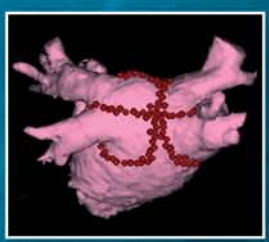
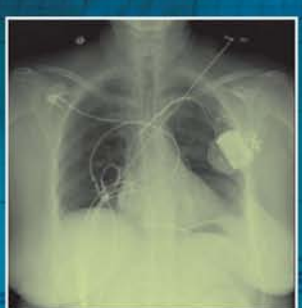
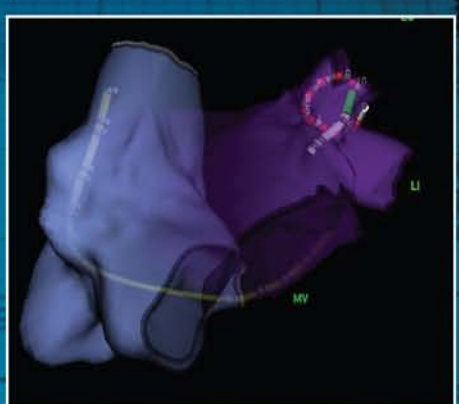


Cardiac Electrophysiology

HANDBOOK OF





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Handbook of Cardiac Electrophysiology

Dedication

To my family and parents for their patience, support, understanding and love Alice and Yasmine, Musbah and Zahra

OMW

Handbook of Cardiac Electrophysiology

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Preface

The *Handbook of Cardiac Electrophysiology* is a repository of information for the in-training, the academic and the practicing electrophysiologist. Each chapter was earnestly authored by our fellows and was conscientiously supervised by members of our electrophysiology staff. This handbook has been written in a perspicuous and concise manner in the hopes of making the challenging and exciting topic of cardiac electrophysiology accessible to all interested individuals. Furthermore, it instructs our readers on the concepts and practices taught at our institution.

The first chapter of this handbook elucidates the 'electricity' of the heart by covering the basic arrhythmia physiology and mechanisms, providing a rudimentary foundation upon which later chapters are based.

The second section allows the reader 'to tour' the device, arrhythmia, Holter and event labs. This section introduces the equipment and setup that are found and conventionally used in electrophysiology laboratories around the world. Our goal is to demystify the plethora of complex equipment that may intimidate individuals who are new to the field of electrophysiology.

Sections III, IV, and V cover the pathophysiology of bradyarrhythmia and how to manage it clinically with the use of devices; an introduction to supraventricular tachycardias, atrial flutter and atrial fibrillation; and ventricular arrhythmias. Our objective is to provide the latest information on the most frequently encountered clinical arrhythmias based upon the most recent guidelines published by the American College of Cardiology and Heart Rhythm Society. Additionally, these sections will provide an electrophysiological base which is vital to understanding the procedures that eradicate arrhythmias.

Section VI thoroughly explores the nature of syncope. Syncope is a malady often clinically encountered in all electrophysiology services. Unfortunately, as many physicians have discovered, the etiology of syncope is often difficult to isolate and treat. In this section, we want our readers to appreciate the elusiveness of this disorder and to provide an organized method to best isolate the cause and manage the problem.

The second half of our handbook is in the vein of a cookbook. It provides the reader with insight on how to perform the 'bread and butter' of electrophysiology procedures. While we realize it is impossible for any book to replace observing and participating in procedures, we hope to be able to provide the reader with a 'taste' of what awaits them in the electrophysiology laboratory and a better appreciation of the cases they may have already observed.

Section VII discusses implantation of permanent pacemakers, ICDs, CRTs and extraction of devices. This section is particularly appropriate considering the epidemic of coronary artery disease and congestive heat failure. Consequently, these devices have been particularly successful in some large clinical trials in improving the quality of patient lives and thus, are the current zeitgeist. Therefore, as a clinician, familiarity with these devices is imperative.

Section VIII covers venous and arterial access, basic intervals and intracardiac ECGs, basic EP study protocols and tilt table testing, which are all staples for any student of electrophysiology.

Section IX covers catheter ablation techniques for SVT, atrial flutter, atrial fibrillation, and idiopathic dilated cardiomyopathy. The newest mapping techniques are presented, and our approach to catheter ablation of atrial fibrillation and ventricular tachycardia is discussed in detail. We are the most experienced center in the United States in the use of pulmonary vein isolation for the management of atrial fibrillation, as we have performed over 3250 cases over the last five years. Over time, our technique has evolved and while no procedure is perfect, we believe that our method is presently the best method of performing AF catheter ablation.

Overall, our readers will understand the bases of the mechanisms responsible for arrhythmias, how to identify commonly encountered clinical arrhythmias, and how to treat them electrically, surgically or pharmacologically. We want our readers to benefit from our experience. We understand that electrophysiology is a rapidly evolving field, and that it is impossible to comprehensively and definitively cover such a dynamic topic, but we believe that the ideas and the techniques presented within this handbook will help make electrophysiology accessible to those individuals who have a desire to learn it.

Dimpi Patel DO and Andrea Natale MD

Acknowledgment

We wish to thank Dr. Dimpi Patel for all her dedication, determination and hard work, which made this book possible. We also wish to thank all of the authors and staff members who worked diligently to produce outstanding chapters. Finally, we would like to thank our team of nurses, families and all those who support us in all our endeavors.

AN and OMW

Section I
Introduction

1

Basic arrhythmia physiology and mechanisms

Mohamed Kanj and Walid Saliba

Sodium channels • Calcium channels • Potassium channels • Membrane action potential • Electrical coupling (GAP junction) • Mechanism of cardiac arrhythmias

SODIUM CHANNELS

The sodium (Na) channel is a voltage-gated channel that is responsible for the rapid depolarization of conducting myocardial cells. This is important for mechanical synchrony. It has been mapped to chromosome 3 (SCN5A). It consists of one alpha and occasionally one or multiple beta subunits. The beta subunits are auxiliary units and their role in cardiac myocytes is not well understood. The alpha subunit consists of four charged domains arranged in a clockwise manner to form a single-pore, highly selective, monovalent channel.[1]

Activation and inactivation of these channels are very complex processes governed by phosphorylation/dephosphorylation and glycosylation of the alpha subunit, and they are summarized in Figure 1.1.[2] While neurotoxins cause inactivation by physically blocking the channel pore, local anesthetics bind to the open inactivated channel and facilitate closure.

Abnormalities in structure or function of the Na channel, causing changes in activation/inactivation characteristics, have been involved in many diseases including Brugada's syndrome, long QT syndrome (LQTS), sick sinus syndrome (SSS), and congenital conduction disease (CCD) (Table 1.1).[3]

CALCIUM CHANNELS

Cardiac myocytes have two types of voltage-gated calcium (Ca) channels, L-type and T-type (Table 1.2). Other types are found in autonomic neurons innervating the heart. L-type channels plays a role in contraction and T-type channels plays a role in automaticity and impulse conduction. Activation is initiated by membrane depolarization and is dependent on intracellular calcium concentration ([Ca]i) and membrane potential (E_m). Inactivation is dependent on time, Em, and [Ca]i. During pathologic longer action potentials (APs), these channels will be inactivated,

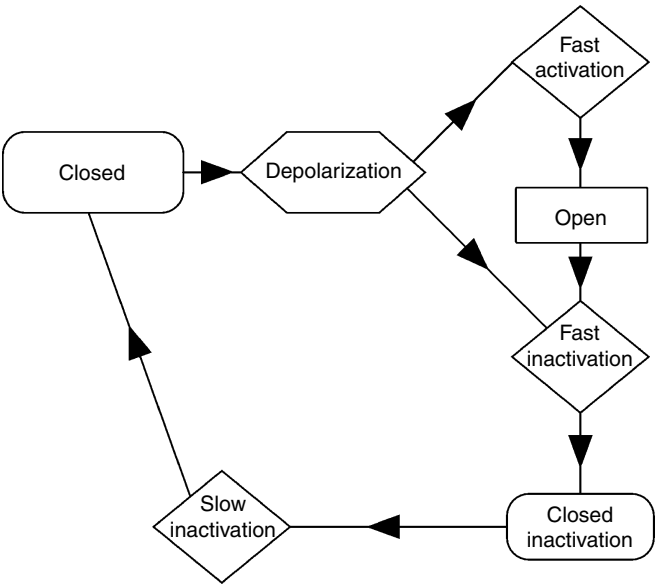

Figure 1.1 Activation and inactivation of Na channels.

Table 1.1 Current types, channel locations and diseases associated with channel abnormality

Type	Current	Location	Phase contribution	Genetic disease
Inward	I_{Na}	A, V, P	0	SSS CCD
	I_{CaL}	A, V, P, N	1, 2	
	I_{CaT}	A, N		
	I_f	N	4	SSS
Outward	$I_{to,\ f}$	A, V, P	1	
	$I_{to,\ s}$	V	1	
	I_{Kr}	V	1, 2	LQTS-2, 6
	I_{Ks}	V	3	LQTS-1, 5 AF
	I_{Kur}	A	2	
	I_{Kp}	V	0, 1, 2, 3, 4	
	I_{K1}	A, V	3, 4	LQTS-7 (Anderson-Tawil syndrome) AVN block
	I_{KATP}	A, V	1, 2	
	I_{KAch}	A, N	4	

A, atrium; V, ventricle; AVN, atrioventricular node block; P, Purkinje system; SSS, sick sinus syndrome; CCD, congenital conduction disease; LQTS, long QT syndrome.

Table 1.2 T-type and L-type Ca channels

	T-type	L-type
Location	Atria, Purkinje, pacemaker cells	Ventricular and atrial
Current amplitude	Minimal	Significant
Function	Automaticity, pacemaker cells	SR Ca release trigger
Dihydropyridine sensitivity	No	Yes
Isoproterenol sensitivity	No	Yes

SR, sacroplasmic reticulum

causing a drop in [Ca]i. This inactivation will then partly recover as [Ca]i decreases, causing early after depolarization (EAD) arrhythmias.[4] While there are many specific L-type antagonists (e.g. dihydropyridine), there are no specific T-type antagonists. Mibfradil is the most specific T-type antagonist; however, it still has significant L-type antagonistic effects.

POTASSIUM CHANNELS

Potassium (K) channels are responsible for repolarization currents along with Na/Ca and Na/K exchangers. There are three kinds of K channels: background (TASK-1, TWIK-1, TWIK-2), voltage-gated (I_{to}, I_{kslow}, I_{kr}, and I_{ks}), and inward rectifier K-channels (I_{k1}, I_{kACh}, and I_{kATP}).[5,6] Background K currents established the baseline diastolic E_m. These currents are very responsive to metabolic changes, playing a role in metabolic arrhythmias. Additionally, downregulation of voltage-regulated K channels can lead to AP prolongation, promoting early (EAD) and delayed (DAD) after depolarization.

MEMBRANE ACTION POTENTIAL

Cardiac myocytes are divided into two groups depending on the driving ion behind cell depolarization and action potential formation: Na or Ca.

Sodium-channel-dependent AP cells (Figure 1.2)

When a cell receives depolarizing current, Na channels are activated resulting in a net inward (depolarizing) current manifested as phase 0 of the AP (Figure 1.3).

Phase 1 starts with the opening of a rapid outward potassium current (I_{to}). This results in a fast early repolarization that drives E_m to 0 mV. I_{to} is activated in response to membrane depolarization and is spontaneously inactivated in a time-dependent manner. Angiotensin II and alpha-agonists reduce I_{to} current velocity, hyperthyroidism increases I_{to} current density, and aldosterone mediates a receptor-specific downregulation of these channels.

During loss of activity of Na channels (Brugada syndrome) a functioning I_{to} can cause full repolarization by driving E_m towards its resting state (–90 mV). This may result in an intercellular voltage gradient sufficient to generate a depolarizing current that is capable of initiating re-entrant wavefronts. These re-entrant

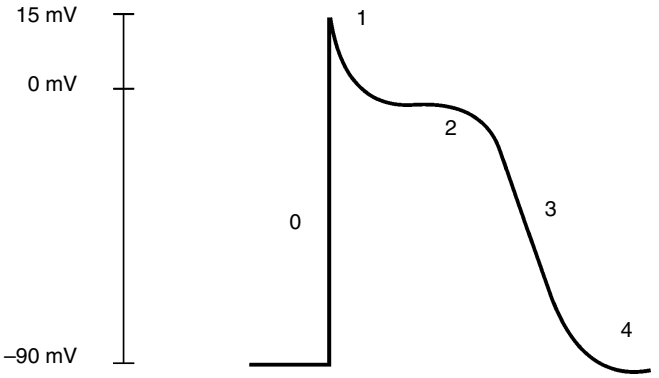

Figure 1.2 Action potential in Na-channel-dependent cells.

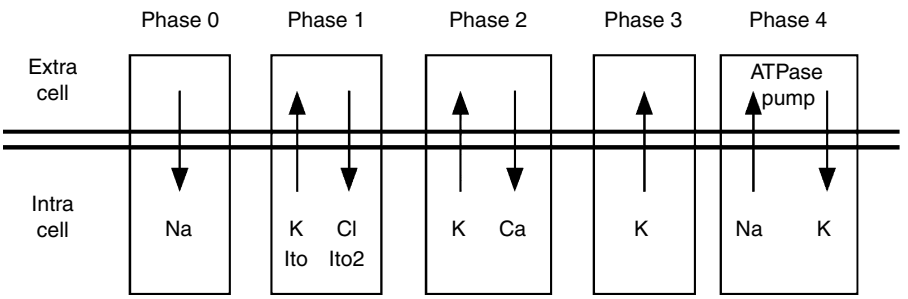

Figure 1.3 Predominant currents during the different phases of Na-channel-dependent action potential.

wavefronts could, in turn, initiate ventricular fibrillation or polymorphic ventricular tachycardias.

Phase 2 or the plateau phase of the AP (Figures 1.2 and 1.3) is the result of an L-type Ca current stabilizing E_m by counteracting the outward K currents. With time, L-type Ca channels are inactivated and the plateau subsides. At the same time, the increase in [Ca]i acts as a trigger for release of more Ca stored in the sarcoplasmic reticulum (SR), which in turn provides a contraction signal to the myocyte contractile elements.

Phase 3 (Figures 1.2 and 1.3) is due to 'delayed rectifier' outward K currents, IKr and IKs. Abnormalities in either type of these channels can cause long QT syndrome.

Phase 4 (Figures 1.2 and 1.3) constitutes a steady, stable, polarized membrane due to voltage-regulated inward rectifiers (I_{K1}). In contrast to the delayed rectifier channels, these channels open at the resting state and are closed during depolarization.

Compared to atrial action potential (AP), ventricular AP has a longer duration, a higher phase 2 due to the absence of IKur in the ventricular myocytes, a shorter

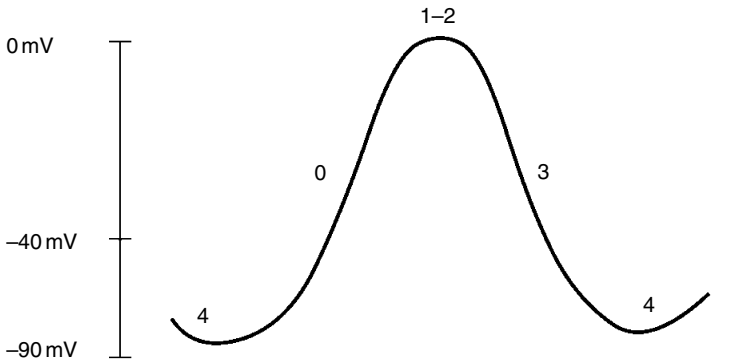

Figure 1.4 Action potential in Ca-channel-dependent cells.

phase 3, and more negative phase 4 due to the presence of I_{K1} in ventricular myocytes.

Calcium-channel-dependent AP cells (Figure 1.4)

These cells are found in the sinus node and the specialized conduction system. They have the ability to generate a spontaneous action potential using I_f 'funny', T-type Ca and K rectifier currents.[7] These currents confer the unstable electrical property of phase 4, causing these cells to develop rhythmic spontaneous slow diastolic depolarization. Once E_m reaches –40 mV, L-type Ca channels are activated, generating the slow upstroke of the action potential in these types of cells (phase 0). The first cloned I_f channel was BCNG1 and further cloning resulted in identifying hyperpolarization-activated cyclic nucleotide gated channels, HCN1–4. These channels are mixed Na and K channels (Na/K ratio = 0.27) with a slow kinetic mode of activation and deactivation, and they are modulated by cyclic AMP.

ELECTRICAL COUPLING (GAP JUNCTION)

GAP junction channels are the functional units that allow direct ionic communication between cardiac cells, facilitating fast propagation of the AP. It is formed of two proteins called connexin. The expression of these channels is affected by protein kinase activity, low intracellular pH, and dephosphorylation.[8]

GAP junction channels are not uniformly distributed around the heart tissues. The distribution varies from almost absent in the sinus node, to low concentrations in different areas of the atrioventricular node (AVN), to significant expression in the faster conducting atrial and ventricular muscle as well as His Purkinje fibers. In these cells, the distribution of the connexins is not uniform. They are more concentrated along the ends of the myocytes than along the sides of the cell, thus giving a directional propensity for propagation of the action potential. This gives rise to anisotropic propagation of depolarization with faster conduction velocities along the cardiac muscle fiber orientation than across the fiber

orientation. Abnormalities in connexins have been found to play a key role in bradyarrhythmias and tachyarrhythmias (mainly through re-entry).

MECHANISM OF CARDIAC ARRHYTHMIAS

The mechanisms of cardiac arrhythmias are often the results of many factors including fluctuation in [Ca]i, after depolarization currents, refractory period shortening or lengthening, autonomic nervous system innnervation, repolarization dispersion, and changes in excitability and conduction. For example, bradyarrhythmia is often caused by abnormalities in excitability. This could be caused by dysfunction in the Na channels or by ischemia-induced elevation in extracellular potassium concentration, $[K]_o$. Furthermore, inherent or metabolically induced abnormalities in Na channels, Ca channels, or connexin have been shown to play a role in conduction diseases.

Mechanisms of tachyarrhythmias can be grouped into three categories: automaticity, re-entry, and triggered activity. The characteristics of each are summarized in Table 1.3.

Re-entry

Re-entry is a depolarizing wave traveling through a closed path. The exact path of the re-entrant circuit is constant and predefined in zero dimension (single cell automatic impulse) and one dimension re-entrant circuits (single cell width re-entrant circuit). On the other hand, the exact cellular path might be different in a higher dimension re-entrant circuit where an impulse can travel transversely through myocytes.

There are three prerequisites for re-entry:

1. *At least two pathways:* slow and fast AV nodal pathways, accessory pathway or the presence of barrier (anatomic: tricuspid valve; pathologic: incisional scars, myocardial infarction, and functional scar) (Figure 1.5).
2. *Unidirectional block*: This block can be physiologic: caused by a premature complex, or increased heart rate; or pathologic: caused by changes in repolarization gradients.
3. *Slow conduction to prevent collision of the head and the tail of the depolarizing wave*: physiologic: caused by AV nodal slow pathway (AVNRT), AV node (AVRT),

Table 1.3 Classification of arrhythmia mechanisms

		Automatic	Triggered	Re-entry
Programmed stimulation	Initiation	−	+	+
	Termination	−	+	+
	Entrainment (E) or overdrive suppression (OS)	OS	OS	E
After depolarization recordings		−	+	+
Adenosine sensitivity		−	+	+/−

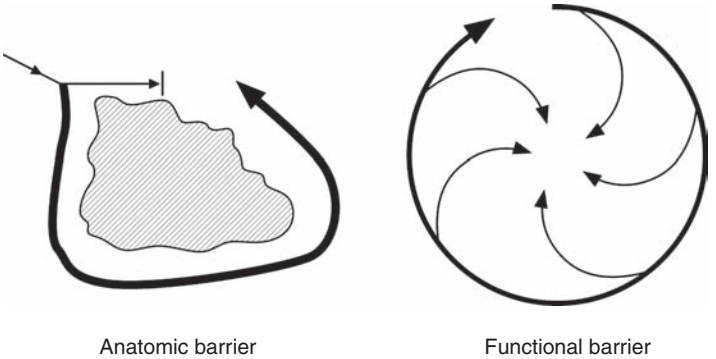

Figure 1.5 Schematic diagrams showing two pathways generated by anatomic or functional barriers.

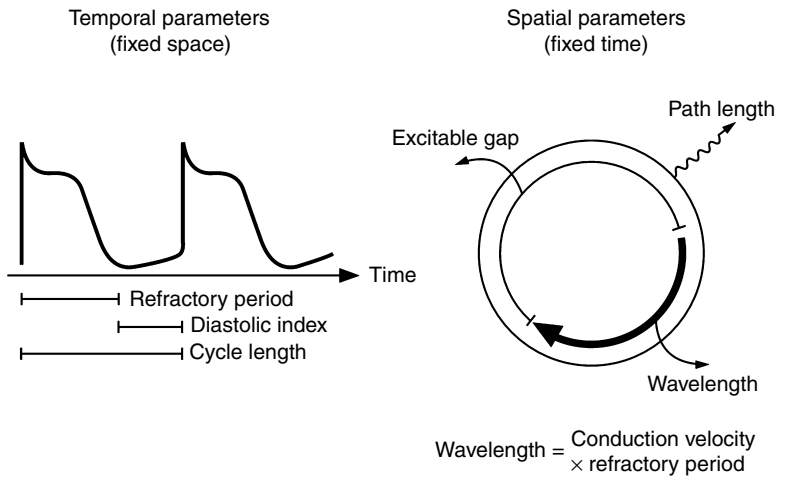

Figure 1.6 Temporal and spatial characteristics of a re-entrant wave.

cavotricuspid isthmus (AFL), slow conduction across the crista terminalis (upper loop tachycardia); pathologic: ischemic or remodeled cells in atrium and ventricle (ventricular tachycardia, atrial flutter).

In functional re-entry, unidirectional block can be due to dispersion of refractoriness (repolarization) or dispersion of conduction velocity (anisotropic re-entry). The former can be caused by repolarization gradients due to spatial heterogenicity of repolarization (ischemia, drugs), discordant repolarization alternans (T-wave alternans during ischemia, autonomic abnormalities), and transmural gradients from cell-to-cell uncoupling (drugs, heart failure).

A re-entrant circuit can be defined with the following (Figure 1.6):

- *Cycle length (CL)/period*: time required for the depolarizing impulse to return to its spatial origin.

- Refractory period (RP): the shortest coupling interval that could capture the re-entrant circuit.
- *Temporal excitable gap (diastolic interval)*: CL–RP.
- *Path length*: spatial length of the physical re-entrant circuit.
- *Wavelength (WL)*: spatial length of the active tissue that is refractory to excitation which is RP $\times$ CV (conduction velocity).
- *Spatial excitable gap (EG)*: pathlength – wavelength.

Triggered activity

Triggered activities are caused by after depolarization currents. They are classified as early (EAD occurring inside AP: phases 2 and 3) or delayed (DAD: phase 4) (Figure 1.7). These currents can in turn be responsible for both focal and re-entrant arrhythmias. The former is caused by eliciting an excitatory response exceeding the activation threshold and the latter can be developed when these currents cause prolongation in action potential which facilitates the development of a unidirectional block due to dispersion of refractoriness.[9]

1. *Early after depolarization*: there are two types of EAD, plateau EAD (phase 2) and late EAD (phase 3). Plateau EAD is caused by inward L-type Ca current (I_{CaL}), resulting from either a loss of function of I_{Kr} channel during a prolonged pause (LQTS-2) or a gain of function of mutant Na channel (LQTS-3). Late phase 3 EAD, on the other hand, is caused by Na/Ca exchange current ($I_{Na/Ca}$), which is also the cause of delayed after depolarization (Figure 1.7).
2. *Delayed after depolarization*: These are the result of Na/Ca exchange and non-specific Ca-activated currents (I_{NS}). They are often seen in digitalis toxicity and catecholamine excess states (Figure 1.8).

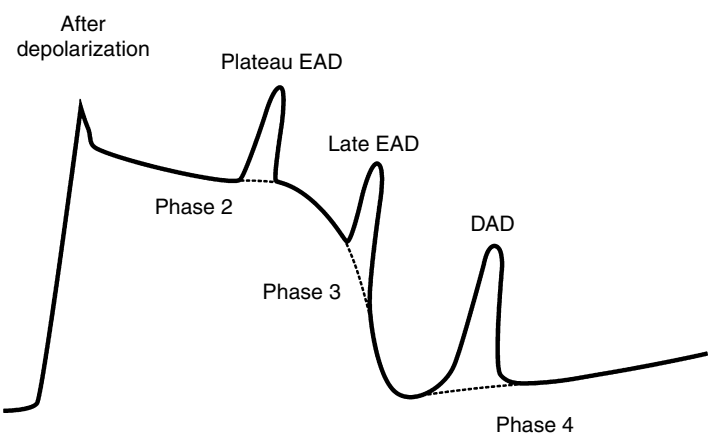

Figure 1.7 Types of after depolarization currents. EAD, early after depolarization; DAD, delayed after depolarization.

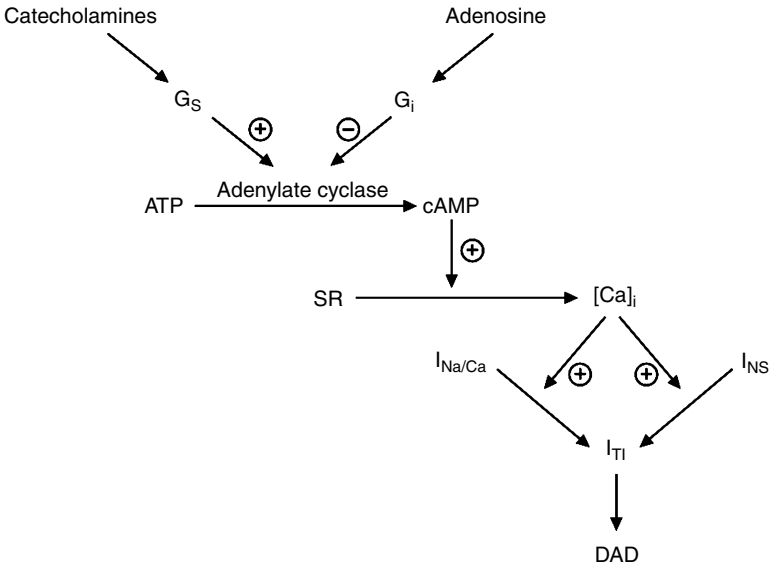

Figure 1.8 Cellular mechanism of delayed after depolarization. G_i: inhibitory G protein, G_s: stimulatory G protein, ATP: Adenylate triphosphate, cAMP: cyclicadenylate monophosphate, SR: Sarcoplasmic reticulum, [Ca]i: intracellular calcium concentration, $I_{Na/Ca}$: Sodium/Calcium exchange current, I_{NS}: nonspecific calcium channels, I_{TI}: transient inward current, DAD: Delayed after repolarization.

Automaticity

Automaticity is driven by spontaneous phase 4 depolarization. Automatic depolarizations in the atria and ventricles are not manifested normally due to overdrive suppression by the faster depolarization caused by the sinoatrial node. However, during excess catecholaminergic states, phase 4 depolarization may exceed sinus node depolarization, causing depolarization to be driven by the abnormal tissue. Ventricular tachycardias during the acute ischemic and reperfusion phases are good examples of automaticity. They often originate from the border zone between normal and ischemic cells. During the acute ischemic phase, elevation in extracellular $[K]_o$ concentration elevates the resting E_m, rendering it more excitable. Additionally, the formation of an intercellular current resulting from non-homogeneous depolarization in the border zone between reperfused and normal tissue may play a role in the formation of these arrhythmias.

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Section II

Basic EP lab set-up and equipment

2
Device lab set-up

Michael McWilliams, Robert Schweikert, and Mina Chung

The purpose of this chapter is to discuss the laboratory equipment and set-up necessary for device implantation. Pacemaker and defibrillator implantation may be performed in an operating room, catheterization suite, or a dedicated electrophysiology laboratory. The device implantation team usually consists of a physician, a nurse dedicated to the management of conscious sedation, and a circulating nurse. A nurse, technician, or device company representative may be present to assist with lead testing and device programming.

- The patient table should be radiolucent and freely movable to allow fluoroscopy from the patient's neck to groin. Ample space is necessary on the left and right side as well as the head of the bed, where personnel can monitor vital signs, oxygen saturation, patient status, and conscious sedation. Complex cases, such as device extractions or extractions with contralateral re-implants, may require space for bilateral pectoral, groin, or neck vascular access for a temporary pacer wire or arterial access for invasive blood pressure monitoring. It is helpful for a table to have options for Trendelenberg and reverse Trendelenberg positioning, although foam wedges may be placed under the legs to facilitate venous return during venous access, or under the head for patients unable to lay flat.
- Fluoroscopy remains essential to optimal lead placement. The fluoroscopy source can be either portable or fixed and should be maneuverable in oblique and lateral views. Maneuverability is important for obtaining access, venograms, and lead positioning. An option for magnification is used to visualize extension and retraction of the lead screw. The ability to record cine loops is helpful for guidance of vascular insertion and lead placement (e.g. coronary sinus venogram), as well as for teaching purposes. Cinefluoroscopy is the most commonly used recording mode, with some machines having the option to record loops from fluoroscopy.
- Anesthesia, either using conscious sedation or general anesthesia, requires a dedicated nurse or physician for continuous monitoring of the level of sedation, pulse oximetry, rhythm, and vital signs. State and local regulations vary as to who can administer sedation, ranging from nurses, implanting physicians, to anesthesiologists. Monitoring vital signs requires an automatic or manual blood pressure cuff and pulse oximetry. Supplemental oxygen should be easily accessible and is often necessary with conscious and deep sedation. A continuous electrocardiographic display should be visible to both the physician and nursing staff, using radiolucent leads and wires if possible.
- Once the pacing and/or defibrillation leads are positioned, lead impedance, capture threshold, and amplitude are tested. The electrodes are connected using alligator clips to a pacing system analyzer (PSA) and display. The signal can

be displayed with standard bipolar intracardiac electrogram filtering (0.5 hertz (Hz) high pass, 500 Hz low pass), as well as with a wider bandpass filter to facilitate assessment for an injury current on the intracardiac electrograms (30 Hz high pass filter and 500 Hz low pass filter). The injury current helps to confirm appropriate fixation to the tissue. It is also helpful to have a second monitor to display the PSA or device programmer screens to the implanting physician.

- Many labs have instrument sets specially designed for device implantation. Basic sterile surgical instrument sets often include hemostats, forceps, fine forceps, suture scissors, Metzenbaum scissors, a needle holder, Weitlaner retractor, and manual retractors (Figure 2.1). Vascular ultrasound devices used to obtain vascular access may be helpful to avoid unnecessary arterial punctures. Electrocautery is used to control local bleeding, and suction should be available in case needed.
- In-room stocking or easy availability of single-use items adds to convenience during the procedure. Items that are used during device implantation include scalpels, absorbable and non-absorbable suture, splittable vascular sheaths, the implanted leads and device, stylets, sterile programming wand covers, drape clips, sterile fluoroscopy cover, and often steerable mapping catheters.
- Every lab should be equipped with emergency equipment. A combination defibrillator/external pacemaker is essential. The most frequent use of the defibrillator is for cardioversion and as a back-up to an internal cardiac defibrillator in defibrillation threshold testing. There should also be a cart stocked with emergency medications used for cardiopulmonary arrests (code cart), pericardiocentesis kit, and in centers performing high risk procedures, an open chest kit can be stocked. A pericardiocentesis kit should be available in the event of a lead perforation.

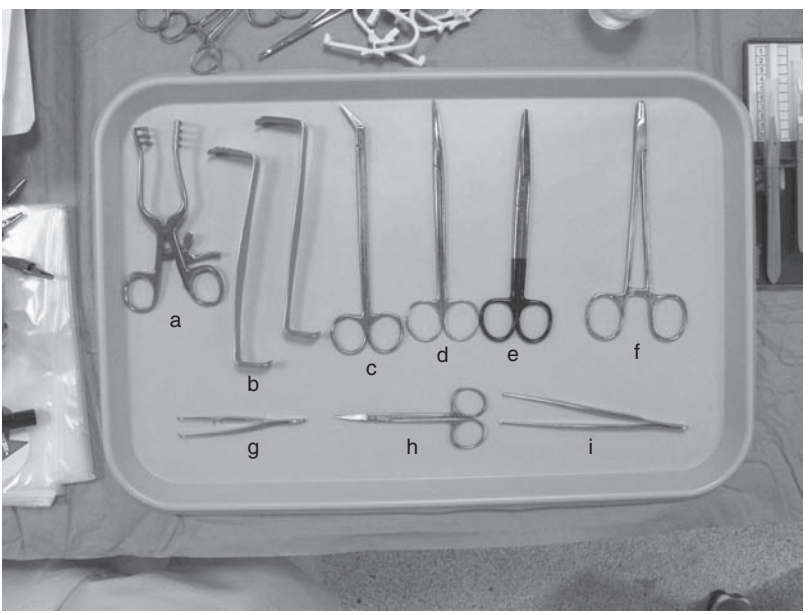

Figure 2.1 Example of a basic pacemaker lab instrument set. Starting from left to right: a. Weitlaner retractor, b. manual retractors, c. Potts scissors, d. Metzenbaum scissors, e. suture scissors, f. needle holder, g. forceps, h. small scissors, i. tissue forceps.

3

Organization of the arrhythmia lab

Shane Bailey, Robert Schweikert, and Mina Chung

Set-up of the interventional electrophysiology laboratory • Mapping systems

Setting up an electrophysiology laboratory for cardiac ablations requires specifics in the layout of laboratory, personnel, and equipment requirements. Conventional electrophysiology (EP) studies and ablation procedures should be performed with adequately trained personnel. One or two physicians are responsible for catheter manipulation and ablation. Two nurses are generally required, one to assist with tasks related to ablation and the other responsible for sedation of the patient. For most electrophysiologic procedures, conscious sedation is preferred to allow for assessment of symptoms and minimization of risks associated with anesthesia. Support for complications related to EP studies and ablations should be readily available, including cardiac and vascular surgery and neurologic imaging modalities.

SET-UP OF THE INTERVENTIONAL ELECTROPHYSIOLOGY LABORATORY

An electrophysiology laboratory capable of performing EP studies and ablations must be equipped with a radiographic system, the ability to separately monitor vital signs, and data acquisition capabilities.

- The *cinefluoroscopic equipment* includes the patient table and the C-arm, which allows for variable angulation of the X-ray beam. Biplane imaging provides simultaneous viewing of cardiac structures from different angles and can be useful in certain procedures, such as the transseptal puncture. The video system should consist of 1–2 monitors and have the ability to store cine images. Above the patient table, one monitor displays fluoroscopic images and another displays tracings from the physiologic recorder and hangs from a mounted movable ceiling bracket, allowing the physician manipulating catheters to achieve the optimal viewing angle (Figure 3.1). Given the amount of fluoroscopy used in prolonged ablations or device implantation procedures, reduced fluoroscopy intensity is generally used in the EP lab as compared to catheterization laboratories.

Figure 3.1 Above the patient table, one monitor displays fluoroscopic images and another displays tracings from the physiologic recorder and hangs from a mounted movable ceiling bracket, allowing the physician manipulating catheters to achieve the optimal viewing angle.

- *Vital signs monitoring* should be performed on independent equipment so that monitoring may continue if the data acquisition system fails. A cardioverter/defibrillator may be used for monitoring rhythm, and combined modality devices may be used to monitor vital signs. Through the defibrillation pads and ECG leads, several lead configurations can typically be viewed separately from the physiologic recorder. Additionally, non-invasive measurements of blood pressure and pulse oximetry can be followed. Many newer models of defibrillators can also monitor arterial pressures and end-tidal CO_2 levels.
- The *data acquisition system* includes the physiologic recorder which displays and stores surface and intracardiac electrograms. The equipment console consists of this system as well as a slave monitor for radiographic images and an electrophysiologic stimulator. Input signals are displayed on computer screens and stored on archivable media, such as optical disks.

Electrical safety must be ensured in the set-up of the electrophysiology laboratory to reduce the risk of current leakage to the patient which can precipitate ventricular arrhythmias. Leaking of current should remain less than 10 mA.

Junction box

The junction boxes receive the intracardiac signals from the catheters and provide an interface into the physiologic recorder (Figure 3.2). Multiple switches within the junction box are designated to a recording and stimulation channel which can be selected through the recording apparatus. The junction boxes are mounted at the foot of the patient table and connected to the physiologic recorder, which is kept as close as possible. This helps to minimize noise on the channels as well as reduce floor clutter.

Figure 3.2 The junction boxes receive the intracardiac signals from the catheters and provide an interface into the physiologic recorder.

Recording apparatus

The physiologic recorder records, displays, and stores intracardiac and surface recordings. It consists of filters, amplifiers, display screens, and recording software. From the junction box, the physiologic signals are introduced into the recorder. These signals are typically low in amplitude and require amplification prior to displaying and recording. The recording system amplifies and filters each input channel separately, with most current systems supporting up to 64 or more channels. The amplifiers have the ability to automatically or manually adjust gain control. The amplifiers should be mounted as close to the patient table as possible. This will reduce the cable length of the intracardiac connections and surface ECGs, which minimizes the signal noise. The amplifier is then connected to the main physiologic recorder through a floor channel, which, ideally, should run separately from electric power cables. Filters are used to eliminate unnecessary signals that distort electrograms (EGMs). High pass filters eliminate signals below a given frequency and low pass filters eliminate signals above a given frequency. Most intracardiac electrograms are clearly identified when the signal is filtered between a high pass of 40 Hz and a low pass of 500 Hz. Several pages can be simultaneously recorded and one of these typically includes a 12-lead ECG. The page displayed during studies typically shows several intracardiac electrograms with 3 to 4 surface ECG leads which allows for axis determination, activation timing, and P/QRS morphology (Figure 3.3). Pressure channels, if used, allow for simultaneous hemodynamic monitoring.

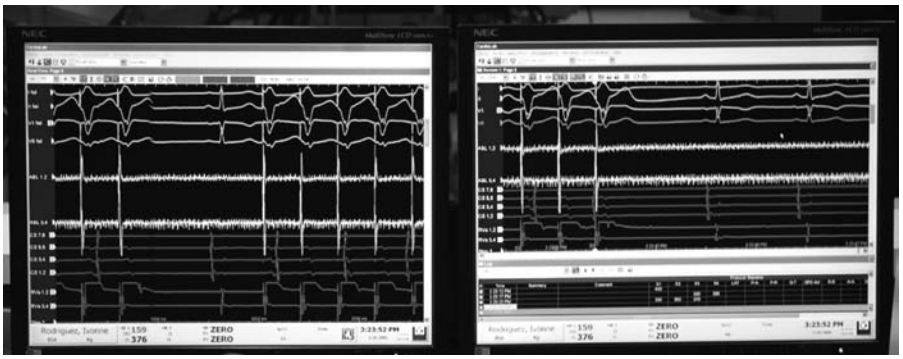

Figure 3.3 The page displayed during studies typically shows several intracardiac electrograms with 3 to 4 surface ECG leads which allows for axis determination, activation timing, and P/QRS morphology. (See color plate section.)

Stimulator

A programmable stimulator is necessary to obtain electrophysiologic data beyond measurements of conduction intervals. Stimulators are capable of various modes of pacing, including rapid pacing, delivery of single or multiple extra stimuli following a paced drive train, and delivery of timed extra stimuli following sensed beats. Stimulators should be capable of delivering variable currents, ranging from 0.1 to 10 mA. With satisfactory positioning of catheters, current thresholds under 2 mA (with 2 ms pulse width) can usually be achieved in both the atrium and ventricle. Higher outputs are seen with diseased myocardium, within the coronary sinus, and with the use of anti-arrhythmic medications. Output is usually set at twice the diastolic threshold. Most stimulators have the ability to pace through more than one channel; however, one channel generally suffices for all studies unless dual chamber pacing is required.

Cardioverter/defibrillator

A primary and back-up cardioverter/defibrillator should be available throughout all EP studies (Figure 3.4). Current defibrillators deliver energy in a biphasic waveform which offers enhanced defibrillation success. Defibrillation pads are attached to the patient and electrically grounded. In our laboratory, the defibrillator and energy delivered by RFA share a common ground patch on the patient which connects through the *Booker box*. ECGs can be recorded through the defibrillation pads separate from the data acquisition system.

Radiofrequency ablation

Radiofrequency ablation uses alternating current delivered between the catheter tip and grounding source to deliver energy to tissue, resulting in necrosis. Radiofrequency generators deliver current with a frequency between 300 and 750 kHz, with generation of heat occurring as a result of resistive and conductive heating.

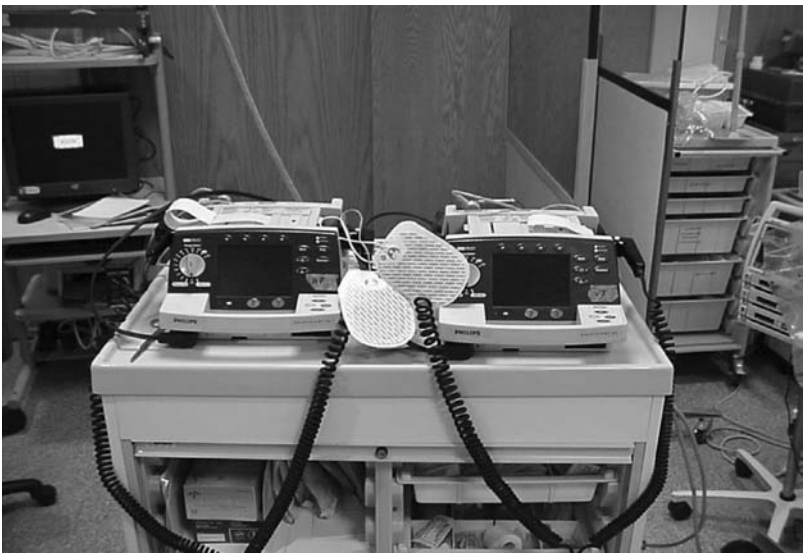

Figure 3.4 A primary and back-up cardioverter/defibrillator should be available throughout all EP studies.

Monitoring of time, power, and impedance is necessary to ensure safe and effective ablation lesions. Through the generator, limits on impedance and temperature are programmed and the desired power level is set (Figure 3.5).

MAPPING SYSTEMS

Cardiac mapping is the process by which arrhythmias are characterized and localized. Conventional mapping involves acquiring electrogram data from fixed and moving catheters and creating mental activation maps with fluoroscopic two-dimensional (2D) images. More sophisticated mapping techniques provide three-dimensional (3D) anatomic localization of the catheter to assist in mapping and ablation. These technologies involve the acquisition of multiple electrogram locations to provide a high resolution activation, voltage, or propagation map. In addition to correlating local electrograms to 3D cardiac structures, these newer mapping techniques reduce the radiation exposure to the patient and physician. The most widely used is an electroanatomic mapping system (e.g. the Biosense Webster CARTO system), which localizes the mapping and ablation catheter through a magnetic field. Three coils located beneath the patient generate ultra low magnetic fields that temporally and spatially code the area within the patient. With a magnetic field sensor in its tip that is referenced to an externally located patch on the patient, the catheter can be displayed and recorded in three dimensions with intracardiac electrograms (Figure 3.6). Another technology offers electroanatomic mapping by creating electrical fields between opposing pairs of patch electrodes located on the patient's chest (e.g. St Jude Endocardial Solutions, Incorporated, ESI). Six patches are placed on the body to create three orthogonal axes with the heart located centrally. A transthoracic electrical field is

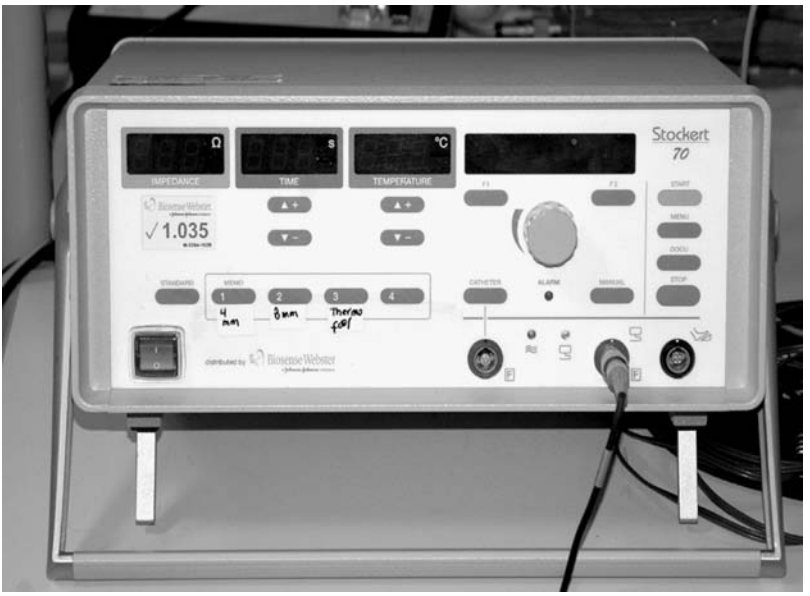

Figure 3.5 Through the generator, limits on impedance and temperature are programmed and the desired power level is set.

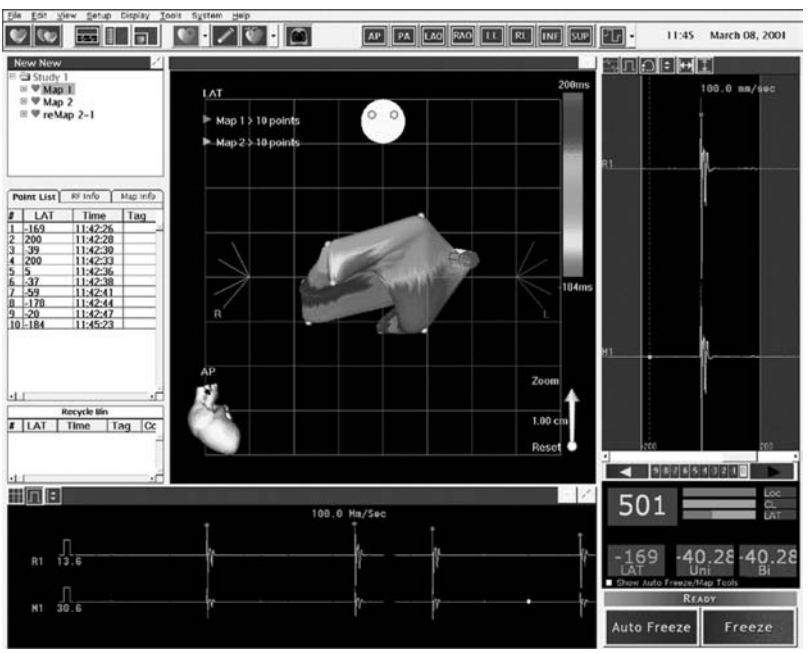

Figure 3.6 With a magnetic field sensor in its tip that is referenced to an externally located patch on the patient, the catheter can be displayed and recorded in three dimensions with intracardiac electrograms. (See color plate section.)

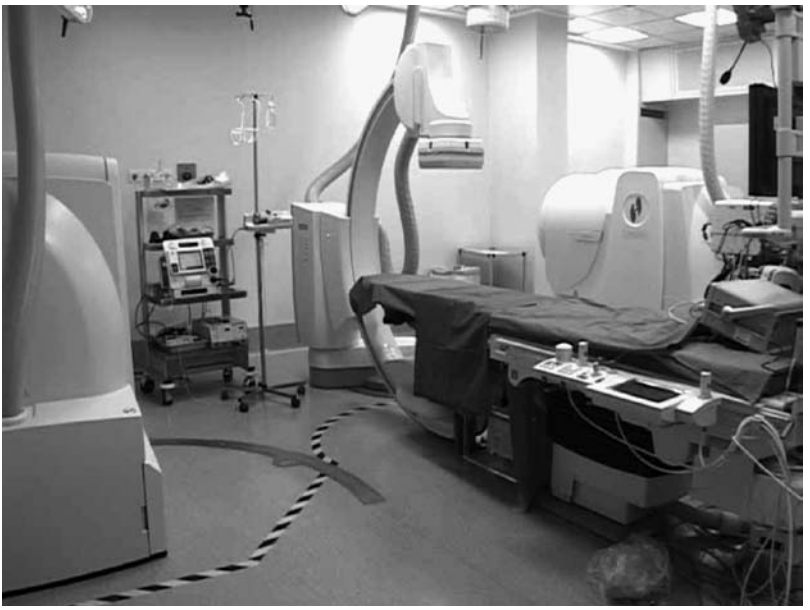

Figure 3.7 *Magnetic navigational systems* are more frequently being utilized for mapping and ablation of various arrhythmias as well as for guidance in the placement of left ventricular leads.

created through each pair of opposing patch electrodes and the mapping catheter delivers this signal for processing.

Magnetic navigational systems are more frequently being utilized for mapping and ablation of various arrhythmias as well as for guidance in the placement of left ventricular leads (Figure 3.7). This system uses large external magnets that sit closely on each side of the patient allowing for magnetic navigation of percutaneous devices. The catheters or guide-wires have small magnetic tips that respond to changes in magnetic field vectors that are programmed by the physician remotely. Advantages of this approach include a softer catheter tip which likely reduces trauma that can occur with stiffer ablation catheters as well as decreasing physician exposure to radiation. Other robotic navigation systems are also in development.

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4

Holter and event monitor laboratory set-up

Subramanya Prasad, Robert Schweikert, and Mina Chung

Introduction • Indications • Components of an ambulatory ECG monitoring laboratory • Recording devices and storage of transmitted data • Continuous ambulatory ECG monitoring • Intermittent and memory loop AECG monitoring • Artifacts and errors • Scanning and analysis techniques • Personnel, training requirements, and quality control • Recorder maintenance and preparation • Preparation • Selection of lead system • Electrode placement • Preparation of electrode site • Patient instruction, pre-examination procedures • Removal of the Holter recorder • Device selection and duration of recording for AECG monitoring • Conclusions

INTRODUCTION

- Cardiac arrhythmias are common disorders with a spectrum ranging from benign premature atrial conditions (PACs) to lethal ventricular fibrillation (VF) causing stroke or sudden cardiac death. The occurrence of these arrhythmias during a brief physical examination or a standard 12-lead electrocardiogram (ECG) is low. In addition, certain cardiac events are seen only during sleep, exercise or mental and emotional stress, thus requiring longer periods of monitoring. ECG recordings for extended periods can provide an accurate diagnosis and symptom–arrhythmia correlation.
- When compared to the 75 lb (34 kg) device introduced by Holter and Gengerelli, ambulatory ECG (AECG) monitoring has become an essential tool in the diagnosis, characterization, quantification risk stratification and management, and prognostic stratification of cardiac arrhythmias, particularly among patients with structural and ischemic heart disease.[1]
- In addition to recording over extended periods of time, the effects of physical and psychologic changes on the autonomic tone during routine activities can be reflected.
- Various studies have demonstrated the increased sensitivity of ambulatory ECG monitoring for detecting spontaneous cardiac arrhythmias.[2,3]

INDICATIONS

- Though earlier monitors were designed to document tachycardia or bradycardia, due to improvements in solid-state digital technology and increased accuracy of software analysis systems, modern AECG monitors are used for:
    - Assessment of symptoms possibly related to arrhythmia.
    - Identification of high-risk post-MI patients with complex and frequent ventricular arrhythmias potentially benefitting from ICD implantation or amiodarone as shown by CAMIAT and EMIAT.[4,5]
    - Assessment of risk of future cardiac events in patients without arrhythmia.
    - Measuring heart rate variability (to assess the risk of future events).
    - Monitoring arrhythmia reduction after anti-arrhythmics or ablation.[6]
    - Assessment of pacemaker and ICD function.
    - QRS complex measurements (specific intervals, e.g. QT interval, T-wave changes), long QT, and Brugada syndromes.[7,8]
    - Documenting triggers of ventricular and supraventricular arrhythmias (PVCs, NSVT, PACs).
    - Monitoring ST segment changes (myocardial ischemia).
    - High resolution signal average ECG recognizing abnormal structural myocardial substrate by identifying fractionated late potentials.[9]
- A list of indications for Holter monitoring is given in Table 4.1.[10]

COMPONENTS OF AN AMBULATORY ECG MONITORING LABORATORY

- The three main components of a long term ambulatory ECG monitoring laboratory set-up are (Figure 4.1):
    - Recording devices
    - Storage of recorded or transmitted data
    - Playback and analysis systems.

RECORDING DEVICES AND STORAGE OF TRANSMITTED DATA

- Improvements in solid-state digital technology have allowed superior transtelephonic recordings increasing the potential uses of long term ambulatory recording devices.
- AECG monitoring can be continuous or intermittent.
- Continuous AECG (usually performed for 24 to 48 hours) is obtained either by tape or solid-state (digital) recording.
- Intermittent ambulatory recordings (obtained for longer periods) are achieved by implanting memory loop recorders.
- Table 4.2 lists the various types of recording devices and their features.

Table 4.1 Indications for Holter monitoring

Indication	Class I	Class IIa	Class IIb	Class III
Assess symptoms possibly related to rhythm disturbances	• Patients with unexplained syncope, near syncope, or episodic dizziness in whom the cause is not obvious • Patients with unexplained recurrent palpitation		• Patients with episodic shortness of breath, chest pain, or fatigue that is not otherwise explained • Patients with neurologic events when transient atrial fibrillation or flutter is suspected • Patients with symptoms such as syncope, near syncope, episodic dizziness, or palpitation in whom a probable cause other than an arrhythmia has been identified, but in whom symptoms persist despite treatment of this other cause	• Patients with symptoms such as syncope, near syncope, episodic dizziness, or palpitation in whom other causes have been identified by history, physical examination, or laboratory tests • Patients with cerebrovascular accidents, without other evidence of arrhythmia
Arrhythmia detection to assess risk for future cardiac events in patients without symptoms from arrhythmia	None		• Post-MI patients with LV dysfunction (ejection fraction $\leq$ 40%) • Patients with CHF • Patients with idiopathic hypertrophic cardiomyopathy	• Patients who have sustained myocardial contusion • Systemic hypertensive patients with LV hypertrophy • Post-MI patients with normal LV function • Preoperative arrhythmia evaluation of patients for non-cardiac surgery • Patients with sleep apnea • Patients with valvular heart disease

(Continued)

Table 4.1 (Continued)

Indication	Class I	Class IIa	Class IIb	Class III
Measurement of HRV to assess risk for future cardiac events in patients without symptoms from arrhythmia	None		• Post-MI patients with LV dysfunction • Patients with CHF • Patients with idiopathic hypertrophic cardiomyopathy	• Post-MI patients with normal LV function • Diabetic subjects to evaluate for diabetic neuropathy • Patients with rhythm disturbances that preclude HRV analysis (i.e., atrial fibrillation)
Assess anti-arrhythmic therapy	To assess anti-arrhythmic drug response in individuals in whom baseline frequency of arrhythmia has been characterized as reproducible and of sufficient frequency to permit analysis	• To detect pro-arrhythmic responses to anti-arrhythmic therapy in patients at high risk • To assess rate control during atrial fibrillation	• To document recurrent or asymptomatic non-sustained arrhythmias during therapy in the outpatient setting	None
Assess pacemaker and ICD function	• Evaluation of frequent symptoms of palpitation, syncope, or near syncope to assess device function to exclude myopotential inhibition and pacemaker-mediated tachycardia and to assist in the programming of enhanced features such as rate responsivity and automatic mode switching		• Evaluation of immediate postoperative pacemaker function after pacemaker or ICD implantation as an alternative or adjunct to continuous telemetric monitoring • Evaluation of the rate of supraventricular arrhythmias in patients with implanted defibrillators	• Assessment of ICD/pacemaker malfunction when device interrogation, ECG, or other available data (chest radiograph and so forth) are sufficient to establish an underlying cause/diagnosis • Routine follow-up in asymptomatic patients

	• Evaluation of suspected component failure or malfunction when device interrogation is not definitive in establishing a diagnosis • To assess the response to adjunctive pharmacologic therapy in patients receiving frequent ICD therapy			
Ischemia monitoring	None	• Patients with suspected variant angina	• Evaluation of patients with chest pain who cannot exercise • Preoperative evaluation for vascular surgery of patients who cannot exercise • Patients with known CAD and atypical chest pain syndrome	• Initial evaluation of patients with chest pain who are able to exercise • Routine screening of asymptomatic subjects
Monitoring in pediatric patients	• Syncope, near syncope, or dizziness in patients with recognized cardiac disease, previously documented arrhythmia, or pacemaker dependency • Syncope or near syncope associated with exertion when the cause is not established by other methods	• Syncope, near syncope, or sustained palpitation in the absence of a reasonable explanation and where there is no overt clinical evidence of heart disease	• Evaluation of asymptomatic patients with prior surgery for congenital heart disease, particularly when there are either significant or residual hemodynamic abnormalities, or a significant incidence of late postoperative arrhythmias	• Syncope, near syncope, or dizziness when a non-cardiac cause is present • Chest pain without clinical evidence of heart disease • Routine evaluation of asymptomatic individuals for athletic clearance • Brief palpitation in the absence of heart disease

(Continued)

Table 4.1 (Continued)

Indication	Class I	Class IIa	Class IIb	Class III
	• Evaluation of patients with hypertrophic or dilated cardiomyopathies • Evaluation of possible or documented long QT syndromes • Palpitation in the patient with prior surgery for congenital heart disease and significant residual hemodynamic abnormalities • Evaluation of anti-arrhythmic drug efficacy during rapid somatic growth • Asymptomatic congenital complete AV block, non-paced	• Evaluation of cardiac rhythm after initiation of an anti-arrhythmic therapy, particularly when associated with a significant pro-arrhythmic potential • Evaluation of cardiac rhythm after transient AV block associated with heart surgery or catheter ablation • Evaluation of rate-responsive or physiologic pacing function in symptomatic patients	• Evaluation of the young patient (<3 years old) with a prior tachyarrhythmia to determine if unrecognized episodes of the arrhythmia recur • Evaluation of the patient with a suspected incessant atrial tachycardia • Complex ventricular ectopy on ECG or exercise test	• Asymptomatic Wolff–Parkinson–White syndrome

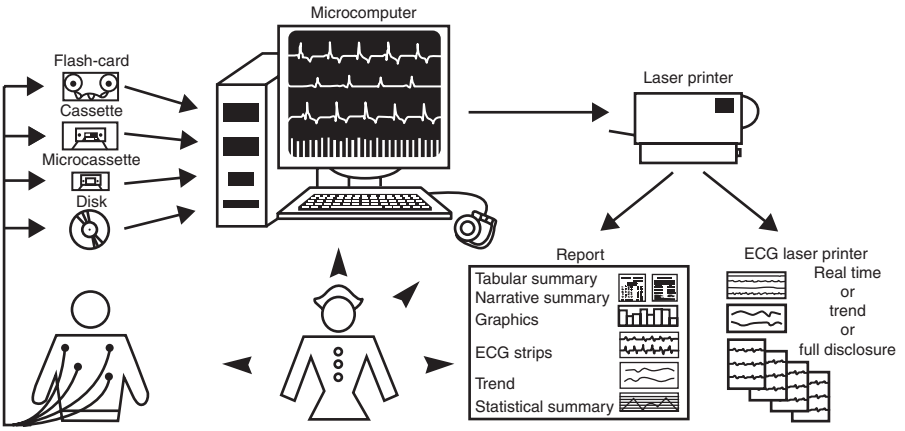

Figure 4.1 Modern conventional ambulatory electrocardiographic system. Reprinted with permission from Kennedy HL, Podrig PJ. Role of Holter monitoring and exercise testing for arrhythmia assessment and management. In: Podrid PJ, Kowey PR, (eds). Cardiac Arrythmia, 2nd edn. Philadelphia, PA: Lippincott, Williams & Wilkins, 2001; p 168, Figures 6.1–6.4.[11]

CONTINUOUS AMBULATORY ECG MONITORING

- There are two types of continuous recording systems:
  - Tape-based
  - Solid-state.
- Table 4.2 lists the recording, scanning, transmitting, and additional features of the two types.

INTERMITTENT AND MEMORY LOOP AECG MONITORING (Table 4.2)

- Intermittent recorders are lightweight patient-activated devices with limited capacity for storage useful in patients with infrequent symptoms.
- Though the memory loop recorders have to be worn continuously, they provide ECG data prior to the onset of the event, which could aid in the diagnosis of the mode of onset of arrhythmia. This is particularly useful in patients with significant symptoms that occur infrequently.
- A study of transtelephonic transmissions in 5052 patients postpacemaker implant showed that 95% of events with suspected transient cardiac arrhythmias occurred within 5 weeks of using the device, with serious arrhythmia in 52% of patients.[15] When this device was used in patients with recurrent syncope, a diagnosis was made in 25% of them.[16] Despite adequate patient education, improper device activation was seen in 20% of patients.
- Recent use of implantable memory loop recorders allows continuous ECG recordings for extended periods of up to 18 months.[17] The device can be patient-activated or programmed to record automatically based on preset heart rate limits.
- A study using ILR in 85 patients with recurrent syncope (negative HUT, AECG, and EPS), showed recurrent syncope in 68% at a mean of 10.5 months post-implantation, 30% of whom were secondary to bradycardia.[17]

Table 4.2 Recording, scanning, and transmitting features of the two types of recorders

Type	Recording	Scanning	Transmitting	Comments, advantages, and disadvantages
Holter				
Analog	• Battery powered device; records at extremely slow speeds at frequencies (0.05–100 Hz) similar to the standard ECG • All ECG complexes 'full disclosure'	• Technicians digitize data with computer assistance, templating, area determination and superimposition	None	• Discrepancies in the range of recording frequency among devices can cause inaccuracies in measuring dynamic ST segment changes • Irregularities in the tape drive can create artifacts that simulate bradycardia/tachycardia
Digital – continuous recording	• Recording on digital or compact disk or flash card • ECG from multiple channels is stored in solid-state memory • Unlike older systems, newer systems record each beat within a 24 h period. This creates full disclosure similar to tape systems • All ECG complexes 'full disclosure'	• Technician with computer assistance, templating, area determination and super-imposition • Algorithms for arrhythmia recognition measuring HRV and tabulation of ectopics enable real-time analysis by microprocessor with retrospective technician editing	Transtelephonic	• Patient-activated markers or time-encoded markers enable symptom arrhythmia correlation. The playback instrument system which is operator-interaction-dependent has an arrhythmia analyzer, ST segment detector, RR interval analyzer, and a signal-averaging computer with software capable of generating ECG recordings, trends or statistical summaries
Digital – real-time analysis	• Computer analysis of ECG and selected ECG	• With microprocessor and electronic memory real-time analysis of digitized recordings online[12]	None	• Though usually done for 24 h, can be extended up to 5 days with battery change[11] • Though reports can be generated upon completion of the test, absence of continuous storage of ECG data makes subsequent analysis and verification difficult

In-hospital telemetry	• Recent improvements permit ECG recording from 2 channels with arrhythmia and ST segment change analysis[13]	• Solid-state storage of ECG recordings online permits full disclosure with capability for re-examining at a later date		• The continuously looping stored telemetry signal is presented as hourly full disclosures for review of all continuous events during the previous 12 to 24 h[14]
Event recorder				
Post-event non-looping, without memory				
Hand-held (including credit card size) wristwatch type	• ECG selected by patient activation	• Direct visualization	Transtelephonic	• When compared to continuous recorders, they can provide recordings during events thus increasing the likelihood of symptom event correlation
Automatic electronic sensor, in DDD pacemaker	• ECG when activated automatically by sensor	• Direct visualization of analysis or ECG	Direct telemetry	
Pre-event looping, with memory	• Various electrodes are placed and the device is worn continuously for 3–4 weeks	• After activation, permanently stored ECG recordings are obtained, 1–4 min before and 30–60 s after device activation[15]	While the older versions required immediate telephone access for transmitting, newer devices have limited (2 to 5 min) of solid-state memory which can be transmitted telephonically at the patient's convenience	• Though these devices are invaluable in documenting the onset and offset of a paroxysmal cardiac arrhythmic event, patient error and device malfunction are potential limitations[16]
Wristwatch type monitor worn with attached electrodes	• ECG, selected by patient activation, with memory of pre-event	• Direct visualization	Solid state storage of ECG data on the device is transmitted transtelephonically at the patient's convenience	• Solid-state technology allows 1–5 min of ECG recording up to 3–5 times during events

(Continued)

Table 4.2 (Continued)

Type	Recording	Scanning	Transmitting	Comments, advantages, and disadvantages
	• The circuitry is completed by index finger and thumb or hand contact			
ILR (implantable loop recorder) Subcutaneous, implanted digital recorder	• ECG selected by patient activation with memory of pre-event. After event, patient places a pager-like device over the loop recorder. By pressing a button, the ECG data are recorded to the hand-held device, which is available for later analysis by the physician	• Direct visualization	Direct telemetry	• Though it involves an invasive procedure, the ability to record pre- and post-event, independent of patient activation, which is available for microprocessor-based analysis is a significant advantage. The ILR permits ECG recordings during water immersion, unlike other event recorders
Automatic electronic sensor, in ICD or pacemaker	• ECG, when activated by firing of ICD or recognized by sensor in pacemaker, with memory	• Direct visualization of analysis of ECG	Direct telemetry	
Real-time				
Real-time transtelephonic monitoring	• ECG at central monitoring station – no recording at device	• Direct visualization	Transtelephonic	

ARTIFACTS AND ERRORS

- Due to technical problems during recording and analysis, a large amount of invalid data during AECG recording is possible.
- For accurate analysis and interpretation of AECG recordings it is important to recognize artifacts that can simulate arrhythmia.
- With earlier tape-based recorders, tape slippage, excessive damping, inappropriate calibration, or saturation of the amplifier can cause artifacts.[18] Tape distortion can falsely prolong intervals that simulate sinus pauses.
- Changes in body position (supine vs erect), and breathing patterns, can change P-wave, QRS, and T-wave morphology.
- A major cause of inaccurate arrhythmia and ST-segment recognition and analysis is noise interference from multiple sources.
- Electrical artifacts can simulate pacemaker malfunction.
- Most current devices use solid-state digital recordings, rendering the problems associated with tape recordings obsolete.

SCANNING AND ANALYSIS TECHNIQUES

- Earlier scanners were capable of full disclosure of ECG recordings with no data processing or tabulation facilities. Though analysis by experienced technicians revealed significant rhythm abnormalities, sophisticated processing was difficult.
- Current scanning systems incorporate computer-assisted analysis with algorithm-based software systems capable of generating ECG recordings, arrhythmia analysis, ST segment detection, RR interval analysis, and providing trends or statistical summaries.
- It has been shown that when operator analysis is done without computer assistance, up to a third of supraventricular or ventricular arrhythmias are missed.[19] Computer-assisted analytic systems significantly improve the sensitivity and specificity of ECG monitoring.[20,21]

Table 4.3 compares the technical and clinical attributes of ambulatory ECG and the transtelephonic loop recorder.[21]

PERSONNEL, TRAINING REQUIREMENTS, AND QUALITY CONTROL

- In addition to a technician/nurse trained in the technical aspects of the device recorder who places the electrodes and hooks up the device, the base station must be equipped with a cardiovascular technician or nurse on a 24-hour basis, or with a microcomputer capable of receiving and storing data for later analysis.
- Guidelines established by the American College of Cardiology/American Heart Association (ACC/AHA) have outlined the minimum knowledge and training necessary for acquiring and maintaining competence in AECG interpretation.
- Table 4.4 lists the ECG diagnoses that can be made with AECG.
- Due to various technical differences among devices, physicians who interpret AECG need to

    - acquire cognitive skills which in addition to basic electrocardiography include assessment of HRV, cardiac pacemakers, and ICDs (Table 4.5);

Table 4.3 Technical and clinical differences of ambulatory ECG and transtelephonic loop recorder[21]

	Ambulatory ECG	Transtelephonic loop
Technical		
ECG data	24–48 h of 2- or 3-channel ECG Continuous ECG data	4–5 min of 1-channel ECG intermittent and patient-activated ECG data
Resources needed	Holter recorder Holter playback analysis system Operator interaction	Transtelephonic loop recorder Telephone communication with audio modem Base station printout recorder (24 h availability) Operator interaction
Cost	24 h $150–300	30 d surveillance $200–300
Patient participation	Minimal (diary for symptoms)	Moderate/substantial (sending and recording ECG data)
Clinical		
Indications	To diagnose cardiac arrhythmias with qualitative/quantitative assessment	To diagnose infrequent or rare cardiac arrhythmias qualitatively only
As first-line diagnostic test	Often	Never
As arrhythmic follow-up	Often	Rarely or special situation (e.g. sudden death cohorts or effects on QT interval)
As pacemaker follow-up	Often	Often

Table 4.4 List of AECG diagnoses[22]

Type of AECG disorder	List of diagnoses
Sinus node rhythms and arrhythmias	Sinus rhythm Sinus tachycardia (>100 beats per minute) Sinus bradycardia (<50 beats per minute) Sinus arrhythmia Sinus arrest or pause Sino-atrial exit block
Other supraventricular rhythms	Atrial premature complexes Atrial premature complexes, non-conducted Ectopic atrial rhythm Ectopic atrial tachycardia, unifocal Ectopic atrial tachycardia, multi-focal Atrial fibrillation Atrial flutter Junctional premature complexes Junctional escape complexes or rhythm Accelerated junctional rhythm Junctional tachycardia, automatic Supraventricular tachycardia, paroxysmal

(Continued)

Table 4.4 (Continued)

Type of AECG disorder	List of diagnoses
Ventricular arrhythmias	Ventricular premature complexes Ventricular escape complexes or rhythm Accelerated idioventricular rhythm Ventricular tachycardia Ventricular tachycardia, polymorphous (including torsade de pointes) Ventricular fibrillation
Atrial ventricular conduction	First-degree AV block Mobitz type 1 second-degree AV block (Wenckebach) Mobitz type 2 second-degree AV block AV block or conduction ratio, 2:1 AV block, varying conduction ratio AV block, advanced (high-grade) AV block, complete (third-degree) AV dissociation
Intraventricular conduction	Left bundle branch block (fixed or intermittent) Right bundle branch block (fixed or intermittent, complete or incomplete) Intraventricular conduction delay, non-specific Aberrant conduction of supraventricular beats Left posterior fascicular block Ventricular pre-excitation (Wolff–Parkinson–White pattern)
QRS axis and voltage	Right axis deviation (–90 to –180 degrees) Left axis deviation (–30 to –90 degrees) Low voltage (less than 0.5 mV total QRS amplitude in each extremity lead and less than 1.0 mV in each precordial lead)
Chamber hypertrophy or enlargement	Left atrial enlargement, abnormality, or conduction defect Right atrial abnormality Left ventricular hypertrophy with secondary ST-T abnormality Right ventricular hypertrophy with or without secondary ST-T abnormality
Repolarization (ST-T, U) abnormalities	Early repolarization (normal variant) Juvenile T-waves (normal variant) Non-specific abnormality, ST segment and/or T-wave ST and/or T-wave suggests ischemia ST suggests injury ST suggests ventricular aneurysm Q-T interval prolonged Prominent U waves
Pacemaker	Ventricular-paced rhythm Atrial-sensed ventricular-paced rhythm AV dual-paced rhythm Failure of appropriate capture, atrial Failure of appropriate capture, ventricular Failure of appropriate inhibition, atrial Failure of appropriate inhibition, ventricular Failure of appropriate pacemaker firing Retrograde atrial activation Pacemaker mediated tachycardia

Table 4.5 Skill sets required for competency in AECG interpretation[22]

Cognitive skills needed to interpret AECGs competently (from ACC/AHA guidelines 2001)[22]
1. Knowledge of the appropriate indications for ambulatory electrocardiography
2. Knowledge of cardiac arrhythmias, their diagnosis, and significance in normal subjects and in patients with heart disease
3. Appreciation of the wide range of variability in arrhythmia occurrence in the ambulatory patient throughout a diurnal cycle, and the influence of the autonomic nervous system on the rhythm of the heart
4. Knowledge of changes in the ECG that may result from exercise, hyperventilation, conduction disorders, electrolyte shifts, drugs, meals, temperature, Valsalva maneuvers, ischemia, and transient repolarization phenomena related to a variety of cardiac diseases
5. Knowledge of cardiac drugs and how they may affect conduction and repolarization on the ECG, particularly for suspected pro-arrhythmic phenomena
6. Knowledge of the sensitivity, specificity, and diagnostic accuracy of ambulatory electrocardiography in various age groups and populations, particularly with respect to ST segment changes and the application of Bayes' theorem
7. Knowledge of the most widely accepted criteria for ischemic ST segment changes
8. Knowledge of ambulatory electrocardiographic evidence of failure to capture, failure to sense, or failure to pace for cardiac pacemakers and ICDs
9. Knowledge of ambulatory electrocardiographic evidence of appropriate and inappropriate anti-tachycardia pacing or defibrillation in the ICD patient
10. A basic understanding of the advantages and disadvantages of the instrumentation used in continuous and intermittent ambulatory electrocardiography from a recorder, and the possible causes for false-positive or false-negative test results that are due to inherent instrumentation or signal processing limitations
11. Knowledge of the particular characteristics of the AECG instrumentation used to process the recordings for which the electrocardiographer is responsible
12. Appreciation of the skills required by the technologist to interact with the AECG instrumentation in editing the computer output, and the need to be assured of the competence of the technologist

  - understand the equipment and computer algorithms including problems during editing;
  - have knowledge of artifactual and transient physiologic changes and the false-positive and false-negative findings during arrhythmia detection and classification (Table 4.6).

- A minimum of 150 supervised AECG interpretations is recommended to expose the trainee to most of the technical and physiologic phenomena known to confound AECG interpretation.[22]
- Hands-on experience with operation of the Holter instrumentation enables the trainee to appreciate artifacts and errors encountered during recording and analysis.
- A minimum of 25 interpretations per year is recommended to maintain competence in AECG interpretation.[22]
- Quality assurance in AECG interpretation by physicians can be achieved by conducting periodic reviews of random samples of their prior AECG interpretations by an acknowledged expert.

Table 4.6 Technical pitfalls responsible for false-positive/negative findings[22]

Causes of technical false-positive/false-negative findings in arrhythmia detection and classification	Causes of false-positive/false-negative findings in detection and interpretation of cardiac ischemia
1. Inadequate computer QRS detection and classification algorithms 2. Noise interference or lead-electrode baseline drift or artifact 3. Low-voltage recording 4. Recorder malfunction with variable tape drive or inaccurate storage 5. Physiologic variations in QRS form and voltage 6. Incomplete degaussing or erasure of data from previously used tapes or memory storage 7. Inadequate or incorrect technician interpretation during analysis 8. Incorrect time stamping of AECG tracings	1. Positional changes on the ST segment 2. Hyperventilation 3. Sudden excessive exercise-induced ST segment changes 4. Vasoregulatory or Valsalva-induced ST segment changes 5. Intraventricular conduction disorders 6. Undiagnosed or unappreciated left ventricular hypertrophy 7. ST segment changes secondary to tachyarrhythmias 8. False ST segment changes from atrial fibrillation or atrial flutter 9. ST segment changes secondary to electrolyte disturbance or drugs 10. Inadequate lead system employed 11. Incorrect or lack of lead calibration 12. Inadequate recording fidelity 13. Recording signal processing that compresses or filters the data, altering the ST segment characteristics

RECORDER MAINTENANCE AND PREPARATION

- Optimal and reliable performance of Holter monitors requires routine maintenance depending on the frequency of use. Continuous recording Holters need weekly maintenance.
- Older tape-based Holter recorders (seldom used currently) have oxide build-up on the magnetic tape which can decrease the ECG signal amplitude, which can be easily removed by wiping the cassette recorder head with alcohol pads or cleaning fluids like Freon.

PREPARATION

- Before device application to the patient, a blank magnetic tape should be inserted into the recorder.
- Adequately charged or new batteries should be available. If rechargeable batteries are used they must be charged for 4 to 16 hours prior to use depending on the manufacturer's recommendation.
- Calibration standards of 1 mv are available in most Holter recorders. Brief ECG recordings with these standards should be obtained on each tape, to serve as a baseline for subsequent analysis.

SELECTION OF LEAD SYSTEM

- Unlike the standard 12-lead ECG, most Holter recorders use 1 to 2 leads (current devices use 5 to 6 leads). Using fewer leads improves the reliability of

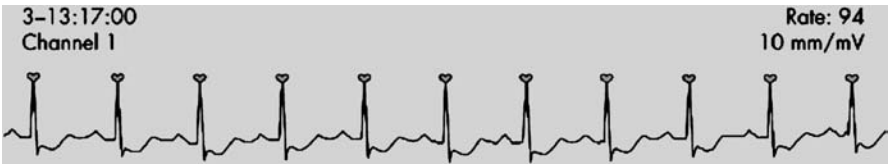

Figure 4.2 Ambulatory electrographic strip demonstrating significant ST segment depression.

recording ECG data and the detection of ectopic beats and myocardial ischemia.
- Despite a lack of studies establishing the superiority of using one lead vs the other, the expert consensus is that a modified V1 lead system (P-wave and QRS morphology) and V3 to V5 lead system (ST segment depression or elevation) are best for identifying ectopic beat patterns and myocardial ischemia, respectively[23] (Figure 4.2).

ELECTRODE PLACEMENT (FIGURE 4.3)

- The ground electrode is placed in the lateral one-third of the right infraclavicular fossa immediately medial to the shoulder.
- For V1, the positive exploring electrode is placed in the fourth intercostal space (ICS) on the anterior chest 1 inch from the right sternal border; the negative electrode is placed in the lateral one-third of the left infraclavicular fossa medial to the shoulder.
- For V3, the positive electrode is placed in the left lower fourth ICS midway between the left sternal border and the left midclavicular line (MCL); the placement of the negative electrode is similar to V1.
- For V5, the positive electrode is placed on the anterior chest in the fifth ICS space midway between the left MCL and the left midaxillary line; the negative electrode is located 1 inch below the inferior angle of the right scapula on the posterior chest.
- For AVF, the positive electrode is placed in the ninth to tenth ICS at the left anterior axillary line; the negative electrode is placed in the lateral third of the left infraclavicular fossa medial to the shoulder.[24]

PREPARATION OF ELECTRODE SITE

- The patient removes clothing from the waist up and the positions of the five electrodes as described earlier are prepared.
- Body hair in and around the site of the electrode placement should be removed by light shaving.
- Skin surface oil and dirt are rubbed off with alcohol-soaked gauze. Adequate skin preparation is crucial for optimum ECG signal. Alcohol prep pads lack the abrasive quality of gauze, and therefore should not be used.
- The central area of the electrode where the skin will make contact with the electrode pad should be gently abraded by wiping 3 to 4 times with extra fine

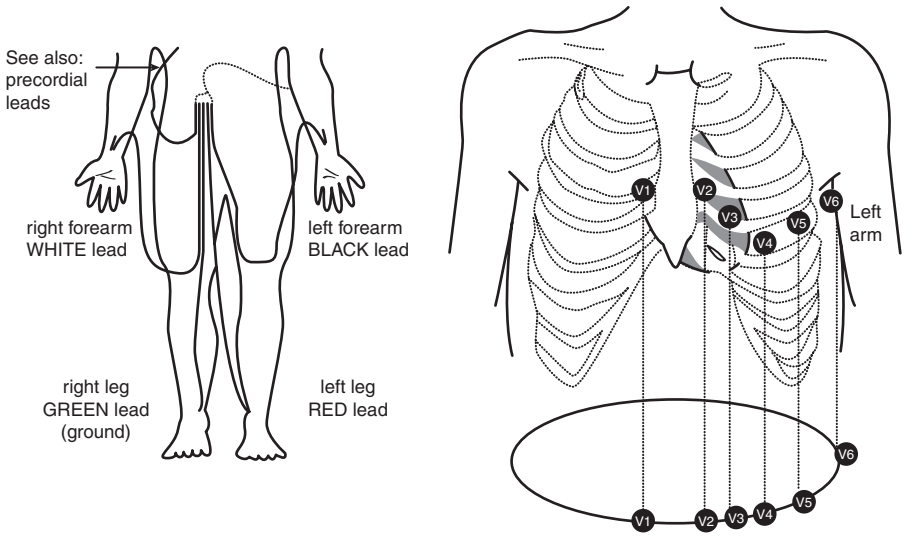

Figure 4.3 Placement of limb leads and chest leads.

grade sandpaper. Removal of this extra layer of dead superficial skin will enhance contact and improve the quality of the electrode signal.

- The adhesive disk should be securely attached to the skin. A prolonged period ($\geq$72 hours) of contact is achieved with Huggable (brand of tape based electrodes that are capable of achieving longer periods of contact) ambulatory monitoring electrodes. Applying a thin layer of tincture of benzoin serves as a useful adjunct, particularly on hot humid days, to negate the effect of excessive sweating. In patients with hypersensitivity to electrode gel or adhesive material, a non- or hypoallergenic electrode type or tape should be used to avoid serious local skin reactions.
- After the electrodes are placed, the electrical impedance between the poles of each bipolar lead should be checked to ensure optimal ECG signal. Using a standard impedance meter with a 10 Hz signal the impedance should always be $<$5000 ohms, preferably $<$3500 ohms.[25]
- An electrode lead wire is snapped on to each of the electrode pads. The five lead wires are connected to a single patient cable. Accidental pull-out of the lead wires is avoided by using a lead wire brace retainer around the area of the patient's cable interface to serve as a stabilizing support. Additional protection with adhesive tape wrapping around the lead wire retainer is desirable.

PATIENT INSTRUCTION, PRE-EXAMINATION PROCEDURES

- A log book containing patient identifiers, contact information, diagnosis, date, the serial number of the recorder used, and battery identification, if it is rechargeable, should be kept in the Holter recording examination area.

- In the patient's diary, in addition to demographic information and dates of examination, the patient records the time of activities (including major changes), symptoms with time of occurrence, and medication ingestion that occur during AECG examination. This facilitates correlation of activities and symptoms with detected electrocardiographic phenomena.
- It should be emphasized that the patient should engage in his routine activities.
- The recording starts either with the connection of the patient cable to the Holter recorder or by activation of the recorder. The start time per the patient's watch is noted in the patient's diary and also entered into the clock of the Holter recorder.
- Once recording begins, the clarity of the electrical signal has to be verified before the patient is sent home. The clarity of ECG signal should be tested while manually tapping the various electrodes and vigorously moving the corresponding lead wires for both bipolar leads. If a wandering baseline or muscular or electrical artifacts are seen, the electrode/lead wire responsible for the artifact is identified using an impedance meter and replaced.
- Due to assumption of different positions by the ambulatory patient, ECG rhythm strips should be recorded in at least 5 positions (standing, sitting, supine, left lateral supine, and right lateral supine). This provides accurate baseline comparisons for the changes that normally occur during a 24-hour AECG.
- Finally, the lead wire retainer and the patient cable should be taped to the anterior chest wall. The Holter recorder can be worn on the hip (with a belt) or carried over the shoulder (with a strap).

REMOVAL OF THE HOLTER RECORDER

- Following completion of the time period (usually 24 hours), the Holter recorder is removed as follows:
  - the patient cable is disengaged from the Holter recorder;
  - the diary and recorder are removed from the patient;
  - lead wires are removed from the electrodes;
  - micropore tape holding the patient cable to the chest wall is removed;
  - electrode pads can be removed by the patient or the technician;
  - excessive electrode gel is wiped off with alcohol pads; any skin irritation or reaction is treated by application of 1% hydrocortisone gel;
  - the patient's diary is always kept with the corresponding patient's tape.

DEVICE SELECTION AND DURATION OF RECORDING FOR AECG MONITORING

- Selection of continuous vs intermittent ECG recording is individualized based on the frequency of symptoms.
- Table 4.7 shows the type of device to be selected depending on the symptoms and the diagnostic yield.[26]
- The presence of symptom–arrhythmia correlation is diagnostic.
- While most patients are monitored for 24 to 48 hours, it is possible to monitor for longer periods (days).
- While the presence of arrhythmia without associated symptoms does not contribute towards diagnosis, lack of arrhythmia during symptoms excludes arrhythmia as a possibility.

Table 4.7 Device selection based on symptoms and diagnostic yield

Symptom	Type of recorder	Duration of recording	Diagnostic yield (%)	Comments
Palpitations	Intermittent	During symptoms up to 4 weeks	35	Depending on frequency, if daily symptoms present, continuous monitoring can also be used
Syncope/ pre-syncope	Intermittent	Depending on frequency of the event	31 to 58	Recording up to 24 months with ILR is possible
Atrial fibrillation and cerebrovascular events	Intermittent		Low diagnostic yield, not routinely recommended	Class IIb indication
Ischemic episodes	Continuous or intermittent	>48 to 96 hours	27 to 94	Diagnostic yield depends on length of recording
Prognosis of myocardial infarction	Continuous or intermittent	HRV analysis		For HRV analysis at least 5 PVCs are needed
Drug therapy	Continuous	24 to 48 hours		Established indication only for atrial fibrillation on rate control medications

- A randomized cross-over trial of 43 patients with palpitations randomized to event monitoring and 48-hour monitoring showed that event monitors were more than twice as likely to detect a clinically important arrhythmia.[27]

CONCLUSIONS

- AECG monitoring is a cost-effective tool for evaluating patients with suspected arrhythmias and myocardial ischemia. Setting up a long-term arrhythmia monitoring laboratory involves costs in the form of personnel and equipment (devices and computerized analysis systems); the spectrum of uses renders it cost-effective.
- Rapidly emerging technologic advances have not only changed the size and ease of carrying recording devices but have added a wide spectrum of possibilities ranging from mundane recognition of ectopic beats and recognizing ST segment changes to complex QT interval analysis, diagnosing unexplained syncope by ILR implantation, and HRV assessment. Troubleshooting of technical problems is summarized in Table 4.8.

Table 4.8 Problems in interpretation due to technical problems

	Decreased signal amplitude	Wide signal	Narrow signal tachycardia	Loss of signal	Wandering baseline	Premature cessation of record-ing	60 Cycle noise	Muscle artifact	Electrical artifact
Electrode	X				X		X	X	X
Skin placement	X				X			X	
Disengaged	X			X	X			X	
Type					X			X	
Lead wire									
Broken	X			+					X
Disengaged				X					
Inadequately grounded							X		
Patient cable									
Short in wire	X			+					X
Loosely fitting to lead wires	X			+					X
Loose connection into recorder				X		X	X		X
Holter recorder									
Oxide accumulation	X			X	X				
Recording tape									
Inadequately erased									X
Wrong type of recording tape	X			X					

Battery								
Defective	+	+			+			
Inadequate charge	X	X			X			
Body interference								
Fat tissue	X			X				
Musculature				X			X	
Outside interference								
Electric blanket or heating pad				X		X		X
Sudden fall or blow			X					X

X: source of a particular type of artifact.
+: can occur intermittently.

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Section III
Bradyarrhythmia

5
Bradycardia

Shane Bailey, J David Burkhardt, and Mandeep Bhargava

Bradycardia – pathophysiology • Disorders of the sinus node • Disorders of atrioventricular and His-Purkinje conduction • Conduction abnormalities after myocardial infarction • Neurally mediated bradycardia • Post-surgical bradyarrhythmias • Bradyarrhythmias secondary to medications • Diagnostic testing

BRADYCARDIA – PATHOPHYSIOLOGY

Bradyarrhythmias and conduction blocks are common electrocardiographic findings. These arrhythmias can result from a wide variety of disorders of the cardiac conduction system. Bradycardias are generally divided into disorders involving either the sinus node or atrioventricular conduction or as neurally mediated arrhythmias. Bradyarrhythmias may be discovered as incidental electrocardiographic abnormalities or may be found after investigation for symptoms suggestive of their presence. A wide variety of symptoms may be caused by the different etiologies of bradycardia, often times adding diagnostic difficulty to patients with coexisting medical problems.

DISORDERS OF THE SINUS NODE

Sinus node dysfunction includes any abnormality involving the sinus node, including sinus bradycardia, sino-atrial arrest, sino-atrial exit block, and tachycardia–bradycardia syndrome. The clinical presentation may include fatigue, dyspnea, and syncope. Palpitations may be the primary complaint in patients with tachycardia–bradycardia syndrome. The most common etiology of sinus node dysfunction includes idiopathic degenerative disease with the incidence increasing with age. Other intrinsic factors include coronary disease, hypertension, and infiltrative disorders. Extrinsic factors include drug effects, autonomic influences, and electrolyte imbalances.

Sinus bradycardia exists in an adult when the sinus node discharges less than 60 beats per minute (bpm). This occurs normally in young adults from vagal tone or in older individuals from medications or underlying sinus node dysfunction. During sleep, the normal heart rate can decrease to 35–40 bpm with marked sinus arrhythmia and asymptomatic pauses. Inappropriate sinus bradycardia, or chronotropic incompetence, refers to a failure to increase the sinus rate with exercise.

Sinus arrest, or sinus pause, is a disorder of automaticity in which no impulses are generated within the sinus node and may last from seconds to several minutes. The length of the pause is not an exact multiple of the PP interval, suggesting that the mechanism is due to slowing or interruption of sinus node automaticity and not conduction block.

Sinoatrial exit block is recognized electrocardiographically as a sudden pause in atrial depolarization with the length of the pause an exact multiple of the PP interval. Unlike sinus arrest, this arrhythmia is not due to a disorder of impulse formation, but rather conduction block. Sinoatrial exit block can be divided into type I (SA Wenkebach), type II (SA Mobitz II), and high-degree SA block (Figure 5.1). Type I SA block can be recognized electrocardiographically as a group beating of P waves with shortening of the PP intervals and pauses that amount to less than twice the shortest PP cycle. In contrast, type II SA block demonstrates intermittent failure of conduction to the atrium as manifested by fixed PP intervals with pauses that equal twice the PP interval.

Sick sinus syndrome (SSS) is characterized by episodes of bradycardia with sinus pauses, arrest, or exit block associated with poor atrial and junctional escape rhythms. Alternating atrial tachyarrhythmia, mainly atrial fibrillation, is seen in many cases and is termed the *tachycardia–bradycardia syndrome*. Atrial fibrillation is likely associated with SSS due to the increased dispersion of refractoriness or early after depolarizations (EADs) occurring in the setting of bradycardia. Pauses are often observed after cessation of tachycardia, posing difficulty in pharmacologically managing the tachyarrhythmia. Atrioventricular (AV) conduction disturbances occur in approximately half of patients with SSS. Most commonly, atrial fibrillation with a slow ventricular response in the absence

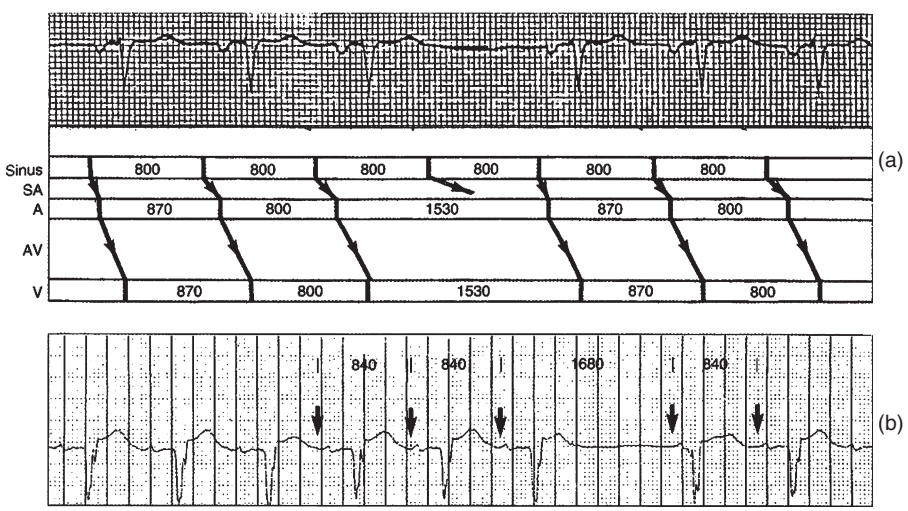

Figure 5.1 (a) SA Wenkebach with 4:3 conduction to the atrium. The PP interval is greatest in the initial cycle with subsequent decrease in PP interval until block in the atrium. (b) Mobitz II block – no change in the PP interval is seen prior to a dropped P-wave. (Courtesy of: Wellens, Hein JJ, The ECG in emergency decision making, second edition, Saunders Elsevier, 2006.)

of AV nodal blocking medications indicates AV node dysfunction. Etiologies for SSS include sinus node fibrosis, coronary disease (involving the SA nodal artery), drugs, and infiltrative diseases such as amyloidosis and sarcoidosis.

DISORDERS OF ATRIOVENTRICULAR AND HIS-PURKINJE CONDUCTION

The most common etiologies of AV conduction disturbances include fibrosis, degeneration of the conduction system, ischemia, and drugs. In the young, the most common etiology is congenital AV block or AV block from surgery for congenital heart disease. Among the elderly, idiopathic fibrosis and calcification of the conduction system is a frequent cause. Ischemic heart disease accounts for approximately one-third of cases of AV block, either the result of chronic coronary disease or myocardial ischemia. AV nodal conduction disturbances are seen frequently in acute coronary syndromes (described below).

Lev's disease refers to the sclerotic process that is seen in older individuals involving the fibrous ring. Associated echocardiographic findings include calcification of the mitral and aortic valves. *Lenegre's disease* refers to a fibrotic process specifically involving the conduction system and is felt to be hereditary, most often observed in younger individuals. A comprehensive list of causes of AV conduction disorders is given in Figure 5.2.

First-degree AV block is a misnomer in that every P-wave is conducted to the ventricles, however with a PR interval exceeding 200 ms. *Prolonged PR conduction,* a more appropriate classification for this conduction disturbance, may be the result of conduction delay within the atrium, AV node, His bundle or bundle branches. Prolongation of the PR interval most often indicates AV nodal conduction delay.

Second-degree AV block is characterized by a failure of one or more atrial impulses to reach the ventricles. Block can be either at the level of the AV node or infranodal structures. *Type I second-degree AV block, or Wenkebach*, requires prolongation of the PR interval prior to the blocked impulse with subsequent shortening of the PR interval with the next conducted impulse. On the ECG, the RR interval progressively shortens up to the point of the blocked ventricular impulse. This occurs because the largest increment in the PR interval occurs between the first and second cycles. The site of block in type I second-degree AV block is the AV node. This conduction disturbance most often is physiologic and is seen with high vagal tone and during sleep. Pacing is rarely indicated.

Type II second-degree AV block, or Mobitz II, is instead characterized by a constant PR interval prior to and following a blocked impulse. Mobitz II second-degree block originates from an intra- or infra-Hisian location and often is associated with a bundle branch block pattern. On electrophysiologic evaluation, constant HV intervals are typically seen with spontaneous block within or below the His. Type II second-degree AV block often progresses to complete AV block and can manifest as syncope. When development of this type of block or new bundle branch block is seen in association with anterior myocardial infarction, it implies a proximal LAD occlusion.

Two-to-one AV block can represent benign block within the AV node or disease of the His-Purkinje system. Certain electrocardiographic features and maneuvers can help in distinguishing where the location of block exists. A long PR interval

Drug effects
  Digoxin
  Beta-blockers
  Non-dihydropyridine calcium-channel blockers
  Membrane-active anti-arrhythmic drugs
Ischemic heart disease
  Acute myocardial infarction
  Chronic coronary artery disease
Idiopathic fibrosis of the conduction system
  Lenègre's disease
  Lev's disease
Congenital heart disease
  Congenital complete heart block
  Ostium primum atrial septal defect
  Transposition of the great vessels
  Maternal systemic lupus erythematosus
Calcific valvular disease
Cardiomyopathy
Infiltrative disease
  Amyloidosis
  Sarcoidosis
  Hemochromatosis
Infectious and inflammatory diseases
  Endocarditis
  Myocarditis (Chaga's disease, Lyme disease, rheumatic fever, tuberculosis, measles, mumps)
  Collagen vascular diseases (scleroderma, rheumatoid arthritis, Reiter's syndrome, systemic lupus erythematosus, ankylosing spondylitis, polymyositis)
Metabolic
  Hyperkalemia
  Hypermagnesemia
Endocrine: Addison's disease
Trauma
  Cardiac surgery
  Radiation
  Catheter trauma
  Catheter ablation
Tumors
  Mesothelioma
  Hodgkin's disease
  Malignant melanoma
  Rhabdomyosarcoma
Neurally mediated
  Carotid sinus syndrome
  Vasovagal syncope
Neuromyopathic disorders
  Myotonic muscular dystrophy
  Slowly progressive X-linked muscular dystrophy

Figure 5.2 Etiologies of atrioventricular conduction disorders. (Courtesy of: Topol ET. Textbook of Cardiovascular Medicine, 1st edition. Philadelphia: Lippincott-Raven, 1998.)

with a narrow QRS suggests an intranodal block. A short PR interval with intraventricular conduction delay or bundle branch block suggests disease below the node. Responses to atropine, exercise, and carotid sinus massage can be helpful in diagnosis. Atropine will improve AV nodal conduction but will worsen block within diseased His-Purkinje fibers. Exercise has a similar effect, improving conduction in cases where block exists only in the node, but worsening when block is subnodal. Alternatively, carotid sinus massage will slow conduction when block occurs in the AV node, but will improve conduction in diseased His-Purkinje tissue by allowing for refractoriness to recover (Figure 5.3).

Not all atrial impulses that fail to conduct to the ventricles are necessarily second-degree AV block. If an atrial impulse reaches the AV junction early enough in the cycle while the node is refractory, the impulse is not conducted. This is a common scenario seen with early premature atrial complexes (PACs). Block, which infers pathology of conduction, is an incorrect description of this phenomenon. Likewise, 2:1 conduction, rather than block, is a more apt description of atrial flutter that conducts to the ventricles in this pattern.

Third-degree heart block results in no conduction of atrial impulses to the ventricles and may be acquired or congenital. Block can occur in either the AV

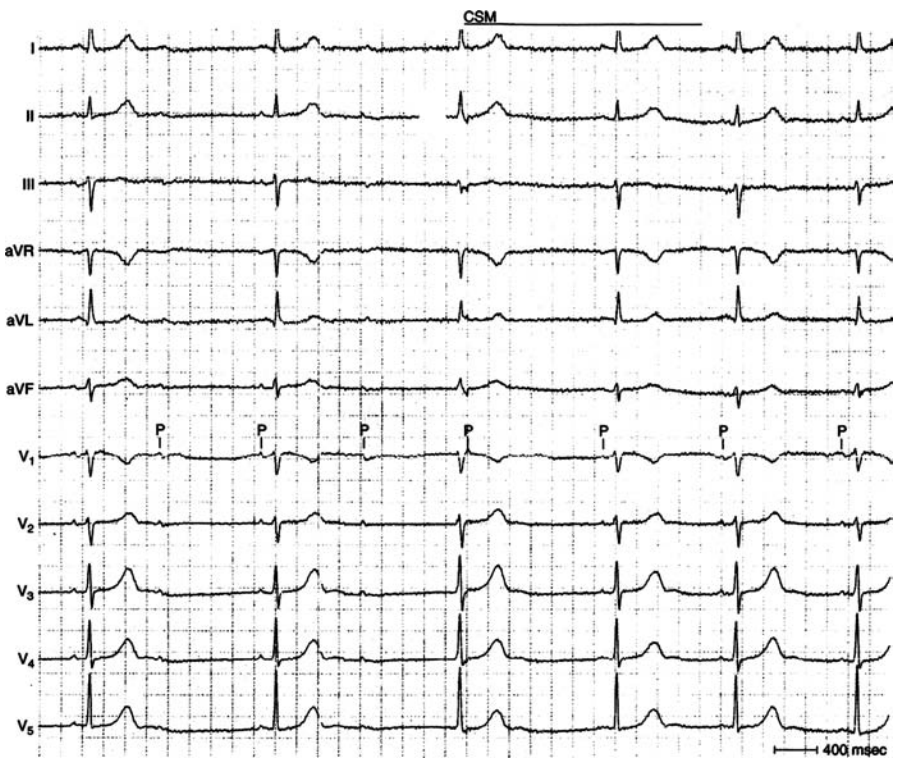

Figure 5.3 Improvement in AV conduction with carotid sinus pressure. Two-to-one AV block improves to one-to-one AV block with prolongation of the cycle length, indicating His-Purkinje disease. (Courtesy of: Wellens, Hein JJ. The ECG in emergency decision making, second edition, Saunders Elsevier, 2006.)

node or His-Purkinje system. The site of block can be somewhat inferred by the nature of the escape rhythm, with narrow QRS escape complexes and rates greater than 40 bpm suggestive of block in the AV node or proximal His. Conversely, block within the distal His or the branching structures will manifest as wide QRS escape complexes with slower rates. Use of atropine will accelerate the escape rate in instances of AV nodal block, and will fail to do so otherwise.

Congenital third-degree AV block occurs in approximately 1 in 20 000 children. In over half, AV block is discovered as a result of bradycardia *in utero* or neonatally and is secondary to maternal lupus in over 90% of cases. Mortality in AV block from neonatal lupus tends to be high. When AV block is diagnosed later in childhood, maternal lupus is rarely responsible and etiologies include structural heart defects and myocarditis. Initially, AV block may be transient but most often progresses to permanent AV block with junctional escape.

Intraventricular conduction disturbances (IVCDs) occur below the AV node and do not in themselves result in bradyarrhythmias. Conduction delay can occur anywhere along the His-Purkinje system and etiologies are similar to those causing AV block. The most common etiologies include idiopathic fibrosis and ischemia. IVCDs are more commonly seen in structurally abnormal hearts. These are generally classified by the number of fascicles affected. The His-Purkinje system is a trifascicular system, with *bifascicular block* referring to conduction delay within either both the right bundle and left anterior or posterior fascicle or the left bundle branch in itself. Chronic bifascicular block in asymptomatic patients has a low risk of progression to AV block; however, in the setting of an anterior infarction and new bifascicular block, the risk is substantial. *Trifascicular block* is a confusing description that is most often applied to those with bifascicular block and prolonged PR intervals. Like bifascicular block, the risk for progression to AV block is less than 1% per year.

Paroxysmal AV block, an unusual but formidable form of conduction block, occurs when one-to-one conduction abruptly changes to complete AV block. As shown in Figure 5.4, following a conducted PAC, the following PP interval is prolonged secondary to sinus node suppression. Complete AV block is seen following the lengthening in sinus cycle length after the PAC. This is secondary to phase 4 block. *Phase 4 block* occurs in the setting of bradycardia secondary to reduction of transmembrane potential during a prolonged electrical diastole. This type of block is not physiologic and indicates diseased His-Purkinje tissue.

Bradycardia-dependent bundle branch block is a similar, but less extreme, phenomenon related to phase 4 block. In this case, bundle branch block (almost always left bundle branch block) is seen after the end of a longer diastolic cycle (Figure 5.5). This, as well, indicates organic heart disease and results from diastolic depolarization of the membrane potential with a deterioration of membrane responsiveness so that conduction is impaired through the affected bundle branch.

CONDUCTION ABNORMALITIES AFTER MYOCARDIAL INFARCTION

Both bradyarrhythmias and conduction disturbances can be seen with myocardial infarctions and are generally related to ischemia or autonomic disturbance.

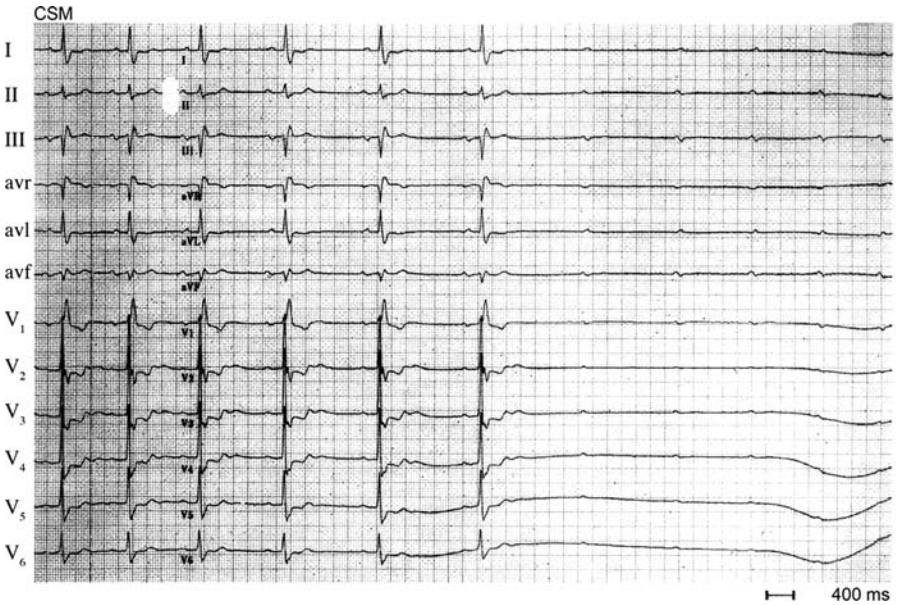

Figure 5.4 Paroxysmal AV block – phase 4 infranodal block precipitated by carotid sinus massage. Note the lengthening of the PP interval until block is seen. No increase in PR interval is observed prior to block. (Courtesy of: Josephson, Mark E, Wellens, Hein JJ. How to approach complex arrhythmias. EP Fellows Course, 2006.)

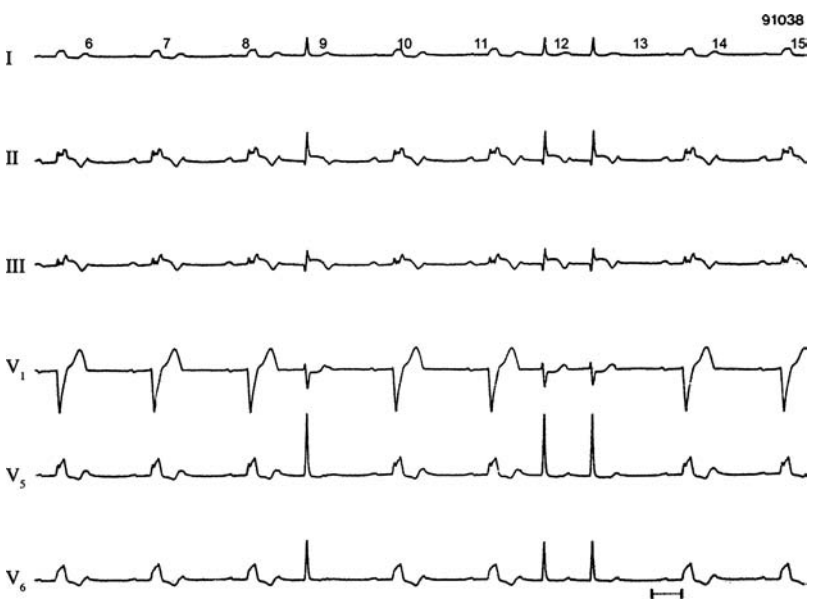

Figure 5.5 Bradycardia-dependent bundle branch block. Note the development of left bundle branch block after a longer diastolic interval. (Courtesy of: Josephson, Mark E, Wellens, Hein JJ. How to approach complex arrhythmias. EP Fellows Course, 2006.)

The clinical features and management of bradyarrhythmias and conduction block depend on the location of the infarction. The right coronary artery supplies the SA node in 60% of people and the left circumflex the remaining. In over 90% of people, the RCA feeds the AV node and proximal His. The terminal portion of the His and main left bundle and right bundle branch are supplied by septal perforators of the LAD.

Sinus bradycardia, prolonged PR conduction with Wenkebach, and complete heart block are common in inferior myocardial infarctions (IMIs). Complete AV block occurs in approximately 10% of patients with IMI. This rarely occurs suddenly, being most often seen with prolonged PR conduction gradually progressing to complete AV block. AV block occurs within the node in over 90% of cases and typically results in a transient block. The escape complex is usually narrow and infrequently requires pacing. Bradyarrhythmias occurring in the setting of inferior infarctions are generally responsive to atropine.

With anterior infarctions, conduction disturbances are not as benign and are related to the size of the infarction. The development of fascicular or bundle branch block is correlated to the size of infarct. Complete AV block in anterior MI can occur abruptly in the first 24 hours, developing without warning. AV block may also be preceded by the development of an intraventricular conduction delay or by type II second-degree block. Escape complexes are unstable and wide-complex requiring pacing. Complete heart block occurs secondary to necrosis of the distal His and bundle branches within the septum. When AV block occurs with anterior infarctions, mortality is greatly increased.

NEURALLY MEDIATED BRADYCARDIA

Autonomic stimulation can lead to sinus node slowing or AV nodal blockade in the absence of sinus or AV node dysfunction. Neurocardiogenic syncope and carotid sinus hypersensitivity are the most common etiologies of autonomically mediated bradycardia. Both occur in the setting of excess vagal tone and have similar clinical manifestations which include a cardioinhibitory response. This results from an increase in parasympathetic tone which can lead to sinus bradycardia, prolonged PR conduction, and second- and third-degree AV block.

The pathophysiology involving the cardioinhibitory response in neurocardiogenic syncope is felt to result from an exaggerated response to a physiologic reflex. The syndrome begins with relative hypovolemia that triggers a sympathetic reflex with an increase in heart rate, myocardial contractility, and peripheral vasoconstriction. Increased contractility results in ventricular cavity obliteration which, in turn, generates pressure sensed by mechano C fibers. In predisposed individuals, this results in vasodepression and cardioinhibition manifested as hypotension and slowing of the sinus rate or AV nodal block, respectively.

POST-SURGICAL BRADYARRHYTHMIAS

Bradyarrhythmias following open heart surgery are common. Most commonly, AV block is seen following aortic and mitral valve surgery. Septal myectomy invariably leads to resection of the left bundle and can often require permanent pacing secondary to subsequent AV block. Permanent pacing is required in 2–3%

of surgeries involving valve replacement and in approximately 10% of cardiac transplant recipients.

In cardiac transplant recipients, resting sinus rates are usually elevated due to denervation of vagal input. Sinus node dysfunction occurs in 50% of patients postoperatively resulting from prolonged donor ischemia or injury to the SA nodal artery. Injury to the SA node or artery can be avoided by performing bicaval, rather than atrial anastomosis. AV block is infrequently seen postoperatively in cardiac transplants. The most frequent intraventricular conduction disturbance is right bundle branch block, likely secondary to repeated biopsies required in these patients.

BRADYARRHYTHMIAS SECONDARY TO MEDICATIONS

Multiple cardiac medications are known to cause bradycardia. Beta-blockers, calcium-channel blockers, digoxin, and anti-arrhythmic medications include the most common agents. Through blockade of beta receptors, beta-blockers result in sinus bradycardia and prolong AV conduction. Similarly, calcium channels, specifically the non-dihydropyridines, verapamil and diltiazem, slow sinus depolarization and AV conduction. Digoxin, through altering vagal tone and increasing intracellular calcium concentrations, is well known to cause sinus bradycardia, block, and arrest as well as junctional bradycardia and AV block.

DIAGNOSTIC TESTING

Diagnostic testing for suspected bradyarrhythmias is generally limited to non-invasive methods. The initial work-up includes a 12-lead ECG followed by 24–48-h Holter monitoring. For patients with infrequent symptoms, an event monitor may be used to monitor the cardiac rhythm for up to 4 weeks. Implantable loop recorders are also available for prolonged continuous diagnostic monitoring. In instances where inappropriate sinus bradycardia is suspected, stress testing can be performed to assess chronotropic competence.

Assessment of autonomic tone includes carotid sinus massage and tilt table testing. Carotid sinus pressure with concomitant ECG monitoring can be helpful in identifying patients with *carotid sinus hypersensitivity*. Pauses exceeding 3 secs in response to carotid pressure are abnormal. Carotid sinus pressure should not precipitate sinus pauses, although slowing in the sinus rate or AV block can be normal responses. Tilt table testing can be helpful in differentiating bradycardia from sinus node disease and autonomic dysfunction. Bradycardic responses to tilt testing are the result of autonomic dysfunction.

Pharmacologic testing can also be useful in differentiating sinus node dysfunction from autonomic dysfunction. Autonomic blockade with atropine (0.4 mg/kg) and propanolol (0.2 mg/kg) can be used to determine the intrinsic heart rate (IHR), which represents the sinus node rate without autonomic influences. IHR can be calculated from the formula: $118 - (0.57 \times \text{age})$. Intrinsic sinus rates lower than the calculated value suggest sinus node dysfunction while sinus rates closer to this value represent autonomic dysfunction.

Electrophysiologic evaluation of bradyarrhythmias includes assessment of sinus node function and AV conduction. Sinus node function cannot be measured directly.

The two most common tests for sinus node function measure sino-atrial function indirectly. Sinus node recovery time (SNRT) is the time taken for sinus rhythm to resume after 30 s of overdrive atrial pacing. This interval is measured in the high right atrium from the last paced beat to the first spontaneous sinus beat. A delay of longer than 1500 ms is abnormal. The corrected value (CSNRT) can be determined by subtracting the intrinsic sinus cycle length from the SNRT value. Values of CSNRT longer than 550 ms suggest sinus node dysfunction.

The second indirect measurement of sinus node function is the sino-atrial conduction time (SACT). This technique is used for detecting delayed conduction between the sinus node and surrounding atrial tissue. This involves resetting the sinus node with atrial extra stimuli delivered in the high right atrium. After measurement of the intrinsic sinus rate, atrial extra stimuli are delivered during sinus rhythm over a range of coupling intervals (A1A2). Earlier coupled atrial extra stimuli invade and reset the sinus node. The interval of the returning sinus impulse following the atrial extra stimulus is measured and SACT is calculated as: (A2A3 – A1A1)/2. SACT values greater than 115 ms are considered abnormal.

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6

Indications for permanent pacing and cardiac resynchronization therapy

Kenneth Civello, Mandeep Bhargava, and J David Burkhardt

The indications for pacemaker therapy have increased over recent years and now include both the treatment of bradyarrhythmias and heart failure. The American College of Cardiology (ACC) and the American Heart Association (AHA) have published guidelines for permanent pacemaker implantation,[1] with recommendations presented in the standard ACC/AHA format (Table 6.1). These guidelines discuss indications for pacing in patients with sinus node dysfunction, acquired atrioventricular block, chronic bifascicular and trifascicular block, hypersensitive carotid sinus, and neurally mediated syndromes. They serve to direct the treating physician in selecting which patients would benefit from device therapy.

Sinus node dysfunction encompasses any dysfunction of the sinus node and includes inappropriate sinus bradycardia, sino-atrial exit block, sino-atrial arrest, and tachycardia–bradycardia syndrome. It is important to document the presence of symptomatic bradycardia in patients with sinus node dysfunction. Correlation with symptoms is imperative when deciding whether a permanent pacemaker is indicated. Work-up should start with a 12-lead ECG, followed by a 24- to 48-hour ambulatory monitoring. If less frequent events occur, a loop recorder, event monitor, or implantable loop recorder may be required. If non-invasive tests fail to make a diagnosis, invasive testing using the sinus node recovery time (SNRT) may be required to indirectly measure the sinus node function. The sinus node recovery time is the time it takes the sinoatrial node to recover following paced overdrive suppression of the node. This is performed by placing a catheter in the high right atrium near the sinus node at the junction of the superior vena cava and the right atrium for 4–6 trials of 30 s each. Each trial should use successively shorter pacing cycle lengths, beginning with a cycle length just shorter than the resting sinus cycle length. SNRT is the time interval between the last paced captured beat to the first spontaneous sinus beat. Secondary pauses can also occur after the initial recovery interval in sinus node dysfunction. If the longest interval for the recovery interval or secondary pause exceeds 1500 ms, the SNRT is prolonged. To adjust for heart rate the

Table 6.1 Standard ACC/AHA guidelines format

Class I: conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective
Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
Class IIa: weight of evidence/opinion is in favor of usefulness/efficacy
Class IIb: usefulness/efficacy is less well established by evidence/opinion
Class III: conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful

resting sinus cycle length is subtracted from the SNRT, and the corrected SNRT is obtained. Its upper range limit is 550 ms, thus if the SNRT exceeds the SCL by more than 550 ms, the SNRT is abnormal.

Another form of sinus node dysfunction frequently encountered is *chronotropic incompetence*, which is defined as an inadequate sinus rate response to stress or exercise. The severity of chronotropic incompetence can be diagnosed and documented with the use of an exercise stress test.

Permanent pacing in the setting of sinus node dysfunction is indicated in patients with symptomatic bradycardia, which is defined in the guidelines as a documented bradyarrhythmia that is directly responsible for development of the clinical manifestations of frank syncope or near syncope, transient dizziness or lightheadedness, and confusional states resulting from cerebral hypoperfusion attributable to slow heart rate. The guidelines for implantation of a pacemaker for sinus node dysfunction are listed below.

- Class I
  1. Sinus node dysfunction with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms. In some patients, bradycardia is iatrogenic and will occur as a consequence of essential long-term drug therapy of a type and dose for which there are no acceptable alternatives.
  2. Symptomatic chronotropic incompetence.
- Class IIa
  1. Sinus node dysfunction occurring spontaneously or as a result of necessary drug therapy with a heart rate $<$40 beats per minute (bpm) when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented.
- Class IIb
  1. In minimally symptomatic patients, chronic heart rate $<$30 bpm while awake.
- Class III
  1. Sinus node dysfunction in asymptomatic patients, including those in whom substantial sinus bradycardia (heart rate $<$40 bpm) is a consequence of long-term drug treatment.
  2. Sinus node dysfunction in patients with symptoms suggestive of bradycardia that are clearly documented as not associated with a slow heart rate.

3. Sinus node dysfunction with symptomatic bradycardia due to non-essential drug therapy.

Indications for pacing in patients with atrioventricular (AV) block are also influenced by the presence or absence of symptoms. Pacing for patients with first-degree AV block is rarely an indication unless the patient has symptoms suggestive of pacemaker syndrome. This has been found in patients with marked first-degree AV (PR greater than 300 ms).[2] In patients with type I second-degree AV block the level of delay is usually in the AV node irrespective of QRS width. Pacing is usually not indicated unless the patient is symptomatic or intra-His or infra-His block is found incidentally at EP study. On the other hand, type II second-degree AV block is usually infranodal, especially when the QRS is wide. In these patients progression to third-degree AV block is common. Thus, type II second-degree AV block constitutes an indication for pacing even in the absence of symptoms. Patients with third-degree heart block, asymptomatic or symptomatic, have an indication for pacing. It is important to note that even when the average heart rate is greater than 40 bpm in patients with advanced AV block there is a IIa indication for pacing because it is not the escape rate that is necessarily critical for safety, but rather the site of origin of the escape rhythm. Indications for permanent pacing in acquired AV block in adults are listed below.

- Class I
  1. Third-degree AV block at any anatomic level associated with any one of the following conditions:
     a. Bradycardia with symptoms presumed to be due to AV block.
     b. Arrhythmias and other medical conditions that require drugs that result in symptomatic bradycardia.
     c. Documented periods of asystole $\geq$3.0 s or any escape rate $<$40 bpm in awake, symptom-free patients.
     d. After catheter ablation of the AV junction.
     e. Postoperative AV block that is not expected to resolve.
     f. Neuromuscular diseases with AV block such as myotonic muscular dystrophy, Kearns–Sayre syndrome, Erb's dystrophy (limb-girdle), and peroneal muscular atrophy.
  2. Second-degree AV block regardless of type or site of block, with associated symptomatic bradycardia.
- Class IIa
  1. Asymptomatic third-degree AV block at any anatomic site with average awake ventricular rates of 40 bpm or faster.
  2. Asymptomatic type II second-degree AV block.
  3. Asymptomatic type I second-degree AV block at intra- or infra-His levels found incidentally at electrophysiologic study for other indications.
  4. First-degree AV block with symptoms suggestive of pacemaker syndrome and documented alleviation of symptoms with temporary AV pacing.
- Class IIb
  1. Marked first-degree AV block ($>$0.30 s) in patients with LV dysfunction and symptoms of congestive heart failure in whom a shorter

AV interval results in hemodynamic improvement, presumably by decreasing left atrial filling pressure.

- Class III
  1. Asymptomatic first-degree AV block.
  2. Asymptomatic type I second-degree AV block at the supra-His (AV node) level or not known to be intra- or infra-Hisian.
  3. AV block expected to resolve and unlikely to recur (e.g., drug toxicity, Lyme disease).

Conduction disturbances due to block below the AV node are classified on the basis of the intraventricular conduction system. Bifascicular block refers to electrocardiographic (ECG) evidence of impaired conduction below the AV node in two fascicles of the right and left bundles. Alternating bundle-branch block (also known as bilateral bundle-branch block) refers to situations in which clear ECG evidence for block in all three fascicles is seen on successive ECGs. Examples are right bundle-branch block and left bundle-branch block on successive ECGs, or right bundle-branch block with associated left anterior fascicular block on one ECG and associated left posterior fascicular block on another ECG. A strict definition of trifascicular block is block documented in all three fascicles, whether simultaneously or at different times. Alternating bundle-branch block also fulfills this criterion. This term has also been used to describe first-degree AV block in association with bifascicular block.

Although, there is considerable evidence that the rate of progression of bifascicular block to third-degree AV block is slow,[3] symptomatic advanced AV block that develops in these patients is associated with a high mortality rate and a significant incidence of sudden death.[4] Thus, pacing is indicated in patients with bifascicular block or trifascicular block who have intermittent symptomatic complete heart block or intermittent Mobitz II AV block. It is also important to comprehensively work up the cause of syncope in patients with intraventricular conduction disturbances because there is evidence that syncope in this setting is associated with an increased incidence of sudden cardiac death.[5,6] Therefore, if the cause of syncope in the presence of bifascicular or trifascicular block cannot be determined, prophylactic permanent pacing is a Class IIa indication for pacing.

Investigators have also attempted to identify possible predictors of third-degree AV block and sudden death in the presence of underlying bifascicular block. Some have suggested that an EP study can assist in identifying patients at risk. If an asymptomatic patient with bifascicular block is found to have a prolonged HV interval ($\geq$100 ms) at an EP study they should be considered for permanent pacing.[7] Other maneuvers that can be performed during an EP study include atrial pacing in asymptomatic patients as a means of identifying patients at increased risk of future high- or third-degree AV block.[8] If atrial pacing induces nonphysiologic infra-His block, this is a IIa indication for implantation of a pacemaker. Indications for permanent pacing are listed below for patients with chronic bifascicular or trifascicular block.

- Class I
  1. Intermittent third-degree AV block.
  2. Type II second-degree AV block.

- Class IIa
  1. Syncope not proved to be due to AV block when other likely causes have been excluded, specifically ventricular tachycardia (VT).
  2. Incidental finding at electrophysiologic study of markedly prolonged HV interval ($\geq$100 ms) in asymptomatic patients.
  3. Incidental finding at electrophysiologic study of pacing-induced infra-His block that is not physiologic.
- Class IIb
  None.
- Class III
  1. Fascicular block without AV block or symptoms.
  2. Fascicular block with first-degree AV block without symptoms.

Hypersensitive carotid sinus syndrome is an infrequent cause of syncope or presyncope. It is due to an exaggerated response to carotid sinus baroreceptor stimulation which is manifested by a cardioinhibitory response, vasodepressor response, or a combination. The cardioinhibitory response results in a decreased heart rate due to sinus bradycardia, atrioventricular block, or asystole. The vasodepressor response results in a drop in blood pressure without a change in heart rate. It is important to determine the relative contribution of these two components of carotid sinus stimulation before concluding that permanent pacing is clinically indicated, because patients with symptoms due entirely to the cardioinhibitory response of carotid sinus stimulation can be effectively treated with permanent pacing.

A significant number of syncopal events are due to a variety of neurally mediated syndromes, the most common being vasovagal syncope. Cardiac pacing can be useful in some patients with vasovagal episodes and orthostatic hypotension.[9–11] The guidelines recommend that neurally mediated syncope with significant bradycardia reproduced by a head-up tilt with or without isoproterenol or other provocative maneuvers is a IIb indication for pacing. However, considerable controversy exists concerning permanent pacing in refractory neurally mediated syncope associated with significant bradycardia or asystole because there is conflicting evidence regarding the efficacy of permanent pacing in neurally mediated syncope. The guidelines for pacing in hypersensitive carotid sinus and neurally mediated syndromes are listed below.

- Class I
  1. Recurrent syncope caused by carotid sinus stimulation; minimal carotid sinus pressure induces ventricular asystole of $>$3 s duration in the absence of any medication that depresses the sinus node or AV conduction.
- Class IIa
  1. Recurrent syncope without clear, provocative events and with a hypersensitive cardioinhibitory response.
  2. Syncope of unexplained origin when major abnormalities of sinus node function or AV conduction are discovered or provoked in electrophysiologic studies.
- Class IIb
  1. Neurally mediated syncope with significant bradycardia reproduced by a head-up tilt with or without isoproterenol or other provocative maneuvers.

- Class III
  1. A hyperactive cardioinhibitory response to carotid sinus stimulation in the absence of symptoms.
  2. A hyperactive cardioinhibitory response to carotid sinus stimulation in the presence of vague symptoms such as dizziness, light-headedness, or both.
  3. Recurrent syncope, light-headedness, or dizziness in the absence of a hyperactive cardioinhibitory response.
  4. Situational vasovagal syncope in which avoidance behavior is effective.

Cardiac resynchronization therapy (CRT) has been demonstrated to improve heart failure symptoms, quality of life, exercise capacity (6-minute walking test, peak oxygen consumption during exercise), hospitalizations, and echocardiographic variables (LV volumes, LV ejection fraction, mitral regurgitation).[12–16] With the addition of a cardiac resynchronization therapy defibrillator (CRT-D) it has been shown to reduce the risk of all-cause mortality by 36%.[17] The MIRACLE trial (Multicenter InSync Randomized Clinical Evaluation) was the first large, controlled, randomized trial to confirm the improvement in quality of life and functional capacity.[18] Based on the available data, CRT is indicated in patients with drug refractory, symptomatic, New York Heart Association (NYHA) functional class III–IV heart failure of either ischemic or non-ischemic origin with a prolonged QRS complex ($>$130 ms), left ventricular end-diastolic diameter $\geq$55 mm, and LVEF $\leq$35%. However in the more recently published CARE-HF (Cardiac Resynchronization Heart Failure) Trial[19] and the trials in the past, benefits have been shown to extend to patients with a QRS of up to 120 ms or more, especially if they have additional markers of mechanical dyssynchrony in the echo cardiogram.

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Section IV

Supraventricular tachyarrhythmia

7
Introduction

Umamahesh Rangasetty, Sergio Thal, Walid Saliba, and Robert Schweikert

Epidemiology • Classification • Clinical presentation • AV nodal re-entrant tachycardia • AV re-entrant tachycardia • Wolff–Parkinson–White syndrome • Sinus nodal re-entrant tachycardia • Inappropriate sinus tachycardia • Atrial tachycardia • Multi-focal atrial tachycardia • Junctional tachycardia • Non-paroxysmal junctional tachycardia • Differentiation between VT and SVT with bundle branch block • Management of PSVT • Management of tachycardia associated with WPW syndrome

Supraventricular tachycardia (SVT) can be defined as any tachycardia requiring the atrium or the atrioventricular (AV) node, either in whole or in part, for its perpetuation. SVT is a very common group of arrhythmias (90%) seen in clinical practice.[1] The QRS complex duration is typically narrow (<120 ms), reflecting conduction over the AV node and His-Purkinje system, but sometimes can have a wide QRS complex due to pre-existent or rate-dependent bundle branch blocks or other aberrant interventricular conduction disturbances. Irregular SVT includes atrial fibrillation, which is the most common sustained arrhythmia encountered in clinical practice. This chapter briefly discusses the ECG diagnosis, clinical presentation, and management excluding atrial flutter and atrial fibrillation (see Chapter 4, sections B & C).

EPIDEMIOLOGY

The frequency of this group of rhythm disorders is about 1–3 per 1000 persons.[2] A population-based study in Wisconsin reported an incidence of 35/100 000 person-years and a prevalence of paroxysmal SVT (PSVT) of 2.25/1000 persons.[3] The prevalence is twice as high in women as compared to men and it increases with age. The incidence of ventricular pre-excitation (Wolff–Parkinson–White ECG pattern) is 0.1–0.3% in the general population.[4] Atrioventricular nodal re-entrant tachycardia (AVNRT) is by far the most common regular re-entrant SVT. AVNRT is more common in patients who are of middle age or older, while adolescents are more likely to have SVT mediated by an accessory pathway. PSVT is most commonly seen in patients without structural heart disease. Supraventricular tachycardias rarely cause sudden cardiac death.[2]

CLASSIFICATION

Supraventricular tachycardias can be classified into two types based on the site of origin or re-entry: (i) atrial tachycardias and (ii) atrioventricular tachycardias. Other classifications based on ECG criteria include the following: (i) regular vs irregular tachycardia; (ii) narrow vs wide QRS complex; (iii) AV node dependent vs AV node independent; (iv) short RP/long PR interval vs long RP/short PR interval tachycardias (Tables 7.1 and 7.2).[4]

CLINICAL PRESENTATION

Symptoms are variable and depend on the presence of underlying heart disease, rate of ventricular response, and the overall condition of the patient. Typical presentation includes palpitations or a sensation that the heart is beating rapidly or fluttering or racing. This may last from a few seconds or minutes to several hours. Occasionally, patients may have shortness of breath or 'air hunger', chest pressure, or pain. Sometimes patients will feel lightheaded or dizzy, and rarely they will feel presyncopal or syncopal.[6] SVT with uncontrolled ventricular rates can cause tachycardia-related cardiomyopathy and present with features of congestive heart failure.

AV NODAL RE-ENTRANT TACHYCARDIA

AVNRT is by far the most common cause of PSVT and accounts for 50–60% of patients who present with rapid, regular, narrow QRS tachycardia.[7,8] Most of the patients with AVNRT are young, healthy females and do not have structural heart disease.[9] Electrocardiographically AVNRT is characterized by regular narrow QRS

Table 7.1 Classification of supraventricular tachycardias

Atrial tachyarrhythmias

(1) Sinus tachycardia
(2) Sinus nodal re-entrant tachycardia (SNRT)
(3) Inappropriate sinus tachycardia (IST)
(4) Atrial tachycardia
(5) Multi focal atrial tachycardia (MAT)
(6) Atrial flutter[5]
    Typical, counterclockwise
    Reverse-typical, clockwise
    Left atrial flutter
    Lesion atrial flutter
    Atypical flutter
(7) Atrial fibrillation

Atrioventricular tachyarrhythmias

(1) AV nodal re-entrant tachycardia (AVNRT)
(2) AV re-entrant tachycardia (AVRT)
(3) Junctional ectopic tachycardia (JET)
(4) Non-paroxysmal junctional tachycardia (NPJT)
(5) Tachycardia associated with WPW syndrome
(6) Permanent junctional reciprocating tachycardia (PJRT)

Table 7.2 Mechanisms and recognition of supraventricular tachycardias

Arrhythmia	Mechanism	ECG features
Sinus tachycardia (ST)	Secondary to other factors such as physiologic response to stressors (e.g. fever, pain, anxiety, exercise, hyperthyroidism)	Similar to normal sinus rhythm, P-waves similar to SR
Inappropriate sinus tachycardia (IST)	Unclear mechanism, may be enhanced automaticity of the sinus node or hypersensitivity to sympathetic tone	Similar to ST, P-waves similar to sinus rhythm (SR), but may have a more inferior axis
Sinus node re-entrant tachycardia (SNRT)	Re-entrant circuit either in or near the sinus node	P-waves similar to SR; abrupt onset and offset
Atrial tachycardia (AT)	Enhanced automacity or re-entry or triggered activity	HR 120–250 bpm; different P-wave morphology
Multifocal AT (MAT)	Originates from multiple atrial foci; often associated with hypoxia and sympathetic stimulation	HR 100–200 bpm; three or more different P-wave morphologies to establish ECG diagnosis
Atrioventricular nodal re-entrant tachycardia (AVNRT)	*Typical*: PAC conducts antegrade over slow pathway (to set up re-entrant circuit); premature ventricular contraction-initiated; initiates the re-entrant circuit in 1/3 of patients with AVNRT *Atypical*: occurs in the opposite direction with antegrade conduction over fast (B) pathway, and retrograde conduction over slow (A) pathway '*Slow-slow*' AVNRT: less common; re-entrant circuit occurs over two slow pathways	HR 150–200 bpm; P-wave within or after the QRS; short RP interval in typical AVNRT; long RP in atypical AVNRT. Typical AVNRT (antegrade conduction via slow pathway); PR $>$ RP; P-wave is usually within or at the terminal portion of the QRS complex. Atypical AVNRT (antegrade conduction via fast pathway, and retrograde conduction via slow pathway); RP $>$ PR
Atrioventricular reciprocating tachycardia (AVRT)	*Orthodromic* AVRT: re-entry circuit is created by impulse which conducts retrograde via accessory pathway, and antegrade via AV node; typical narrow complex tachycardia *Antidromic* AVRT: re-entry circuit created by impulse which conducts retrograde via AV node, and antegrade via accessory pathway; typically a bizarre, wide-complex tachycardia	HR 150–250 bpm; P-wave occurs after QRS complex; narrow QRS complex in orthodromic conduction; wide QRS complex in antidromic conduction. Short PR interval and delta wave may be present if ventricular pre-excitation occurs (as a result of impulse conduction anterograde down the accessory pathway)
Non-paroxysmal junctional tachycardia and junctional ectopic tachycardia (JCT)	Increased automaticity, triggered activity, or both; uncommon in adults	ECG: regular narrow QRS complex, but P-waves may not be visible
Permanent junctional reciprocating tachycardia (PJRT)	Circus movement tachycardia, the impulse transverse antegrade through A-V node and His-Purkinje system and retrograde through accessory pathway with decremental properties	Broad P-waves, negative in inferior leads, RP interval longer than PR interval

tachycardia with heart rates in the range of 150–250 beats per minute (bpm). Usually P-waves are not seen and are buried in the QRS complex due to simultaneous activation of ventricles and atria. At times atrial activity may be seen to distort the terminal part of the QRS complex, producing pseudo S-waves in leads II, III, and aVF, and pseudo R-waves in V1 (Figure 7.1).[4]

Mechanism of AVNRT

Physiologically, the AV nodal tissue may have functionally multiple pathways with different electrophysiologic properties. A slow pathway is located at the low posteroseptal region of the right atria inside the triangle of Koch, which conducts impulses slowly with a short refractory period. A fast pathway is located in the anteroseptum of the right atria, near to the His bundle potential recording that conducts rapidly but with a long refractory period. The presence of these anatomic/functional pathways is the requirement for AVNRT to exist.[1,7,8] An electrophysiologic study usually shows evidence of dual AV nodal pathway physiology in 40% of patients (Figure 7.2).[2] Usually AVNRT is triggered by a premature atrial contraction (PAC), which reaches the AV node when the fast pathway is refractory from the previous sinus impulse. By the time the PAC completes its course in the slow pathway, the fast pathway is fully recovered and is ready to conduct it in a retrograde manner and initiates the tachycardia cycle (Figure 7.1). Since the conduction of the premature atrial beat is anterograde through the slow pathway and retrograde over the fast pathway, the PR interval is longer than the RP interval. In 10% of patients the re-entry circuit is reversed, with

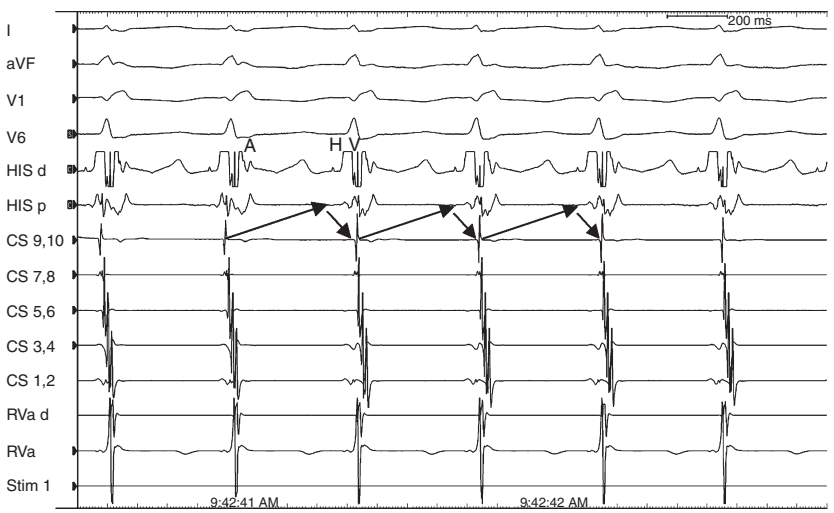
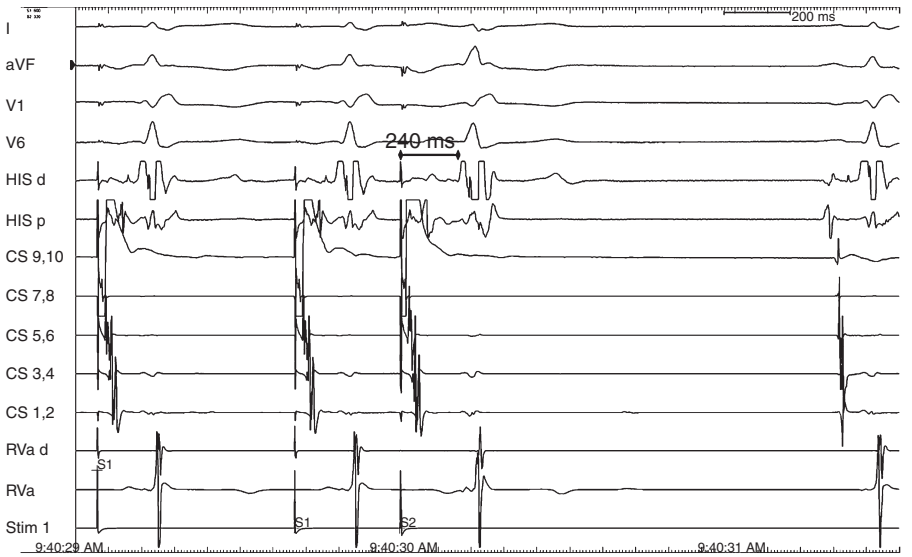
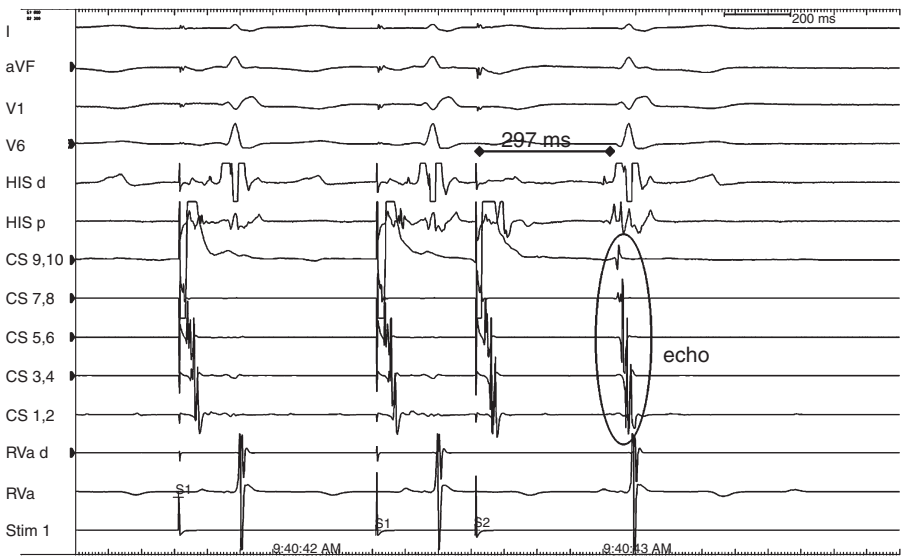


Figure 7.1 Recording of AVNRT during EP study. Note the activation timing of the atria superposed with the ventricle activation. Note also antegrade conduction over the slow pathway (longer arrows) and retrograde conduction over the fast pathway (shorter arrows). From top to bottom: leads I, aVF, V1, and V6 surface ECGs; His d and His p: distal and proximal recordings respectively at the His-bundle; CS: coronary sinus from electrodes 10 to 1 (proximal to distal); RVa d: right ventricular apex distal; RVa: right ventricular apex; Stim I: stimulation channel. A: atrial electrogram; H: His electrogram; V, ventricular electrogram.



(a)



(b)

Figure 7.2 Dual AV node physiology. (a) Pacing proximal CS 600/320; (b) Pacing proximal CS 600/310. Note the increment in AV nodal to His bundle conduction time higher than 50 ms after decreasing 10 ms in the S1S2. The S2 blocked antegrade in the fast pathway and conducted to the AV node through the slow pathway. Also note the presence of a typical echo beat associated with the conduction over the slow pathway. From top to bottom: leads I, aVF, V1, and V6 surface ECGs; His d and His p: distal and proximal recordings respectively at the His-bundle; CS: coronary sinus from electrodes 10 to 1 (proximal to distal); RVa d: right ventricular apex distal; RVa: right ventricular apex; Stim I: stimulation channel.

the anterograde conduction over the fast pathway and retrograde conduction over the slow pathway.[8] Hence the RP interval is longer than the PR interval, also known as atypical AVNRT. Ventricular premature beats typically initiate this type of arrhythmia and P-waves are usually inverted in leads II, III, and aVF.[10]

AV RE-ENTRANT TACHYCARDIA

AV re-entrant tachycardia (AVRT) is the next most common cause of PSVT, accounting for 30% of the cases. AVRT, also known as orthodromic tachycardia, is more common in males and presents at a younger age than patients with AVNRT. AVRT occurs in the presence of an accessory pathway or bypass tract. It could be located on the left side or the right side of the AV junction; the right ones are commonly associated with Ebstein's anomaly.[11] From an anatomopathology point of view, these accessory pathways are extra bundles of conducting tissue that bridge the atria and the ventricles.[1,7,12,13] The arrhythmia could be initiated by a premature atrial beat, which conducts anterograde through the normal AV node–His-Purkinje system and retrograde through an accessory pathway located along the AV junction. If the accessory pathway conducts only retrogradely, it is not seen on the surface electrogram and is therefore said to be concealed. Another way to initiate the tachycardia is with a premature ventricular contraction (PVC) early enough to be blocked retrogradely in the AV node–His-Purkinje system, but able to be retroconducted to the atria through the accessory pathway. By the time the impulse arrives at the atria the AV node has recovered and is able to conduct antegrade the impulse and initiate the tachycardia circuit (Figure 7.3).

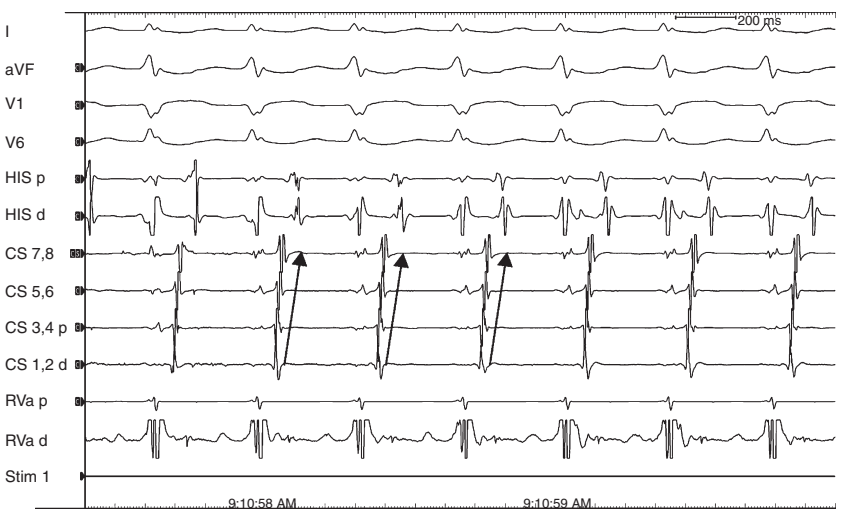


Figure 7.3 AVRT: recording during EP study. Note activation of the atria takes place more than 70 ms after the ventricle and the activation sequence in this case is eccentric earlier in distal coronary sinus recordings due to a left lateral accessory pathway. From top to bottom: leads I, aVF, V1, and V6 surface ECGs; His p and His d: proximal and distal recordings, respectively, at the His-bundle; CS: coronary sinus from electrodes 8 to 1 (proximal to distal); RVa p: right ventricular apex proximal; RVa d: right ventricular apex distal; Stim I: stimulation channel.

WOLFF–PARKINSON–WHITE SYNDROME

Pre-excitation, or the Wolff–Parkinson–White (WPW) syndrome ECG pattern, is characterized by (i) a PR interval less than 120 ms during sinus rhythm; (ii) a QRS complex duration exceeding 120 ms with a slurred, slowly rising onset of the QRS in some leads (delta wave) and usually a normal terminal QRS portion; and (iii) secondary ST-T wave changes that are generally directed in an opposite direction to the major delta wave and QRS vectors. This pattern results from a fusion of activation of the ventricles over both the bypass tract and the AV node–His-Purkinje system. The reported prevalence is 0.1 to 0.3% in the general population.[2] It is twice as common in males as females.[14] The term Wolff–Parkinson–White syndrome is applied to patients with both pre-excitation on the ECG and paroxysmal tachycardias. Ebstein's anomaly is the most common congenital anomaly associated with WPW syndrome and often consists of multiple bypass tracts.

The most common manifestation of WPW syndrome is PSVT with conduction similar to AVRT. Rarely (10%), the conduction may exhibit a reverse pattern with anterograde conduction through the bypass tract and retrograde conduction through the normal AV system.[15,16] This produces a tachycardia with a wide QRS complex, in which the ventricles are totally activated by the bypass tract, and is referred to as antidromic tachycardia. Antidromic tachycardia is more common among patients with multiple accessory pathways.[16] Atrial flutter and atrial fibrillation (AF) also may occur more commonly in patients with WPW syndrome. The development of AF in these patients is thought to be most commonly due to degeneration of an AVRT. Since the bypass tract does not have generally the same decremental conducting properties as the AV node, the ventricular responses during atrial flutter or fibrillation may be quite rapid and, in rare circumstances, may cause VF. Syncope or sudden cardiac death may occur by this mechanism.[17,18] Surface ECG may provide clues to the localization of accessory pathways and direct mapping. The approach described by Arruda et al appears to be more precise[19] (Figure 7.4).

SINUS NODAL RE-ENTRANT TACHYCARDIA

Sinus nodal re-entrant tachycardia (SNRT) is due to a re-entry circuit, either in or near the sinus node. Therefore, it has an abrupt onset and offset. The heart rate is usually 100–150 bpm. Electrocardiographically, the P-waves are identical or very similar to the sinus P-wave and the RP interval is long, with a shorter PR interval.[13,20,21] AV block can occur without affecting the tachycardia, and vagal maneuvers can slow and then abruptly terminate the tachycardia. Electrophysiologically, the tachycardia can be initiated and terminated by premature atrial and, uncommonly, premature ventricular stimulation. Initiation of sinus nodal re-entry does not depend on a critical degree of intra-atrial or AV nodal conduction delay, and the atrial activation sequence is the same as during sinus rhythm. Sinus nodal re-entry accounts for 5–10% of re-entrant SVTs. Drugs such as beta-blockers, calcium-channel blockers, and digitalis may be effective in terminating and preventing recurrences of sinus node re-entrant tachycardia. Catheter ablation is highly effective in treating this arrhythmia and has a low risk to produce sinus node dysfunction.[22]

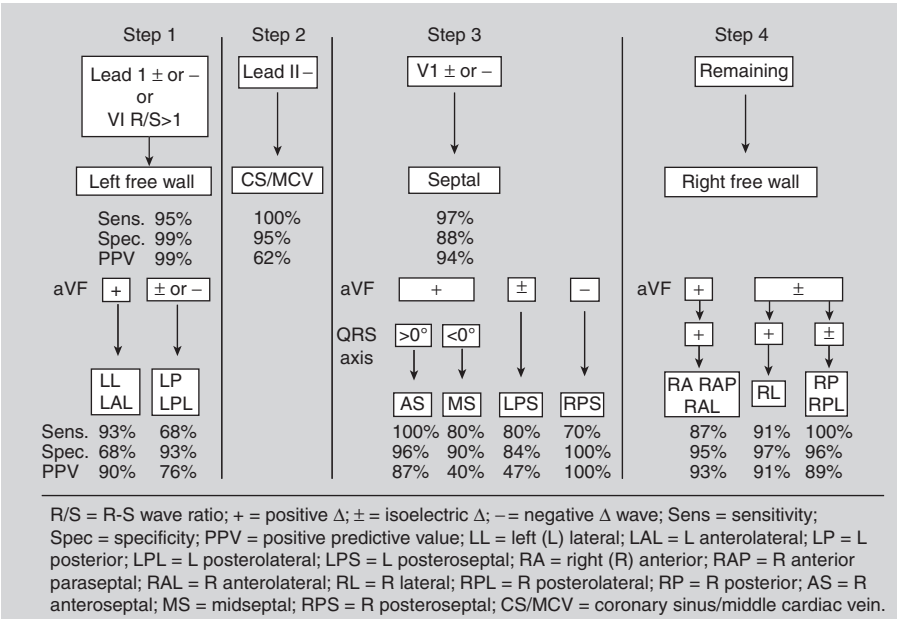


Figure 7.4 Algorithm to localize accessory pathway in pre-excitation syndrome.[19]

INAPPROPRIATE SINUS TACHYCARDIA

Inappropriate sinus tachycardia (IST) is an accelerated baseline sinus rate in the absence of secondary causes such as physiologic stressors or metabolic derangements. It has been described in otherwise healthy persons (especially women), possibly secondary to increased automaticity of the sinus node or an automatic atrial focus located near the sinus node.[13,20,21] Patients often have an exaggerated heart rate response to minimal exercise. This abnormality can result from a defect in either sympathetic or vagal nerve control of sinoatrial (SA) automaticity, or an abnormality of the intrinsic heart rate. IST behavior is generally incessant with gradual onset/offset, but can also be paroxysmal less commonly.

ATRIAL TACHYCARDIA

Atrial tachycardia (AT) is an uncommon arrhythmia in the adult population (0.34% and 0.46% of asymptomatic and symptomatic patients, respectively)[23] and includes several types of differing mechanisms generally related to different atrial anatomic structures. The mechanisms involved include abnormal automaticity, triggered activity, and re-entry.[24] In 2001, a consensus of experts from the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (NASPE, now Heart Rhythm Society) established a classification for atrial tachycardias based on the mechanism and anatomy.[25] Electrocardiographically, AT is characterized by an atrial rate of 150 to 200 bpm with P-wave morphology different from that of the sinus P-wave. At onset, there

may be some 'warming up' of the rate, resulting in a slight increase in heart rate over the initial several complexes. Characteristic isoelectric intervals between P-waves, in contrast to atrial flutter, are usually present in all leads. AV block can be present without affecting the tachycardia cycle. When tachycardias arise in the right atrium they are usually associated with a P-wave that is inverted in lead aVR and upright in leads aVL and I. Tachycardias arising in the left atrium usually manifest a P-wave that is inverted in leads I and aVL and that has an upright deflection in lead aVR[4] (Figure 7.5).

Automatic atrial tachycardia

This is usually due to an ectopic focus present around the crista terminalis in the right atrium or around the base of pulmonary veins in the posterior left atria. A typical ECG finding, apart from the usual atrial tachycardia, is the rate accelerating after its initiation (warm-up phenomenon). It is seen more often in younger patients, does not respond to vagal maneuvers, and is more likely to be incessant.[26] Intra-atrial re-entry is usually seen in patients with structural heart disease and who also have atrial arrhythmias (flutter or fibrillation). *Triggered atrial tachycardia* is the least common variety, more likely seen in older individuals secondary to digitalis toxicity or sympathetic discharge. The ECG in such cases typically shows 2:1, 3:1, or variable AV conduction, so called paroxysmal atrial tachycardia with block (PAT).[27]

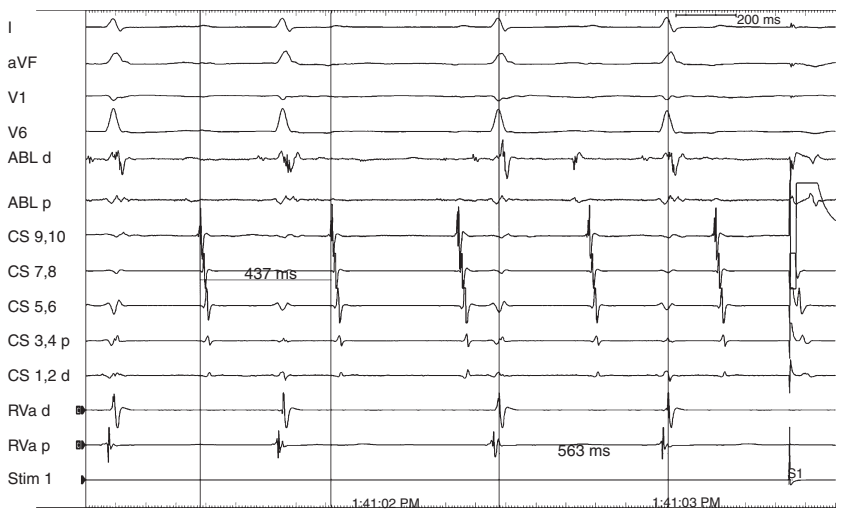


Figure 7.5 Atrial tachycardia recording during EP study of atrial tachycardia. Note atrial cycling faster than ventricular cycling with near 2:1 ventricular response. From top to bottom: leads I, aVF, V1, and V6 surface ECGs; ABL d and ABL p: distal and proximal recordings, respectively, at the ablation catheter; CS: coronary sinus from electrodes 10 to 1 (proximal to distal); RVa d: right ventricular apex distal; RVa p: right ventricular apex proximal; Stim I: stimulation channel.

MULTI-FOCAL ATRIAL TACHYCARDIA

Multi-focal atrial tachycardia (MAT) is a rare arrhythmia characterized electrocardiographically by P-waves of at least three different morphologies and variable PR and RR intervals. The ventricular rhythm is irregular, with rates ranging from 100 to 200 bpm, and may be confused with AF. In addition, the finding of discrete P-waves and isoelectric periods between adjacent P-waves helps to distinguish this arrhythmia from atrial fibrillation. The typical patient with MAT has a chronic obstructive airway disease with exacerbations and hypoxemia. The electrophysiologic mechanism underlying the arrhythmia is an enhanced automatism triggered by several pathologic conditions. The most frequent causes are hypoxia, high catecholamine levels, or drug toxicity. The arrhythmia carries a poor prognosis due to severe pulmonary or heart disease (45–50% death rate). It is generally fairly resistant to any anti-arrhythmic therapy and in some cases high doses of calcium-channel blockers may be effective, but medical treatment is in general quite challenging or impossible unless directed toward the underlying condition.[4]

JUNCTIONAL TACHYCARDIA

Junctional tachycardia (JT) is a narrow QRS complex tachycardia with a regular rate, usually between 60 and 140 bpm. The distinguishing feature of this ECG is retrograde conduction of the atrium causing an inverted P-wave, best observed in leads II, III, and aVF. P-waves may not always be seen and intermittent AV dissociation may also be present.

Junctional ectopic tachycardia (JET), also known as automatic AV junctional tachycardia, primarily manifests in two forms: idiopathic chronic junctional ectopic tachycardia, observed in the setting of a structurally normal heart, and a transient postoperative junctional ectopic tachycardia that occurs following repair of congenital heart disease. The onset of congenital JET is often insidious. Prolonged moderate tachycardia may not be recognized until myocardial dysfunction and signs of congestive heart failure ensue.[14] Heart rate variability is decreased; also the heart rate is very regular except for occasional sinus capture beats. Postoperative JET usually begins 6–72 hours following cardiopulmonary bypass surgery for repair of congenital heart lesions. It is usually identified during monitoring in the intensive care unit and usually leads to a fall in blood pressure and cardiac output. This arrhythmia is not commonly seen in the adult patient population.

The mechanism of JET is not clear. It may be due to automaticity or triggered activity. Postmortem studies in congenital JET have shown an abnormal location of the normal AV node or an accessory AV node and His bundle within the central fibrous body or surrounding it, as the anatomic substrate for the arrhythmia. Histamine, eosinophil cation protein, or other products of mast cell, eosinophil, or basophil degranulation that are liberated in response to cardiopulmonary bypass have been implicated in the genesis of transient postoperative JET. The relative levels of various cytokines may also play a role. Low magnesium levels have been noted in children who develop JET following cardiopulmonary bypass surgery. The ECG typically demonstrates a rate of 130 to 200 bpm and mimics AVRT. The presence of AV dissociation and irregular QRS differentiates this rhythm from AVRT. Congenital JET has been managed with oral propafenone. Other therapies are anecodotal and exceed the goal of this chapter.

NON-PAROXYSMAL JUNCTIONAL TACHYCARDIA

Non-paroxysmal junctional tachycardia (NPJT) is a junctional tachycardia that occurs primarily in the setting of digitalis toxicity. The ECG shows a narrow QRS complex and the ventricular rate is between 70 and 130 bpm. Intermittent AV dissociation is frequently present. When the rate is less than 100 bpm, the term accelerated junctional rhythm is applied. The postulated underlying mechanisms are enhanced automaticity or triggered activity.[28] Other causes of NPJT include structural heart disease such as inferior myocardial infarction, myocarditis as a result of rheumatic fever, or after surgery for aortic or mitral valve disease.[29,30] The tachycardia is usually managed by treating the underlying disease or correction of electrolyte abnormalities and withdrawal of digitalis. Anti-arrhythmics and shocks are usually ineffective. Catheter ablation has been used in selected cases.[4]

Differentiating SVT with aberrancy from that of VT

Although SVTs are typically narrow QRS tachycardias, at times they may be wide and mimic VT. It is very important to differentiate wide QRS tachycardia with an SV origin from that of VT as it carries different treatment and prognosis. Wide QRS in a setting of SVT may be due to one of the following: (i) pre-existing bundle branch block; (ii) functional bundle branch block (tachycardia-dependent); (iii) ventricular pre-excitation; and (iv) aberrancy due to sodium channel-blocking anti-arrhythmic drugs.[31]

Clinical features

Age can be a useful factor in determining the origin of a broad complex tachycardia: a tachycardia in patients aged over 35 years is more likely to be ventricular in origin. A history that includes coronary artery disease (CAD) or congestive heart failure (CHF) associated with wide complex tachycardia is highly predictive of ventricular tachycardia. The availability of previous ECGs (pre-existing conduction disturbances) for comparison and the knowledge of the current medical therapy can also be helpful. Symptoms associated with the tachycardia are less useful as they depend on the hemodynamic consequences of the arrhythmia – that is, they relate to the heart rate and the underlying cardiac reserve rather than to the origin of the arrhythmia. Presence of cannon 'a' waves in the jugular venous pulse or variable intensity of the first heart sound indicates a diagnosis of ventricular tachycardia. Slowing or termination of the tachycardia by a vagal maneuver may indicate its supraventricular origin.[32,33]

ECG differentiation

The presence of independent P-wave activity or AV dissociation is highly suggestive of ventricular tachycardia, as is the presence of fusion or capture beats. Other features that may suggest VT include QRS duration $>$140 ms, concordance of QRS or absence of RS complexes in precordial leads, and a Q-peak S interval $>$100 ms.[34]

However, these ECG criteria are not helpful in cases of SVT with aberrant ventricular conduction due to class IA or IC drugs, or in the presence of pre-excited tachycardias. Whenever a diagnostic doubt exists, the arrhythmia has to

be considered and treated as ventricular tachycardia.[35] Drugs such as verapamil or diltiazem must be avoided because, by depressing contractility and lowering blood pressure, they might worsen the clinical status. A bolus of adenosine, an ultra-short acting agent that profoundly depresses AV node conduction, has been proposed as a first-line drug for the differential diagnosis in these cases.

DIFFERENTIATION BETWEEN VT AND SVT WITH BUNDLE BRANCH BLOCK[4]

If the tachycardia has right bundle branch block morphology (a predominantly positive QRS complex in lead V1), a ventricular origin is suggested if there is:

- QRS complex with duration >0.14 s.
- Axis deviation.
- A QS-wave or predominantly negative complex in lead V6.
- Concordance throughout the chest leads, with all deflections positive.
- A single (R) or biphasic (QR or RS) R-wave in lead V1.
- A triphasic R-wave in lead V1, with the initial R-wave taller than the secondary R-wave and an S-wave that passes through the isoelectric line.

If the tachycardia has left bundle branch block morphology (a predominantly negative deflection in lead V1), a ventricular origin is suggested if there is:

- Axis deviation.
- QRS complexes with duration >0.16 s.
- A QS or predominantly negative deflection in lead V6.
- Concordance throughout the chest leads, with all deflections negative.
- An RS complex in lead V1.

MANAGEMENT OF PSVT

AVNRT and AVRT are both re-entrant tachycardias that involve and depend on the AV node to occur. They account for most of the cases of PSVT. Hence, interruption of the AV node by drugs or maneuvers is the mainstay of therapy in hemodynamically stable patients. Synchronized cardioversion starting at 50 J should be used immediately in patients who are hypotensive, have pulmonary edema, have chest pain with ischemia, or are otherwise unstable. Vagal maneuver, particularly carotid sinus massage (Table 7.3), is quite useful in the termination of the tachycardias and as a tool for differential diagnoses. Carotid sinus massage is usually reserved for young patients due to the risk of stroke from emboli, hence carotid bruits should be ruled out before attempting this maneuver.[36]

When maneuvers fail, intravenous adenosine should be tried first.[37,38] Adenosine, an endogenous nucleoside, has negative chronotropic, dromotropic, and inotropic actions of very short duration (half-life 10 s), with minimal hemodynamic consequences. It transiently blocks the AVN conduction and sinus node automacity. Adenosine should terminate >90% of AVNRT and AVRT. It is also effective for sinus re-entry and less common in automatic atrial tachycardia originating near the crista terminalis. Because of its short duration of action, it

Table 7.3 Vagal stimulation maneuvers

Maneuver	Technique	Disadvantages
Valsalva	Forced expiration with closed glottis	Needs patient cooperation
Müeller	Forced inspiration with closed glottis	Needs patient cooperation
Carotid sinus message	Pressure over the carotid artery at the level of angle of the mandible	Risk of stroke in the presence of carotid artery stenosis
Diving reflex	Ice bag on the face	Low efficacy, first choice in children
Eye globe pressure	Bilateral	Risk of retinal detachment

can also be used to differentiate SVT from VT. Typical adverse effects of adenosine include flushing, chest pain and dizziness. These effects are temporary because of its very short half life.[39] Beta-blockers and calcium-channel blockers may also be used to slow or terminate the tachycardia, but are agents of second choice. Digitalis glycosides have a slower onset of action and should not be used for acute therapy.[1,39,40]

When these drugs fail to terminate the tachycardia, or when the tachycardia is recurrent, atrial or ventricular pacing via a temporary pacemaker inserted pervenously may be used to terminate the arrhythmia. Sinus node re-entry is managed in a similar way to that of AVNRT or AVRT. Automatic atrial tachycardia is difficult to manage with pharmacotherapy. Precipitants should be treated or eliminated whenever possible.

Management of atrial tachycardia is directed primarily towards the underlying disease, withdrawal of digitalis, and correction of the underlying electrolyte abnormalities. Anti-arrhythmics are usually ineffective in this type of arrhythmia. The use of beta-blockers is preferred when they are hemodynamically tolerated. Catheter ablation is the treatment of choice when it is more frequent or incessant.[41]

Acute management of intra-atrial re-entry is similar to atrial fibrillation in the absence of an accessory pathway. Following acute therapy, subsequent management should be individualized based on the type of arrhythmia, frequency and duration, and the presence or absence of structural heart disease. Patients in whom drug treatment is considered may initially be treated with calcium-channel blockers, digoxin, and/or beta-blockers because the risk–benefit ratio associated with these agents is more favorable than that of IA or IC agents.[1,4]

Treatment of IST includes beta-blockers, calcium-channel blockers, or digitalis, alone or in combination. In severe cases, sinus node radiofrequency modification or surgical ablation may be indicated.[22]

MANAGEMENT OF TACHYCARDIA ASSOCIATED WITH WPW SYNDROME

Management of tachycardia associated with WPW syndrome is similar to AVNRT or AVRT without WPW, with the following exceptions. Verapamil should not be given IV as it may block conduction in the AV node and enhance conduction through the accessory pathway, and result in ventricular fibrillation.

Similarly, IV digoxin is also contraindicated. When patients present with wide complex tachycardia due to anterograde conduction through the accessory pathway, agents like procainamide that selectively depress accessory pathway should be considered.[1,14]

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8
Atrial flutter

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Risk factors • Clinical presentation • Diagnosis of AFL • Re-entrant mechanism of AFL • Tools for diagnosing atrial flutter • Nomenclature

There are 200 000 new cases of atrial flutter (AFL) in the United States each year. Of these, 88 000 present solely as AFL.[1,2] The number of AFL cases rises exponentially in relationship to advancing age. Atrial fibrillation (AF) has a 10 times greater prevalence than AFL.[2] It has been reported that over a year's follow-up, 56% of patients presenting with typical AFL develop AF.[3] AFL is associated with an increased risk of morbidity. However, not as profoundly as when it is coupled with AF.[4]

RISK FACTORS

See Table 8.1.

CLINICAL PRESENTATION

AFL, an organized macroreentrant arrhythmia, often presents as paroxysmal, short episodes ranging from seconds to hours; however, it can also present as sustained and persistent.[5] The atria usually contract at a rate of 250–350 beats per minute (bpm) while in AFL.[6] The ventricular rate is generally a 2:1 ratio. A 1:1 ratio can be seen in cases where the atrial rate is relatively slower or when atrioventricular (AV) nodal conduction is enhanced due to increased sympathetic tone or anticholinergic medications.[7]

Acutely, patients often complain of shortness of breath, palpitations, diaphoresis, chest discomfort, dizziness, and weakness. Patients may also complain of polyuria, which occurs as a result of increased atrial pressure from rapidly contracting atria against a closed AV valve, and the subsequent release of atrial natriuretic factor (ANF). AFL may also present more subtly in the form of exercise-induced fatigue, worsening heart failure, or pulmonary disease. Patients tend to be more symptomatic when the ventricular response rate is rapid and/or when they present with episodes of both AF and AFL. AFL can coexist with AF in 25% of patients with AF. On physical examination, the peripheral pulse is generally rapid

Table 8.1 Risk factors for atrial flutter

Independent risk factors
- Advanced age
- Male gender
- Congestive heart failure
- Chronic pulmonary disease
- Prior CVA
- Myocardial infarction

Conditions associated with AFL
- Thyrotoxicosis
- Valvular heart disease (rheumatic, mitral, tricuspid)
- Pericardial disease
- Congenital heart disease
- After open heart surgery
- After major cardiac surgery (primarily in cases of congenital heart defect repair)
- Possible genetic predisposition
- Alcohol intoxication
- Pulmonary embolus
- Hypertrophic cardiomyopathy
- Cardiac tumors
- Secondarily to Na channel blocking agents to treat AF (5%)

Adapted from Lee et al.[5]

and regular (less often irregular); cannon 'a' waves may be observed, and S_1 is of variable intensity.[8]

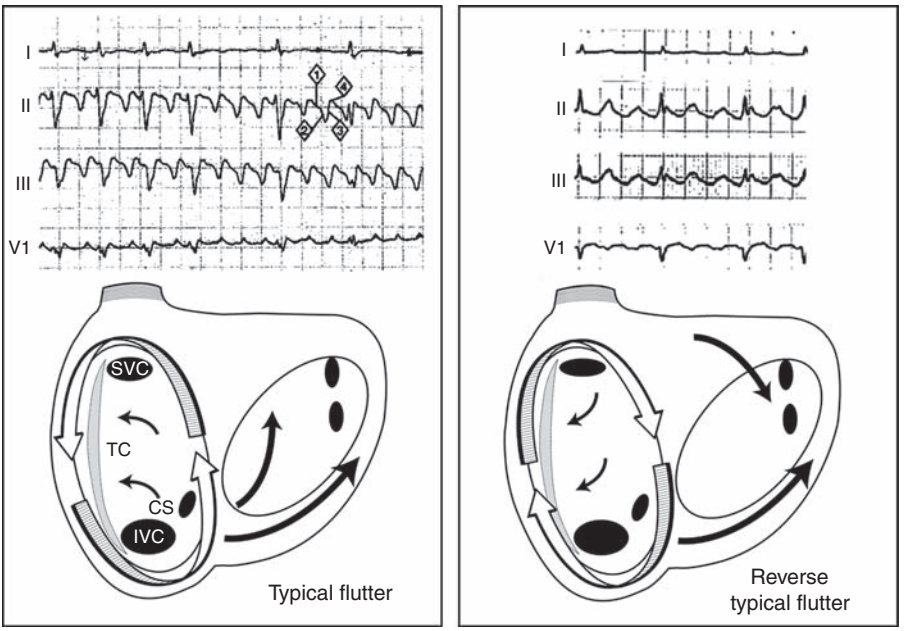
DIAGNOSIS OF AFL

Generally, the diagnosis of AFL can be made on a 12-lead surface ECG by identifying flutter waves in leads II, III, aVF, and V1. When it is difficult to distinguish flutter waves, AV nodal blockers (e.g. adenosine or diltiazem) remove QRS complexes. Vagal maneuvers (Valsalva or gentle carotid sinus message) can also assist in slowing the heart rate down enough to distinguish flutter waves. Flutter waves resemble the edge of a wood saw, hence the name 'saw-tooth' wave. In 'typical' flutter the saw-tooth waves are negative in the inferior leads and positive in V1. The negative waves can be described in succession: (i) a slowly descending segment, (ii) a rapid negative deflection, (iii) a sharp upstroke, that (iv) with a slight overshoot leads to the slowly descending segment of the next cycle (Figures 8.1 and 8.2).[9]

RE-ENTRANT MECHANISM OF AFL

In a primary sense, re-entry occurs as a repetitive excitation of an area of the heart and transmission of that impulse around a conduction or functional barrier. In order for re-entry to initiate, propagate, and perpetuate certain criteria must be present:

1. Initiation of the tachycardia circuit requires unidirectional block in one limb of the circuit. A unidirectional block can occur as an acceleration of the heart rate or a blocked premature beat that affects the refractory time of the circuit.



(a) (b)

Figure 8.1 (a) 12-lead ECG of counterclockwise (CCW) atrial flutter (AFL) below which is a schematic drawing of the flutter circulating within the atrium. Note that in leads II, III, and aVF negative flutter waves and in V1 positive flutter waves are present. Negative flutter waves can be described as: (i) a slowly descending segment (ii) a rapid negative deflection (iii) a sharp upstroke, that (iv) with a slight overshoot leads to the slowly descending segment of the next cycle. (b) A 12-lead ECG of clockwise (CW) AFL. Note that in leads II, III, and aVF positive flutter waves and in V1 negative flutter waves are present. Figure adapted from Cosio et al.[9]

2. A zone of slowed conduction is required for both initiation and perpetuation (Figure 8.3).[6,9]

Atrial flutters circus around an unexcitable anatomic or functional barrier. In 1940 Rosenbleuth[10] demonstrated that creating a crushing lesion on the posterior wall of the right atrium extending from the IVC to the SVC provided an obstacle which could support atrial flutter. The wavefront was demonstrated to circulate in a clockwise direction up the septum, around the roof down the free lateral wall and bounded anteriorly by the tricuspid orifice. Rosenbleuth further demonstrated that the circulating wavefront could be extinguished by creating a lesion between the IVC and the inferior edge of the tricuspid orifice, thus providing the first stepping stones which would later give insight into how to successfully ablate atrial flutters.[9,11]

Re-entrant circuits include normal anatomic boundaries such as the tricuspid ring, mitral ring, and orifices of the superior vena cava (SVC), inferior vena cava (IVC), pulmonary veins, and the coronary sinus (CS). Functional barriers are created due to an inability to conduct action potentials as rapidly as that seen in AFL. In 1980, Spach[12] suggested that the right atrium is able to support re-entry due to anisotropic conduction. The crista terminalis (CT) is a thick bundle of

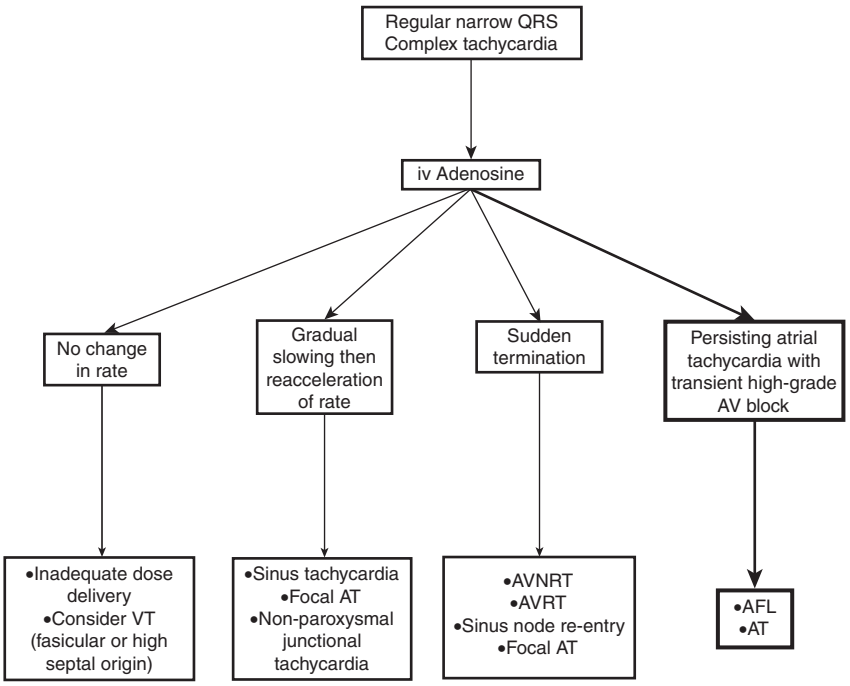


Figure 8.2 The response that a narrow complex tachycardia has to adenosine can assist in the identification of the rhythm. Adapted from Blomstrom-Lundqvist C and Scheinman M.[6]

myocardial fibers that run in a superior/inferior direction, extending from the roof of the right atrium adjacent to the SVC opening laterally and inferiorly to the IVC. This band of tissue is able to conduct rapidly in the longitudinal direction but very slowly in the transverse direction. The conduction ratio is 10:1. This remarkable difference in conduction is due to the non-homogeneous distribution of gap junctions. The longitudinal spindle-shaped cells have ten times as many gap junctions in an end-to-end direction for conduction compared to the transverse ones in a side-to-side direction. This property allows for a functional barrier. The openings of the IVC and the SVC linked by the CT constitute the posterior obstacle, the tricuspid orifice (TR) constitutes the anterior obstacle; this creates a ring that is able to support re-entry in either a clockwise or counterclockwise direction.[9,10]

TOOLS FOR DIAGNOSING ATRIAL FLUTTER

A multi-polar reference catheter that covers the septal and anterior walls allows recording of almost the entire circuit (Figure 8.4). An electrogram of the IVC–TR isthmus, recorded with a mapping/ablation catheter, will provide information on the remaining circuit. When a characteristic ECG pattern is identified and the endocardial activation map is 'circular' a diagnosis can be made without pacing studies. However, it is routine to test local return cycles after a couple of pacing runs to verify isthmus involvement. This practice should not be ignored in patients with multiple different ECG patterns recorded or in those with any

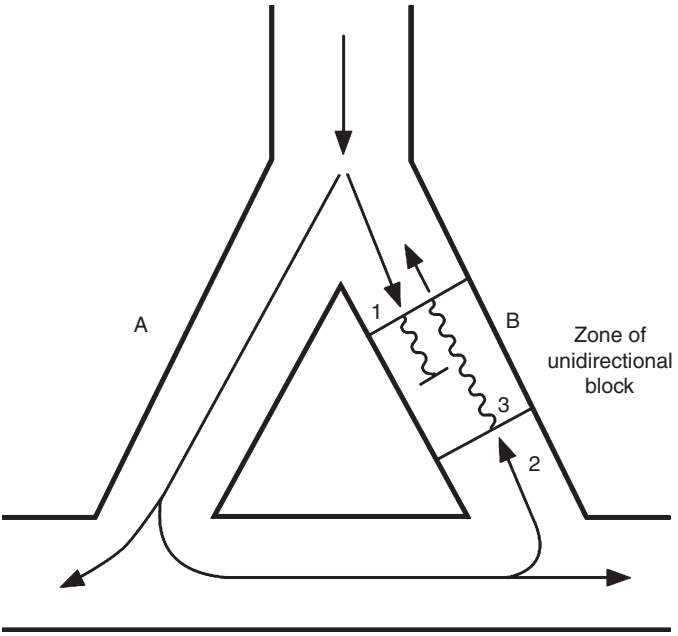


Figure 8.3 Classic re-entrant circuits with the three factors required for re-entry: an anatomic obstacle, a zone of slow conduction, and a unidirectional block. Limbs A and B are independent units that are formed by the anatomic obstacle and are capable of electrical conduction. Because the two pathways have different electrophysiologic properties (e.g., a refractory period longer in one pathway than the other), the impulse (1) is blocked in one pathway (B) and (2) propagates slowly in the adjacent pathway (A). If conduction in this alternative route is sufficiently depressed, especially when a premature impulse occurs, the slowly propagating impulse excites tissue beyond the blocked pathway and returns in a reversed direction along the pathway initially blocked to (3) zone of unidirectional block. Figure reproduced with the permission of Topol EJ (ed.), Textbook of Cardiovascular Medicine, 2nd edn. Philadelphia, PA: Lippincott, Williams and Wilkins, 2002.[33]

history of cardiac surgery or structural damage. The length of the pacing cycle should be similar to that of the cycle length of the atrial flutter thus not to disturb the arrhythmia. This is especially true if there are multiple circuits as in those cases of scar-dependent macro-re-entry. In the face of this activation sequence it is not necessary to show the presence of double potentials on the posterior or posterior lateral RA.[9]

NOMENCLATURE

In the past, there has been some confusion about how to describe the different types of AFL. Recently, Scheinman and his colleagues have provided a classification system based on the location and mechanism of AFL (Figure 8.5, Table 8.2).[5,6]

Right atrial cavotriscuspid-isthmus-dependent flutter

Counterclockwise (CCW) atrial flutter

This represents 90% of clinical AFL cases.[13] ECG findings include negative saw-tooth waves in the inferior leads and positive waves in V1 that transition to

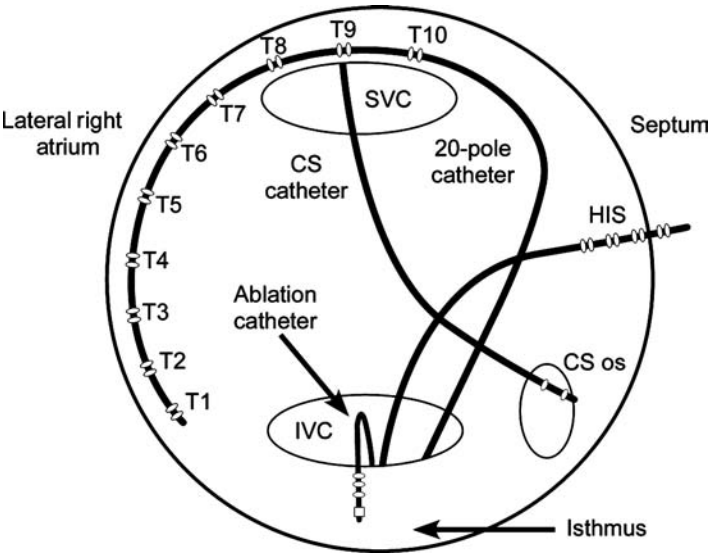


Figure 8.4 A diagram of a 20-pole 'halo' catheter in the right atrium which is used to analyze the activation sequence during the tachycardia. IVC, inferior vena cava; SVC, superior vena cava; CS, coronary sinus; os, ostium; HIS, His bundle region. Figure reproduced with the permission of Lee et al.[5]

negative in V6 (Figure 8.1). The wavefront of the CCW–AFL circuit propagates up the posterior and septal wall of the right atrial (RA) and down the RA anterior and lateral walls when viewed from left atrial oblique (LAO) perspective. This wavefront perpetuates in a circular CCW direction until it is interrupted (Figure 8.6). Anatomically, the circuit is anteriorly bound by the tricuspid orifice, and posteriorly bound by the vena cava orifices, Eustachian ridge, and the coronary sinus (cs).[14–18]

Clockwise (CW) atrial flutter

This represents 10% of clinical AFL cases. ECG findings include positive saw-tooth waves in the inferior leads and negative waves in V1. The wavefront of the CW-AFL circuit propagates down the posterior and septal wall of the RA and up the RA anterior and lateral walls when viewed from the LAO perspective. This wavefront propagates in a circular CW direction until it is interrupted (Figure 8.7). The CW–AFL circuit has the same anatomic boundaries as CCW–AFL.[5]

Double-wave re-entry (DWR)

DWR flutter occurs when a carefully timed stimulus is delivered to the isthmus between the tricuspid annulus and the Eustachian ridge, resulting in a unidirectional antidromic block of the paced impulse and acceleration of the CCW–AFL. The acceleration of the tachycardia is due to two successive activation fronts traveling in the same direction in the re-entrant circuit. DWR flutter is not sustained. Termination of DWR AFL results in complex atrial arrhythmias which include AF.[5,19,20]

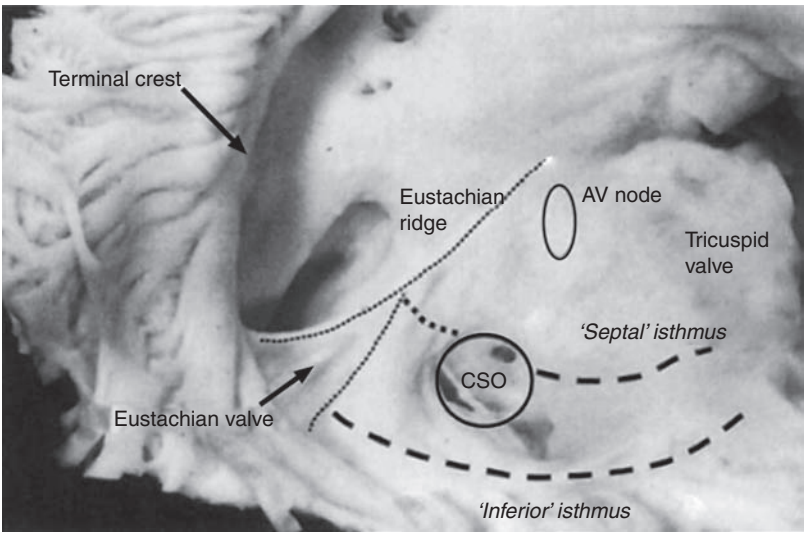


Figure 8.5 Photograph of the key anatomic structures involved in cavotricuspid isthmus-dependent AFLs. Figure reproduced with the permission of Lee et al.[5]

Table 8.2 Classification of atrial flutter

Right atrial CTI-dependent flutter
- Counterclockwise flutter
- Clockwise flutter
- Double-wave re-entry
- Lower loop re-entry
- Intra-isthmus re-entry

Right atrial non-CTI-dependent flutter
- Scar-related flutter
- Upper loop flutter

Left atrial flutter
- Mitral annular flutter
- Scar and pulmonary vein related flutter
- Coronary sinus flutter
- Left septal flutter

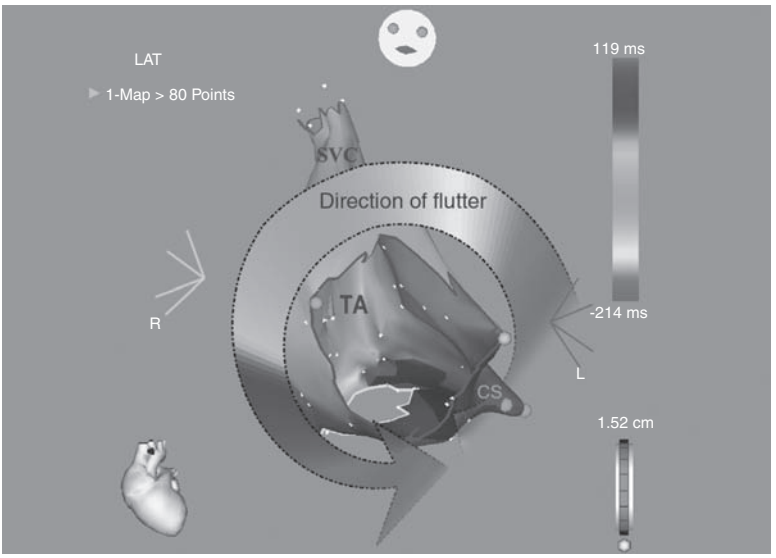
Adapted from Lee et al.[5]
CTI: cavotricuspid isthmus.

Lower loop re-entry

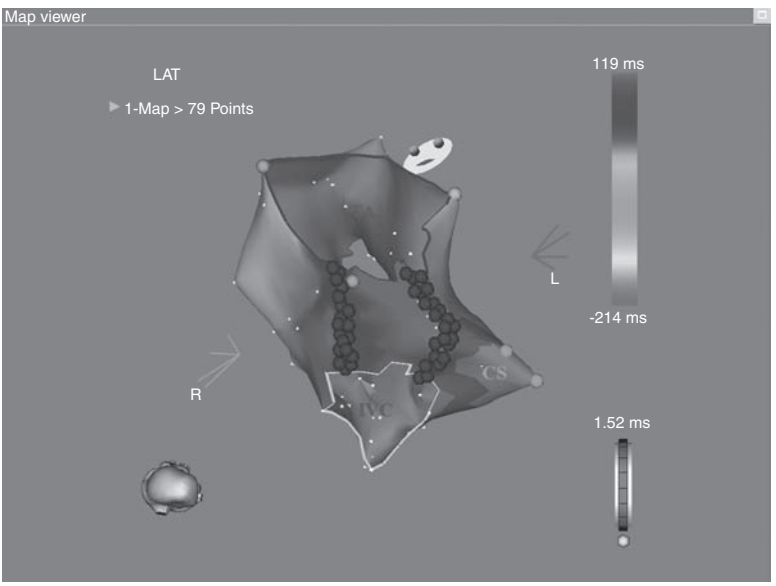
Lower loop re-entry AFL propagates around the IVC in either a CW or CCW direction or around the IVC and tricuspid annulus in a figure of 8 double-loop configuration (Figure 8.7).[5,21,22]

Intra-isthmus re-entry

The intra-isthmus re-entry AFL circuit is localized to the CTI. The circuit is bound medial CTI and the coronary sinus ostium the lateral CTI is not involved.



(a)



(b)

Figure 8.6 Electroanatomic activation map of the right atrium during flutter. (a) In the AP view, the activation wave is seen propagating up the septum and down the lateral wall, where 'early meets late' at the inferior wall (CCW direction). (b) Inferior view of the right atrium showing the CT isthmus. Two ablation lines are designed to encompass the broad CTI; line A joins the Tricuspid annulus to the CS os and further down to the IVC (septal isthmus), while line B joins the lateral tricuspid annulus to the IVC (lateral annulus). (See color plate section.)

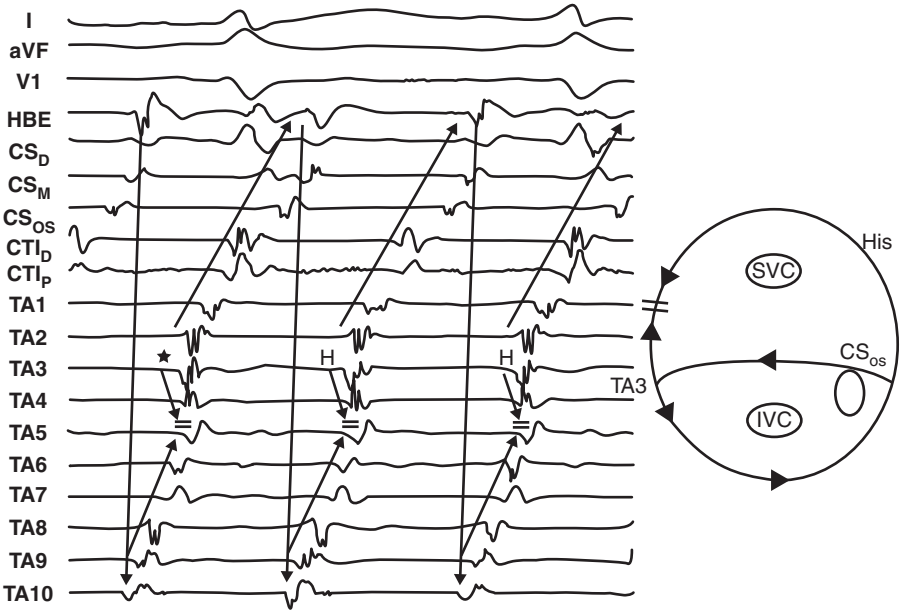


Figure 8.7 Lower loop re-entry. The left panel shows simultaneous recordings of a surface ECG (I, aVF, and V1), and intracardiac electrogram recorded from the His bundle region (HBE), the ostium of coronary sinus (CS_{OS}), and the middle and distal of the coronary sinus (CS_M and CS_D) during lower loop re-entry. Note the early breakthrough at the low lateral tricuspid annulus (TA3) (marked by an asterisk) and wavefront collision at the high lateral annulus (TA5). The right panel is an illustration of lower loop re-entry. Note that the activation pattern circles the IVC rather than the tricuspid annulus, but still uses the CTI. The arrow denotes a CCW direction of activation around the IVC. His, HIS; SVC, superior vena cava; IVC, inferior vena cava; CS_{OS}, coronary sinus os; TA3, low lateral tricuspid annulus. Published with permission of Leo et al

Fractionated or double potentials can be recorded at the CTI just outside the coronary sinus ostium and the circuit can be entrained.[5,23,24]

Right atrial non-cavotricuspid-isthmus-dependent flutter

Scar-related atrial flutter

Macro-re-entrant circuits can occur at sites other than the CTI. Areas that have low voltage provide an anatomic obstacle for macro-re-entry. Surgical repair of congenital heart defects may cause a right atrial scar, resulting in regions of low voltage. Scar tissue located within the posteriolateral and inferiolateral right atrium, and in regions of low conduction within the scar located in the free right atrial wall can all create and support re-entrant circuits.[5,25–27]

Upper loop re-entry

Upper loop re-entry circuits are due to functional obstacles rather than anatomic obstacles. Upper loop re-entry circuits are localized to the upper portion of the right atrium with the crista terminalis and its slowed conduction serving as the functional obstacle. Maintenance of the conduction gap is vital for the perpetuation

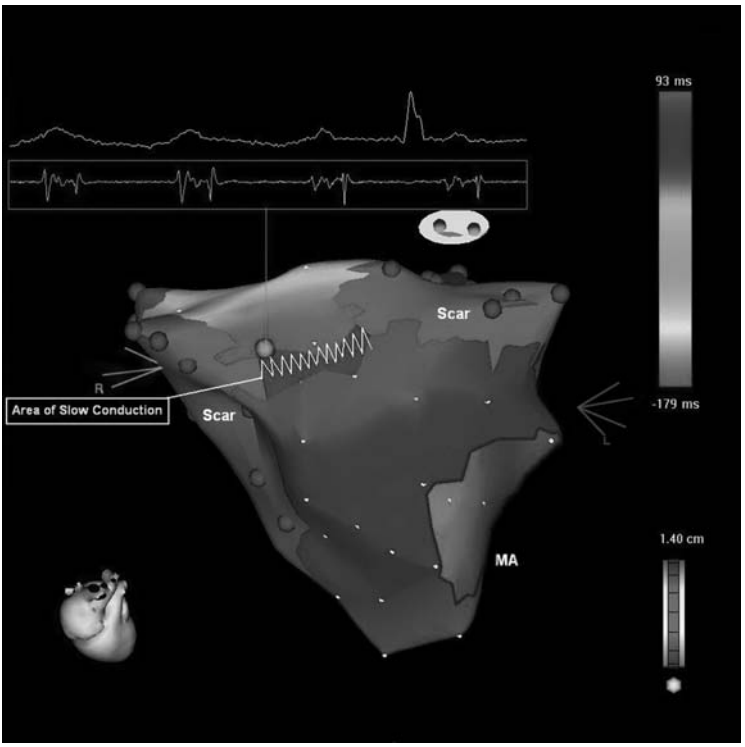


Figure 8.8 Electroanatomic map of the left atrium in a previously ablated patient. Two scars at the location of the PVs on both sides provide anatomic obstacles around which a flutter propagates. The flutter activation wave is seen traveling down the posterior wall, around the mitral annulus, and up the anterior wall. An area of slow conduction is shown between the two scars anteriorly where fractionated potentials are recorded. MA, mitral annulus. (See color plate section.)

of the circuit. The circuit can travel in either a clockwise or counterclockwise direction (Figure 8.9).[5,28]

Left atrial flutter

Left atrial flutter occurs less frequently than right atrial CTI-dependent tachycardias and often co-exists with AF. Left atrial flutters arise in structurally damaged left atria. Areas of slowed conductance, block, or electrically silent areas serve as a substrate for left atrial flutter. ECG findings of CCW left atrial circuits include low amplitude flutter waves and positive waves in leads V1 and V2. (Figure 8.7)[5]

Mitral annular atrial flutter

The anatomic boundaries of the circuit include the mitral annulus and low voltage area or scar in the posterior wall of the left atrium. The circuit rotates around the mitral annulus in either a CW or CCW direction (Figure 8.10).[5,29,30]

Scar and pulmonary vein related atrial flutter

This circuit rotates around one or more of the pulmonary veins or scar in the posterior wall.[5,29,30]

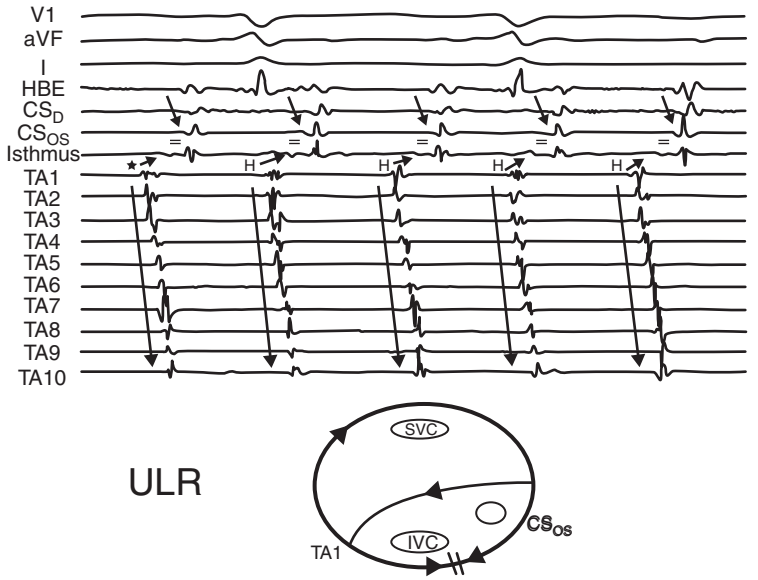


Figure 8.9 Upper loop re-entry (ULR). Upper panel shows simultaneous recordings of a surface ECG and intracardiac electrogram in a patient with sustained ULR flutter. The lower schematic illustrates the re-entrant circuit in the upper part of the right atrium. The cavotricuspid isthmus is *not* a critical part of the circuit. His, recording from the His bundle region; CS_D, distal coronary sinus; CS_{OS}, ostium of coronary sinus; TA, recordings from the 20-pole, 'halo' electrode catheter positioned along the tricuspid annulus with its distal pole (TA1) at 7 o'clock in the left anterior oblique projection, and proximal at the high right atrium (TA5); SVC, superior vena cava; IVC, inferior vena cava. Reproduced with the permission of Lee et al.[5]

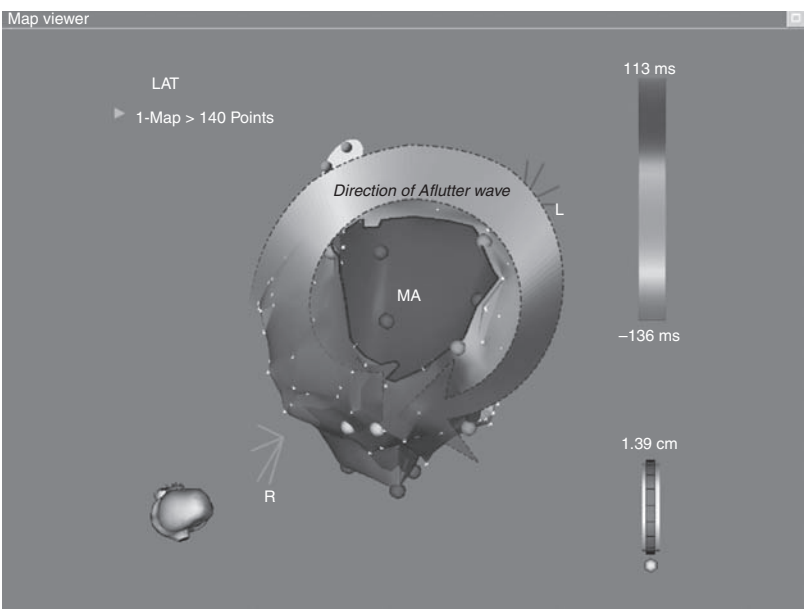


Figure 8.10 Electroanatomic map of the left atrium. Sequential activation around the mitral annulus in a clockwise fashion. (See color plate section.)

Coronary sinus atrial flutter

The circuit travels from the coronary sinus to the lateral left atrium down the interatrial septum and back to the cs. One case has been reported in a patient with no structural abnormality.[31]

Left septal atrial flutter

The circuit rotates in either a CW or CCW manner around the left septum primum. ECG findings include dominant positive waves in V1. The critical isthmus is located between the septum primum and pulmonary veins or between the septum primum to the right inferior pulmonary vein and the mitral annular ring. In the cases that have been reported with left septal atrial flutter the patients had no prior history of surgery but low-voltage areas were found on the posterior wall and the roof of the left atrium. It is hypothesized that atrial conduction slowing is secondary to either atrial dilated cardiomyopathy or anti-arrhythmics (sotalol, amiodarone).[32]

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9

Atrial fibrillation

Bai Rong, Dimpi Patel, Luigi Di Biase, Robert Schweikert, and Walid Saliba

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained supraventricular tachyarrhythmia. An estimated 2.3 million individuals are affected in the United States, thus making it a cardiovascular epidemic. More than 160 000 new cases a year are reported. The total mortality rate is doubled in patients with AF compared with those in sinus rhythm and can be correlated to the magnitude of underlying cardiac disease. AF is associated with a significant risk of morbidity and mortality, therefore, the epidemiology, the risk factors, the classification, and the elucidation of its mechanism become vital to managing patients.

RISK FACTORS

Independent risk factors

- Male gender
- Age
- Diabetes
- Hypertension
- Congestive heart failure
- Valvular heart disease (rheumatic especially mitral valve)
- Myocardial infarction

Other predisposing conditions

- Non-rheumatic valvular disease
- Cardiomyopathies
- Congential heart disease
- Sick sinus syndrome/degenerative conduction system
- Wolff–Parkinson–White syndrome

- Pericarditis
- Pulmonary embolism
- Thyrotoxicosis
- Chronic lung disease
- Diabetes
- Structurally normal hearts affected by high adrenergic states such as alcohol (holiday heart), stress, drugs (sympathomimetics), excessive caffeine, hypoxia, hypokalemia, hypoglycemia, or systemic infection.

CLASSIFICATION

- *First detected AF*.
- *Paroxysmal*: AF is self-terminating within 7 days of recognized onset. Most episodes last less than 24 hours.
- *Persistent*: AF is not self-terminating within 7 days or is terminated electrically or pharmacologically.
- *Permanent*: cardioversion failed or not attempted.
- *Recurrent*: when a patient has two or more episodes.

PATHOGENESIS

The mechanism of AF has yet to be completely elucidated; it is more than likely multi-factorial. The most popular theory is that AF is triggered by spontaneous electrical activities originating from the pulmonary veins (90%), SVC (4%), ligament of Marshall, inferior versa cava (IVC), and coronary sinus (CS), and is maintained by substrate that is conducive for perpetuating the arrhythmia. It has been observed that dilated atria, scar, fibrous tissue, and the electrical remodeling of the myocardium all provide a likely substrate for AF. In some situations, the triggering mechanisms may also be the driving mechanism sustaining AF. Sympathetic and vagal stimulation may also play a role in the initiation and maintenance of AF.

CLINICAL PRESENTATION

Patients with AF present with palpitations, fatigue, dizziness, presyncope, dyspnea, and less commonly with chest pain and syncope. Some AF patients, especially the permanent ones, report no symptoms. The patient's symptoms also depend on the pattern of AF breaking out, the duration of the AF episode, the ventricular response (heart rate) to the index AF attack, and severity of the underlying cardiac disease. Physical examination may reveal irregular heart beats, pulse deficits, and variable intensity of the first heart sound during any episode of AF (Figure 9.1). Systemic evaluation is required in patients with suspected or proven AF in order to characterize the pattern of the arrhythimia, determine its cause, define associated cardiac and extracardiac factors and plan therapy (Table 9.1).

MANAGEMENT OF AF (TABLES 9.2–9.4)

The management of AF entails: (i) rate control, (ii) rhythm control, and (iii) anticoagulation.

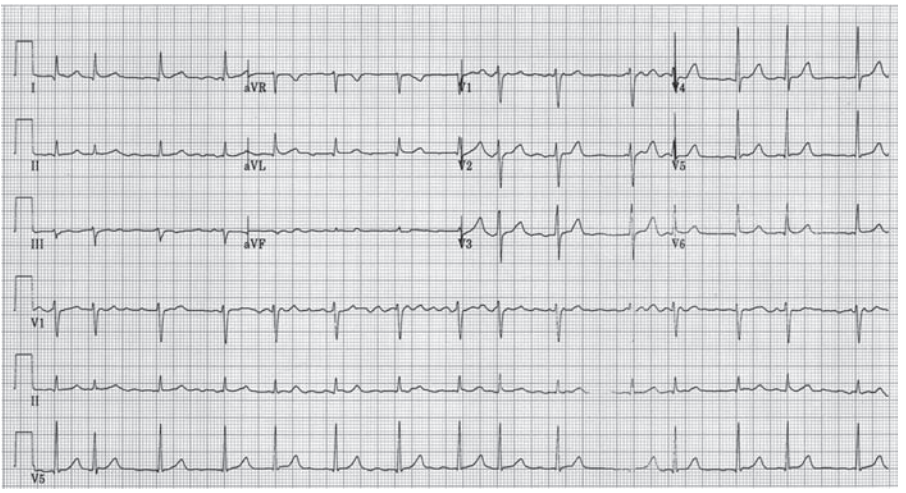


Figure 9.1 ECG of patient with atrial fibrillation.

Rate control during AF

The goal of rate control is to achieve a heart rate of 60–80 bpm at rest and 90–110 bpm with moderate exercise. This can be assessed using a 24-hour or a 48-hour Holter monitor. A rate control only strategy may be used in asymptomatic patients or in patients with very slight symptoms and no evidence of worsening heart failure or ejection fraction (Table 9.2):

- Agents that slow AV nodal conduction including digoxin, beta-blockers, and calcium antagonists (non-dihydropyridine).
- Class I or III anti-arrhythmic drugs (AAD) (sotalol, amiodarone, propafenone, and flecainide) can also contribute to ventricular rate control.
- AVN ablation and pacemaker implantation may also be performed in those patients with poor rate control and who have failed or are not candidates for rhythm control strategies.

Restoration and maintenance of sinus rhythm

- *Restoration of sinus rhythm*: a rhythm control strategy should probably be the first-line strategy in newly diagnosed AF and in patients with symptomatic AF. Depending on the agent of choice and on the type of AF this could be performed in the hospital or on an outpatient basis. Anticoagulation should be optimized as discussed in the next section before attempting to restore sinus rhythm, especially if AF has been present for longer than 48 hours.
- *Pharmacologic conversion*: medications may convert the AF into sinus rhythm and their recommended doses are shown in Table 9.3.

OUTPATIENT TREATMENT OF AF

Self-administration of a single oral dose of drug after the onset of symptomatic AF (the 'pill-in-the-pocket') can be used to terminate an episode. Such a strategy

Table 9.1 Minimum and additional clinical evaluation in patients with atrial fibrillation

Minimum evaluation

1. *History and physical examination, to define*
   - Presence and nature of symptoms associated with AF
   - Clinical type of AF (first episode, paroxysmal, persistent, or permanent)
   - Onset of the first symptomatic attack or date of discovery of AF
   - Frequency, duration, precipitating factors, and modes of termination of AF
   - Response to any pharmacologic agents that have been administered
   - Presence of any underlying heart disease or other reversible conditions (e.g., hyperthyroidism or alcohol consumption)
2. *Electrocardiogram, to identify*
   - Rhythm (verify AF)
   - LV hypertrophy
   - P-wave duration and morphology or fibrillatory waves
   - Pre-excitation
   - Bundle-branch block
   - Prior MI
   - Other atrial arrhythmias
   - To measure and follow the RR, QRS, and QT intervals in conjunction with anti-arrhythmic drug therapy
3. *Transthoracic echocardiogram, to identify*
   - Valvular heart disease
   - LA and RA size
   - LV size and function
   - Peak RV pressure (pulmonary hypertension)
   - LV hypertrophy
   - LA thrombus (low sensitivity)
   - Pericardial disease
4. *Blood tests of thyroid, renal, and hepatic function*
   - For a first episode of AF, when the ventricular rate is difficult to control

Additional testing

One or several tests may be necessary.

1. *Six-minute walk test*
   - If the adequacy of rate control is in question
2. *Exercise testing*
   - If the adequacy of rate control is in question (permanent AF)
   - To reproduce exercise-induced AF
   - To exclude Ischemia before treatment of selected patients with a type IC anti-arrhythmic drug
3. *Holter monitoring or event recording*
   - If diagnosis of the type of arrhythmia is in question
   - As a means of evaluating rate control
4. *Transesophageal echocardiography*
   - To identify LA thrombus (in the LA appendage)
   - To guide cardioversion
5. *Electrophysiologic study*
   - To clarify the mechanism of wide-QRS-complex tachycardia
   - To identify a predisposing arrhythmia such as atrial flutter or paroxysmal supraventricular tachycardia
   - To seek sites for curative ablation or AV conduction block/modification
6. *Chest radiograph, to evaluate*
   - Lung parenchyma, when clinical findings suggest an abnormality
   - Pulmonary vasculature, when clinical findings suggest an abnormality

Table 9.2 Pharmacologic rate control for atrial arrhythmias

Agent	Loading dose	Maintenance dose	Side-effects/toxicity	Comments
Digoxin	0.25–0.5 mg iv or po, then 0.25 mg q 4–6 to 1 mg in 1st 24 h	0.125–0.25 mg po or iv qd	Anorexia, nausea; AV block; ventricular arrhythmias; accumulates in renal failure	Used in CHF; vagotonic effects on the AVN; delayed onset of action; narrow therapeutic window; less effective in postoperative, paroxysmal AF with high adrenergic states
Beta-blockers				
Propranolol	1 mg iv q 2–5′ to 0.1–0.2 mg/kg	10–80 mg po tid–qid	Bronchospasm; CHF; ↓BP	Effective in heart rate control; rapid onset of action; esmolol short acting
Metoprolol	5 mg iv q 5′ to 15 mg	25–100 mg po bid–tid		
Esmolol	500 μg/kg iv over 1′	50 μg/kg iv for 4′; repeat load prn and ↑maintenance 20–50 μg/kg/min q 5–10′		
Calcium-channel blockers				
Verapamil	2.5–10 mg iv over 2′	5–10 mg iv q 30–60′ or 40–160 mg po tid or 120–480 mg/day, sustained release	↓BP, CHF ↑digoxin lev	Rapid onset, can be used safely in COPD and DM
Diltiazem	0.25 mg/kg over 2′, repeat prn p 15′ at 0.35 mg/kg	5–15 mg/h iv or 30–90 mg po qid or 120–360 mg sustained release qd		Often well tolerated with low LVEF pts

can be used in patients with lone AF without structural heart disease. In such patients class IC drugs may be initiated on an outpatient basis. Adequate AVN blockade with beta-blockers or non-dihydropyridine calcium channel antagonists is recommended to prevent rapid AV conduction prior to taking the pill-in-the-pocket.

Electrical cardioversion

This may be performed electively after 3 weeks of effective anticoagulation, emergently in cases of hemodynamic instability, or in conjunction with transesophageal echocardiography.

- Most effective method of restoring sinus rhythm.
- Requires conscious sedation with a short-acting anesthetic.
- Monophasic (200–360 J) and biphasic (50–200 J) external cardioversion.
- Urgently indicated with clinical instability (e.g., hypotension, ischemia, pulmonary edema).
- Electively indicated in patients who remain in symptomatic AF after a pharmacologic attempt.
- This may be enhanced with anti-arrhythmic medications such as amiodarone, flecainide, or ibutilide.
- May be guided by transesophageal echocardiography. Such a strategy can help rule out left atrial clot and expedite cardioversion in patients who are tolerating AF poorly. In this strategy anticoagulation should be started with unfractionated heparin or low molecular weight heparin before cardioversion and continued until a therapeutic international normalized ratio (INR) is achieved with warfarin therapy.

Maintenance of sinus rhythm

Maintenance of sinus rhythm often requires an anti-arrhythmic agent, particularly in patients with persistent or resistant AF, underlying cardiovascular disease, enlarged atria, or other continuing disease factors that predispose to AF. Anti-arrhythmic agents available that can be effective in maintaining sinus rhythm include class IA (quinidine, procainamide, disopyramide), IC (flecainide, propafenone), IA/B/C (moricizine), and III (sotalol, amiodarone, dofetilide) anti-arrhythmic drugs (Table 9.4). Patients with recurrent symptomatic AF who

Table 9.3 Pharmacologic conversion regimens

Drug	Route	Dose	Success rate (%)
Quinidine	po	200–324 mg tid to 1.5 g/d	48–86
Procainamide	iv	1 g over 20–30 min	48–65
Propafenone	po	600 mg	55–87
	iv	2 mg/kg over 10 min	40–90
Flecainide	po	300 mg	90
	iv	2 mg/kg over 10 min	65–90
Amiodarone	iv	1.2 g over 24 h	45–85
Sotalol	po	80–160 mg, then 160–360 mg/d	52
Dofetilide	po	125–500 μg bid, based on CrCl	30
Ibutilide	iv	1 mg over 10 min, repeat in 10 min as required	31

Table 9.4 Drugs for maintenance of sinus rhythm

Anti-arrhythmic drug	Dose	% Maintenance SR (6–12 mos)	Side-effects/comments
Class IA			
Quinidine	200–400 mg po tid–qid	30–79	↑QT, pro-arrhythmia/TdP, potential ↑ AVN conduction, diarrhea, nausea, ↑ digoxin levels, thrombocytopenia
Procainamide	10–15 mg/kg iv at ⩽50 mg/min or 2–6 g/day po in bid or qid sustained release	N/A	↓ BP, CHF, drug-induced lupus, agranulocytosis; active metabolite NAPA with class III activity accumulates in renal failure
Disopyramide	100–300 mg po tid	44–67	Anticholinergic effects (e.g., urinary retention, dry eyes/mouth), CHF
Class IC			
Flecainide	50–200 mg po bid	34–81	Pro-arrhythmia, visual disturbance, dizziness, CHF, avoid in CAD or LV dysfunction
Propafenone	150–300 mg tid	30–76	CHF, avoid in CAD/LV dysfunction
Class IA/B/C			
Moricizine	200–300 mg tid	N/A	Pro-arrhythmia, dizziness, GI/nausea, headache, caution in CAD/LV dysfunction
Class III			
Sotalol	80–240 mg bid	37–70	CHF, bronchospasm, bradycardia, ↑ QT proarrhythmia/TdP
Amiodarone	600–1600 mg/d loading in divided doses, 100–400 mg qd maintenance	40–79	Pulmonary toxicity, bradycardia, hyper- or hypothryroidism, hepatic toxicity, GI (nausea, constipation), neurologic, dermatologic, and ophthalmologic side-effects, drug interactions
Dofetilide	CrCl (ml/min) >60: 500 μg bid 40–60: 250 μg bid 20–40: 125 μg bid	58–71	Exclude CrCl <20 ml/min. ↑ QT, pro-arrhythmia/ TdP, headache, muscle cramps

have failed at least one anti-arrhythmic medication may be considered for AF ablation.

PREVENTION OF THROMBOEMBOLISM

Atrial fibrillation is associated with increased risk of thromboembolic events and stroke. AF is one of the most common causes of stroke in the elderly and the most common cause of cardiogenic stroke. AF-induced strokes appear to be due to

cardiac emboli, presumably from thrombi formed in fibrillating atria. Rate of stroke is clustered at the onset of the arrhythmia, with 25% of the patients suffering a stroke, while another 14% had a stroke within the first year.

Risk factors for stroke with AF

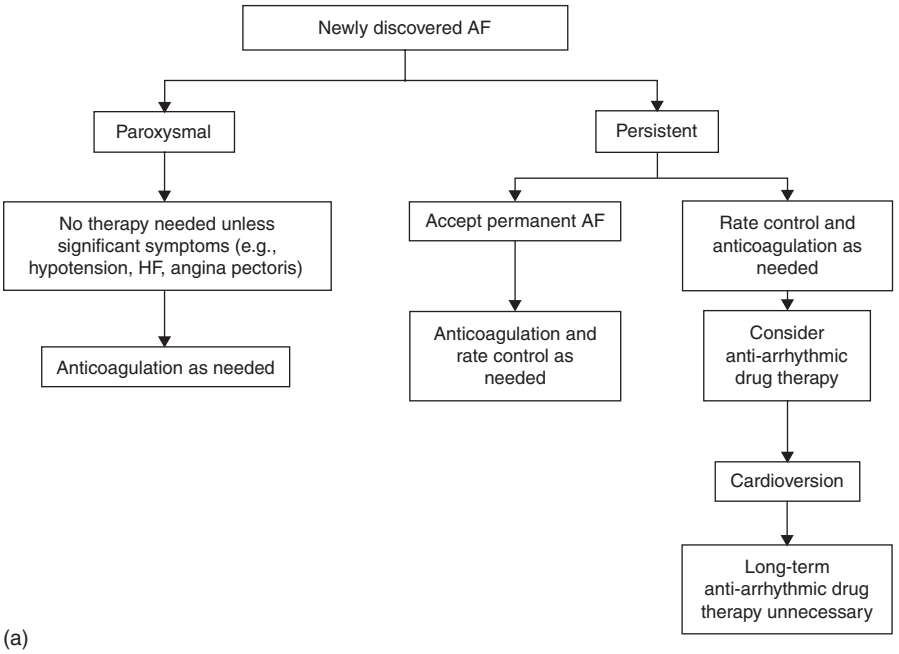
- TIA or previous stroke
- Diabetes
- Hypertension
- Age
- Left ventricular dysfunction
- Increased left atrial size
- Rheumatic mitral valve disease
- Prosthetic valves
- Women >age 75
- Mitral annular calcification
- Increased wall thickness
- Thyrotoxicosis

Guidelines for antithrombotic therapy for AF

- Anticoagulation is recommended if AF persists longer than 48 hours, particularly if cardioversion is anticipated after this time or AF continues to recur after cardioversion.
- Anticoagulation with warfarin (target INR 2.5, range 2.0–3.0 for AF) should be recommended for all anticoagulation-eligible patients >75 years old, as well as in patients <75 years old who have any of the following risk factors for thromboembolism:
    - Prior transient ischemic attack, systemic embolus or stroke
    - Hypertension
    - Poor left ventricular function
    - Rheumatic mitral valve disease
    - Prosthetic heart valves
- Patients aged 65–75 years with no risk factors can be treated with aspirin or warfarin.
- Aspirin is recommended for patients <65 years old and who have no risk factors.
- Anticoagulation therapy with warfarin might be contraindicated for patients who have one of the following risk factors of bleeding complication:
    - Advanced age >80 years old
    - Uncontrolled hypertension, particularly when systolic is >160 mmHg
    - Prior history of cerebrovascular disease
    - Prior history of subdural hematoma
    - These recommendations apply to paroxysmal as well as persistent and permanent AF

SUMMARY

The overall strategies of AF management are summarized in Figure 9.2.



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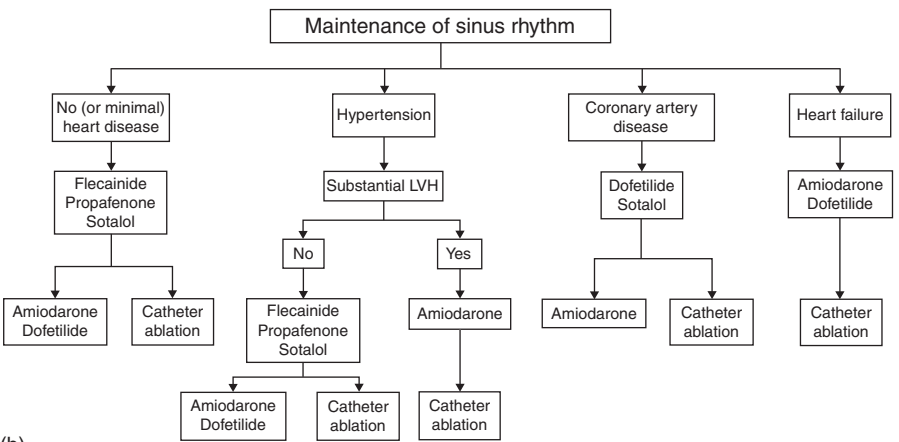
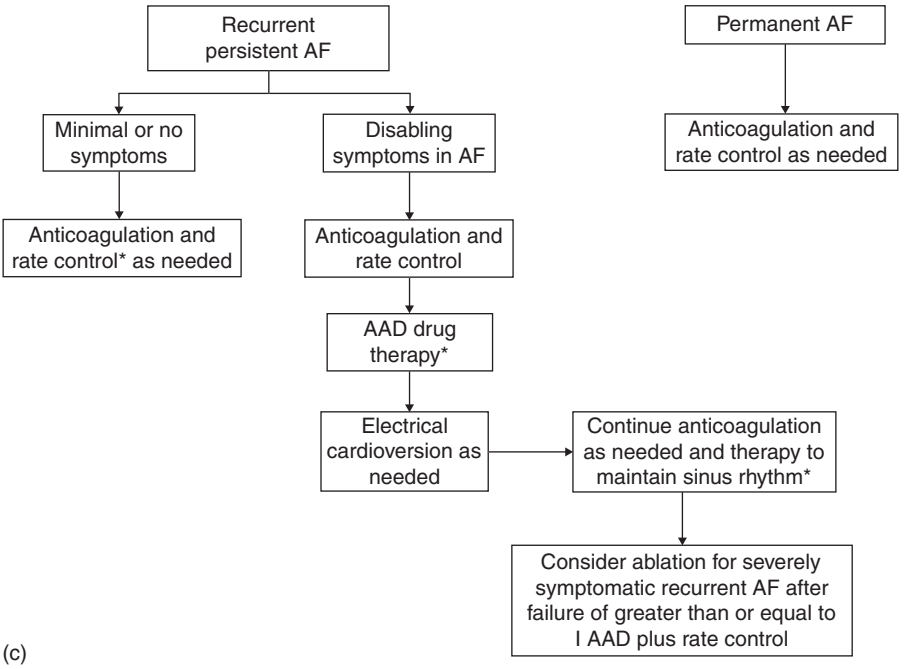


(b)

Figure 9.2 Summary of overall strategies of AF management



(c)

Figure 9.2 (Continued).

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Section V
Ventricular tachyarrhythmia

10

Genetically determined ventricular arrhythmias

Atul Khasnis, Jennifer Cummings, and Patrick Tchou

Long QT syndrome • Short QT syndrome (SQTS) • Brugada syndrome • Idiopathic ventricular fibrillation (IVF) • Catecholaminergic polymorphic ventricular tachycardia (CPVT) • Summary and future directions

Genetics has permeated every domain of medicine offering diagnostic insight and promising therapeutic solutions in various diseases. This chapter will focus on the genetically determined ventricular arrhythmias; some are potentially lethal. We are yet faced with few markers for early identification and unfortunately a limited therapeutic armamentarium in dealing with these complex conditions.

LONG QT SYNDROME

Long QT syndrome (LQTS) is a heterogeneous electrical disorder that manifests with increased corrected QT interval (QTc) on the ECG. The estimated prevalence of LQTS is 1:5000 persons in the US (over 50 000 people) and it may cause up to 3000 deaths (mostly in children and young adults) each year.[1] Prolonged QT interval may occur secondary to many medications (including anti-arrhythmics), electrolyte disturbances, and ischemia. This review will focus on the primary form of long QT syndrome (congenital LQTS). LQTS can be broadly divided into Romano–Ward syndrome (AD inheritance, QT prolongation, and VT) and Jervell–Lang–Nielsen (JLN) syndrome (AR inheritance, congenital deafness, QT prolongation, and VT). The characteristic ventricular arrhythmia observed with LQTS is 'torsade de pointes' (TdP), a form of polymorphic VT characterized by an undulating QRS axis (resembling 'twisting of the points'). This term was coined in 1966 by Dessertenne in an 80-year-old female patient with intermittent complete AV block.[2] QT prolongation in LQTS is due to overload of myocardial cells with positively charged ions during ventricular repolarization. LQT1, due to mutations of KCNQ1 (KVLQT1), is the most common form (Table 10.1).

The various cardiac channels that derive from the responsible genes and their role in the genesis of the action potential are shown in Figure 10.1. The common cut-off used to diagnose LQTS is 440 ms.

Table 10.1 Genetics of long QT syndrome (LQTS)

LQTS type	Gene	Chromosome locus	Ion channel	Effects	Percent of LQTS
Autosomal-dominant (Romano–Ward)					
LQT1 (1991)	KCNQ1 (KVLQT1)	11p15.5	α-subunit of I_{Ks}	↓ I_{Ks}	50
LQT2 (1994)	KCNH2 (HERG)	7q35–36	α-subunit of I_{Kr}	↓ I_{Kr}	45
LQT3 (1994)	SCN5A	3p21–24	α-subunit of I_{Na}	↑ I_{Na}	3–4
LQT4 (1995)	Ankyrin-B	4q25–27		↑ late I_{Na}?	<1
LQT5 (1997)	KCNE1 (minK)	21q22.1–22.2	β-subunit of I_{Ks}	↓ I_{Ks}	<1
LQT6 (1999)	KCNE2 (MiRPI)	21q22.1–22.2	β-subunit of I_{Kr}	↓ I_{Kr}	<1
LQT7 (2001)	KCNJ2	17q23	$I_{Kir2.1}$	↓ $I_{Kir2.1}$	<1
Autosomal-recessive (Jervell and Lange–Neilsen)					
JLN1 (1997)	KCNQ1 (KVLQT1)	11p15.5	α-subunit of I_{Ks}	↓ I_{Ks}	<1
JLN2 (1997)	KCNE1 (minK)	21q22.1–22.2	β-subunit of I_{Ks}	↓ I_{Ks}	<1

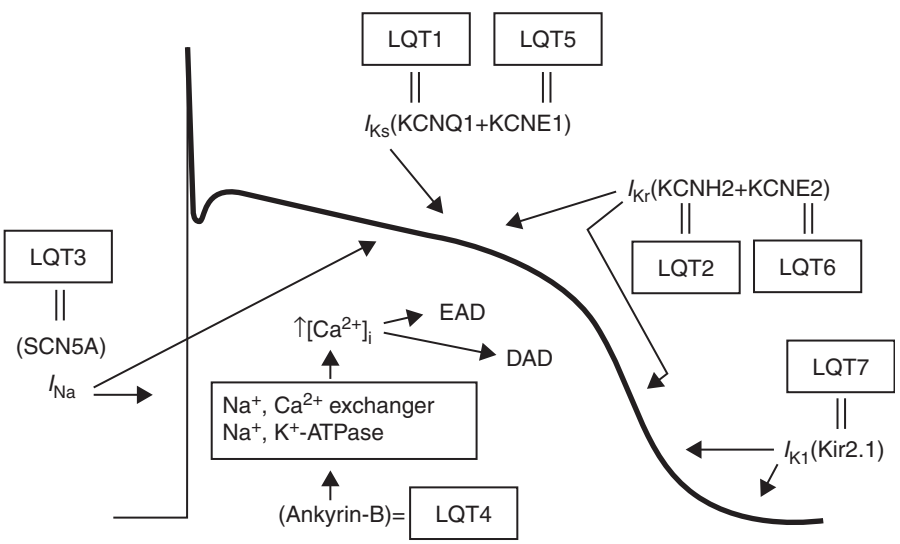

Figure 10.1 Channels in subtypes of long QT syndrome.

Characteristics of familial LQTS[3]

1. First member of a family to be identified was younger
2. More likely to be female
3. Higher frequency of syncope or sudden cardiac death (SCD) with resuscitation
4. Congenital deafness
5. Resting HR $<$ 60 bpm
6. QTc $\geq$ 500 ms
7. History of VT in other affected and unaffected family members
8. Arrhythmogenic syncope associated with acute physical, emotional, or auditory arousal.

Ventricular arrhythmias in various LQTS genotypes are triggered by different stimuli – exercise-related cardiac events for LQTS1 patients, auditory stimuli for LQTS2 patients, and sleep for LQTS3 patients.[4]

Genetic and clinical characteristics

- The channelopathy for LQTS3 is shared by patients with Brugada syndrome.
- The risk of cardiac events is significantly higher in patients with LQT1 or LQT2, but the percentage of lethal cardiac events is significantly higher in patients with LQT3.[5]
- Syncope, seizure-like activity, and cardiac arrest are the common clinical presentations related to physical activity and emotional stress.

Schwartz et al have devised diagnostic criteria for patients with LQTS – first described in 1985[6] and then revised in 1993 (Table 10.2).[7] Molecular screening of family members of patients with LQTS has been emphasized as the silent gene carrier status in family members is more common than thought to be and puts them at risk of ventricular arrhythmias when provoked by medications or other specific triggers.[8]

ECG in long QT syndrome

Clinical history and presentation remain extremely central to triggering the hunt for these channelopathies. However, the 12-lead ECG is an invaluable source of information:

- To confirm the suspicion of LQTS
- To provide clues to the possible underlying channel defect
- To assist risk stratification
- To guide effective and safe therapy.

The accurate measurement of the QT interval is the most important part of making the diagnosis of LQTS. This might not be simple in patients with underlying atrial fibrillation, the presence of 'U' waves, paced ventricular rhythms, pre-excitation syndromes, or low amplitude waves on the ECG. The anteroseptal leads (V2 or V3) provide the best estimate of the longest QT interval. Variability in QT interval measurement is mainly at the end of the T-wave, rather than the onset of the QRS complex, and attributable to variability in cycles, observers, or

Table 10.2 Diagnostic criteria for long QT syndrome[7]

	Points
ECG findings*	
A. QT†	
≥ 480 ms$^{1/2}$	3
460–470 ms$^{1/2}$	2
450 ms$^{1/2}$ (in males)	1
B. Torsade de pointes‡	2
C. T-wave alternans	1
D. Notched T-wave in three leads	1
E. Low heart rate for age§	0.5
Clinical history	
A. Syncope‡	
With stress	2
Without stress	1
B. Congenital deafness	0.5
Family history‖	
A. Family members with definite LQTS#	1
B. Unexplained sudden cardiac death below age 30 among immediate family members	0.5

LQTS, long QT syndrome.
*In the absence of medications or disorders known to affect these electrocardiographic features.
†QT_c calculated by Bazett's formula, where $QT_c = QT / \sqrt{RR}$.
‡Mutually exclusive.
§Resting heart rate below the second percentile for age.[25]
‖The same family member cannot be counted in A and B.
#Definite LQTS is defined by an LQTS score ≥4.
Scoring: ≤1 point, low probability of LQTS; 2 to 3 points, intermediate probability of LQTS; ≥4 points, high probability of LQTS.

measurement error. It is therefore important to measure the longest QT interval observed in any lead of the 12-lead ECG.[9]

Corrected QT interval

Various formulae are then applied to estimate the corrected QT interval. The *Bazett correction* (QT/RR$^{1/2}$),[10] though imperfect and unsatisfactory, is still most commonly used. Other formulae used to correct QT interval include the cube root *formula of Fridericia* (QTc = QT/RR$^{1/3}$)[11] and linear regression formula obtained from the Framingham study (QTc = QT + 0.154 (1 RR).[12] Each of the formulae has been reported as having problems at under- or over-correcting the QT interval. The *Framingham formula* has been suggested to be better as it makes a greater physiologic attempt to factor in the dynamicity of the QT/RR relationship.[13] This QT/RR relationship is individualized and accounts for the shortcomings of the 'global' heart rate correction formulae. The Bazett correction for QT interval is unsuitable for paced QRS complexes on the 12-lead ECG.[14] Using the JT interval has been suggested as remedial in combating the confounding QT correction formulae.

There is immense influence of the autonomic nervous system on the QT interval.

Importance of T-wave morphology in LQTS

The most important clue to the presence and subtype of LQTS in addition to the QTc is T-wave morphology.[15] The classic T-wave morphology in the setting of LQTS can help to diagnose the genotype and therefore direct risk stratification and management.

- LQTS1 show QTc intervals > 550 ms and an extremely broad-based T-wave
- LQTS2 show moderately prolonged QTc intervals and low amplitude T-waves with bifid T-waves in 60% or more of the carriers
- LQTS3 show prolonged QTc with late-onset, peaked T-waves preceded by a long, isoelectric ST segment
- LQTS7 show a low-amplitude T-wave, modestly prolonged QTc, and indistinct termination of the T-wave as it approaches the isoelectric baseline.

Notched, double-hump T-waves with a distinct second protuberance above the apex of the T-wave have been reported exclusively in LQTS2 patients (Figure 10.2). Epinephrine causes a differential diagnostic response in LQTS1, LQTS2, and LQTS3.[16] Computer-analyzed ECG interpretation alone has been reported to miss identifying many at-risk family members of patients with LQTS1.

The interval between the peak and the end of the T-wave (transmural dispersion of repolarization) increases with exercise in patients with LQTS1, but not LQTS2.[17] In patients with sinus arrhythmia, applying the Bazett correction to the QT interval following the shortest RR interval has been suggested.[18]

Torsade de pointes in LQTS

Torsade de pointes is the classical arrhythmia associated with LQTS. TpP shows three patterns of onset:[19]

1. *Short-long-short* sequence defined as one or more short-long cardiac cycles followed by an initiating short-coupled PVC.
2. *Increased sinus rate* pattern defined as a gradual increase in sinus rate with or without T-wave alternans.
3. *Changed depolarization* pattern defined as a sudden long-coupled PVC or fusion beat followed by short-coupled PVC.

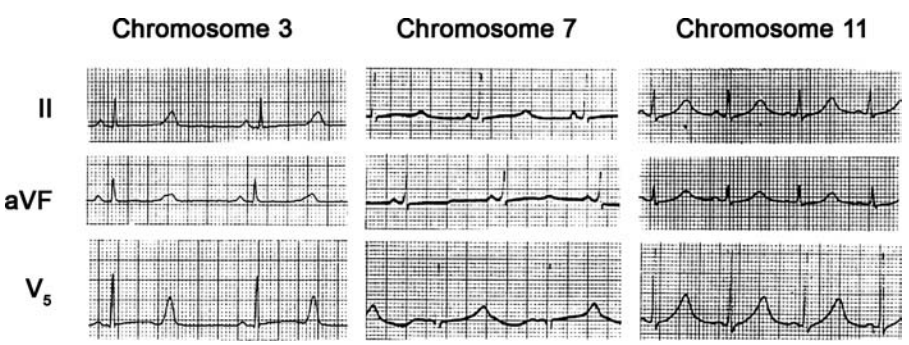

Figure 10.2 T-wave morphology correlation with genotype in LQTS.

Medications and LQTS

There are many classes of medications that may prolong QTc. These must absolutely be avoided in patients with LQTS. Special caution must be exercised in the following groups of patients:

- Female
- Electrolyte disturbances: hypokalemia and hypomagnesemia
- Diuretic use
- Bradycardia
- Congestive heart failure
- Baseline QT prolongation
- Known congenital LQTS
- Patients on other QT prolonging agents.

Medications include anti-arrhythmics (class IA and III), antibiotics (macrolides), antihistaminics (terfenadine, astemizole), SSRIs (ketanserin), diuretics, antipsychotics, and many others. The list continues to grow every day. An updated list can be found at the Sudden Arrhythmia Death Syndromes Foundation website (www.sads.org).[1] Different strengths of association exist between medication use and LQTS. Some drugs may prolong QTc by indirect effects such as bradycardia, ischemia, or interacting with other medications that have similar cardiac effects.

Therapy for LQTS

Definitive therapies for prevention of sudden death in patients with LQTS include use of beta-blockers, implantation of pacemakers, defibrillators, and left-sided cervical sympathectomy.

Drug therapy

Experimental studies suggest that drug therapy may need to be catered to specific genotypic and cellular substrates:[20]

- Beta-blockers are protective in LQTS1, less so in LQTS2, but not protective in LQTS3
- Mexiletine was most effective in LQT3 but less so in LQT1 and LQT2
- Nicorandil was capable of preventing torsades in LQT1 and LQT2 but not in LQT3.

Wedekind et al followed a family with LQTS1 (common mutation at V254M) on beta-blockers for 23 years and reported no cardiac events.[21] Beta-blockers are more effective in LQTS1 and more effective in males. This seems logical as adrenergic stimulation is the most sensitive trigger for VT in patients with LQTS1. Failure of beta-blockers has been reported in studies with atenolol, young age at diagnosis, initial presentation with aborted cardiac arrest, LQTS1 genotype, and non-compliance.[22]

In the International LQTS Registry, *asthma* was identified in as many as 5.2% of 4310 studied LQTS family members. Longer QTc duration was associated with

a higher incidence of asthma. An increased risk of cardiac events was mitigated by beta-blockers.[23] In women with LQTS, the *postpartum interval* is associated with a significantly increased risk for cardiac events among probands with LQTS, but not among first-degree relatives. Prophylactic treatment with beta-blockers during the pregnancy and postpartum intervals in these patients is recommended.[24] It appears paradoxical to use beta-blockers, which can cause bradycardia and prolong the QTc; it must be remembered that in LQTS1, tachycardia causes worsening of QT prolongation. Bradycardia can prolong the QT interval; pacing therefore seems a logical option to shorten it. Other options for LQTS include combination therapy with beta-blockers and pacing.[25] However, permanent pacing does not provide complete protection against sudden death in these patients.[26]

SCD survivors in LQTS

Patients who have experienced cardiac arrest and recurrent syncope despite beta-blockers are considered high risk and benefit significantly from implantable cardioverter defibrillators (ICDs). QTc interval and cardiac arrest survival are prognostic factors for appropriate ICD shocks. Increasing the pacing rate, adding beta-blockers, or starting the rate-smoothing algorithm can reduce the incidence of these shocks.[27] T-wave oversensing can occur in patients with LQTS following ICD placement. ICDs provide a fail-safe modality for prevention of SCD. At present, they are implanted in selected high-risk patients. The definition of 'high-risk' in patients with LQTS is not entirely clear. Future studies may help elucidate the answer to this complex question. *Left cardiac sympathetic denervation (LCSD)* is another modality that has been reported to reduce the risk of SCD in high-risk patients (very prolonged QTc, 99% symptomatic, 48% had had a cardiac arrest, and 75% symptomatic despite treatment with beta-blockers). The mean yearly number of cardiac events per patient was reduced by 91%.[28] A world-wide study of 85 patients who underwent LCSD for LQTS reported reduction in cardiac events from 99% to 45%. A microinvasive approach to LCSD may make it more feasible for LQTS.

Prognosis of LQTS

The prognosis of LQTS is determined by the genotype. Female first-degree relatives of patients with the LQTS have a higher risk of cardiac events independent of recorded ECG findings. Not only bradycardia, but tachycardia also increases risk of cardiac events in family members of patients with LQTS.[29] Better variables or markers for risk stratification of patients and families with LQTS are needed. For asymptomatic patients with LQTS, treatment is recommend for the following groups:[30]

- Patients with J-LN syndrome
- Neonates and infants
- Affected siblings of children who have died suddenly because of the emotional stress in the family
- Patients with documented T-wave alternans
- Patients with a very long QTc ($\geq$600 ms)

- Group thought to be more symptomatic and
- Anxiety and an explicit request for treatment in a family after thorough explanation.

SHORT QT SYNDROME (SQTS)

Short QT syndrome is a recently described familial disorder that also manifests with sudden cardiac death.[31] To date 22 cases of SQTS have been described. The familial form is characterized by a QT interval < 280 ms (QTc < 300 ms).[32] There are three subforms of SQTS:

- SQTS1, caused by a gain of function substitution in the HERG (I_{Kr}) channel
- SQTS2, caused by a gain of function substitution in the KvLQT1 (I_{Ks}) channel
- SQTS3, caused by a defect in the gene coding for the inwardly rectifying Kir2.1 (I_{K1}) channel.

These mutations result in an accelerated action potential, thus shortening its duration and consequently manifesting a shortened QT interval. The patients in the first paper describing SQTS as a familial entity presented with syncope, palpitations, and resuscitated cardiac arrest in the presence of a positive family history for SCD (Figure 10.3).

Electrophysiologically, SQTS is characterized by short atrial and ventricular refractory periods, which explain increased vulnerability to AF and VF. The mechanism of VF in SQTS has been proposed to be heterogeneous abbreviation of the action potential duration among different cell types spanning the ventricular wall.

ECG in SQTS

The 12-lead ECG is useful in quantitating the short QT interval and careful observation of T-wave morphology may provide clues to SQTS3 subtype (tall and asymmetric T-waves). ECG features also include:

1. Symmetric tall T-waves in V1–6
2. Near absence of the ST segment
3. Apparently long TP interval.

Other causes of QT shortening such as digitalis and hypercalcemia must be excluded. The problems with correction of the QT interval that haunt LQTS also apply to SQTS. Any formula that underestimates the actual corrected QT may lead to the erroneous diagnosis of SQTS. The *suggested formula* to calculate the lower limit of the QT interval (based upon the heart rate) is QT $=$ 57728/(100 $+$ heart rate).[33]

Therapy in SQTS

Therapy for SQTS includes *quinidine*, which has been reported as most potent in prolonging the QT interval compared to class IC and III agents. It was also found to effectively prolong the ventricular refractory period and suppress induction

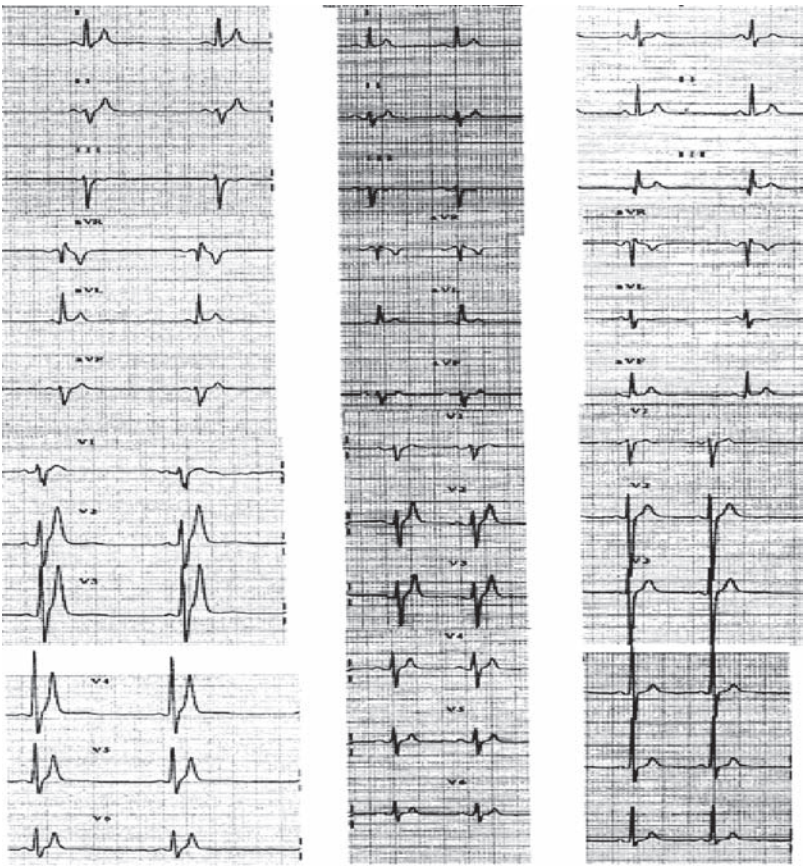

Figure 10.3 12-lead ECG in three patients with short QT syndrome.

of VF.[34] Other studies have confirmed the efficacy of quinidine in blocking the HERG channel under experimental and clinical conditions. Implantation of ICD has also been attempted successfully as primary prevention in SQTS.[35] Inappropriate therapy due to T-wave oversensing is also seen in patients with SQTS. This may be due to the tall T-waves seen in some of these patients. As stated above, consequent upon very few reported cases so far, diagnostic criteria or guidelines have not been devised at the present time. In the future, increased number of patients and longer follow-up will lead to better patient identification, risk stratification, and management of this complex electrical disorder.

BRUGADA SYNDROME

Brugada syndrome is a distinct electrical abnormality characterized by specific ECG abnormalities and predisposing to sudden death. The first patients reported in 1986 were a 3-year-old boy from Poland with multiple episodes of loss of consciousness (some requiring resuscitation) and a sister who had experienced

SCD at 2 years of age.[36] The syndrome was formally described by Brugada and Brugada in 1992 in a series of eight patients with aborted SCD.[37] The ECG hallmark during sinus rhythm in these patients showed right bundle branch block, normal QT interval, and persistent ST segment elevation in precordial leads V1 to V2–V3 in all and rapid polymorphic VT initiated by ventricular extrasystoles (spontaneous or programmed) in five patients.

Mechanisms of Brugada syndrome

- Defective sodium channel (common to LQTS3) leading to depression or loss of the action potential duration (APD) peak in the RV epicardium during repolarization creating a transmural voltage gradient responsible for the ST-segment elevation.[38]
- Abnormal depolarization in the RVOT.
- Overexpression of transient outward current (I_{to}) in the epicardial ventricular myocardial cells leads to shortened APD, making those cells more vulnerable to re-excitation by surrounding cells with normal APD (phase 2 re-entry).

The mutated sodium channel dysfunction is worsened by *elevated temperatures*.

Unmasking the Brugada ECG

Blocking the sodium channel with various pharmacologic agents can help unmask the Brugada ECG pattern.

1. Flecainide and ajmaline have been traditionally for this purpose; ajmaline has been reported to be superior in studies using the patch clamp technique.[39]
2. A combination of sodium and calcium channel blockade is also more effective in unmasking the Brugada ECG pattern.[40]
3. The Brugada ECG pattern has been described in myriad entities such as vagal nerve manipulation during deep neck dissection, thioridazine overdose, use of tricyclic antidepressants, propranolol overdose, vasospastic angina, and patients on sodium-channel blocking drugs such as flecainide and propafenone.

It is suggested that the Brugada ECG pattern begins to appear during junior high school and increases until late adulthood.[41] The presence of symptoms and spontaneous abnormal ECG in patients with Brugada syndrome are markers for future cardiac events.[42]

ECG in Brugada syndrome

There are three distinct ECG patterns of Brugada syndrome:

- Type 1 – diagnostic and characterized by coved ST-segment elevation $\geq$2 mm (0.2 mV) followed by a negative T-wave.
- Type 2 – saddleback appearance with high takeoff ST-segment elevation of $\geq$2 mm, a trough displaying $\geq$1 mm ST elevation, and then either a positive or biphasic T-wave.

- Type 3 has either a saddleback or coved appearance with an ST-segment elevation of ≥1 mm. Type 2 and type 3 ECG are not diagnostic of the Brugada syndrome

The diagnosis of Brugada 'syndrome' requires a type 1 ST-segment elevation in >1 right precordial lead (V1 to V3) in the presence or absence of a sodium channel blocker, and in conjunction with one of the following: documented VF, polymorphic VT, family history of SCD at <45 years of age, coved-type ECGs in family members, inducibility of VT with programmed electrical stimulation, syncope, or nocturnal agonal respiration (Table 10.3 and Figure 10.4).[43]

Table 10.3 ECG characteristics of the subtypes of Brugada syndrome

	Type 1	Type 2	Type 3
J-wave amplitude	≥2 mm	≥2 mm	≥2 mm
T-wave	Negative	Positive or biphasic	Positive
ST-T configuration	Coved type	Saddleback	Saddleback
ST-segmental (terminal portion)	Gradually descending	Elevated ≥1 mm	Elevated <1 mm

1 mm = 0.1 mV; the terminal portion of the ST-segment refers to the latter half of the ST-segment.

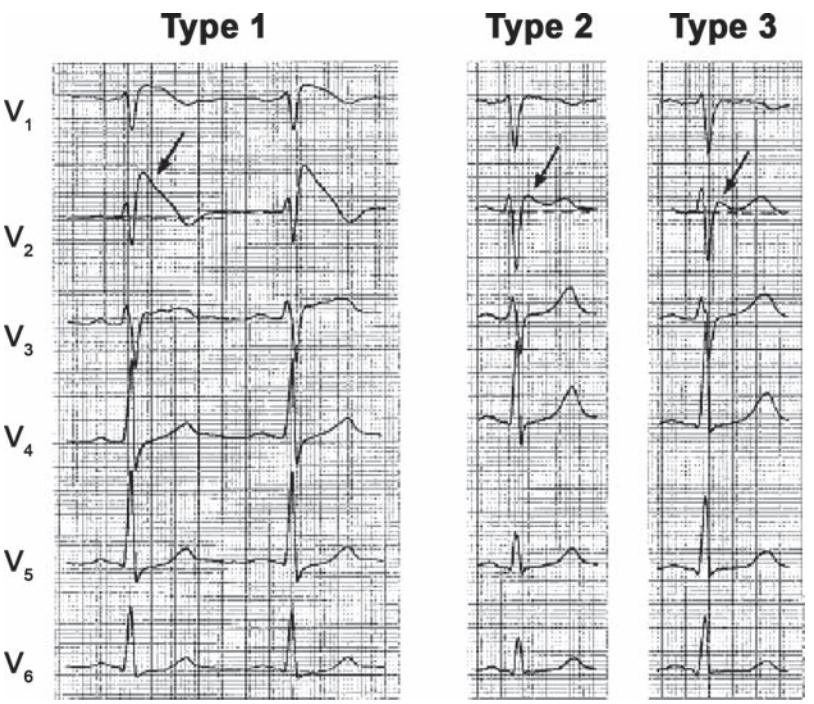

Figure 10.4 ECG features of the subtypes in the Brugada syndrome.

In doubtful cases, recording the ECG from higher intercostal spaces has also been recommended to unmask abnormalities.[44]

In provocative testing[43] the following guidelines apply:

- Monitor continuously with ECG (at 10 mm/s throughout the test, interposed with 25 or 50 mm/s).
- *It should be terminated* when the diagnostic type 1 Brugada ECG develops, ST-segment in type 2 ECG increases by >2 mm, premature ventricular beats or other arrhythmias develop, or QRS widens to >130% of baseline.
- Intravenous sodium-channel blockers should always be infused slowly and closely monitored, with necessary back-up for resuscitation.
- Patients at high risk for drug-induced AV block, such as older adults with syncope, should be studied in the EP lab after a temporary pacemaker has been inserted.
- For younger patients, sodium blocker challenge can be safely performed as a bedside test, provided the drug is discontinued as soon as excessive ST-segment elevation, QRS widening, or ventricular ectopy is observed.

Other observed ECG abnormalities in patients with established SCN5A mutations include significantly longer conduction intervals on baseline ECG (PQ and HV interval; aggravated by class I drugs).[45] Other causes for ST elevation and a Brugada-like ECG pattern must be excluded.

Therapy for Brugada syndrome

Various treatment options exist for Brugada syndrome: again, defibrillators are the only fail-safe choice. Quinidine is effective in preventing VF in these patients; selective I_{to} blocking agents have also been effective experimentally.[43] Inducibility of ventricular arrhythmias at EPS translates into poor prognosis.[46] The free wall of the RVOT appears to be the site of origin of PVCs that trigger VF in Brugada syndrome; it also is the most successful site for arrhythmia induction.[47] Prophylactic ICD placement has been recommended in patients with Brugada syndrome with inducible arrhythmias at EPS, irrespective of symptoms. Following ICD placement, patients with Brugada syndrome have been reported to have a high DFT, and short ventricular ERP and VF cycle length.[48] T-wave oversensing has also been observed. RF ablation of foci in the RVOT and Purkinje fiber network is successful in patients with Brugada syndrome.[49] There are no data regarding the long-term outcome of ablation in this group of patients.

Risk stratification in Brugada syndrome

Risk stratification is based on presentation, family history, ECG features, non-invasive electrophysiologic testing, and electrophysiology study. The prognosis is worst in those presenting with aborted SCD compared to those presenting with syncope.[50] Family history of SCD also elevates the risk. The spontaneous presence of a classic Brugada type I pattern on the ECG (without alternative pathology or pharmacologic provocation) also augurs a worse outcome. The presence of late potentials on the signal averaged ECG (SAECG) is suggestive of a higher risk.[51] ST elevation >0.15 mV at baseline with pilsicainide-induced

additional ST elevation >0.10 mV and positive late potentials together have been reported as having high sensitivity (92%) and specificity (89%) in predicting VF induction at EP study in asymptomatic patients with Brugada syndrome.[52] Isoproterenol has been used to unmask the abnormal late potentials on the SAECG.[53] *High-risk patients are candidates for ICD placement*. ARVC has been reported to possibly co-exist with the Brugada syndrome. A single SCNA5 mutation has been observed to manifest as atrial flutter, conduction disease, and Brugada syndrome to sudden cardiac death.[54] Further studies may clarify the relationship between Brugada syndrome and ARVC, leading to a unifying genetic explanation for this co-existence.

IDIOPATHIC VENTRICULAR FIBRILLATION (IVF)

Idiopathic VF is another important cause of SCD. In the absence of clinical or laboratory findings that could account for the occurrence of major arrhythmic events, the diagnosis of IVF can be made once a survivor of cardiac arrest has been extensively studied. This definition does not imply that the heart of the patient is completely free of structural or functional abnormalities but simply that, if an abnormal finding is present, it is not considered responsible for the VF.[55] In most cases, it is almost impossible to state that there is 'no underlying cardiac disease'. Certain minimal structural cardiac abnormalities have therefore been regarded as consistent with the diagnosis of IVF (Table 10.4).

Idiopathic VF accounts for 5 to 10% of survivors of out-of-hospital cardiac arrest.[56] The proposed mechanism is *abnormal depolarization and repolarization* responsible for electrical heterogeneity resulting in VF. The *Purkinje fiber network and RVOT* have been sites of successful ablation, thus suggesting their role in the genesis of IVF.[57] A subset of patients with IVF has a short QTc; VF in these patients has been suppressible using agents that lengthen the QT interval. Another subset has been described with torsade de pointes preceded by a short coupling interval of the first beat or of the isolated premature beats. Verapamil was found to be effective in arrhythmia suppression.[58]

In a meta-analysis,[59] the observed mean age of these patients is 36 years, with a male:female ratio of 2.5:1. Over 90% of the patients required resuscitation; syncope occurred in the rest. Diagnosis of VF was preceded by syncope in one fourth of the patients. Eleven percent experienced SCD within a year of diagnosis.

Table 10.4 Structural cardiac abnormalities acceptable for diagnosis of IVF[55]

- MVP (lack of regurgitation, redundant valves, QT or ST-T wave abnormalities)
- Modest regional dyskinesia
- Thickening of septum or left ventricular wall (<10%)
- Paroxysmal AF
- Chronic AF
- AV block (first- or second-degree)
- Bundle-branch block
- Age >60 years
- Hypertension (no hypertrophy)
- Non-specific abnormalities at myocardial biopsy

VF frequently recurs in these patients and shortly after the index event. Stress, vagal activity, and fever have been reported as precipitants of VF. In the study involving patients with IVF precipitated by vagal stimulation, transient late r'-waves and ST elevation in leads V1 through V3 before and after VF episodes were observed.

Therapy in idiopathic VF

EPS has been used to guide therapy in these patients. Patients with inducible VF at EPS, which is suppressible by class IA anti-arrhythmic drugs, may be candidates for long-term pharmacologic therapy.[60] Success has also been reported with a combination of amiodarone and mexiletine. The inducibility of VF at EPS does not predict future cardiac events. RF ablation has been successful in eliminating possible arrhythmogenic foci, the most common sites being the RVOT and Purkinje network.[61] Other sites such as the RV free wall have been identified using non-contact mapping. The procedure for ablation of RVOT foci triggering VF is similar to that used for RVOT VT. Clinically, patients with RVOT foci have frequent PVCs but few episodes of VF; the converse is true for patients with Purkinje foci. A family history of SCD has not been described for the RVOT VF patients compared with 25% of the Purkinje VF cases. The PVCs initiating from the RVOT show a wide QRS with a classic left bundle branch block inferior axis pattern. Ventricular ectopics originating from the Purkinje fibers are narrow when they originate from the left-sided Purkinje network, while those from the right side are usually monomorphic with an LBBB pattern (Figure 10.5).[62]

Activation mapping is performed to localize the earliest electrogram relative to the onset of the ectopic QRS complex identifying the Purkinje potential as a

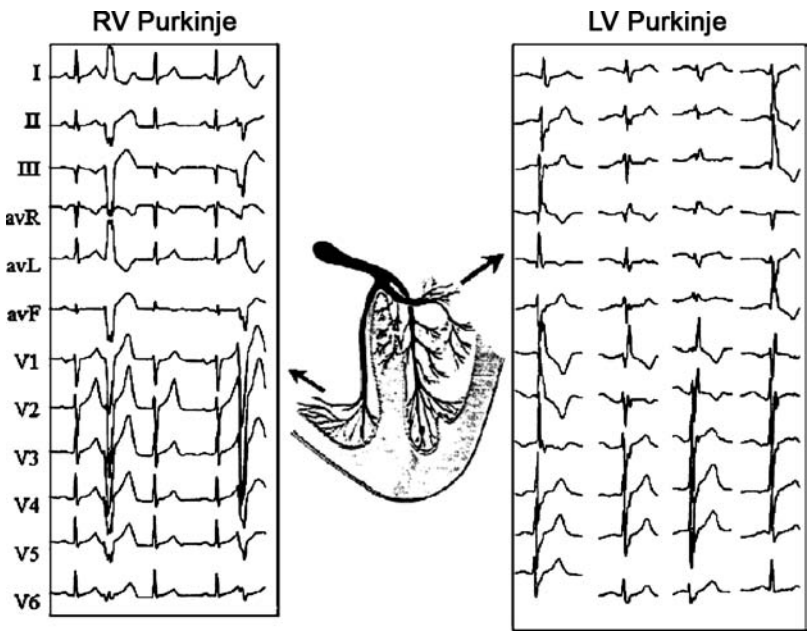

Figure 10.5 Localization of Purkinje fiber origin in idiopathic VF.[62]

sharp potential (< 10 ms in duration) preceding the ventricular electrogram during sinus rhythm as well as during ectopics. The absence of a Purkinje potential at the site of earliest activation indicates a muscular origin. The endpoint is the absence of premature beats and abolition of local Purkinje potentials in the area of origin.[63] However, the lethal consequence of an arrhythmic event can be averted only by the placement of a defibrillator. ICDs have been useful not only in preventing future cardiac events but providing a window on the events leading to VF. This retrospective analysis can guide better future therapy. Cardiac arrest survivors are candidates for ICD placement; device interrogation shows a 30% incidence of appropriate ICD therapy suggesting a high rate of recurrence.[64] No absolute recommendations can be made at this time regarding ICD placement as there are studies of patients without therapy who remained free of recurrences for over 45 ± 33 months.[65] *The concept of prophylactic ICD implantation cannot be applied to IVF as these individuals cannot be identified before the index episode of VF.* There are no clinical, electrocardiographic, or electrophysiologic variables that can help risk stratify patients with IVF. The use of non-invasive modalities such as body surface QRST integral mapping, monophasic action potentials, and computer simulation of a cardiac model have been reported in isolated case reports as useful in identifying high-risk patients. RVOT and the Purkinje network are the most common offenders generating PVCs triggering VF; the favorable outcome resulting from their ablation suggests molecular substrates in these areas that are not yet well defined. Better imaging and molecular mapping may unlock the door to better risk stratification and drug therapy in these patients.

CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA (CPVT)

CPVT is a rare idiopathic ventricular arrhythmia that arises as a consequence *of mutation in genes responsible for myocardial calcium handling*. Classically, the arrhythmias are triggered by *exercise or adrenergic stimuli*. The mutation in the *ryanodine 2 receptor* gene (RyR2) located on chromosome 1q42–43[66] leads to delayed afterdepolarization (DAD)-induced extrasystolic activity from defective calcium handling. The resulting transmural dispersion of repolarization provides the substrate for the development of re-entrant tachyarrhythmias.[67] The RyR2 gene shows AD inheritance. The *calsequestrin* (CASQ2) gene is also located on chromosome 1p13–21[68] and is responsible for AR inheritance. A familial occurrence has been observed in 30% of cases. Other unidentified genes are also believed to result in CPVT. The ryanodine receptor is located on the sarcoplasmic reticulum and allows the release of calcium into the cell, thus facilitating excitation contraction coupling in the myocardium. Calsequestrin gene mutations interfere with sarcoplasmic calcium storage. Abnormalities in RyR2 have been reported in patients with ARVC.[69] Patients with this subset have fatty infiltration of the RV myocardium. Genotype-phenotype analysis shows that patients with RyR2 mutation have events at a younger age than do patients with unknown mutations, resulting in CPVT, and that male gender is a risk factor for syncope.[70]

CPVT has an ominous course, with estimates of mortality ranging from 30 to 50% by the age of 20 to 30 years.[71] Most cases present in the *first or second*

decade, while delayed presentations are not unknown. The typical history is that of syncope induced by exercise or emotional stress. In some cases, the absence of symptoms or classical arrhythmias may warrant genetic testing as the only means to an early diagnosis. The absence of calsequestrin has been reported to result in severe CPVT, suggesting that the degree of the mutation correlates with the phenotype.[72] *Exercise testing, either on a treadmill or using Holter monitoring, is often sufficient to document the arrhythmia*. EPS has limited value in CPVT as the tachycardia is seldom inducible by programmed stimulation.[72] No specific electrophysiologic abnormality has been demonstrated. The different VT morphologies observed in these patients include polymorphic, polymorphic and bidirectional, bidirectional, or polymorphic with VF.[73] Exercise appears to be the best trigger although isoproterenol infusion has been used with success.[74,75] The typical pattern is the development of 'warm-up' PVCs followed by a sudden increase in the heart rate and onset of bidirectional and polymorphic VT. On cessation of exercise or isoproterenol infusion, there is prompt termination of the arrhythmia and development of 'cool-down' PVCs before restitution of sinus rhythm. Programmed stimulation often fails to elicit the arrhythmia or provide prognostic information. It is logical that such an arrhythmia would respond well to beta-blockers. However, variable success has been reported. Verapamil[76] has also been useful in some cases in blocking the excessive 'leakage' of calcium from the sarcoplasmic reticulum. Atrial pacing in addition to beta-blockers was necessary in a single case report to control CPVT (Figure 10.6).[77]

Implantable defibrillators are the only sure modality to prevent sudden cardiac death in these patients. Male patients with the RyR2 mutation who were noted to experience the highest rates of severe cardiac arrhythmic events may be the category that benefits most from ICDs. There are no studies at present regarding risk stratification of these individuals. Given the rarity of this disorder, it is difficult to carry out large-scale studies regarding natural history and risk stratification.

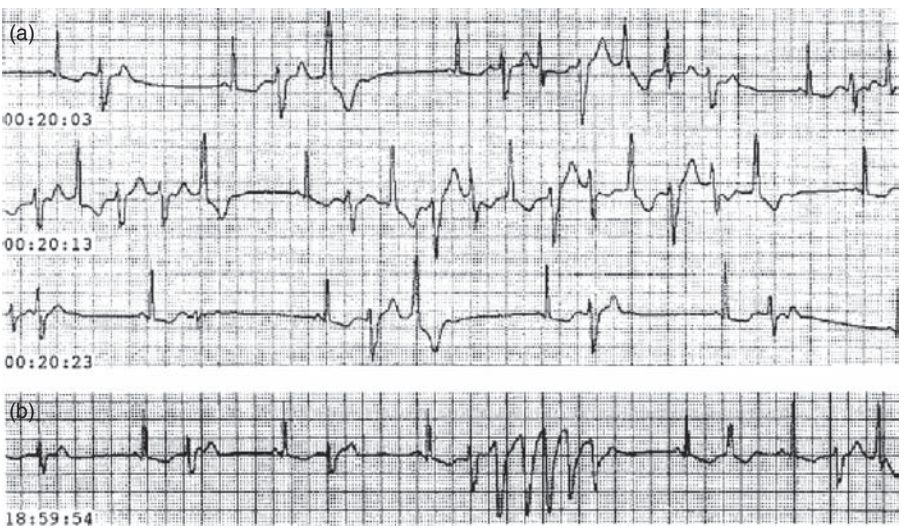

Figure 10.6 (a) Bidirectional ventricular ectopic activity and (b) non-sustained polymorphic VT.

Molecular and genetic analysis seem to be our best bet to better understanding these arrhythmias and possible prevention of unfortunate outcomes by timely intervention.

SUMMARY AND FUTURE DIRECTIONS

Ventricular tachycardias and ventricular fibrillation are seen with myriad electrical abnormalities in the 'structurally normal heart'. They can occur in the assumed 'electrically normal heart' as well as with idiopathic VF. The overlap in these various conditions (RVOT-VT and ARVC, CPVT and ARVC, long QT3 and Brugada syndrome) suggests that there is a common genetic/molecular thread that runs through all these conditions. The search for the 'Holy Grail' of risk stratification is an enduring task in these uncommon to extremely rare conditions. At the present time, the ICD seems to be our only sure means of defense in these conditions. Unfortunately, patients with some of these conditions manifest with an index episode of aborted sudden cardiac death before they can be identified. Further research will shed light on the mechanisms involved in these electrical abnormalities and may generate a unifying common pathway of arrhythmogenesis. This will also translate into better identifying therapeutic targets for pharmacologic intervention. In cases of idiopathic VF, identification of an electrical marker before the first cardiac event would be ideal. Developing better therapy for these unfortunate young patients aims at improving outcomes and extending survival.

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11

Idiopathic ventricular tachycardia

Atul Khasnis, Patrick Tchou, and Jennifer Cummings

INTRODUCTION

Idiopathic ventricular tachycardia (VT) is a broad term encompassing various arrhythmias arising from different anatomic regions of the structurally normal right and left ventricles. They are often benign and amenable to cure by radiofrequency ablation.

OUTFLOW TRACT VENTRICULAR TACHYCARDIA

Outflow tract ventricular tachycardia (OTT) can arise from the right or left ventricular outflow tracts (pulmonary or aortic outflow).

- RVOT VT is more common in females (2:1), LVOT VT is equally common in both genders.[1]
- OTT usually occurs in the third to fifth decade.

Presentation

RVOT VT has two predominant forms:

1. Repetitive monomorphic non-sustained VT and
2. Paroxysmal exercise-induced sustained VT.[2]

Mechanisms of outflow tract tachycardia

- cAMP-dependent triggered activity resulting in increased intracellular calcium concentrations (producing delayed after depolarizations);[3] this explains

tachycardia induction by exercise and isoproterenol[4] and response to beta-blockers and adenosine.[5]
- Re-entry.[6]
- Abnormal automaticity.[7,8]
- Sympathovagal imbalance (increased sympathetic influence).[9]
- TU wave changes.[10]
- Reduced presynaptic norepinephrine re-uptake and beta-adrenoceptor down-regulation due to increased local synaptic catecholamine levels caused by impaired catecholamine re-uptake.[11]
- Mutations in inhibitory G proteins.[12]

ECG in outflow tract tachycardias

The classic ECG pattern in OTT is bundle branch morphology (right with LVOT origin and left with RVOT origin) and inferior frontal axis (Figure 11.1). Various ECG algorithms have been described to attempt to precisely localize the origin of OTT and correlate with findings during pace mapping.[13–15] (Figure 11.2). Algorithms have also been developed to localize the origin of LVOT VT to above or below the aortic valve and further to the culprit aortic sinus, facilitating correct catheter placement for ablation[16,17] (Figures 11.2 and 11.3).

Imaging outflow tract tachycardias

MRI findings

MRI may be superior to echocardiography in detection of RVOT abnormalities:

- Fatty infiltration and wall motion abnormalities in some studies.[18]
- Morphologic changes of the RV free wall.

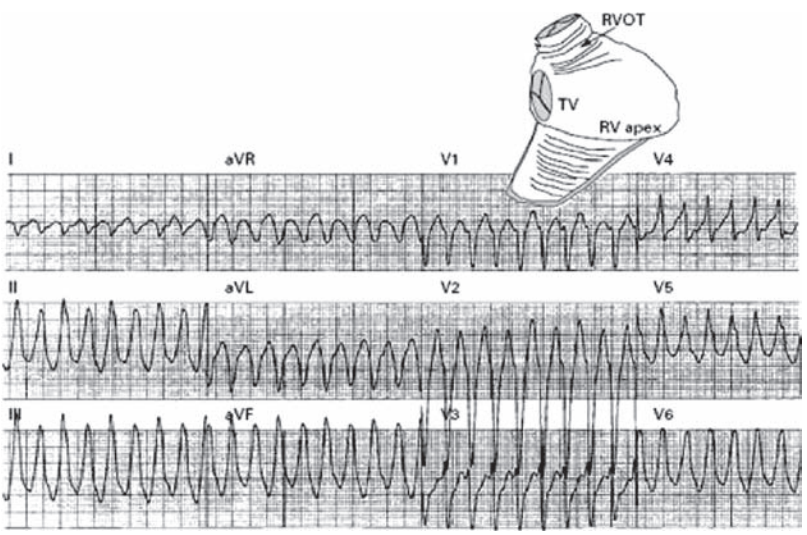

Figure 11.1 RVOT VT – typical origin and axis.

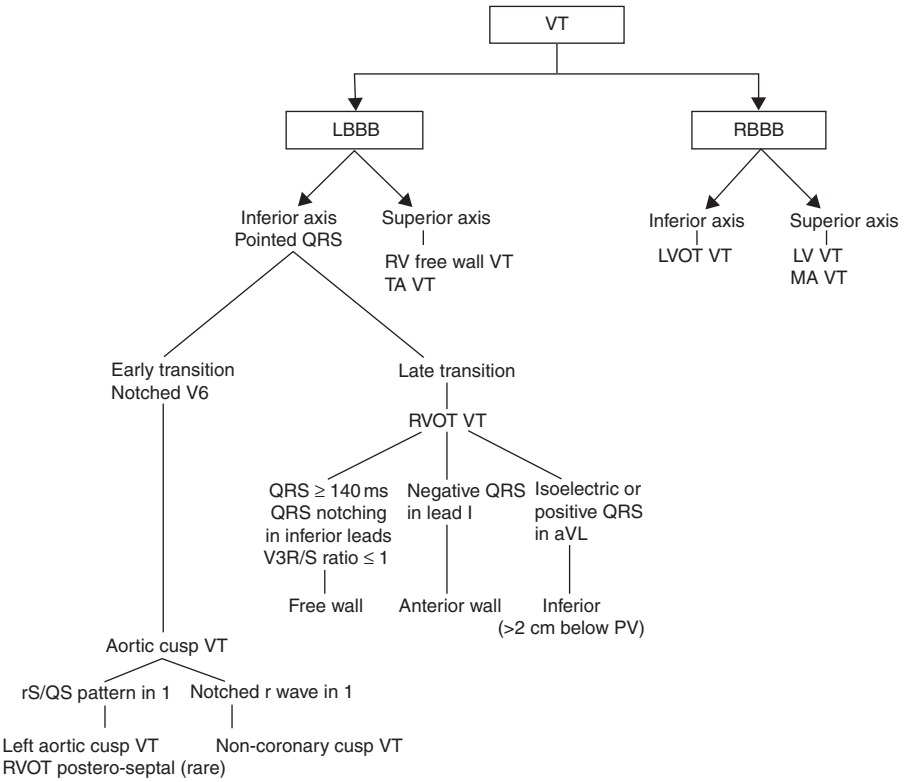

Figure 11.2 Localization of outflow tract tachycardia origin.

- Wall thinning.
- Dyskinetic wall segments.
- Additional fat deposits.
- Thinning and saccular aneurysm in the RVOT.[19]

Involvement of the outflow tract rather than the RV free wall correlates better with the presence of tachycardia.[20] Increased width of the RVOT has also been reported in patients with RVOT premature contractions.[21]

Echocardiography

An abnormal RV echocardiogram has been reported as both a sensitive (73%) and a specific (94%) indicator of an abnormal RV biopsy. Sustained VT on ECG is sensitive (90%) but has a low specificity (56%).[22] This is a chicken and egg situation between the RV abnormalities as a substrate for VT and VT-induced cardiomyopathy.

Tissue tracking ultrasound

Tissue tracking ultrasonography is a new modality being investigated in localization of the idiopathic VT focus.[23]

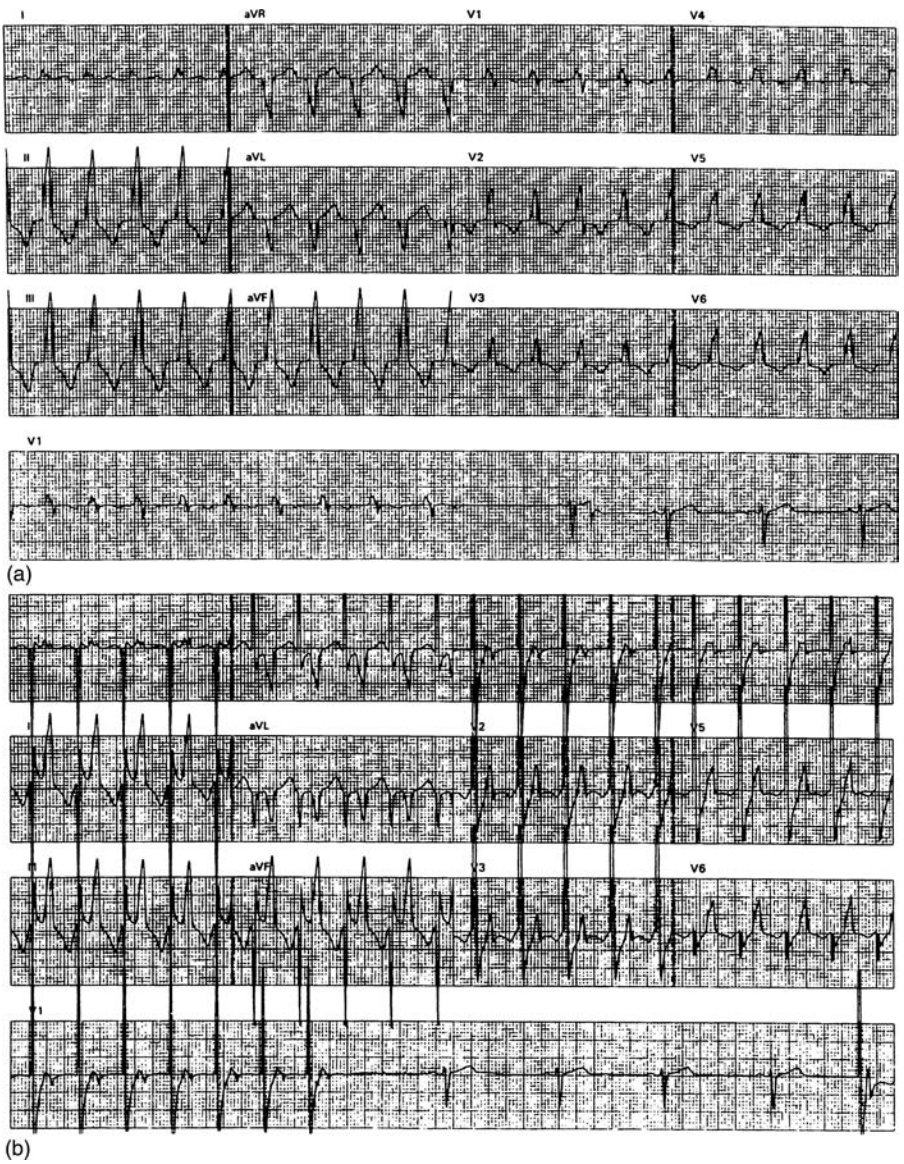

Figure 11.3 Pace mapping of LVOT VT.

Pace mapping

Pace mapping is performed prior to attempting OTT ablation. The use of a 'basket' multi-electrode catheter[24] and electroanatomic mapping (CARTO)[25] aid better precision in tachycardia focus localization.

Intracardiac echocardiography (Figure 11.4)

Intracardiac echocardiography (ICE) has also increased the accuracy of RF ablation.[26]

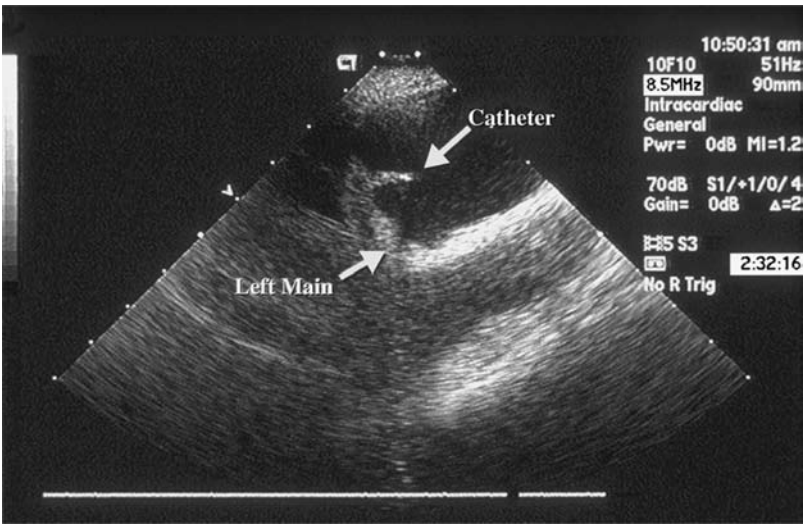

Figure 11.4 Use of ICE to guide catheter placement for ablation.

Ablation of outflow tract tachycardias

Radiofrequency energy is the commonest therapeutic source of energy used for successful ablation of OTT; successful cryocatheter ablation has also been reported.[27] Catheter ablation has a success rate of approximately 85% for RVOT VT.[28]

- *Predictors of unsuccessful ablation* include >1 induced VT morphology, a delta wave-like beginning of QRS, and VT/pace map correlation <11/12 leads.[29]
- VT with LBBB morphology, inferior axis, and early precordial transition (V2/V3) can be successfully ablated in the majority of patients from either the *left or the non-coronary aortic sinus* of Valsalva[30] (Figure 11.5).
- Tall R-waves in the inferior leads, R-wave in V1 and S-wave in V2, precordial R-wave transition in V2–4, deep QS-wave in aVL, absent S-wave in V6, and atypical LBBB morphology with inferior axis suggest an *epicardial origin* of the LVOT VT[31] (Figure 11.6). Successful epicardial ablation of these tachycardias has been reported.[32] Ablation in the region of the coronary cusps may be necessary where endocardial ablation is unsuccessful.[33]
- Other locations that have been successfully ablated include the RV septum *near the tricuspid valve and the LV septum*.[34]
- VT arising from the *mitral annulus* has a favorable outcome with RFA.[35]
- RVOT may co-exist with AVNRT; both have been concomitantly successfully ablated.[36]

Medical therapy

In patients who are not candidates for ablation, who have failed ablation, or who are unwilling, both calcium-channel blockers and beta-blockers are useful.[37] Outflow tract tachycardias are often amenable to potentially curative ablation and this option should be offered to these patients.

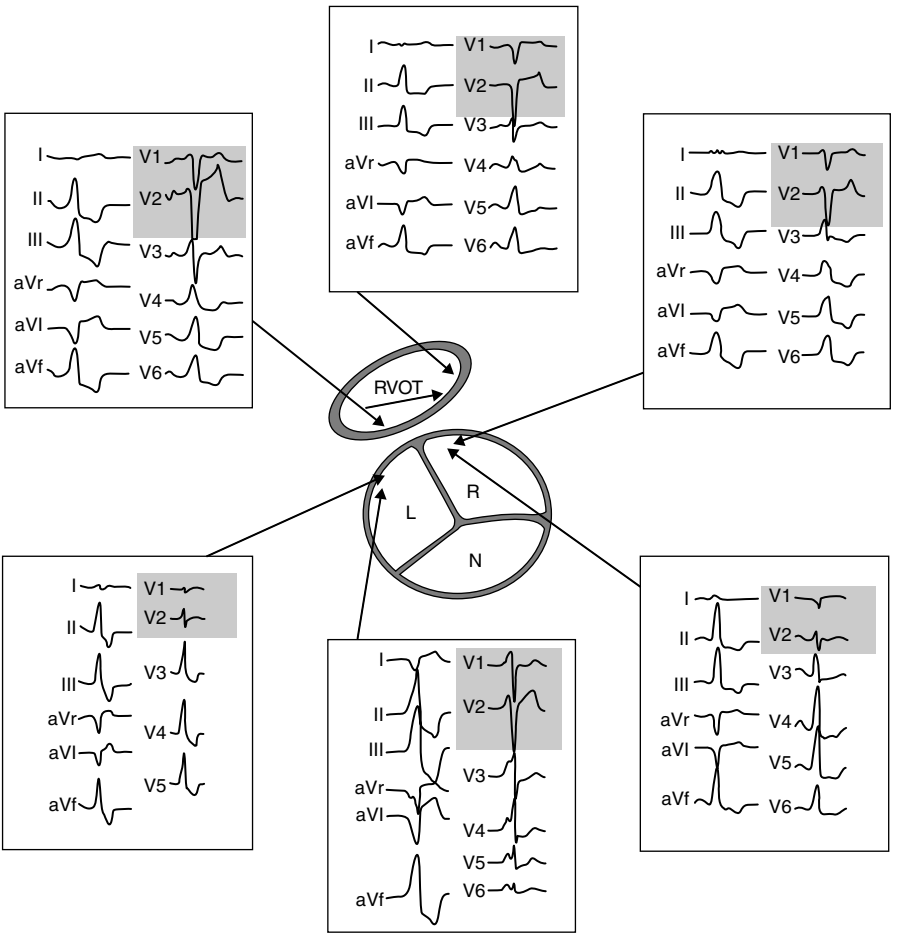

Figure 11.5 RVOT VT origin localization before ablation.

IDIOPATHIC LEFT VENTRICULAR TACHYCARDIA

Idiopathic left ventricular tachycardia (ILVT) based on pharmacologic responses can be:

1. Verapamil sensitive (re-entrant)
2. Adenosine sensitive (triggered activity)
3. Propranolol sensitive (automaticity).

Verapamil-sensitive fascicular tachycardia is the most prevalent form; it can be entrained during pacing and may be mediated by re-entry. Belhassen et al first reported the verapamil sensitivity of this tachycardia.[38] *Adenosine-sensitive fascicular tachycardia* behaves like RVOT VT, is thought to be from cAMP-mediated triggered activity, originates from deep within the interventricular septum, and exits from the left side of the septum. *Propranolol-sensitive fascicular VT* is suspected

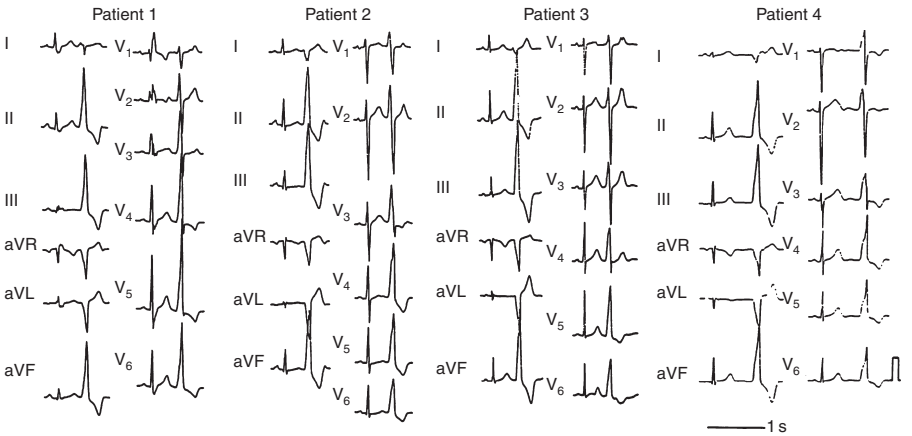

Figure 11.6 Epicardial origin of LVOT VT.

to be from abnormal automaticity.[39] The exact re-entrant circuit for verapamil-sensitive fascicular VT is reported to involve the Purkinje fiber network. *Pre-Purkinje potentials* have been observed and appear to be indicators for successful ablation sites.[40]

The presence of a *false tendon in the LV* extending from the posteroinferior left ventricular free wall to the left ventricular septum has been observed as anatomic substrate and also a suitable site for successful catheter ablation[41,42] (Figure 11.7). Diastolic potentials have been observed in the false tendon, suggesting it is the site of slow conduction.[42] Other studies have exonerated the posterior fascicle of the LBB from participating in the re-entry circuit.[43] Fascicular ILVT can originate from the left anterior fascicle as well.[44] Some studies show verapamil-sensitive ILVT to be a heterogeneous entity with a wide range of electrophysiologic characteristics.[45] The unique responsiveness of some isoproterenol-induced ILVT to adenosine (otherwise insensitive) has strongly implicated cAMP as a mediator of this subset of tachycardia.[46]

ILVT has also been divided into three types based on the ECG pattern (Figure 11.8):

1. Left posterior fascicular VT with a right bundle branch block (RBBB) and superior axis configuration (common form).
2. Left anterior fascicular VT with RBBB and right-axis deviation configuration (uncommon form).
3. Upper septal fascicular VT with a narrow QRS and normal axis configuration (rare form).[47]

Rarely, RBBB morphology with a dual axis (superior and inferior) has been reported in a single patient with ILVT.[48]

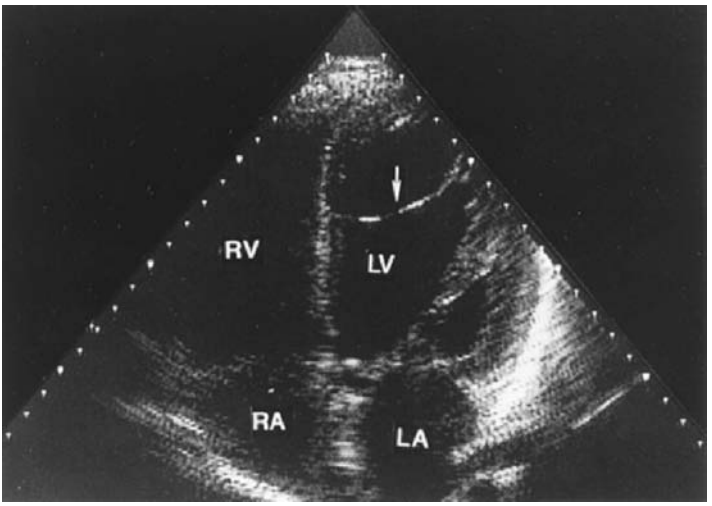

Figure 11.7 False tendon in the LV in ILVT.

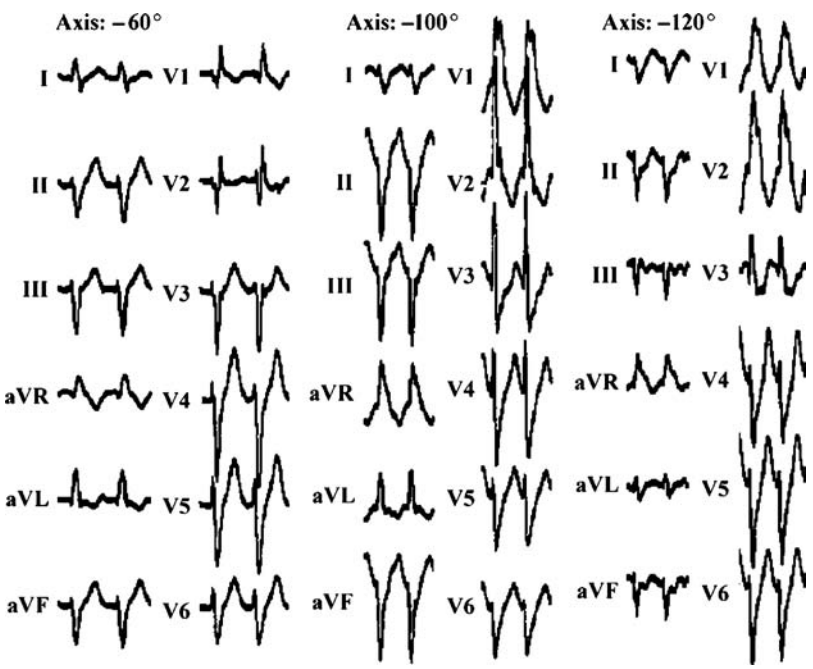

Figure 11.8 ILVT classification based on the ECG axis.

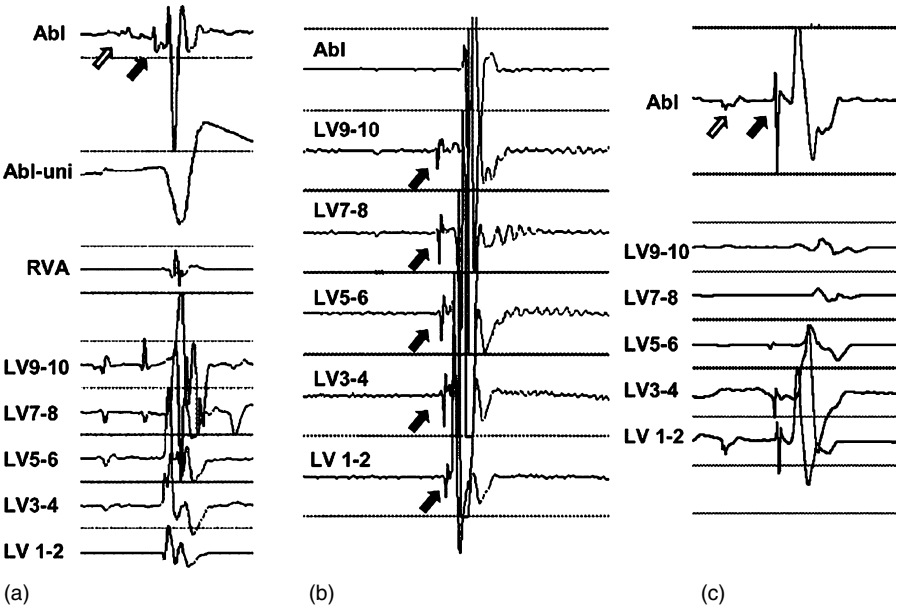

Figure 11.9 Pre-Purkinje potential in patients with ILVT.

Ablation of ILVT

ILVT is effectively treated by RF ablation. The presence of diastolic potentials and the pre-Purkinje potentials provide reliable guidance to ablation sites in the LV for ILVT.[49,50] The earliest Purkinje potential (with or without the concomitant use of diastolic potentials) may be superior for selection of the target site of RF ablation in patients with ILVT[51] (Figure 11.9). Non-contact mapping has also been used to ablate ILVT.[52,53] The long-term success of ILVT ablation varied from 83 to 100% in a small series of followed-up patients.[54,55] Radiofrequency ablation is safe and effective for patients with ILVT. Most patients remain free of recurrences at long-term follow-up.

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Section VI

Syncope

12

Syncope events, definitions, causes, and features

Subramanya Prasad, Oussama Wazni, Mina Chung, and Robert Schweikert

Introduction • Definition • Nomenclature in syncope • Scope of the problem • Pathophysiology • Cerebral autoregulation • Causes and clinical features of transient loss of consciousness (TLOC) • True syncope • Non-syncopal conditions (syncope mimics)

INTRODUCTION

- Syncope is a common clinical problem both in the outpatient and the in-hospital setting.[1] It has been estimated that approximately one-third of individuals experience a syncopal episode during their lifetime,[2] with a 30% recurrence rate.[3]
- Though most syncopal episodes are benign and self-limiting, it can be a presenting symptom of organic heart disease, and accounts for significant injuries in 35% of patients.[4]
- This chapter provides a comprehensive overview of the definition, pathophysiology, classification/causes including clinical features, and initial management.

DEFINITION

- Syncope (Greek origin where 'syn' means with and 'kopto' means cut or interrupt) is defined clinically as a relatively rapid, transient loss of consciousness (LOC) and postural tone followed by complete, spontaneous recovery.
- Presyncope or near-syncope refers to a condition in which syncope is felt to be imminent without LOC.

NOMENCLATURE IN SYNCOPE

- A lack of consensus in syncope-related terminology makes the interpretation of early syncope literature confusing. Table 12.1 lists the guidelines regarding acceptable terminology in syncope issued by the ESC[5] and ACC.

Table 12.1 Acceptable syncope terminology with explanation

Term	Description/recommended terminology
Breath holding spells/ reflex anoxic seizure	They represent a form of VVS in infants. 'Infantile vasovagal syncope' is preferred
Classical vasovagal syncope	Should be reserved for neurally mediated/reflex syncope initiated by triggers (pain, emotional or orthostatic stress, instrumentation)
Convulsive syncope	This term should be used as an abbreviated description of 'syncope accompanied by myoclonic jerks and other involuntary movements'; the term does not imply epilepsy
Drop attacks	Should be strictly restricted to sudden loss of lower extremity tone without LOC
Dysautonomia/ dysautonomic	Should be reserved for Riley-day syndrome
Hyperventilation syncope	Currently it is unclear if hyperventilation can cause syncope. Syncopal symptoms attributable to hyperventilation fall under 'panic attacks' in DSM-IV
Neurally mediated syncope (NMS)	NMS and reflex syncope are synonyms
Neurogenic syncope	NMS is preferred
Neurocardiogenic syncope	Since the term emphasizes the origin of reflex in the heart, it should be strictly used for a putative type of reflex syncope where the trigger is in the heart
Orthostatic intolerance	Erroneously used as synonyms for POH and POTS. Strict restriction of the term to describe patient complaints only is advised
Presyncope	Should be used to describe a collective constellation of symptoms due to compromised CBF, and diminished cortical functioning (dizziness, lightheadedness, blurred vision). Though headache and shoulder pain, sweating and nausea, and paresthesias can occur before syncopal onset, they are not linked to LOC
Psychogenic syncope	Pseudosyncope or psychogenic pseudosyncope is preferred, implying the lack of cerebral hypoperfusion among these patients (factitious disorders, malingering, and conversion)
Seizures	Strictly restricted for epilepsy
Transient LOC (TLOC)	Should be used when 4 criteria are satisfied: LOC Transient Self-limited Absence of head or brain injury
Vasodepressor syncope	Should be used in syncope when a vasodepressor response is seen without an associated cardioinhibitory response

VVS, vasovagal syncope; LOC, loss of consciousness; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; POH, postural orthostatic hypotension; POTS, postural orthostatic tachycardia syndrome; CBF, cerebral blood flow

SCOPE OF THE PROBLEM

- Syncope is a common presenting problem accounting for 3 to 5% of emergency room visits and 1 to 3% of hospital admissions,[2] with an incidence of 3% (men) and 3.5% (women) in the general population.[2]
- Susceptibility to syncope increases with advancing age,[2,6] with a 6% annual incidence and a recurrence rate of 30% among the institutionalized elderly.

- The annual cost of evaluating and treating patients with syncope in the USA is estimated to be 800 million dollars.[7]
- Patients at high risk of recurrent syncope require hospitalization, with diagnostic studies averaging $5281 per patient (1993 dollars).[7] Table 12.2 shows the cost of investigations in syncopal patients.

PATHOPHYSIOLOGY

- The pathophysiology of syncope is complex and incompletely understood.
- *In healthy humans*, assumption of the upright posture causes peripheral venous and splanchnic pooling, displacing 500–800 ml of blood (within the first 10 s), thus reducing preload.[5,8]
- The reducing preload stimulates the central arterial baroreceptor system (carotid body, aortic arch) and cardiopulmonary mechanoreceptors.[9,10]
- The cardiopulmonary mechanoreceptors (inferoposterior wall of the left ventricle and the chest wall) stimulate the brainstem (nucleus ambiguous and dorsal vagal nucleus), causing augmented sympathetic activity and parasympathetic withdrawal.[9,10]
- The resulting increase in circulating catecholamines causes compensatory vasoconstriction of the splanchnic, musculocutaneous, and renal vascular beds, thus maintaining systemic arterial pressure and cerebral perfusion.[10]
- *In neurally mediated syncope (NMS) susceptible individuals*, hypoactive neurocardiovascular reflexes along with a diminished central blood volume result in a reduced preload.
- A reduced preload triggers a paradoxic reflex vasodilatation and bradycardia, mediated by enhanced parasympathetic activity and sympathetic withdrawal.[11] Inadequate vasoconstriction or inappropriate vasodilatation may play a critical role in mediating hypotension seen in the reflex syncopal syndromes.[5]
- Vasomotor center (VMC) stimulation is believed to cause most of the prodromal symptoms (diaphoresis, nausea, vomiting) accompanying NMS.
- The mechanism of syncope in an individual patient could be multi-factorial. In addition to venous pooling and decreased central volume, decreased cardiac output and an inability to increase vascular resistance during upright posture can play significant roles in the causation of syncope.
- In contrast to other viscera, the metabolism of the brain is largely dependent on adequate perfusion. In healthy young to middle-aged individuals, the average cerebral blood flow (CBF) is 50 to 60 ml/min/100 g tissue.
- In the young healthy cerebrovascular bed, cerebral autoregulation maintains the average CBF over a wide range of blood pressures, thus maintaining adequate cerebral O_2 requirements (3.0–3.5 ml O_2/100 g tissue/min) (Figure 12.1).[12,13]
- An abrupt reduction in CBF for 6–8 s is enough to produce reduced blood flow to the reticular activating system, resulting in complete loss of consciousness.[14] Lesser periods of reduced CBF result in presyncope or near-syncope.
- Cerebral autoregulation can be compromised due to increasing age or underlying disease, thus reducing the safety margin for oxygen delivery. Aging alone causes a 25% reduction in CBF, among individuals aged 20–70 years.[15] Hence a small drop (as low as 20%) in cerebral oxygen delivery is sufficient to cause loss of consciousness.[4]

Table 12.2 Clinical features of true syncope and syncope mimics

Type of syncope	Specific syndromes	Clinical features/comments	Diagnostic criteria
DISORDERS WITH True LOC			
Neurally mediated (reflex) $	Vasovagal syncope * (common faint) classic non-classic Carotid sinus syncope Situational syncope acute hemorrhage cough *, sneeze gastrointestinal and/or genitourinary stimulation (swallowing *, defecation #, visceral pain, endoscopy, bladder catheterization) micturition (post-micturition) * postexercise postprandial # others (e.g., brass instrument playing, weightlifting) Glossopharyngeal neuralgia #	NMS: Absence of cardiac disease Long history of syncope After unpleasant sight, sound, smell or pain Prolonged standing or crowded, hot places Nausea, vomiting associated with syncope During or in the absorptive state after a meal With head rotation, pressure on carotid sinus (as in tumors, shaving, tight collars) After exertion	VVS is diagnosed if precipitating events such as fear, severe pain, emotional distress, instrumentation, or prolonged standing are are associated with typical prodromal symptoms Situtional syncope is diagnosed if syncope occurs during or immediately after urination, defecation, cough, or swallowing
Orthostatic hypotension $	Autonomic failure primary autonomic failure syndromes (e.g., pure autonomic failure, multiple system atrophy, Parkinson's disease with autonomic failure) secondary autonomic failure syndromes (e.g., diabetic neuropathy *, amyloid neuropathy) postexercise postprandial Drug (and alcohol)-induced orthostatic syncope	After standing up Temporal relationship with start of medication leading to hypotension or changes of dosage Prolonged standing, especially in crowded, hot places Presence of autonomic neuropathy or Parkinsonism After exertion	POH is diagnosed when there is documentation of POH associated with syncope/ presyncope. Orthostatic BP measurements are recommended after 5 minutes of lying supine, followed by measurements each minute, or more often, after 3 minutes of standing. Measurements may be continued longer if BP is still falling at 3 minutes.

	Volume depletion * Hemorrhage, diarrhea, Addison's disease		If the patient does not tolerate standing for this period, the lowest BP in the upright posture is recorded A decrease in SBP ≥20 mmHg or a decrease in SBP to <90 mmHg, is defined as POH, regardless of occurrence of symptoms[57]
Cardiac arrhythmias as primary cause (see Table 12.5)	Sinus node dysfunction (including bradycardia/tachycardia syndrome) * Atrioventricular conduction system disease (AV block) *, myocardial ischemia, medications * (digoxin, beta-blockers, verapamil), hypertension, valvular heart disease, cardiomyopathy Paroxysmal supraventricular (accessory pathways) (SVT) and ventricular tachycardias (VT) Inherited syndromes (e.g., long QT syndrome # , Brugada syndrome, ARVD #) Implanted device (pacemaker, ICD) malfunction Drug-induced pro-arrhythmias (digoxin, inotropes, drugs causing QT prolongation)	Presence of severe structural heart disease During exertion, or supine Preceded by palpitation or accompanied by chest pain Family history of sudden death	Arrhythmia-related syncope is diagnosed by ECG when there is • sinus bradycardia < 40 beats/min or repetitive sinoatrial blocks or sinus pauses > 3s • Mobitz II 2nd or 3rd degree AV block • Alternating LBBB and RBBB • Rapid paroxysmal SVT or VT • Pacemaker malfunction with cardiac pauses
Structural cardiac or cardiopulmonary disease (see Table 12.5)	Arrhythmias, supraventricular # and ventricular tachycardia * Acute myocardial infarction/ischemia Obstructive cardiac valvular disease (aortic stenosis *, mitral stenosis)	Presence of severe structural heart disease During exertion, or supine Preceded by palpitation or accompanied by chest pain Family history of sudden death	Myocardial ischemia-related syncope is diagnosed when symptoms are present with ECG evidence of acute ischemia with or without

(Continued)

Table 12.2 (Continued)

Type of syncope	Specific syndromes	Clinical features/comments	Diagnostic criteria
	Hypertrophic obstructive cardiomyopathy *, non-ischemic cardiomyopathy with low EF Atrial myxoma # Acute aortic dissection Pericardial disease/tamponade Pulmonary embolus #/pulmonary hypertension #		myocardial infarction, independently of its mechanism
Cerebrovascular disease	Vascular steal syndromes #, migraine # Vertebrobasilar TIA	With arm exercise Differences in blood pressure or pulse in the two arms Vertebrobasilar system TIAs (vertigo, ocular palsy, and dysarthria) caused by atherosclerotic narrowing or extrinsic compression (cervical spondylosis, cervical rib) should be considered if syncope/presyncope is associated with extension or lateral rotation of the neck Subclavian steal syndrome (subclavian artery narrowing at its origin, accounts for < 0.1% of all syncopal episodes[1]) or severe carotid artery disease (atherosclerotic disease, Takayasu's disease) can cause syncope. Syncope or dizziness can be seen during upper extremity exercise due to shunting of blood from the brain via the vertebral artery system to the affected limb Extracranial vasospasm seen during migraine can cause NMS	

* Major common causes; # major uncommon causes; $ NMS and POH account for 33% of all syncopal episodes.

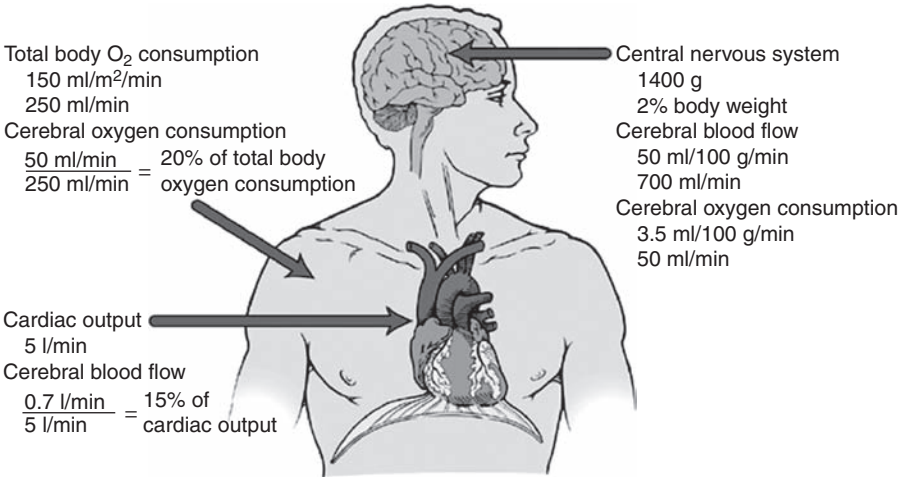

Figure 12.1 Cerebral blood flow as a function of cardiac output.

CEREBRAL AUTOREGULATION

- Adequate cerebral perfusion is largely dependent on systemic arterial pressure and cerebral autoregulation (maintenance of cerebral blood flow over a relatively wide range of mean arterial pressures).
- In the presence of hypertension, the autoregulatory curve is shifted higher, requiring higher arterial pressures to maintain perfusion (Figure 12.2). A decrease in systolic blood pressure $\leq$60 mmHg is associated with syncope.[16]
- Though cerebrovascular autoregulation is largely controlled by local metabolic and chemical mediators ($pCO_2 > 20$ mmHg and <80 mmHg, pH, and $pO_2 <50$ mmHg), baroreceptor responses to changes in systemic arterial pressure play a minor role. These mechanisms are deregulated among the elderly or critically ill patients.[16]
- Presyncope/syncope seen during panic attacks/hyperventilation syndromes is due to reduced CBF, probably secondary to low pCO_2-induced vasoconstriction.

CAUSES AND CLINICAL FEATURES OF TRANSIENT LOSS OF CONSCIOUSNESS (TLOC)[5]

- Clinicians approaching patients with TLOC have to differentiate true syncope from 'non-syncopal' conditions (syncope mimics) to help decide further management.
- A thorough history and a focused physical examination (orthostatic blood pressure measurements and a standard ECG) are usually sufficient to identify the probable cause of syncope in 75% of patients.[17,18]
- In the outpatient/emergency setting, non-cardiac syncope is the commonest cause. In the in-hospital setting, cardiac causes are the most common. A list of the causes and clinical features of true syncope and syncope mimics is seen in Table 12.2.

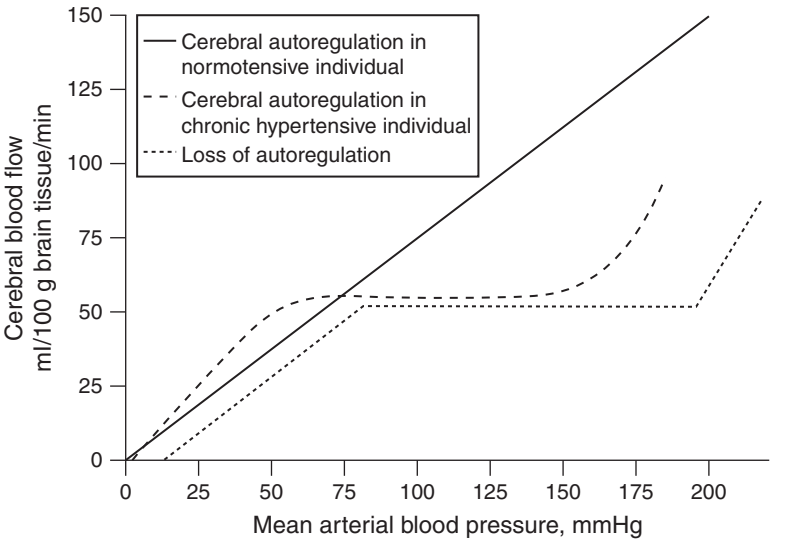

Figure 12.2 Cerebral autoregulation.

TRUE SYNCOPE

Neurally mediated syncopal syndromes (NMSs)

- NMS is the most common variety of syncope among all age groups.
- Though NMS occurs in response to a variety of triggers they share a common pathophysiologic basis.
- Among NMS, vasovagal syncope (VVS) and carotid sinus hypersensitivity (CSH) are the most common types.

Vasovagal syncope

- VVS is the most common form of syncope among the young and the elderly, with a benign and self-limited course.
- Various triggers induce VVS through
  - Neural (Bezold–Jarisch and carotid sinus) reflexes.
  - Neuroendocrine (chemical) pathways.

Neural reflexes (Figure 12.3)

- *Bezold–Jarisch reflex* – mechanoreceptors located in the atria, great veins, left ventricle, and thoracic wall are activated in response to pressure or volume loading, which stimulates afferent C fibers.[19] This activates vagal efferents to induce a cardioinhibitory response and reduce BP.
- *Carotid sinus reflex* – as above, mechanical stimulation (CSM) or increased BP increases baroreceptor firing (carotid sinus and aortic arch), activating vagal efferents.

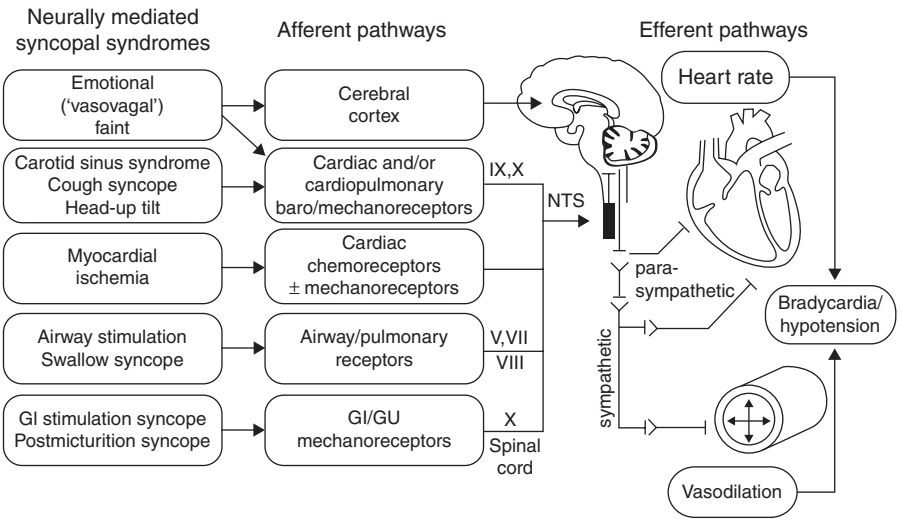

Figure 12.3 Schematic diagram showing the various triggers of NMS syndromes, the afferent and efferent pathways. NTS, nucleus tractus solitarius; V, VII, VIII, IX, and X are cranial nerves.

Neural mechanisms of VVS

- Afferent neural signals originating centrally (CNS in anxiety) or peripherally (baroreceptors, mechanoreceptors, and chemoreceptors) stimulate the VMC.[11,19]
- The vagal efferents mediate bradycardia whereas sympathetic withdrawal mediates vasodepression.[20]
- In classic VVS, prodromal symptoms followed by a vasodepressor and cardioinhibitory (sinus bradycardia to AV block to asystole; Figure 12.4) response are seen in that order.
- Clinically, atypical VVS (absent prodrome with a mixed response) is more common. Interestingly, all three response patterns can be seen in the same patient at different times, and the clinical pattern may differ from the head-up tilt (HUT) response.

Neuroendocrine mechanisms of VVS

- *Central serotoninergic pathways* – these appear to have a role in the pathogenesis of neurocardiogenic syncope. Animal studies have shown that elevated extracellular serotonin levels can inhibit central sympathetic activity responsible for the cardioinhibitory and vasodepressor response of VVS.[21]
- *Adenosine (ATP)* – ATP is a potent AV node depressant with significant negative inotropic and vasodepressor effects.[22] Intravenous administration of ATP can induce VVS and has been used as a pharmacologic adjunct in HUT testing.
- Though recent studies measuring multiple neurohumoral markers (norepinephrine, endothelin, prolactin, cortisol, renin, vasopressin, beta-endorphins, and substance P) have reported differential changes in serum levels during HUT testing, their pathophysiologic significance is unclear at the present time.[23,24]

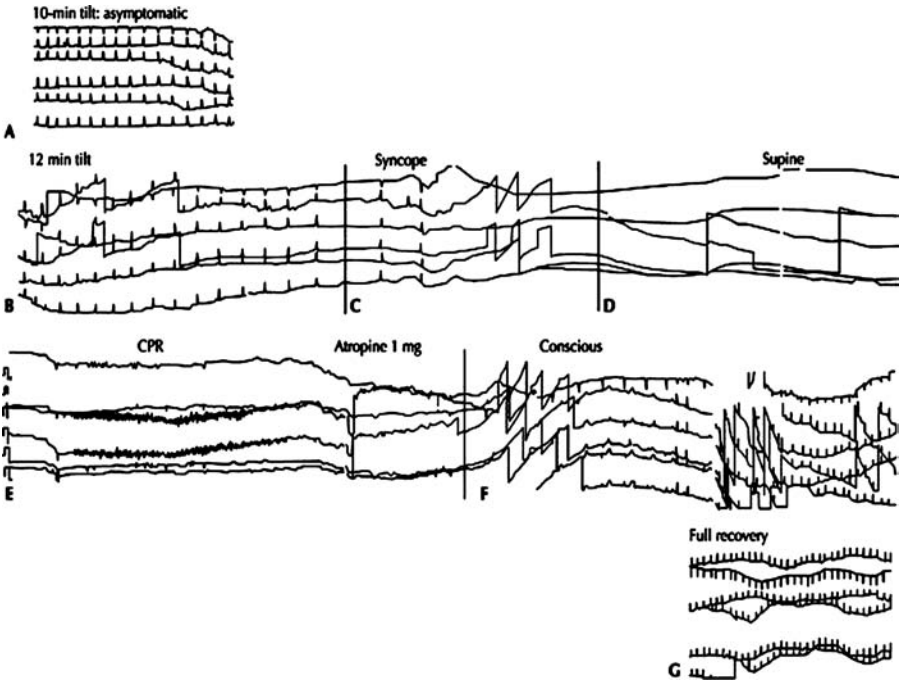

Figure 12.4 ECG recorded during vasovagal syncope. CPR, cardio-pulmonary resuscitation.

Clinical features

- VVS is commonly encountered in crowded warm places. A typical history includes prodromal symptoms (absent in elderly) followed by partial or complete LOC.
- With the exception of pallor, the physical exam is usually benign. Complete recovery is usual although fatigue and nausea may persist for several minutes. Table 12.2 lists the salient clinical features of the various causes of syncope.

Situational syncope

- This applies to the group of NMSs initiated by specific triggers. The most common types are cough, deglutition, defecation, and postprandial syncope. Table 12.3 lists their salient features and pertinent management.
- Most of them result in a cardioinhibitory response (sinus bradycardia, sinus arrest, and AV block). Treatment involves removal or avoidance of the trigger responsible for syncope. When anticipated (e.g. diagnostic endoscopy), prophylactic atropine administration can prevent syncope.

Carotid sinus hypersensitivity (CSH)

- CSH is a syndrome with manifestations very similar to NMS (Table 12.2).
- Carotid sinus stimulation by triggers (washing of the face, shaving, head and neck movements) sends afferent neural signals, mainly from the cervical area

Table 12.3 Clinical features of situational syncopal syndromes

Situational syncope	Clinical features and comments
Cough syncope	Follows a vigorous coughing spell Increase in CSF pressure causes increased cerebrovascular resistance, reducing CBF[25] Cessation of smoking and bronchodilators are useful
Deglutition syncope	Dysphagia induces vagal stimulation, especially in the setting of esophageal disorders (tumors, diverticulum, achalasia, stricture, and diffuse spasm), and with instrumentation (EGD, bronchoscopy) Syncope is due to cardioinhibition
Postprandial syncope	Presyncope/syncope due to hypotension during the postprandial period is common in the elderly Unclear mechanism, most likely explanations are meal-induced splanchnic pooling with an inadequate sympathetic compensation, inadequate postprandial increase in cardiac output, and release of gastrointestinal peptides In a study of 113 elderly nursing home residents, 36% (41/113) showed a one-hour postprandial SBP decrease of 20 mmHg[26] Octreotide infusion has been shown to be effective in reducing postprandial syncope[27]
Defecation syncope	It is commonly seen among elderly people with bowel movements during the night or during manual fecal disimpaction.[28] Many such patients have underlying gastrointestinal malignancy
Valsalva syncope	Forced exhalation against a closed glottis (Valsalva maneuver) can cause peripheral venous pooling and syncope[2] Valsalva syncope can be a harbinger of syncope due to SND or cerebrovascular occlusive disease. Avoiding sustained Valsalva maneuvers can prevent recurrences
Micturition syncope	LOC following urination is commonly seen in patients with nocturia, with consumption of large quantities of beverages, also following drainage of a distended urinary bladder and abdominal paracentesis[29]

(including the ipsilateral sternocleidomastoid) causing cardioinhibitory and vasodepressor responses.

- It is usually seen in men >40 years.[5,30] Prodromal symptoms are usually absent. Two large studies of HUT testing in NMS patients showed a 6–14% incidence of CSH.[4]
- A diagnosis is made by performing carotid sinus massage (CSM), both supine and during a HUT. A fall in systolic blood pressure (SBP) $>$ 50 mmHg or a pause (asystole) $\geq$ 3 s along with symptom reproduction is considered diagnostic of CSH (Figure 12.5).
- During HUT, even though the predominant response is cardioinhibitory, identifying an underlying vasodepressor component can significantly affect management. This can be identified by repeating the HUT after correction of bradycardia (atropine or temporary pacing).

Postural orthostatic hypotension (POH)

- Orthostatic hypotension is defined as a decrease of 20 mmHg in systolic blood pressure, and a 10 mmHg decrease in diastolic blood pressure within 3 minutes

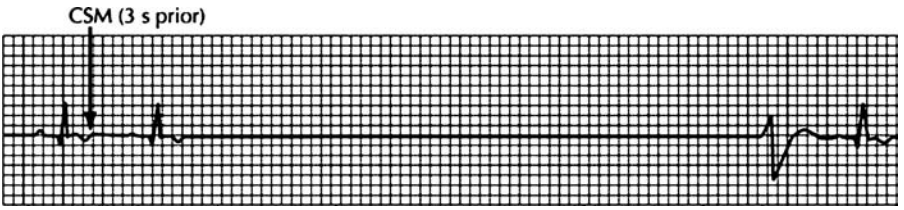

Figure 12.5 Asystole scene CSM. ECG strip of an elderly male showing prolonged asystole following CSM during HUT testing.

of change in posture (recumbent to standing/sitting)[33] or an SBP $<$ 90 mmHg, with or without symptoms.[5]
- Measurement of BP should be done after 5 minutes of lying supine, and after 3 minutes of standing (see Table 12.2).
- POH is usually seen in the early morning hours or following prolonged recumbency. Symptoms of presyncope are seen, while bradycardia, sweating, and pallor are usually absent.
- The most common causes of POH are intravascular volume depletion (transient or chronic) and/or autonomic failure (primary or secondary). Table 12.4 lists the various causes of POH and its salient features.

Cardiac causes

Cardiac causes include arrhythmias and structural heart disease. Tables 12.5 and 12.6 list the various conditions.

Cardiac arrhythmias as a primary cause

- Cardiac arrhythmias are among the most common and potentially hazardous causes of syncope.
- Though hypotension due to arrhythmia (tachycardia/bradycardia) can be obvious, other mechanisms (depressed ventricular function, altered volume status, and impaired vascular reactivity) can be present which can be deciphered by HUT testing.

Cerebrovascular disease

- Cerebrovascular disease is an infrequent cause of syncope. Table 12.2 lists the various conditions with salient features.

NON-SYNCOPAL CONDITIONS (SYNCOPE MIMICS)

- Non-syncopal conditions are several disorders without true LOC (no cerebral hypoperfusion). Table 12.7 lists the syncope mimics and their salient features.

Table 12.4 Causes of POH

Syndrome	Causes	Clinical features/comments
Primary autonomic failure	Pure autonomic failure (Bradbury Eggleston syndrome), POH, widespread autonomic failure (fecal and urinary incontinence, defective sweating and sexual function) decreased supine norepinephrine levels Autonomic failure with multiple system atrophy (Shy–Drager syndrome), autonomic dysfunction, parkinsonism, ataxia Parkinson's with autonomic failure	Autonomic failure is defined as an inadequate vasomotor reflex adaptation to orthostatic challenge; can be primary or secondary
*Secondary autonomic failure	Diabetes mellitus *Volume depletion (gastroenteritis, hemorrhage), third space losses (adrenal insufficiency, diabetes insipidus or hyperglycemia), medications antihypertensives, diuretics, nitrates, beta-blockers Autoimmune (Guillian–Barre syndrome, myasthenia gravis) Malignancy-induced autonomic neuropathy Metabolic (porphyria, Fabry's disease) CNS infections (syphilis, chagas) Hypothalamic and midbrain tumors/lesions (craniopharyngioma) Spinal cord lesions/tumors Prolonged physical inactivity associated with lengthy hospitalization	Volume depletion (mostly due to medications) is a common cause of orthostatic syncope. Medications are the most common causes of POH, especially in the elderly due to (1) reduced baroreceptor sensitivity, (2) reduced CBF, (3) renal sodium wasting, and (4) an impaired thirst mechanism[31]
Drug/toxin-induced autonomic failure	Alcohol Diuretics Sedative/tranquilizers: phenothiazines, barbiturates Vasodilators ACE inhibitors Tricyclic antidepressants	
Acute autonomic failure	Rare acute pan-autonomic failure with POH, fecal and urinary incontinence, chronotropic incompetence, and fixed dilated pupils[32]	
Postural orthostatic tachycardia syndrome (POTS)	Thought to be a chronic form of autonomic failure, probably due to lack of peripheral vasoconstriction during an orthostatic challenge or ineffective norepinephrine clearance in the synaptic cleft (norepinephrine re-uptake gene mutation is shown in POTS patients' family members[33])	Characterized by ≥28 beats/min increase above the resting heart rate within 5 min of upright posture[5]

* Most common types

Table 12.5 Clinical features of arrhythmic causes of syncope

Class	Causes, clinical features	ECG and diagnosis	Comments
Cardiac arrhythmias			
Sinus node dysfunction (SND)	*Medications chamber enlargement, ANS influences, fibrosis Chronotropic incompetence (inability to increase HR in response to physical or emotional stress)	Sinus bradycardia, sinus pauses, sinoatrial exit block, chronotropic incompetence Symptom arrhythmia correlation by Holter/event monitoring	CBF reduction is more pronounced in the elderly. Differential diagnosis includes PE, myocardial ischemia, new onset seizures
AV conduction disturbances	*Acquired progressive idiopathic fibrosis, myocardial ischemia/infarction, medications (digoxin, beta blockers, calcium channel blockers) congenital	Symptom AV block correlation by ambulatory ECG monitoring	Usually seen in patients with structural heart disease
First-degree AV block	Worsened by negative inotropes (beta-blockers, calcium-channel blockers)	PR interval >210 ms	If seen in syncope without structural heart disease, suspect NMS
Second-degree AV block, Mobitz I		With narrow QRS, is benign With wide QRS, especially >70 yrs suggests infranodal block warranting pacemaker placement	
Second degree AV block, Mobitz II	Can progress to high-degree AV block warranting pacemaker placement		
Third-degree AV block, acquired	Acquired: syncope is reported in 38 to 61% of patients[34]	Usually infra-nodal level with HIS region subsidiary pacemakers which are slow and unreliable warranting pacemaker placement	
Third-degree AV block, congenital	Rare	Usually at the AV nodal level hence benign. However if syncope is induced with exercise pacemaker is indicated[35]	
Bifascicular block	Common finding with rare progression to complete AV block		If an HV interval > 100 ms pacing indicated
Supraventricular arrhythmias, atrial fibrillation,	In susceptible individuals (elderly with vascular disease, young with dehydration, hot weather, gravitational	Syncope usually occurs at arrhythmia onset or termination	Even among patients with established arrhythmic cause of syncope, HUT can identify an

atrial flutter, AVNRT	stress) sudden onset tachycardia can cause dizziness/syncope		underlying vasodepressor component, which has therapeutic implications
Ventricular tachyarrhythmias VT, VF, Torsades			Among patients referred for EPS VT (20%) is > likely than SVT (15%) to cause syncope[36] In patients with a high index of suspicion for ventricular arrhythmias and a negative EPS, SAECG can identify VT risk VT-induced syncope increases SCD risk, warranting ICD placement
Long QT syndrome acquired (secondary)	*Medications (Table 12.6), subarachnoid hemorrhage, poisoning (organophosphorus, arsenic), extreme bradycardia, liquid protein diets[37] Exacerbated by hypokalemia/ hypomagnesemia		Though rarely causes syncope, treatable with prompt recognition Torsades induces syncope, usually during sleep (bradycardia) or after PVCs
Long QT syndrome congenital		Abnormal ventricular repolarization (QT prolongation, notched T waves/ T wave alternans)	Affected individuals are at high risk of SCD and recurrent syncope secondary to Torsades de pointes
Structural cardiac disease	LV outflow tract lesions, aortic stenosis, HOCM LV inflow tract lesions, mitral stenosis, left atrial myxoma RV outflow tract lesions, PE, pulmonary hypertension, pericardial tamponade	Ecocardiography	Recognizing structural heart disease among patients with syncope is of pivotal importance because patients with a cardiac cause of syncope have a 24% incidence of SCD at 1 year[1] In AS (fixed) or HOCM (dynamic) arrhythmias and exercise can precipitate syncope due to CBF reduction or mechanoreceptor-mediated bradycardia/ vasodilation[38] In acute PE, syncope is due to both mechanical flow limitation and neurally mediated reflex vasodilation

Table 12.6 Medications causing QT prolongation

Class of medication	Medication
Class IA anti-arrhythmics	Quinidine Procainamide Disopyramide
Class III	Sotalol Ibutilide Amiodarone NAPA (*N*-acetyl procainamide)
Anti-anginal	Bepridil
Psychoactive agents	Phenothiazines Thioridazine
Tricyclic antidepressants	Amitryptiline Imipramine
Antibiotics	Erythromycin Pentamidine Fluconazole
Antihistamines	Terfenadine Astemizole

Table 12.7 Causes of non-syncopal attacks: syncope mimics

	Type of disorder	Clinical features
Disorders without any impairment of consciousness	Falls Cataplexy Drop attacks Psychogenic pseudosyncope (factitious disorder, malingering, conversion reaction) Transient ischemic attacks (TIAs) of carotid origin	Medications used in psychiatric disorders (phenothiazines, tricyclics) can increase the risk of syncope[12] Cataplexy, which is a generalized abrupt loss of muscle tone, can be triggered by emotional reactions and thus can mimic syncope. However in cataplexy, there is no TLOC Drop attacks refer to sudden loss of postural tone with no LOC. Though the cause is unknown, vertebrobasilar atherosclerosis has been shown to compromise blood supply to the corticospinal tracts causing sudden lower extremity atonia[39]
Disorders with partial or complete loss of consciousness	Metabolic disorders, including hypoglycemia *, hypoxia (pneumonia, CHF, pulmonary embolism), panic disorder/hyperventilation * with hypocapnia Epilepsy Intoxications * Vertebrobasilar transient ischemic attack Neurologic disorders (aneurysms, tumors)	Metabolic and endocrine causes of syncope are rare. They usually result in confusional states, but unlike syncope they seldom resolve spontaneously Syncope/dizziness associated with hyperventilation (anxiety) is relatively common Metabolic states including hypoxemia, hypoglycemia/hyperglycemia, severe metabolic acidosis often cause behavioral disturbances and altered mental status, but seldom result in syncope Akinetic/complex partial seizures are particularly difficult to differentiate from syncope[39]

* Major common causes

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13

Syncope management facilities

Subramanya Prasad, Robert Schweikert, Mina Chung, and Oussama Wazni

Background • Guidelines for establishing a syncopal facility
- **Professionals involved at a syncope management facility**
- **Equipment • Existing syncope models**

BACKGROUND

- Syncope is a commonly encountered symptom representing the sixth commonest reason for hospitalization in adults >65 years, with an average length of stay of 5–17 days.[1] The cost of an unstructured syncope evaluation can be high, with hospital admission alone accounting for 74% of the evaluation costs of syncope.[2]
- Currently a wide variation exists among physicians and management facilities in the evaluation strategy for syncope. This has led to unnecessary diagnostic tests and a higher proportion of patients with unexplained syncope.[3–6]
- Establishment of syncope facilities which maximize implementation of the guidelines and establish mechanisms for effective communication with the patient and other involved personnel can reduce costs.
- A coordinated syncope evaluation is vital for appropriate health-care delivery to patients with syncope. Studies have shown that 20% of cardiac syncope in patients >70 years present as non-accidental falls. Studies of 'falls' suggest that a multi-factorial intervention significantly reduces subsequent events among these patients.[7,8]

GUIDELINES FOR ESTABLISHING A SYNCOPAL FACILITY

- The complex nature of symptoms of syncope and presyncope requires a systematic approach to facilitate a cost-effective approach for management of syncope.
- Facilities caring for patients with syncope vary from primary care providers to tertiary care facilities with multiple specialist care. Thus a common management strategy that ensures implementation of the published practice guidelines

Table 13.1 Indications for hospitalization in syncopal patients

Diagnostic	• Suspected or known structural heart disease
	• ECG abnormalities listed in Table 2.3
	• Exertional/exercise syncope
	• Significant injury
	• Family history of SCD
	• Occasionally
	  ○ No structural heart disease, but sudden onset of palpitations shortly before syncope, syncope in supine position, and frequent recurrence
	  ○ No structural heart disease, with high index of suspicion of cardiac syncope

Therapeutic	• Syncope due to cardiac arrhythmia, myocardial ischemia • Syncope due to structural cardiac or pulmonary disease • Cardioinhibitory NMS requiring pacemaker implantation

should be agreed upon among all the personnel involved (patients, referring physicians, Emergency department, nurses, and other professionals) and practiced.

- Syncope is a common presenting symptom both in the outpatient and inpatient setting. The source of referral (Outpatient office vs Emergency department, vs specialists like neurologists) determines the amount of work-up necessary for further evaluation.
- Most patients with syncope can be investigated on an outpatient basis. Table 13.1 lists the criteria for hospitalization in syncope.
- A local integrated syncope clinic should set standards regarding:
  - The diagnostic criteria for the causes of syncope
  - The preferred approach to the diagnostic work-up among selected groups of syncope patients
  - Risk stratification of the patient with syncope
  - Treatment to prevent recurrent episodes.
- An important goal of a syncope facility is to reduce frequent hospitalizations by providing a structured, quick, alternative evaluation pathway (Figure 13.1).
- Careful audit of the activity and performance of the syncope unit effectively maintains quality assurance.

PROFESSIONALS INVOLVED AT A SYNCOPE MANAGEMENT FACILITY

- Though specialized training in management of patients with syncope is desirable it is not a requirement for a dedicated syncope facility.
- The requirements depend on criteria established by the local professional bodies, level of screening prior to referral, and the nature of the patient population encountered. In general, training and experience in key components of cardiology, neurology, emergency medicine, and geriatrics, with access to specialties including psychiatry, physiotherapy, occupational therapy, ENT, and clinical psychology, are desirable. A proposed evaluation protocol is seen in Figure 13.2.

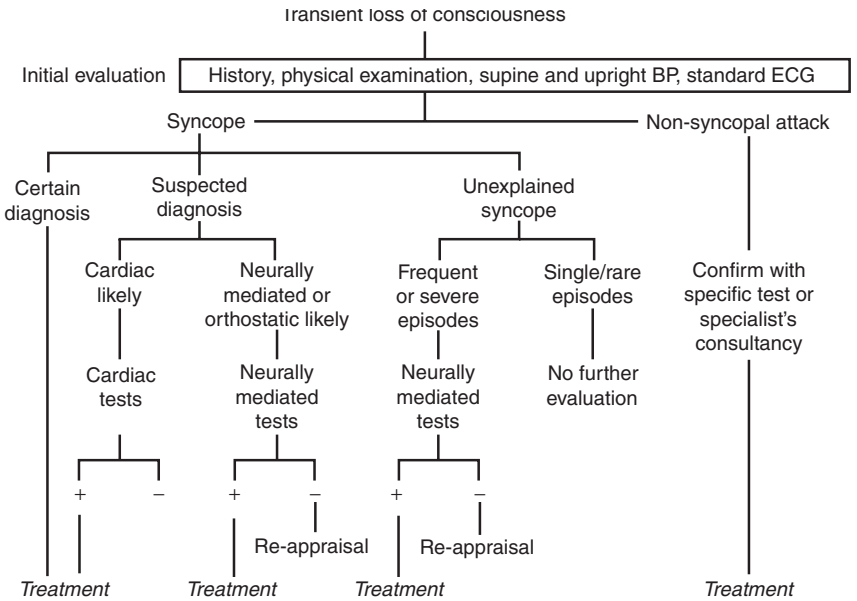

Figure 13.1 Organization model for syncope evaluation in a community setting.[1]

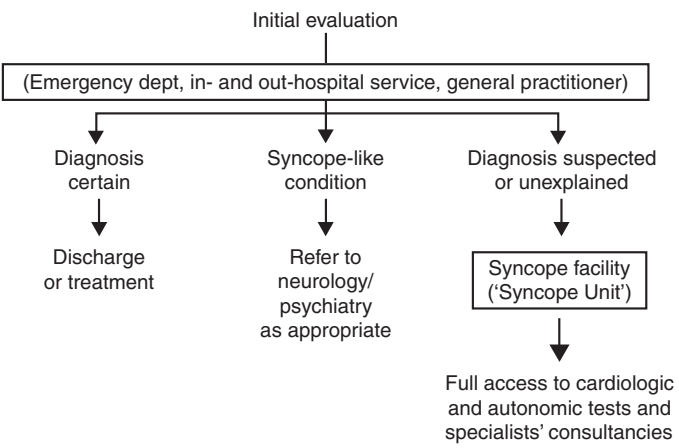

Figure 13.2 Structured protocol for syncope evaluation by syncope task force.[1]

- Core medical and support personnel should be involved in managing the unit on a full time basis.

EQUIPMENT

- Core equipment includes: surface ECG recording, phasic blood pressure monitoring, tilt table testing equipment, external and internal (implantable)

Table 13.2 List of recommendations for a syncope facility[1]

- A cohesive, structured core pathway – either delivered within a single syncope facility or as a more multi-faceted service – is recommended for the global assessment of the patient with syncope
- Experience and training in key components of cardiology, neurology, emergency, and geriatric medicine are pertinent
- Core equipment for the facility includes: surface ECG recording, phasic blood pressure monitoring, tilt table testing equipment, external and internal (implantable) ECG loop recorder systems, 24 h ambulatory blood pressure monitoring, 24 h ambulatory ECG monitoring, and autonomic function testing
- Preferential access to other tests or therapy for syncope should be guaranteed and standardized
- The majority of syncope patients should be investigated as outpatients

ECG loop recorder systems, 24 h ambulatory blood pressure monitoring, 24 h ambulatory ECG monitoring, and autonomic function testing. The syncope clinic at our institution has a blood volume analysis facility as an integral part.

- Access to echocardiography, invasive electrophysiologic studies, stress testing, cardiac imaging, CT and MRI head scans, and EEG, should be present in the facility.
- Preferential access to hospitalization and therapeutic procedures, including pacemaker and defibrillator implantation, and catheter ablation of arrhythmias, should be present. Table 13.2 lists the ESC recommendations for a syncope facility.

EXISTING SYNCOPE MODELS

- Facilities that are involved in the care of syncope patients range from general physicians to geriatricians/neurologists to cardiologists with an interest in cardiac pacing and electrophysiology. No evidence of superiority of any model exists.
- The Newcastle model involves a multi-disciplinary approach, where patients referred with falls or syncope are evaluated by a geriatrician or cardiologist. With this approach a significant reduction in expenditure towards evaluation of syncope has been seen (reduced rehospitalization rates, effective targeted treatment strategies).[2]
- The Italian model (similar to our institution) is a functional unit of cardiologists, with dedicated medical and support personnel. These patients have access to other investigations and specialist referral (neurologists) if deemed appropriate. This model was reported to substantially reduce the number of unnecessary investigations (<2 tests in 66% of patients were enough to make a diagnosis).[9] Table 13.3 lists the common tests done in our syncope facility with their protocols.

Table 13.3 List of common tests with equipment and protocols

Test	Equipment	Protocol or procedure
HUT	ECG defibrillator Automatic BP monitor Tilt table Emergency equipment Oxygen source Medications (atropine) ECG leads	Patient rests for 20 minutes before starting the test Support stockings of patient are removed Venous access obtained, preferably in the antecubital vein After 3 baseline readings, a graded HUT is done at 30 and 45 degrees for 2 minutes, followed by 70 degrees for 45 minutes or appearance of symptoms Recovery for 5 minutes
Isuprel tilt	ECG defibrillator Automatic BP monitor Tilt table Emergency equipment Oxygen source Medications (atropine) ECG leads Isuprel infusion bag at 1 μg/cc	Patient rests for 20 minutes Venous access is obtained Baseline BP and HR obtained for 3 minutes Graded infusion of isoproterenol (at 0.01, 0.03 and 0.05 μg/kg) is done. The patient is tilted at 70 degrees with each dose of isoproterenol, with patient returning to baseline for 5 minutes in between, as tolerated by the patient and occurrence of symptoms
Supine isuprel provocation test	ECG defibrillator Automatic BP monitor Tilt table Emergency equipment Oxygen source Medications (atropine) ECG leads Isuprel infusion bag at 1 μg/cc	Patient rests for 20 minutes Venous access is obtained Baseline BP and HR obtained for 3 minutes Graded infusion of isoproterenol (from 0.01 μg/kg to 0.05 μg/kg) is done with the patient in supine position, as tolerated by the patient and occurrence of symptoms
Blood volume testing Exclude pregnancy, allergy to eggs, shellfish, IVP dye, or iodine	EDTA-coated 6 ml tubes for blood collection Multiple sample adapter	Plasma volume is measured using less than 50 μCi of I-131 radio-iodinated human serum albumin (iv), waiting for an 11 minute equilibrium period. Total blood volume is calculated from the plasma volume and a simultaneously drawn venous hematocrit

(Continued)

Table 13.3 Continued

Test	Equipment	Protocol or procedure
	I-131 RISA syringe STAT–60 Centrifuge Dose calibrator	Venous access established After 20 minutes in supine position, baseline samples are obtained Measure hematocrit by centrifuging method RISA injected over 30 s Post injection samples ×5 are collected at 11, 15, 19, 23, and 27 minutes (with CHF, 6th sample is collected) After centrifugation and serum separation, serum samples are placed in vials in the BVA-100 analyzer (DAXOR) Quality control checked to exclude very high or low radioisotope background counts
Hemodynamics	ECG defibrillator Dinamap BP monitor Technicare 420/450 Gamma camera and computer ADAC 3300 microprocessor Emergency equipment and medications Pyrophospate 1.0 ml injection 99mTcO4 at 0.5 ml, 4 mCi, 8 mCi, and 12 mCi (8 and 12 used with routine hemodynamics)	Venous access preferably in the antecubital vein (right basilic vein preferred) 1 ml of pyrophosphate is injected, waiting for 40 minutes to tag *First cardiac output:* patient is positioned at 45 degrees LAO. Patient lies still with normal breaths and no activity for 12 minutes Simultaneously 4 mCi of 99mTc pertechnetate is injected and the camera is started (90 frame acquisition at 0.5 s intervals) 4 minute recovery *Second cardiac output:* with the same position 8 mCi 99mTc pertechnetate is injected and frame acquisition is started, followed by 4 minute recovery *Third cardiac output:* after checking patient's HR and BP, with the patient at 45 degree tilt, the legs are dropped down, making sure the patient's chest and rest of the body remain still 12 mCi 99mTc pertechnetate is injected and similar frame acquisition is done *Ejection fraction:* frame acquisition (24 frames for 20 minutes) is started during second output with HR and BP during that time frame recorded

Autonomic function testing		Has 4 components
Valsalva:	ECG recorder Automatic beat-by-beat BP monitor (Finapres) Gould recorder* Respirometer Access to emergency equipment and medications Computer	After taking a deep breath, patient blows against the manometer, raising it to 40 mmHg and holding pressure for 15 s, while the gould recorder records breathing and BP
Cold pressor test:		The patient's hand is completely dipped in ice cold water for 2 minutes Somatic pain generates efferent sympathetic input to the heart and peripheral arterioles, resulting in tachycardia and increased BP and peripheral resistance
Phenylephrine:		Injection of 25 μg with 25 μg increments until a 20 mmHg rise in SBP with slowing of HR or maximum dose is reached
Amyl nitrite inhalation:		A vial of amylnitrite is broken under the nose while the patient takes a deep sniff SBP decrease of 20 mmHg from baseline with increasing HR is seen
HRV: (30:15 R-R ratio test)		HR recordings are done during the Valsalva test Analysis of the R-R intervals at the 15th and 30th beats and obtaining the 30th to 15th beat ratio is done by HRV analysis in the software

* Gould recorder also records BP and HR and RR while doing Valsalva for autonomic reflex testing

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14

Syncope management and diagnostic testing

Subramanya Prasad, Oussama Wazni, Robert Schweikert, and Mina Chung

Management • Initial evaluation • History and physical examination • Role of ECG in diagnosis of syncope • Diagnostic testing in syncope • Ambulatory electrocardiographic monitoring (non-invasive and invasive) • Advanced cardiac testing

MANAGEMENT

Throughout this chapter * denotes a class I recommendation, # denotes a class II recommendation and ^ denotes a class III recommendation.

Table 14.1 explains the strength of recommendations and levels of evidence.

Table 14.1 Strength of recommendations and levels of evidence

Class I*	When there is evidence for and/or general agreement
Class II#	Evidence is less well established or divergence of opinion exists
Class III^	Not useful and harmful in some cases
Level of evidence A	Data from multiple randomized clinical trials or meta-analyses
Level of evidence B	Data from one randomized clinical trial or multiple non-randomized studies
Level of evidence C	Expert consensus opinion

INITIAL EVALUATION

- The sporadic and infrequent occurrence of syncopal episodes makes it highly impractical to evaluate the syncopal patient during an episode. Hence the primary goal during the initial evaluation of syncope is to arrive at a presumptive diagnosis.

- An initial evaluation (thorough history including bystander observations, a well focused physical examination including orthostatic blood pressure measurements, and a standard ECG) can identify the probable cause of syncope in 75% of patients.[1,2]

HISTORY AND PHYSICAL EXAMINATION

History

- The history and physical examination can lead to a suspected diagnosis in 40% of patients.
- A careful history should include bystander observations, circumstances surrounding the event, prodromal symptoms, rapidity of LOC, duration of event, and speed of recovery. A list of the historical features and their importance in syncope is given in Table 14.2.
- The history should focus on
  - Differentiating true syncope from 'non-syncopal' conditions
  - Identifying the presence of structural heart disease.
- Medication history including anti-arrhythmic and antihypertensive agents (diuretics, sympathetic blockers) can predispose individuals to POH.

Differentiating seizures from syncopal episodes

- Although typical seizures are easy to diagnose (aura, generalized tonic/clonic movements, tongue biting) differentiating atypical/complex partial seizures from syncope can be challenging.
- Some syncopal patients have convulsive movements similar to seizures attributable to hypoxia due to a paradoxical cerebral vasoconstriction.[5]
- In a recent study of 74 patients with a diagnosis of epilepsy, with persistent episodes in spite of anticonvulsant therapy, HUT testing provided an alternative diagnosis in 31/74 (42%).[5] Table 14.3 lists the differentiating features of seizures from syncope.

Physical examination and maneuvers

- A well focused physical examination, particularly cardiovascular and nervous (central and peripheral) systems, based on the historical clues can aid in diagnosis. A list of such physical findings can be seen in Table 14.4.

ROLE OF ECG IN DIAGNOSIS OF SYNCOPE

- The presence of a normal ECG makes the diagnosis of a cardiac cause unlikely, thus making it an important part of the initial evaluation.
- The initial ECG can establish a diagnosis in 5% and suggests a diagnosis in 5% of cases.[1] ECG findings that contribute to syncopal diagnosis are listed in Table 14.5.

Table 14.2 Historical clues and interpretation

Historical feature	Interpretation
Age[3]	Children, adolescents, young adults: *NMS, POTS, SVT, VT, idiopathic LQTS, cardiomyopathy, ARVD, congenital heart disease, AV block, seizure disorder Middle aged: *NMS, POH, cardiac arrhythmias and obstructive lesions, seizure disorder, medications Elderly: *NMS, cardiac arrhythmias and obstructive lesions, POH, medications, cerebrovascular, CSH, seizure disorders, combined causes
Pre-existing medical conditions/medications	History of cardiac disease is a strong predictor of a cardiac cause of syncope[4] Hyperventilation/anxiety with psychiatric illness Autonomic neuropathy with diabetes, parkinsonism Orthostatic hypotension due to antihypertensive/ anti-arrhythmic medications
Presyncopal features	
Position of the patient during syncopal occurrence	Standing suggests NCS Supine suggests arrhythmia
Activity (rest, during or after exercise) and events preceding syncopal onset (coughing, eating, drinking, micturition, defecation)	Situational syncope (NMS) Shaving, tight collars, head rotation suggests CSH
Exertional syncope	Usually seen in syncope associated with AS or HOCM (reduced flow due to outflow tract obstruction or vagally mediated hypotension) Can be rarely seen in NCS in young patients with structurally normal hearts
Predisposing factors	Crowded or warm places, prolonged standing, postprandial state, fear, pain s/o WS Neck movements s/o VBI, CSH
Onset of syncopal episode	
Prodromal symptoms (nausea, abdominal discomfort, pallor, warmth, lightheadedness, dizziness, blurred vision, diaphoresis)	Usually present in NCS Absent in elderly individuals and CSH
Auras (visual)	Associated with seizures
During syncopal episode	
Onset of symptoms, way of falling, skin color, duration of LOC, breathing pattern, movements with duration, tongue biting	With H/O structural heart disease sudden supine LOC suggests arrhythmia, while exertional LOC suggests AS, HOCM Presyncope s/o WS/ benign causes Prolonged LOC with postictal weakness, tongue biting, and fecal/urinary soiling s/o epilepsy
Associated symptoms/signs	Nausea/vomiting/pallor after an episode suggest WS Dyspnea suggests PE Angina suggests ischemia Focal neurologic deficits suggest CVA/TIA Presence of urination/defecation after episode suggests seizure Injury suggests higher mortality Vertigo, dysarthria, diplopia suggests vertebrobasilar TIA

(Continued)

Table 14.2 (Continued)

	Historical feature	Interpretation
Duration of symptoms	Prolonged LOC suggests seizure or aortic stenosis Brief LOC suggests arrhythmia or NCS (CBF is restored in supine position)	
Number of episodes and time from first episode to subsequent episodes	<1 in lifetime or multiple episodes in many years have benign causes, and longer syncope-free intervals Multiple episodes over a short time have a serious underlying disorder; >50% patients have recurrent episodes	
Recovery	Quick with persistence of nausea, pallor, and diaphoresis suggests NMS Delayed with persistent neurologic changes and confusion suggests CVA/seizure	

*, major common causes; NMS, neurally mediated syncope; POTS, postural orthostatic tachycardia syndrome; SVT, supraventricular tachycardia; VT, ventricular tachycardia; LQTS, long QT syndrome; ARVD, arrhythmogenic right ventricular dysplasia; POH, postural orthostatic hypotension; CSH, carotid sinus hypersensitivity; AS, aortic stenosis; HOCM, hypertrophic obstructive cardiomyopathy; VBI, vertebro-basilar insufficiency; LOC, loss of consciousness; VVS, vasovagal syndrome; PE, pulmonary embolism; CVA, cerebrovascular accident; TIA, transient ischemic attack; CBF, cerebral blood flow.

- Since syncopal episodes are intermittent and unpredictable, documenting symptom–arrhythmia correlation is the gold-standard in syncope evaluation. A 30 to 60 second rhythm strip may aid such documentation in the symptomatic patient.

DIAGNOSTIC TESTING IN SYNCOPE

- An initial evaluation usually provides a probable diagnosis in 75% of syncopal patients. However, appropriate risk stratification, therapy, and prognostic estimates are possible once a reasonably accurate diagnosis has been established.
- Based on the initial evaluation, further testing may be necessary. Diagnostic testing should focus on establishing a strong correlation between symptoms and identified abnormalities, choosing appropriate therapy, and giving prognostic estimates.
- Routine hematologic and biochemical screens and brain CT or MRI, in the absence of focal findings, have a very low yield.[1,6]
- Though the treatment of a patient with syncope should be individualized, a systematic approach that ensures adherence to guidelines is most cost-effective (Figure 14.1). The evaluation of a patient with presyncope is the same as that for a patient with syncope.
- Table 14.6 lists the costs and diagnostic yield of the various cardiac modalities of evaluation used in syncope.

AMBULATORY ELECTROCARDIOGRAPHIC MONITORING (NON-INVASIVE (Table 14.7) AND INVASIVE)

- Due to the unpredictable nature of syncopal episodes, arrhythmic causes of syncope often require long-term ECG monitoring for successful symptom-arrhythmia documentation.

Table 14.3 Distinguishing seizures from syncope

Clinical findings	Seizure likely	Syncope likely	Arrhythmia likely
Demographics/ clinical setting	Young (45 years)	Female > male Younger (<55 years) More episodes (>2) Standing/warm room, emotional upset	Male > female Older (>55 years) Fewer episodes (<3)
Findings during LOC (eyewitness account)	Prolonged syncope (>5 minutes) Tonic-clonic movements are usually prolonged coinciding with LOC onset Hemilateral clonic movement Clear automatisms (chewing or lip smacking, or frothing at the mouth) Tongue biting Blue face Bowel and bladder incontinence Elevated HR and blood pressure	Tonic-clonic movements are always of short duration (15 s), starting after LOC onset, dilated pupils Bradycardia, hypotension	Blue, not pale Incontinence can occur Brief clonic movements can occur
Symptoms preceding the event	Sudden onset Aura (déjà vu, olfactory, gustatory, visual)	Longer duration (>5 s) Nausea/vomiting, abdominal discomfort, cold sweating (neurally mediated), palpitations Lightheadedness, blurring of vision	Shorter duration (<6 s)
Symptoms after the event	Residual symptoms common, prolonged confusion Aching muscles Disoriented Slow recovery The presence of a slow and complete recovery with evidence of soft-tissue injury at multiple sites usually favors epilepsy	Residual symptoms common, usually short duration Prolonged fatigue common (>90%) Nausea, vomiting, pallor (neurally mediated) Oriented	Residual symptoms uncommon (unless prolonged LOC) Oriented
Findings of low specificity	Family history Timing of the event (night) Paresthesias before the event Incontinence, injury, headache, drowsiness after the event		

Table 14.4 Physical findings in the diagnosis of syncope

Physical findings	Implications
Blood pressure	Postural change from supine to sitting or standing for 2–5 mins: an SBP decrease of 20 mmHg, DBP decrease of 10 mmHg *and/or* signs of cerebral hypoperfusion is diagnostic of POH
Heart rate	An increase in 28 beats above resting HR with postural change (supine to standing) is diagnostic of POTS
Heart rhythm and respiratory rate	Marked sinus arrhythmia is indicative of high vagal tone, s/o WS Hyperventilation is s/o anxiety
Cardiac auscultation findings	Ejection systolic murmur s/o AS, HOCM, PS Diastolic murmur s/o left atrial myxoma Sustained parasternal lift with loud P2 s/o pulmonary hypertension Sustained PMI with S3, S4 gallop s/o dilated cardiomyopathy (VT)
Physiologic maneuvers	Change in intensity of systolic murmur with Valsalva maneuver s/o HOCM
Localizing neurologic findings	s/o CVA
Fecal occult blood test	Positive s/o GI bleed
Carotid sinus massage	Positive response s/o CSH

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; POTS, postural orthostatic tachycardia syndrome; VVS, vasovagal syndrome; AS, aortic stenosis; HOCM, hypertrophic obstructive cardiomyopathy; PS, pulmonic stenosis; VT, ventricular tachycardia; s/o, suggestive of; CVA, cerebrovascular accident; GI, gastrointestinal; CSH, carotid sinus hypersensitivity

Table 14.5 ECG abnormalities suggesting an arrhythmic cause of syncope[4]

ECG findings with a high likelihood of making a probable diagnosis	Less specific findings
• QT prolongation • A short PR interval and delta wave with pre-excited QRS complexes • Findings of acute myocardial infarction (MI) • High degree AVB • ARVD (negative T-waves in right precordial leads, epsilon waves, and ventricular late potentials) • Brugada syndrome (right bundle branch block pattern with ST-elevation in leads V1–V3)	• Asymptomatic sinus bradycardia (<50 bpm) • Sinoatrial block or sinus pause >3 s in the absence of negatively chronotropic medications • Evidence of prior MI (Q waves) • BBB, bifascicular block • Ventricular or septal hypertrophy and PVCs • A prolonged QT interval may indicate Torsades de Pointes as the cause of syncope. Patients with LQTS may have a normal QT interval at rest. However, a diagnosis of LQTS can be made if the QT interval increases or fails to shorten during exercise

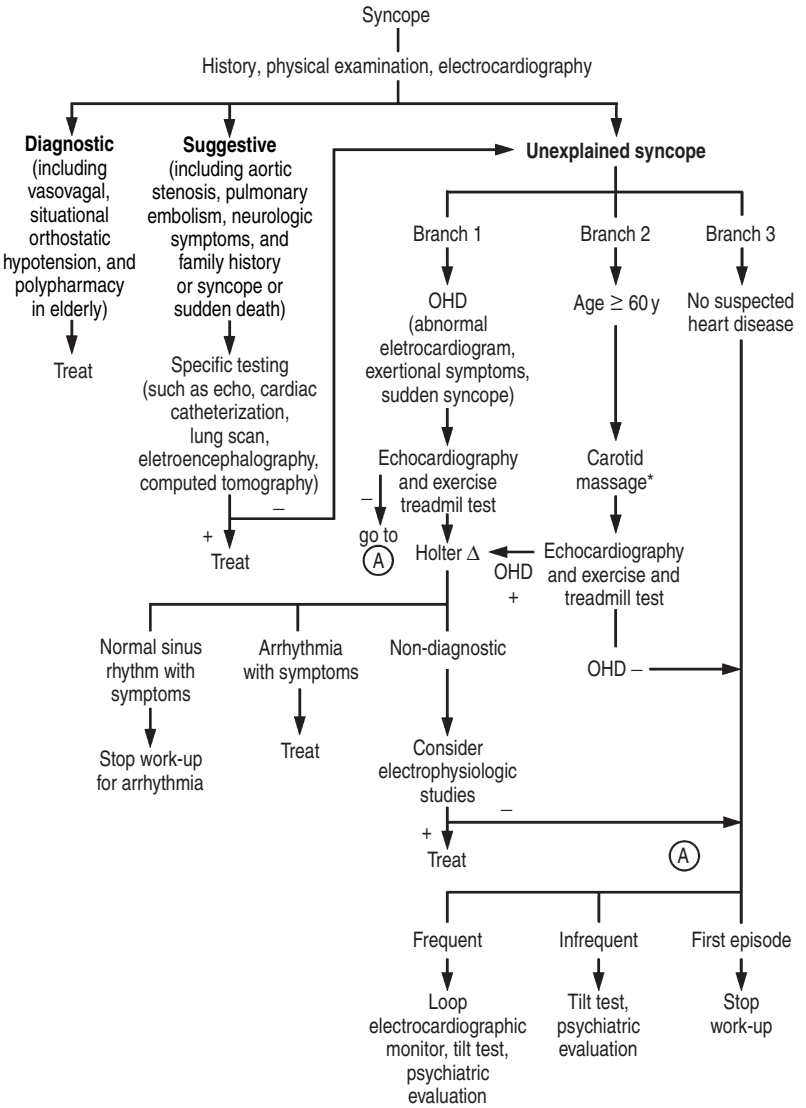

Figure 14.1 Approach to a patient with syncope.
* performed with a Head-up tilt table test (OHD: Orginal heart disease).

- Long-term ambulatory ECG monitoring can be non-invasive (Holter monitor, event monitors/recorders, external loop recorders) or invasive (implantable loop recorder).

Holter recorders (Table 14.8)

- Holter monitors are low-cost external recorder devices used over 24 to 48 hour periods.

Table 14.6 Costs of syncope evaluation[7,8]

Test	Cost ($)	Diagnostic yield (%)	Cost per diagnosis ($)
External loop recorder	201	38	529
Tilt test	594	58	1 024
Holter	328	21	1 562
ILR	4916	88	5 586
EPS with SHD	3663	52	7 044
Echocardiography	1033	3	34 333
EPS without SHD*	3663	5	73 260

*SHD: structural heart disease.

Table 14.7 Recommendations for diagnostic studies based on the initial evaluation

Class I recommendations

- With an unclear mechanism of syncope, the presence of heart disease is associated with a higher risk of arrhythmias and a high 1-year mortality, thus a **cardiac evaluation** (echocardiography, stress testing, prolonged ECG monitoring (Holter, external, or implantable loop recorder as appropriate) and electrophysiological study) is recommended
- As first steps, echocardiography, Holter/event monitoring, and, if non-diagnostic, EPS are recommended
- If syncope with palpitations: Holter/event monitoring and echocardiography
- If chest pain suggestive of ischemia before or after LOC, stress testing, echocardiography, and Holter
- If exertional syncope: echocardiography and stress testing
- If cardiac evaluation is negative for arrhythmic cause, if recurrent/severe syncope present, evaluation for NMS (most patients with single or rare episodes have NMS). An additional consideration is psychiatric illness
- Evaluation for NMS: HUT and CSM (>40 years). If negative Holter or ILR
- Syncope with neck movements; CSM first
- In patients with frequent recurrent syncope and multiple somatic complaints with stress, anxiety, and other psychiatric disorders: psychiatric evaluation is recommended
- Basic laboratory tests are indicated: suspected loss of circulating volume, or a metabolic disorder causing syncope mimics
- Unclear mechanism of syncope despite a complete evaluation, and clinical/ECG features of arrhythmia or recurrent syncope with injury: ILR is indicated

- Holter monitors or event recorders are more useful in excluding an arrhythmic cause than establishing a diagnosis.[10] Many studies of ambulatory monitoring showed symptom–arrhythmia correlation of 1–2% among unselected patients.
- * In-hospital telemetry is valuable in patients with significant structural heart disease, at a high risk of life-threatening arrhythmias, especially within a few days of an episode.[4]
- * While documenting a positive (syncope with arrhythmia) symptom–ECG correlation is diagnostic, a negative (syncope with no arrhythmia) symptom–ECG correlation excludes an arrhythmic cause.
- * Lack of symptom–ECG recording correlation requires additional testing. Exceptions are:

Table 14.8 Modes and indications for electrocardiographic monitoring

Mode of testing	Indications in syncope	Findings and interpretations	Advantages and pitfalls
Long-term ECG monitoring Non-invasive Holter monitor	*High pretest likelihood of arrhythmia (Table 14.5) and frequent (daily) episodes *Holter monitoring may be indicated in patients with clinical/ECG features listed in Table 14.5 to guide an EPS *In unexplained syncope (despite a comprehensive conventional work-up) with features listed in Table 14.5 or a history of recurrent syncope with injury	Continuous ECG recordings of sinus bradycardia, AV block, or non-sustained SVT or VT, obtained during an event can be useful	Holter monitoring can be useful to exclude an arrhythmic cause of syncope. Holter monitors are more productive in patients with frequent (daily) episodes of syncope Since these devices require patient activation and event reproduction within a 24–48 hour period is unpredictable, the diagnostic yield among unselected populations is low (2–3%)[9]
Long-term ECG monitoring Non-invasive event monitor			Event monitors are more useful than Holters among patients with infrequent episodes of presyncope/syncope due to their ability of transtelephonic transmission of ECG recordings A major drawback is that recording is dependent on patient activation which can be unreliable
Long-term ECG monitoring Implantable loop recorder (ILR)	*Initial work-up in patients with clinical/ECG features listed in Table 14.5 with preserved cardiac function *To assess the significance of bradycardia in NMS with frequent syncope/ traumatic injury, before pacemaker implantation		The ILR can be programmed to record when the HR falls outside a predetermined range or manually with magnet application Continuous recording enables device activation after restoration of consciousness
Advanced cardiac testing SAECG	*SAECG[11] of established value*: Risk stratification of patients recovering from MI in sinus rhythm without ECG evidence of BBB or IVCD Identification of IHD patients with unexplained syncope at risk for developing	The recognition of late potentials is a strong predictor (sensitivity 80%, specificity 90%) for ventricular arrhythmias, particularly in structural heart disease with preserved ventricular function	

(Continued)

Table 14.8 (Continued)

Mode of testing	Indications in syncope	Findings and interpretations	Advantages and pitfalls
	sustained ventricular arrhythmias *SAECG valuable, requires further evidence*: Risk stratification for sustained ventricular arrhythmias in non-ischemic cardiomyopathy *SAECG promising:* Detection of acute rejection of heart transplant Assessment of pro-arrhythmic effects of AADs used for ventricular arrhythmias *SAECG not indicated:* IHD patients with documented VT Risk stratification of ventricular arrhythmias in asymptomatic patients without detectable heart disease	(LVEF>40).[12] On the contrary, absence of late potentials on a SAECG is strongly suggestive of inability to induce ventricular tachycardia	
Invasive EPS in sinus node dysfunction (SND)	* An EPS is indicated if clinical/ECG features listed in Table 14.5 are present # Accurate diagnosis of the type of arrhythmia when an arrhythmic cause has been established Exclude an arrhythmic cause of syncope in high-risk occupations (pilots, drivers) ^ In patients with a normal ECG, no structural heart disease and no palpitations, an EPS is not indicated	* An EPS is diagnostic, requiring no additional testing in the following: sinus bradycardia and a very prolonged CSNRT (SNRT > 2 s or CSNRT > 1 s highly suggests SND)	The absence of sinus node dysfunction during EP testing does not exclude it as a cause of syncope
Invasive EPS in atrioventricular block	Same as above	An HV interval >100 ms or infra-His block seen spontaneously or during atrial pacing is diagnostic of AV block as the cause of syncope[13,14] Intra- or infra-Hisian block seen spontaneously or during pharmacologic provocation or incremental atrial pacing/short sequence ventricular pacing is highly predictive of impending	Establishing causation of syncope due to AV nodal dysfunction/AV is difficult

		AV block[15,16] An EPS is diagnostic if: • bifascicular block and a baseline HV interval of >100 ms, or 2nd or 3rd degree His-Purkinje block is demonstrated during incremental atrial pacing, or (if the baseline electrophysiologic study is inconclusive) or high-degree His-Purkinje block is provoked by intravenous administration of ajmaline, procainamide, or disopyramide • induction of sustained monomorphic ventricular tachycardia or rapid supraventricular arrhythmia which reproduces hypotensive or spontaneous symptoms # An EPS is less useful if: • HV interval of >70 ms but <100 ms • Induction of polymorphic ventricular tachycardia or ventricular fibrillation is seen in patients with Brugada syndrome, arrhythmogenic right ventricular dysplasia or among patients resuscitated from cardiac arrest
Invasive EPS in SVT	Same as above	
Invasive EPS in VT	Same as above	^ Induction of Torsades (polymorphic VT) or ventricular fibrillation in patients with idiopathic dilated cardiomyopathy or ischemic cardiomyopathy with poor ventricular function has a low predictive value

* Class I, # class II, ^ class III.

  - Ventricular pauses ≥3 s when awake
  - Transient Mobitz II or 3rd degree AV block when awake
  - Rapid paroxysmal ventricular tachycardia.
- # Presyncopal findings should not guide therapy since they are non-specific.
- ^ In patients with no clinical/ECG features listed in Table 14.5, ECG monitoring is not recommended.

Long-term non-invasive event monitors (Table 14.8)

- Event monitors are patient-activated, portable ECG recording devices that can be used for longer periods of time.
- Event recorders can be prospective, retrospective, or both.
- # A non-invasive external loop recorder may be indicated in patients with clinical/ECG features listed in Table 14.5 with an inter-symptom interval ≤4 weeks.
- Retrospective external loop recorders have a higher yield.[17]
- Studies regarding the use of event monitors are mixed. While Linzer et al, using retrospective external loop recorders, showed a higher yield (25% of patients recorded in a 1 month period),[17] a recent study of syncopal patients (3 ± 4 episodes in 6 months), with a negative HUT test and no structural heart disease, showed event recorders as not useful.[18]
- A study showed that, despite patient education, 23% failed to activate the recorder at the appropriate time.[10]

Implantable loop recorder

- The implantable loop recorder (ILR) is a small subcutaneous device with 2 electrodes, an 18 to 24 month battery life, and is usually implanted in the left prepectoral chest wall.
- It is most useful in patients with unexplained syncope after a negative or inconclusive conventional work-up.[19] A study of 60 patients with unexplained syncope that randomized patients to conventional testing (external loop recorder, HUT, and EPS) vs ILR monitoring showed that ILR use in the initial phase of work-up was more likely to provide a diagnosis (52% vs 20%).[20]
- Pooled data of 287 patients from four studies showed a symptom–arrhythmia correlation in 34% (52% asystole/bradycardia, 11% tachycardia, 37% no rhythm variation).[19,21,22]
- # ILR use is controversial, requiring further studies in patients with:[23]
  - Persistent seizures despite medications.
  - Recurrent unexplained syncope without structural heart disease, in whom understanding the exact mechanism may change therapy.
  - NMS, in whom understanding the exact mechanism may change therapy.
  - Bundle branch block (BBB) with suspected paroxysmal AVB despite negative EPS.
  - Structural heart disease with a strong suspicion of ventricular tachyarrhythmias and a negative EPS.
  - Unexplained falls.[24]

ADVANCED CARDIAC TESTING

- *In patients with a high index of suspicion of an arrhythmic cause of syncope, advanced cardiac testing (SAECG, EPS, ATP infusion) is advocated.
- The role of coronary angiography is limited except in establishing the presence of coronary artery disease.

SAECG

- SAECG is a non-invasive tool used to detect low-amplitude signals in the terminal portion of the QRS complex (late potentials).
- It has also been shown that SAECG is a useful non-invasive tool in early detection of cardiomyopathy (ARVD, dilated cardiomyopathy, amyloidosis, systemic sclerosis, and muscular dystrophy) when ECG and echocardiography are normal.[25]
- Though not evaluated in patients with syncope, T-wave alternans is a stronger predictor of ventricular tachyarrhythmias.[26]
- ^ There is general agreement that ventricular signal-averaged ECG and T-wave alternans are not diagnostic of the cause of syncope. In patients with syncope and no evidence of structural heart disease, the combination of SAECG and T-wave alternans may be useful for guiding the use of EPS. Their systematic use is not recommended.
- SAECG has no role in sinus node or AV nodal assessment.

Electrophysiologic testing

- Electrophysiological studies (EPS) can be non-invasive (transesophageal) or invasive. Invasive EPS tests are considered in patients with recurrent syncopal symptoms due to an unexplained cause.
- The role of transesophageal EPS, which is similar to performing a TEE, is limited to:
  - Screening for rapid AVNRT
  - AVRT in patients with palpitations and a normal ECG
  - Evaluation of SND in syncope due to bradycardia
  - Risk evaluation in accessory pathways.
- Similar to other diagnostic tests, the yield of an EPS depends on the pretest likelihood of an arrhythmic cause. Demonstration of an inducible arrhythmia during an EPS does not prove an arrhythmic cause of syncope, unless there is symptom correlation. Table 14.8 shows the role of EPS in diagnosis of various arrhythmic causes of syncope.
- EPS is considered in patients with recurrent syncope due to an unexplained cause. EPS is used to diagnose sinus node dysfunction, atrioventricular block (AVB) and supraventricular/ventricular tachyarrhythmias.
- In patients with a high likelihood of an arrhythmic cause, a negative EPS does not exclude arrhythmia; further studies (ILR) are recommended.
- Identification of abnormal EP findings is not always diagnostic of an arrhythmic cause.
- Though EPS can easily induce supraventricular tachyarrhythmias and ventricular tachycardia, induction of polymorphic ventricular tachycardia (PVT)/Torsades

de pointes is difficult despite isuprel provocation, or using long–short sequence stimulation.

- The minimum testing required during an EPS for syncope diagnosis per ESC guidelines is:
  - Measurement of sinus node recovery time and corrected sinus node recovery time by repeated sequences of atrial pacing for 30–60 s with at least one low (10–20 beats/min higher than sinus rate) and two higher pacing rates.
  - Assessment of the His-Purkinje system includes measurement of the HV interval at baseline and His-Purkinje conduction with stress by incremental atrial pacing. If the baseline study is inconclusive, pharmacologic provocation with slow infusion of ajmaline (1 mg/kg iv), procainamide (10 mg/kg iv), or disopyramide (2 mg/kg iv) is added unless contraindicated.
  - Assessment of ventricular arrhythmia inducibility by ventricular programmed stimulation at two right ventricular sites (apex and outflow tract), at two basic drive cycle lengths (100 or 120 beats/min), with up to 2 extra stimuli. Use of a third extra stimulus can increase sensitivity but decreases specificity.
  - Assessment of supraventricular arrhythmia inducibility by any atrial stimulation protocol.
- The diagnostic yield of EPS is high among patients with structural heart disease, especially when an SVT with hypotension or sustained monomorphic VT is induced, and low with induction of NSVT, PVT (torsades), or VF. In a study of patients with unexplained syncope, EPS provided a diagnosis in 56% (71% with structural heart disease vs 36% with none).[27] Other predictors of a positive EPS include impaired ventricular function, male sex, prior myocardial infarction, BBB, and non-sustained VT.[28]

EPS in SND

- Though EPS is frequently used to document sinus node dysfunction, it is seen as a cause of syncope in $<5\%$ of patients undergoing EP testing.[29]
- The sinus node recovery time (SNRT) is defined as the interval between the last paced atrial depolarization and the first spontaneous atrial depolarization resulting from the activation of the sinus node.
- A prolonged SNRT or corrected SNRT (CSNRT), sino-atrial conduction time (SACT), or chronotropic incompetence with exercise stress testing indicates SND.
- An SNRT of 1.6 s to 2 s or a CSNRT (SNRT–sinus cycle length) greater than 525 ms is indicative of abnormal sinus node automaticity, sino-atrial conduction, or both (sensitivity 50–80%; specificity 95%).[30] A study by Menozzi et al showed an 8-fold increase in the risk of syncope in patients with a CSNRT $\geq$800 ms.[31]
- When the baseline EPS is inconclusive, pharmacologic challenge with atropine (0.04 mg/kg) or propranolol (0.2 mg/kg) can cause complete autonomic blockade of the sinus node, differentiating intrinsic and extrinsic SND.[32] Although the intrinsic heart rate (IHRp) in relation to age can be calculated using a linear regression equation [$\text{IHRp} = 118.1 - (0.57 \times \text{age})$], its sensitivity is low.[33]

EPS in AV block

- Patients with varying degrees of AV block can present with syncope.
- AV conduction is measured by the HV interval (His bundle to ventricular conduction time) and/or the response of AV conduction to incremental atrial pacing.
- The presence of alternating bifascicular or trifascicular block is an ominous sign due to the possibility of impending or intermittent high-grade AV block. Documenting transient/intermittent bifascicular block requires extended ambulatory ECG monitoring.
- A history of syncope and a prolonged HV interval increase the risk of AV block.
- Ventricular arrhythmias are more common in patients with AV block. Pacemaker implantation reduces recurrent syncope in patients with AV block.[34]
- Studies have shown that although there is a 12% SCD incidence in patients with AV block, it is not associated with syncope or a prolonged HV interval, suggesting that the increased SCD incidence is probably related to the underlying structural heart disease and not syncope.
- The diagnostic yield of EPS in evaluating AV block can be increased by pharmacologic provocation (procainamide: 10 mg/kg; disopyramide: 2 mg/kg, ajmaline: 1 mg/kg) and/or incremental atrial pacing/short sequence ventricular pacing.[35]

EPS in supraventricular arrhythmias

- Among syncopal patients of unknown cause undergoing EPS, SVT causing syncope is seen in $<5\%$.[36] The hemodynamic effects of the SVT causing syncope can be studied by EPS (transesophageal or invasive), with or without isoproterenol/atropine provocation.

EPS in ventricular arrhythmias

- VT is the most common abnormality seen during EPS for syncope (20% of patients undergoing EPS).[28] Ventricular tachycardia can present as syncope with or without palpitations. A study by Moasez et al showed that identification of MMVT on Holter was a strong predictor of inducing MMVT during EPS.[29]
- While induction of MMVT during EPS indicates a high risk of SCD, a negative EPS predicts a low risk of SCD among CAD patients with preserved LV function.[37,38]
- The value of inducing polymorphic ventricular tachycardia (torsades) or VF during EPS depends on the clinical scenario:
  - In the setting of syncope with CAD, the induction of PVT or VF during EPS does not predict syncopal events.[39]
  - However, induction of PVT during EPS predicts survival in patients with (i) Brugada syndrome,[40] (ii) cardiac arrest survivors undergoing coronary bypass surgery, and (iii) idiopathic ventricular fibrillation.[41]

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Section VII
Device procedures

15

Implantation of pacemakers and ICDs

Mohammed Khan, Jennifer Cummings, and Bruce L Wilkoff

Patient selection and preparation • Pocket formation • Vein access • Lead placement • Defibrillation threshold testing • Interrogation and programming after implantation

PATIENT SELECTION AND PREPARATION

- Patients must have an indication for pacemaker or implantable cardioverter defibrillator (ICD) according to ACC/AHA guidelines as discussed elsewhere.[1,2] Patients must have informed consent before proceeding with implantation. This includes discussion of the reasons for implantation, the potential risks associated with the procedure, and alternatives to the procedure. Major risks include pneumothorax, cardiac perforation, pericardial effusion, and pulseless electrical activity associated with defibrillation testing. Minor risks include bleeding and infection. Patients should be aware of lifelong maintenance of the device and the need for generator replacements in the future.
- Before the procedure, screening labs should include coagulation parameters, electrolytes, and complete blood count. Patients should have international ratio (INR) less than 1.5 and heparin should be delayed as long as possible after the procedure, but should not be restarted before 24 hours.
- Once patients are in the EP lab, there should be meticulous attention paid to sterility. The implantation site should be clear of any superficial wounds, be shaven, and be prepped with betadine and a head-to-toe drape. All personnel involved in the procedure should undergo a surgical scrub. Intravenous sedation in the form of intravenous opiates and anxiolytics (e.g., fentanyl and versed) is most often used.

POCKET FORMATION

- Most devices are placed in a left prepectoral pocket due to the fact that most patients are right-handed and due to easier manipulation of leads from the left versus the right side. Other sites include right prepectoral, abdominal, inframammary, and under the pectoralis major muscle positions. The latter two positions may be considered for cosmetic reasons. The pocket should not be

created in the fat layer but just above the pectoral fascia with sharp and blunt dissection and sized to the implanted device. Electrocautery is used for hemostasis.
- There are variations in the location of the incision line. However, most implanters use the clavicle and deltopectoral groove as landmarks. If the subclavian or axillary vein is to be used for venous access then an incision line is extended 2 to 3 cm below the clavicle for a total length of 3 to 5 cm (dependent on the size of the device), which brings the lateral extension of the incision line just medial to the deltopectoral groove. If the cephalic vein is to be accessed then the incision extends over the deltopectoral groove.

VEIN ACCESS

- Veins may be accessed by direct visualization, by anatomic landmarks, or by fluoroscopy. The 'first-rib' approach involves the use of fluoroscopy to access the axillary vein ('extrathoracic' subclavian vein) lateral to the medial edge of the first rib (see Figure 15.1). Once the vein is accessed by any of the methods described a guidewire is inserted through the hollow needle (see Figure 15.2). The guidewire should be advanced to the inferior vena cava to assure that the vein, not the artery, has been entered. The process is repeated for the number of leads to be inserted. Another technique involving retained guidewires requires only one venous access with guidewires left in place to allow for more than one lead to pass through a single venotomy site.
- Of note, in patients who have prior leads or central catheters in the subclavian veins, there may be stenosis that prevents vein access. In such patients, the use of venograms through a peripheral intravenous line placed in the ipsilateral arm can delineate stenosis and guide therapy.

LEAD PLACEMENT

- Sheaths are placed over the guidewires, usually 7 French size for pacemaker leads and 7 and 9 French sizes for ICD leads. The sheaths are either slittable or

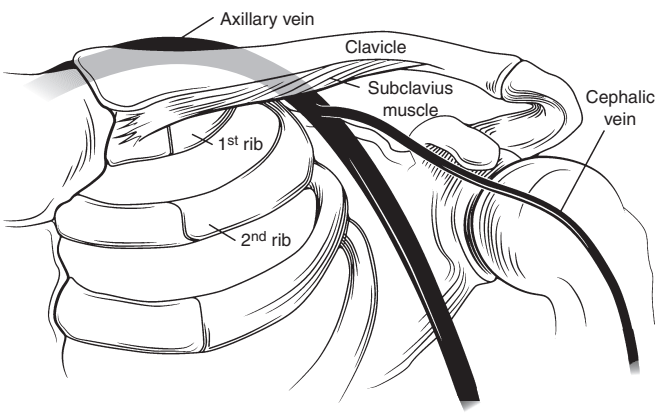

Figure 15.1 Diagram of the relationship of the axillary vein, first rib and clavicle. As long as the needle stays medial to the first rib, there is a very small chance of pneumothorax. Published with the permission of Bellot PH, Reynolds DW. Permanent pacemaker and implantable cardioverter-defrillator implantation. In: Ellenbogen KA, Kay GN, Lau CP, Wilkoff BL, ed. Clinical cardiac pacing, defibrillation and resynchronization therapy 3E, WB Saunders. Philadelphia, PA. 2007.

usually splittable, which allows removal of sheaths once the leads are placed in the endocardium. Leads come in two basic types: those with plastic projections called tines (passive fixation) or those with helical screws (active fixation) at the lead tip. Sometimes the screw is retractable into the lead and sometimes they are designed to always be exposed. Leads are introduced through the sheath with metal stylets into the hollow center of the leads to give the distal aspect of leads both shape and firmness.

- For the ventricular leads, a curved stylet is inserted which allows passage of the lead into the right ventricular outflow tract (RVOT). The presence of ventricular ectopy and placement in the RVOT ensures that the lead is in the right ventricle and not the coronary sinus. From this position, either a curved or straight stylet is inserted to place the lead along the septum or at the apex. If the lead is an active fixation lead, it is screwed into place with confirmation by fluoroscopy. Passive fixation leads are usually only stable in the apex but they can be also trapped in the right ventricular trabeculations above the apex.
- The lead is then tested for sensing, capture threshold, impedance, and injury pattern. Acceptable sensing for the R-wave is usually greater than or equal to 5 mV and acceptable capture threshold is less than or equal to 1 V. Impedance varies with the type of lead and the amount of scar in the myocardium, but should usually be less than 1000–1200 ohms. Acutely, especially after a lead is 'screwed in', an injury pattern (ST-segment-like elevation of the electrogram) is indicative of good contact with myocardium.
- For atrial leads, a straight stylet is used to advance the lead into the right atrium. A preformed J-shaped stylet is used to place the atrial lead into the right atrial appendage (RAA), lateral wall, or septum. The active fixation is

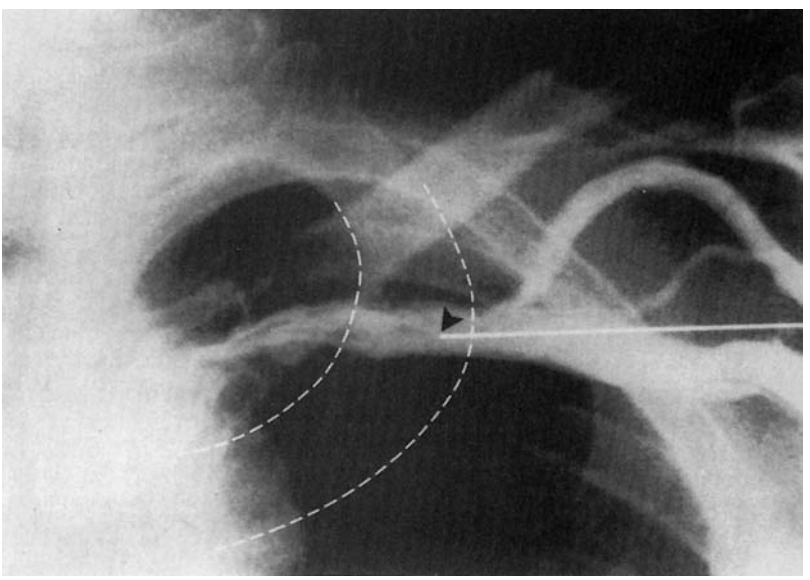

Figure 15.2 Fluoroscopic picture of needle access of the axillary vein using the 'first-rib approach' during a venogram. Published with the permission of Bellot PH, Reynolds DW. Permanent pacemaker and implantable cardioverter-defrillator implantation. In: Ellenbogen KA, Kay GN, Lau CP, Wilkoff BL, ed. Clinical cardiac pacing, defibrillation and resynchronization therapy 3E, WB Saunders. Philadelphia, PA. 2007.

then screwed with fluoroscopic confirmation. Passive fixation leads are usually only placed in the RAA. The acceptable sensing of the P-wave is greater than or equal to 2 mV and the acceptable capture threshold is less than or equal to 2 V. Impedances are similar to ventricular leads.

- Once the leads are positioned properly, suture sleeves are tied down with non-absorable sutures to secure the leads. It is important to allow for enough slack in both leads to accommodate the movement of the heart and diaphragm when the patient stands, for growth (if a pediatric patient), and for shoulder movements. The ventricular lead usually takes the shape of a boot with the curve of the boot just proximal to the tricuspid valve in the right atrium. The atrial lead should have enough slack in its distal loop and should not be intertwined with the ventricular lead.
- Once the leads are secured, the pocket should be re-inspected for hemostasis. The leads are then inserted into the connector block (header) of the pacemaker or ICD and the set-screws tightened. It is important to determine correct placement of leads into the header both in terms of alignment and matching ventricular lead to the ventricular port, and similarly for the shock and atrial leads. Once the device is secured in the pocket, two deeper layers of absorbable suture and one layer of subcuticular suture are used to close the pocket.

DEFIBRILLATION THRESHOLD TESTING

- For ICDs, defibrillation threshold tests (DFTs) are done to assure that the ICD can detect and terminate ventricular fibrillation with an adequate safety margin for defibrillation. DFTs are based on probabilities. If DFTs are successful, then there is a high probability of successful shock in the future, but there is not 100% certainty. However, if DFTs are unsuccessful, then there is a lower probability of success in the future and additional maneuvers will need to be considered.
- What defines a successful DFT? It varies from center to center, but a fairly common definition is defibrillation, often twice, with a 10 joule safety margin in reference to the maximum delivered output of the device. If this is not achieved, then polarity of the shocking coils may be reversed or additional coils may need to be implanted, either subcutaneously or in the azygous vein.

INTERROGATION AND PROGRAMMING AFTER IMPLANTATION

- After the device is implanted and the pocket closed, the device is usually checked, through the device, for atrial and ventricular sensing, capture thresholds, and impedance. This can help identify problems such as early lead dislodgement or loose set-screw.
- In addition, initial programming of the device is often performed at this stage. Programming options have grown over the years, but several key features are often programmed in the lab after implantation. The low pacing rate, high pacing rate (if applicable), rate responsiveness, and the atrioventricular (AV) interval are some of the basic options that are programmed. The AV interval has become more important in recent years with the realization that ventricular pacing could cause left ventricular dysfunction and heart failure symptoms. The AV interval is usually set slightly longer than the native AV interval to allow for AV conduction. Most devices now have a feature which searches for native

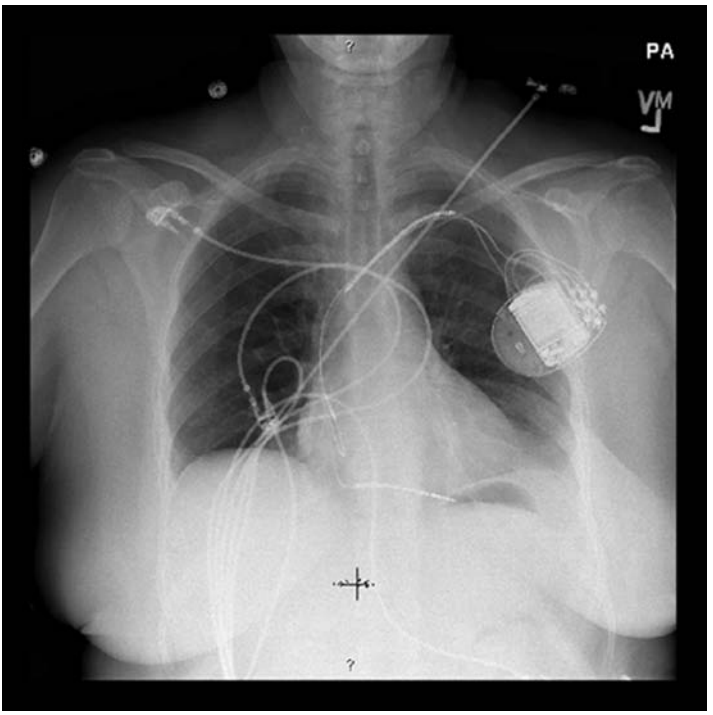

Figure 15.3 Chest X-ray of a typical dual-chamber ICD.

AV conduction by extending the paced AV interval. For ICDs, the number of tachycardia zones is programmable as well as the use of ATP. Empiric use of ATP in the ventricular tachycardia zone has been shown to decrease shocks without compromising patient safety.

- Patients usually require an overnight stay in hospital with inpatient Holter monitoring, follow-up chest X-ray to check positioning of the leads, and a device interrogation to assess sensing, capture thresholds, and impedance. Figure 15.3 shows a chest X-ray with typical location and appearance of a dual chamber ICD. If these tests and the wound are without problems, then the patient is usually seen at 6–8 week follow-up for a device interrogation.
- When a lead is screwed into atrial or ventricular tissue, there is an initial current of injury. Over the next 6 to 8 weeks, the lead matures as the injured myocardium surrounding the lead fibroses. This can cause an increase in the capture threshold from the time of implantation to time of lead maturation at 6 to 8 weeks. Thus, at the time of device implantation, pacing output is set to a high output (usually 5 V). Thresholds checked at 6 to 8 weeks post-implantation are usually stable and pacing outputs are then set to 1.7 to 2 times the capture thresholds.

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16

Implantation of cardiac resynchronization therapy

Kenneth Civello, Mohammed Khan, Bruce Wilkoff, and Jennifer Cummings

BACKGROUND

Cardiac resynchronization therapy (CRT) has proven to be an invaluable tool in improving the quality of life in patients with left ventricular dysfunction, congestive heart failure, and interventricular conduction delay. Patients who receive CRT have improved functional capacity estimated by 6 minute walk, New York Heart Association classification, and quality of life based on Minnesota Living with Heart Failure questionnaires, and they are protected from the associated increased risk of sudden cardiac death when combined with an implantable cardioverter-defibrillator (ICD) system.[1]

The number of implants continues to increase as well as the number of operators comfortable implanting leads in branches of the coronary sinus (CS). Despite the improvements in technology specifically designed to ease the implantation of the CS lead, this step remains the major obstacle in delivering optimal CRT. One of the most important factors in delivering CRT is the placement of the CS lead in the appropriate location. The posterior and lateral locations appear to offer the most benefit. These locations are directly opposite the anterior and apically located right ventricular or ICD lead. Although the anterior branches of the CS tend to be easier to cannulate than the posterior and lateral branches, these locations appear to be less beneficial and may be responsible for some of the patients classified as non-responders.[2] The two major obstacles to delivering optimal CRT are coronary sinus OS cannulation and delivering a lead to the appropriate branch in a posterior and lateral location. Although most implantations of CRT systems are, relatively, uncomplicated, this chapter outlines an approach that allows one to recognize and avoid potential obstacles and continue moving forward when other obstacles are encountered.

CANNULATION OF THE CORONARY SINUS

The first step in delivering a lead to pace the left ventricle is cannulation of the coronary sinus. After cannulation, the system that is present must be stable and provide a 'backbone' to allow force to be applied to the tip of the lead without dislodging the system. Several methods to engage the CS exist. These include dedicated sheaths and guide-wire systems, sheaths with steerable and telescoping inner catheters, and steerable electrophysiologic catheters that provide electrical clues to the location of the CS ostium, with the typical larger atrial electrogram and smaller ventricular electrogram. Fluoroscopy, which is frequently performed in the left anterior oblique (LAO) position, also provides guidance to the location.

Anatomically, there are two potential impediments to entering the CS os. Laterally, the Eustachian ridge may prevent the advancement of a catheter to the ostium. Inferiorly, a thebesian valve may prevent entry to the ostium from an approach below (Figure 16.1). The optimal method of avoiding these impediments is approaching the ostium from the superior and medial approach. Regardless of the equipment used or the fluoroscopic approach, to avoid the Eustachian ridge and the thebesian valve, one should advance the system initially into the right ventricle and withdraw the system, while applying counterclockwise torque. When the catheter or sheath appears to be freed from the tricuspid valve, then it should be advanced while continuing counterclockwise torque. This technique

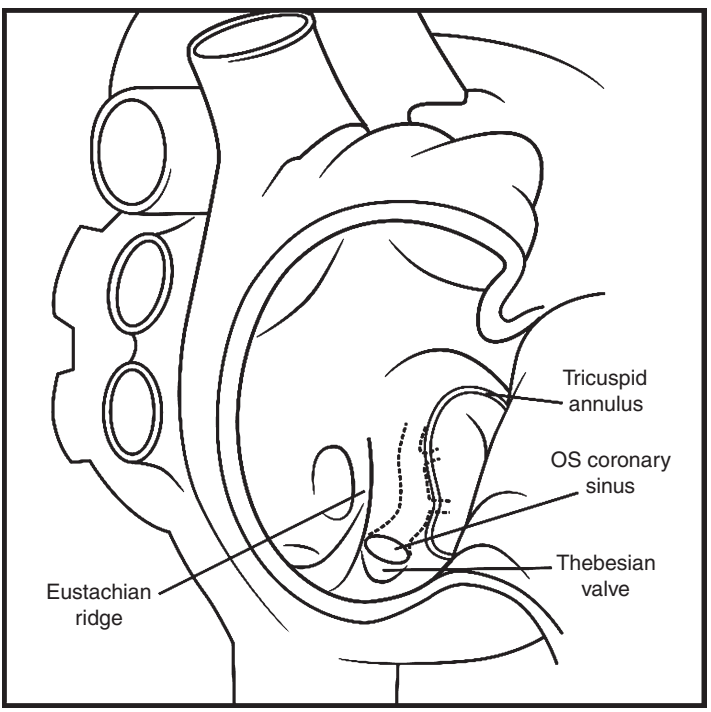

Figure 16.1 Anatomy of the coronary sinus os and surrounding structures.

will avoid both impediments in most cases, and as long as counterclockwise torque is applied, this will also tend to avoid the atrial sulcus inferior and anterior to the CS os, below the tricuspid valve. Using a sheath or catheter with a proximal curve allows one to easily direct it over the Eustachian ridge.

If difficulty persists after performing this maneuver, 'puffing' contrast dye through the sheath or catheter is frequently revealing. It may show the atrial sulcus, in which the approach should be more posterior and superior. Contrast may also reveal either an early or separate take-off of a middle cardiac vein that is preferentially cannulated by the system. Slight manipulation of the system while using contrast may allow the main CS to be selected. Other possibilities include an acutely angled ostium, vertical or tortuous initial segments, or narrowing in the CS from a mid-CS valve or resulting from prior surgery. In these situations, contrast is invaluable to determine the cause of difficulty and aid in determining the optimal remedy. In cases such as these, an inner guide-wire or catheter may facilitate the manipulation and rigidity to allow passage of the outer sheath.

Several fluoroscopic clues may disclose the location of the CS. If an ICD lead has been placed in the RV apex, the ostium is generally in the vicinity of the proximal end of the distal coil in most usual projections. The 'fat stripe' or radiolucency of the atrioventricular groove can be seen best in the right anterior oblique view. In the left anterior oblique view, the coronary sinus will appear to course more toward the left side of the chest, while the right ventricle is *en face*. This orientation may more clearly reveal the posterior position of the sheath or catheter, especially if the operator's difficulty is repeatedly advancing into the right ventricle, indicating that the position is not posterior enough.

LV LEAD DELIVERY INTO THE APPROPRIATE CORONARY SINUS TRIBUTARY

After intubation of the CS, the second major obstacle in delivering optimal CRT is cannulation of the appropriate posterior and lateral branch with the lead. The most important tool to accomplish this is the presence of an appropriate 'backbone' that will allow force to be transmitted to the tip of the lead when advancing it without dislodging the system or pushing the system back. The sheath that is used to deliver the lead needs to be designed so that it rests firmly against the lower lateral right atrium and superior vena cava. These sites provide the best support, and the sheath should be stiff enough to allow pressure at these sites without changing the conformation of the sheath. Appropriate sheaths, generally, have a long straight segment followed by an extended curve, with the proximal curve intended to rest against the lower lateral right atrium. The next straight segment lies anterior to the Eustachian ridge and the secondary curve enters the coronary sinus. The size of the primary curve and length of the segment between the curves may need to be larger if the right atrium is significantly dilated, as is the case in some patients with tricuspid regurgitation. This 'backbone' or workstation provides the support necessary for the force required to advance the lead into the appropriate branch.

At this point, it is frequently helpful to assess the available options in the venous anatomy with coronary venography. Several balloon-tipped catheters are available

for this purpose. Of note, one may wish to use a guidewire to advance the balloon-tipped catheter because this catheter alone may be a source of coronary vein dissections. For this to be a fruitful exercise, the coronary sinus should be occluded during contrast injection. The images should be saved on a separate monitor, if possible, and special attention should be paid to the initial segments of the appropriately located branches and the size of the branches. Several different fluoroscopic views may delineate the 'take-off' of the branches selected.

CORONARY SINUS ANATOMY

After performing coronary venography the operator must then select the coronary vein tributary that will deliver the lead to a posterior and lateral location. Due to discrepancies between physicians in naming the branches of the coronary sinus and tributaries we rely on academic sources and journal reports for the correct nomenclature.[3–11] The coronary veins are described starting with the anterior interventricular vein (AIV), which is defined as originating at the lower or middle third of the anterior interventricular groove. It connects with diagonal veins (DVs) supplying the lateral and anterolateral portion of the left ventricle. It continues to run vertically and as it turns posterior at the AV groove and courses horizontally it becomes the great vein (GV). The GV courses medial over the summit of the left ventricle (Figure 16.2).

The great cardiac vein becomes the CS at the left atrial oblique vein of Marshall (LAOV). In cases where the LAOV is not present the CS begins at the valve of Vieussens.

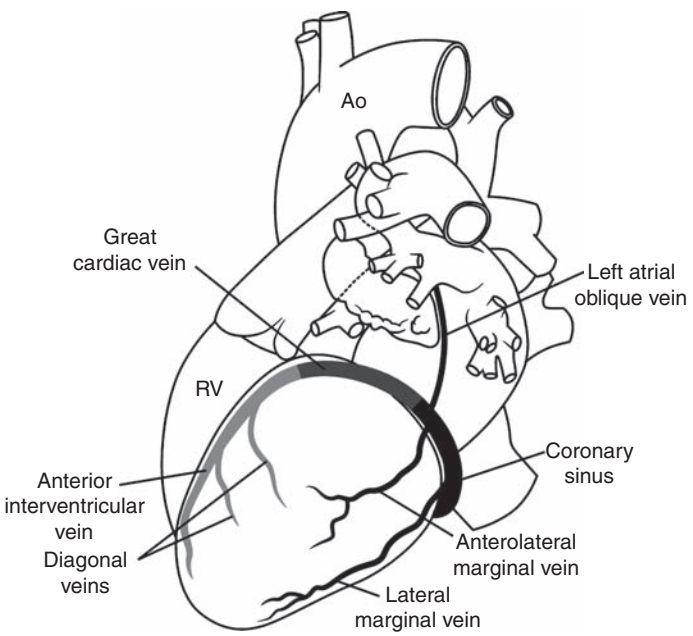

Figure 16.2 Anatomy of the coronary veins. (See color plate section.)

The tributaries of the CS that originate off the lateral wall are referred to as marginal veins. These marginal veins are further defined by the location where they empty into the CS in the LAO projection, such as the anterolateral marginal (AM), lateral marginal (LM), and inferolateral marginal (IM) (Figure 16.3). Since posterior is not an accepted terminology in echocardiographic standards, inferolateral is used in naming the CS tributary here for consistency, but posterolateral marginal may be used.

The posterior ventricular vein (PVV) drains the inferior (posterior) aspect of the left ventricle. The PVV is often confused with the posterolateral marginal vein due to the similar location. The PVV is usually larger in caliber than the posterolateral marginal and sometimes drains into the middle cardiac vein (MCV). The MCV originates near the apex, runs in the posterior interventricular groove, and drains either directly into the right atrium or into the CS just before it opens into the right atrium (Figure 16.4).

We also prefer to use fluoroscopy for the identification of the location of the left ventricular lead tip after completion of the procedure. Since implantation of left ventricular leads occurs in the electrophysiology lab with fluoroscopy we used fluoroscopic views to correspond with the short axis and long axis views of the heart. Using this method an accurate and consistent description of the location of the LV lead tip can be made at the time of implant and entered into the operative report, rather than relying on the CXR for documentation of lead position.

The RAO 30 projection is used to define the location of the left ventricle along the vertical axis of the heart, dividing it into a basal, mid and apical

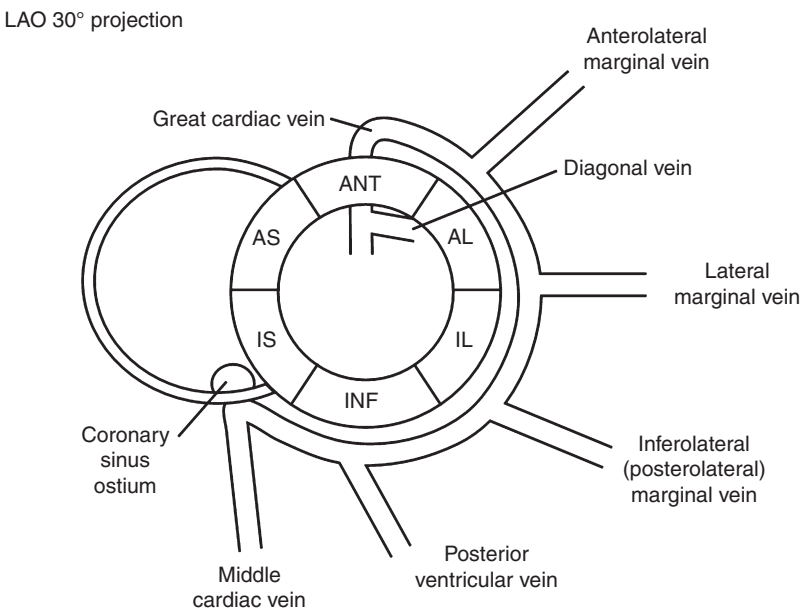

Figure 16.3 Anatomy of the branches of the coronary sinus (CS), including the marginal veins. This projection at LAO 30 projection is also used for the short axis views to define the circumferential location of the lead.

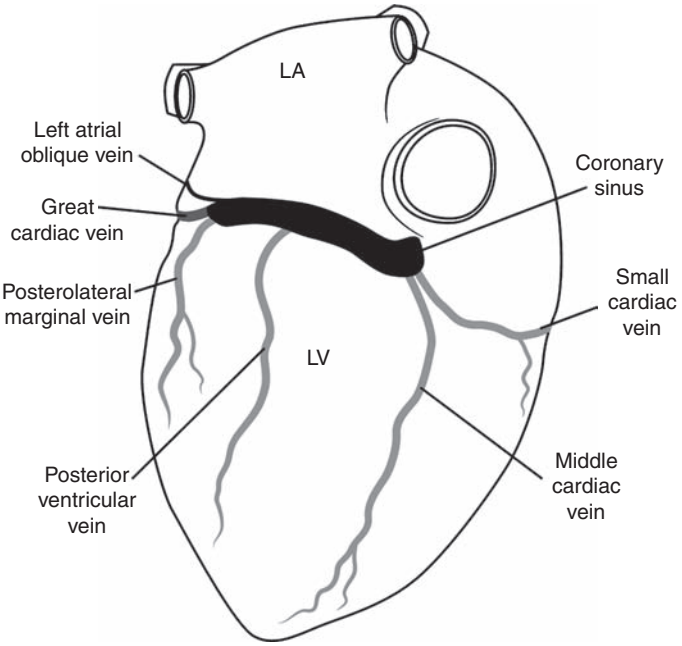

Figure 16.4 Anatomy of the coronary sinus including the posterior interventricular vein or middle cardiac vein and posterior ventricular vein. (See color plate section.)

third (Figure 16.5). The LAO 30 projection is used for the short axis views to define the circumferential location of the lead.

Based on the anatomy, the operator may make several decisions at this point, including the size of the lead used and the approach to the branches. Manufacturers now produce leads that are different sizes and with different shape characteristics, such as a distal coil or sigmoid shapes, that allow a larger lead to be placed in larger branches or make use of the distal lead shape to keep the lead in place. If a large posterolateral branch is present without any obvious impediments to the initial portion of this branch, then a large stylet driven lead may be the appropriate choice; however, if the branches in the appropriate locations appear anything other than straight in their initial segment, then the operator should consider the available options.

The impediments to cannulating branches of the CS include an angulated take-off of the branch, a tortuous initial segment, or a small or stenosed branch. Once again, proceeding from this point necessitates that the outer sheath provides adequate support. If the initial segment of the selected branch is slightly angulated, then using an over-the-wire lead system may be the only tool necessary. The wire is used to navigate the branch, and the lead is inserted over the wire.

Occasionally, it is difficult to even get the wire into the selected branch. For this problem, inner catheters may be used to intubate the selected branches, and the wire is advanced through this catheter into the branch. The catheter is removed, and the lead is advanced over the wire. At points where it becomes

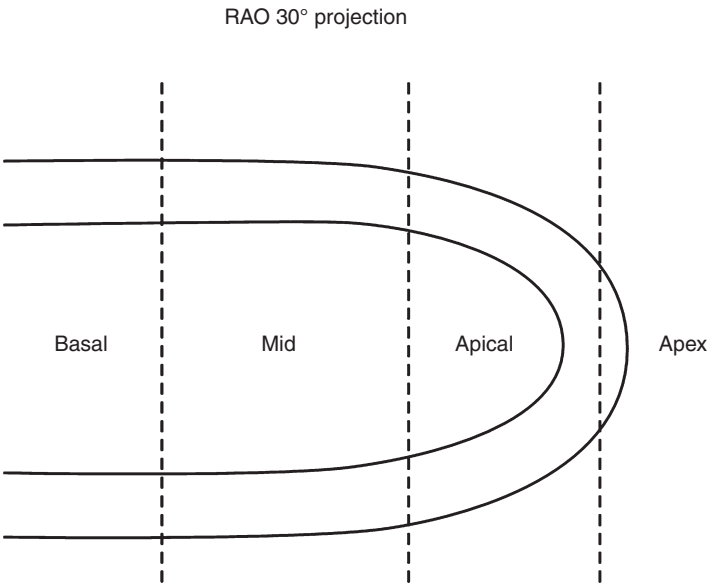

Figure 16.5 The RAO 30 projection is used to define the location of the left ventricle along the vertical axis of the heart dividing it into a basal, mid, and apical third.

difficult to advance the lead, simultaneously advancing the lead and withdrawing the wire is sometimes helpful. The optimal set-up for this is like an angioplasty system. On the tip of the catheter a system with an adjustable valve and side port should be placed. The wire goes through the valve, and the side port allows contrast to opacify the vein and branch, when the valve is closed.

For selected branches that have a very angulated or tortuous initial segment, or are small enough to require that enough direct pressure be applied to the tip of the lead, the ultimate system is using an inner catheter that intubates the selected branch and is large enough to accept and advance the lead. The characteristics of this inner sheath must be similar to the outer sheath. It must be stiff enough to allow pressure to be transmitted to the tip of the lead without buckling. It must also be shaped in a fashion that it uses the wall of the CS opposite the selected branch and the outer sheath for support (Figure 16.6). Currently, there are three available shapes. The multi-purpose shape will provide support for most mild angulations. The renal and hockey stick shapes are appropriate for more severe angulations or very tortuous initial segments. In fact, these inner catheters will, by their shape and stiffness, straighten branches and allow deeper intubations of the branches (Figure 16.7). They can be used like angioplasty catheters with contrast and manipulated to locate the ostium of the selected branch. The lead and wire can be inserted into the branch directly through the catheter. The added support makes advancement of the lead much easier. Another way to straighten tortuous branch segments is the use of a buddy wire. In this case, a relatively stiff wire is used to cannulate the branch, and another wire is used to cannulate the branch and deliver the lead.

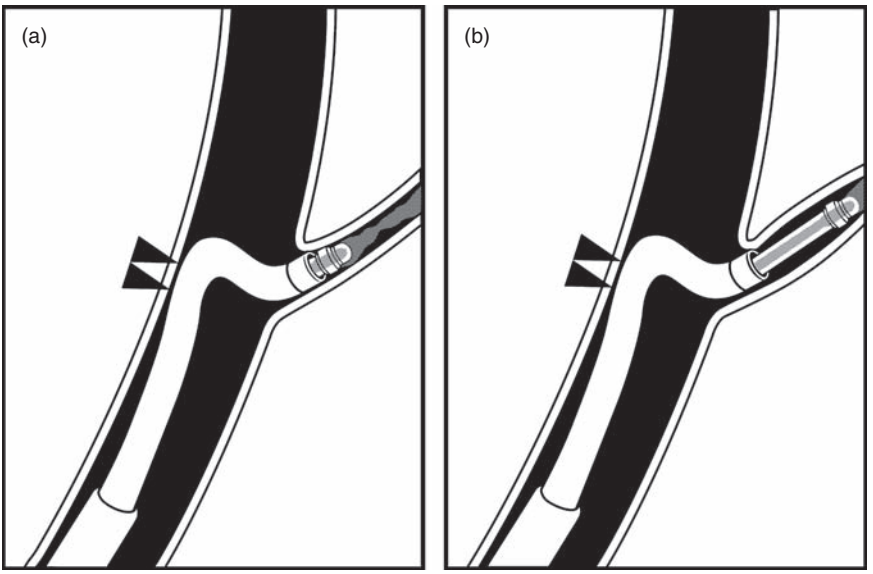

Figure 16.6 (a) An example of an inner catheter that allows the delivery of a lead. The shape of the catheter allows both intubation of the side branch and pressure to be applied to the opposite wall of the coronary sinus. (b) This allows the lead to advance across a narrow segment.

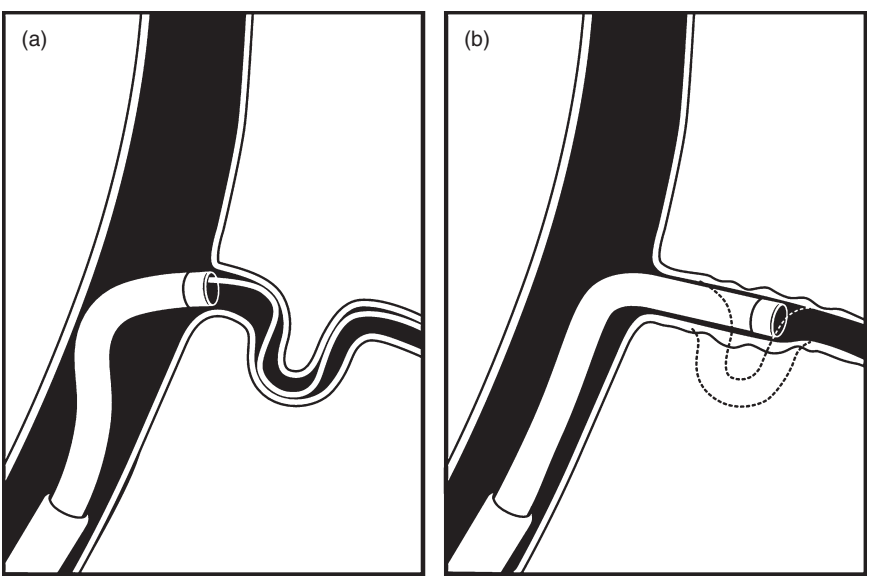

Figure 16.7 (a) An example of an inner catheter and guidewire that allow intubation of a tortuous side branch. (b) When the catheter is fully engaged, the tortuosity is straightened.

VENOPLASTY TECHNIQUES

The final obstacle to delivering the lead may be limitation in the size or a stenosed segment of the appropriately located vein. The solution to this problem is venoplasty. The outer sheath and inner catheter system should be used to intubate the ostium of the branch. A guidewire should be passed to the most distal portion of this vein. A non-compliant balloon of appropriate length for the stenosed or small segment should be used. In general, the sizes necessary for accepting coronary venous pacing leads are 3 to 3.5 mm in diameter. The segment is dilated using a long slow inflation. The balloon is deflated, removed, and replaced with the over-the-wire pacing lead. The dilated vein tends to return to its original size and serves to aid in keeping the lead in place.[12]

SUMMARY

Several obstacles are present that make delivering optimal CRT more difficult. An understanding of the anatomic structure and its variations is an invaluable tool. The method of approaching the CS ostium from the right ventricle avoids the pitfalls of the Eustachian ridge and the overriding thebesian valve. Using an outer sheath that serves as a strong, supportive workstation, and the philosophy of always moving forward with the available tools of an inner sheath that allows selective branch intubation and delivery of the pacing lead as well as venoplasty techniques, permits an operator to overcome most of the challenges presented by difficult anatomy.

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17

Extraction of devices

Sergio Thal, Dhanunjaya Lakkireddy, Jennifer Cummings, and Bruce L Wilkoff

Indications • Extraction tools • Techniques of lead extraction • Procedure success evaluation

Percutaneous intravascular lead extraction has evolved from simple traction through a weight-and-pulley system to a more advanced modern day laser and radiofrequency technique. A more invasive open-heart surgical technique through a midline sternotomy or a limited atriotomy technique was developed, and continues to be a last resort answer to difficult lead extractions that are not suitable for percutaneous techniques.[1,2]

Lead extractions are probably one of the most challenging procedures that a cardiac electrophysiologist has to face today. The indication for device implants has risen tremendously in the last years, and the associated complications that require interventions are expected to rise also. The potential for life-threatening complications like lead breakage, venous or myocardial tear, and tamponade makes lead extraction the least favorable procedure even to the most experienced hands.

INDICATIONS

The indications for transvenous lead extraction can be categorized into two groups – patient-related and lead-related. Patient-related indications are infection, ineffective therapy (high defibrillation threshold), perforation, migration, embolization, induction of arrhythmias, venous thrombosis, unrelenting pain, device interactions, device upgrades, and/or presence of multiple abandoned leads. Lead-related indications include lead recalls, lead failure, and/or lead interactions.[3]

Among the current indications, infected devices are one of the most prevalent. Antibiotic therapy without extraction, named conservative approach, was initially advocated by some authors, but in the experience published by the Cleveland Clinic Foundation in 2000 this approach was shown to be ineffective.[4] In this publication the most frequent symptoms of pocket infection were erythema and local pain and they were caused by coagulase-negative staphylococci in 68% and *Staphylococcus aureus* in 23% of cases. Ninety-five percent of these devices were successfully extracted, with 0% operative mortality.

Until the establishment of the current guidelines in 2000 by the North American Society of Pacing and Electrophysiology (NASPE, currently Heart Rhythm Society) the Byrd classification was used for indications of lead extraction.[5] In April 2000 the NASPE Policy Statement established the current recommendations for chronically implanted transvenous pacing and defibrillator lead extractions,[6] as follows:

Class 1

a. Sepsis (including endocarditis) as a result of documented infection of any intravascular part of the pacing system, or as a result of a pacemaker pocket infection when the intravascular portion of the lead system cannot be aseptically separated from the pocket.
b. Life-threatening arrhythmias secondary to a retained lead fragment.
c. A retained lead, lead fragment, or extraction hardware that poses an immediate or imminent physical threat to the patient.
d. Clinically significant thromboembolic events caused by a retained lead or lead fragment.
e. Obliteration or occlusion of all useable veins, with the need to implant a new transvenous pacing system.
f. A lead that interferes with the operation of another implanted device (e.g., pacemaker or defibrillator).

Class 2

a. Localized pocket infection, erosion, or chronic draining sinus that does not involve the transvenous portion of the lead system, when the lead can be cut through a clean incision that is totally separate from the infected area.
b. An occult infection for which no source can be found, and for which the pacing system is suspected.
c. Chronic pain at the pocket or lead insertion site that causes significant discomfort for the patient, is not manageable by medical or surgical technique without lead removal, and for which there is no acceptable alternative.
d. A lead that, due to its design or its failure, may pose a threat to the patient, though is not immediate or imminent if left in place.
e. A lead that interferes with the treatment of a malignancy.
f. A traumatic injury to the entry site of the lead for which the lead may interfere with reconstruction of the site.
g. Leads preventing access to the venous circulation for newly required implantable devices.
h. Non-functional leads in a young patient.

Class 3

a. Any situation where the risk posed by removal of the lead is significantly higher than the benefit of removing the lead.
b. A single non-functional transvenous lead in an older patient.
c. Any normally functioning lead that may be reused at the time of pulse generator replacement provided the lead has a reliable performance history.

EXTRACTION TOOLS

The tools used for extractions are shown in Table 17.1.

Locking stylets

Locking stylets provide tensile strength to the lead all the way to the tip electrode. This permits the advancement of the telescoping sheaths and withdrawal of the entire lead, without leaving fragments behind.

Telescoping sheaths

The inner and outer telescoping sheaths provide for flexibility and strength as they are passed over the lead to the endocardial surface. Balanced traction on the locking stylet allows first the inner and then the outer sheath to break through the scar tissue and down over the lead to the endocardium. Their use is based on the two important concepts of *counterpressure* and *countertraction*.[8] They are available in 11 to 16 French sizes.

Table 17.1 Extraction tools

Locking stylets	Liberator (Cook-Vandergrift, PA)	3rd generation locking stylet, locks at the distal end of the conductor coil. One size fits all leads
	Lead Locking Device (Spectranetics, Colorado Springs, CO)	Locking mechanism locks along the entire length of the conductor coil, 4 sizes are used depending on the coil inner diameter
	VascoMED (Weil am Rhein, Germany)[7]	T-shaped end screws down the conductor coil to the tip. Available in Europe only
Telescoping sheaths	Stainless steel sheaths	Used to break through the tissue at the vein entry site. Once access to the vein is obtained, replacement with flexible sheaths that adapt better to the vein's shape is recommended[7]
	Plastic sheaths (Teflon or polypropylene)	Used to maneuver around curves and forcing through circumferential bands of fibrous tissue in the vein tracts
Laser ablation	Excimer laser light (Spectranetics, Colorado Springs, CO)	Light dissolves the fibrotic tissue along the entire circumference as it advances over the lead. The sheaths are provided in 12, 14, and 16 French
Electrosurgical ablation	Electrosurgical energy, modified from a standard surgical Bovie unit	The spark is produced between two tungsten wires and cuts the fibrosis along about 15% of the arc of the Teflon sheath
Byrd femoral workstation and femoral snares	Teflon sheaths used to snare the snare in the heart or veins (Cook-Vandergrift, PA)	Several snares (needle's eye snare, Dotter basket with tip deflecting guidewire, Amplatz gooseneck snare) are used to grasp the lead and the Teflon sheath is advanced over the lead to the heart to provide counter-traction[10,11]

Laser ablation

The sheath is used to dissolve proximal scar adherences, but once near the tip of the lead it could be used to apply countertraction against the heart wall and free the distal tip of the lead.

Byrd femoral workstation and femoral snares

Some leads that have been cut or fractured are not accessible from the venous entry site. In these cases, the femoral approach for lead extraction may be favored. Femoral extraction requires the use of a large 16 French sheath (Byrd workstation), which is carefully inserted via the femoral vein.[9] The sheath has many functions, including protection of the vein or heart from damage during femoral snare insertion, and it acts as the outer telescoping sheath for countertraction. A snare can then be inserted through the sheath to grasp the lead and pull it down from the superior veins and from the heart with countertraction.

TECHNIQUES OF LEAD EXTRACTION

Femoral venous and arterial access must be obtained before the extraction starts. The anesthesia method would depend on the team preferences, general status of the patient, and the quality and quantity of leads to be extracted. Measures must be taken to provide appropriate temporary pacing in pacer-dependent patients.

The following are the basic *principles* for a successful lead extraction:

1. Control of the lead body and tip, which could be achieved by binding of its elements with the application of uniform force on the entire length of the lead, to remove it in one piece with minimal disruption. The locking stylets previously described are the appropriate tool to use.
2. Controlled disruption of the fibrous tissue using counterpressure.
3. Bracing the cardiac wall using countertraction, which involves opposing the traction placed on the lead by bracing the myocardium with the overlying blunt sheath. This focuses the traction force perpendicular to the heart wall and limits the counterpressure to the scar tissue immediately surrounding the lead tip (Figure 17.1).

General technical principles

1. A linear incision is made to obtain better access to the vein of insertion and the generator is explanted.
2. The terminal pin of each lead is cut, leaving sufficient length of the proximal end outside the venous insertion. The cut end is prepared by circumferentially incising the insulation.
3. A standard pacemaker stylet is passed through the electrode to its distal tip to ascertain the distance through which the locking stylet has to travel and to clear the debris.
4. A locking stylet is advanced to the farthest reach of the lead and a 0 gauge suture is tied around the insulation tightly with a square knot. The long end of the suture is then tied to the looped end of the locking stylet, providing

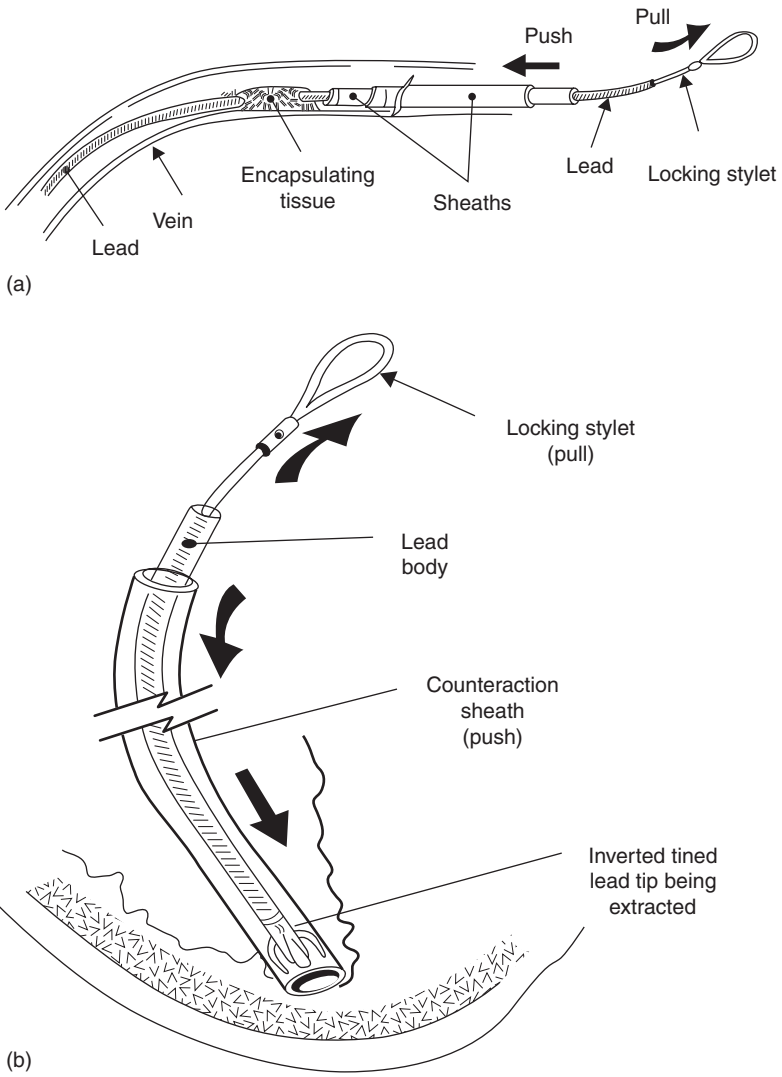

Figure 17.1 Diagrammatic representation of (a) counterpressure and (b) countertraction used during lead extraction.

for parallel and simultaneous traction on the outer insulation and on the conductor coil.

5. Sheaths:
   - A retraction force is applied on the looped end of the locking stylet equal to which allows advancement of the sheaths while holding the lead away from the outer arc of the insertion vein and into the heart.
   - The sheaths should always be advanced under direct fluoroscopic guidance.

- Sheaths should not be advanced directly against the vessel wall but rather the leads should be peeled away from the wall of the vessel, bringing the lead into the center of the vascular lumen.

6. With infected devices, the generator pocket should be completely excised to prevent microbial reseeding, and closed with mattress sutures, allowing healing by secondary intention. In a non-infected extraction new hardware can be implanted during the same procedure.

Specific procedures

Table 17.2 summarizes the principal extraction techniques.

Excimer laser extraction

The laser sheath is one of the most effective extraction tools and has been prospectively studied in the randomized PLEXES trial in comparison to traditional extraction with locking stylets and telescoping sheaths.[12] Laser resulted in a higher percentage of complete lead removal (94% versus 64%, $p = 0.001$) and also reduced the time required for removal (10.1 $\pm$ 11.5 min versus 12.9 $\pm$ 19.2 min, $p < 0.04$). Life-threatening complications (including one death) occurred in the laser group, while none occurred in the traditional group, but this difference was not statistically different given the small numbers overall. Whether a true difference exists requires further evaluation, but there is little doubt that the laser has improved the efficacy and speed of lead extraction. Further trials were performed using the larger diameter 14 and 16 French laser sheaths for larger leads, such as defibrillator leads.[13,14] The efficacy and complication rates were similar to those reported above, and the extraction time was only 2 to 4 minutes longer per lead (Figure 17.2).

Radiofrequency extraction

The electrosurgical sheath provides hypothetical advantages over the laser. First, the sheath is designed to be more supple and therefore may be better able to maneuver around bends in the vein compared to the laser sheath. Second, the radiofrequency energy is supposed to be gentler than the laser, allowing more careful dissection of the tissue and reducing the chance of vascular damage. Finally, the electrosurgical sheath is less expensive.[10] While there are no randomized trials published to date using the electrosurgical sheath, our preliminary experience from the Cleveland Clinic Foundation suggests that this tool compares

Table 17.2 Specific procedures

Conventional mechanical extraction	Conventional tools including the blunt but angled Teflon or steel telescoping sheaths with appropriate locking stylets using the principles of counterpressure and countertraction
Excimer laser extraction	Conventional technique plus Excimer laser inner telescoping sheaths for dissolution of the fibrotic tissue
Radiofrequency extraction	Conventional technique plus electrosurgical sheath for cutting the fibrotic tissue

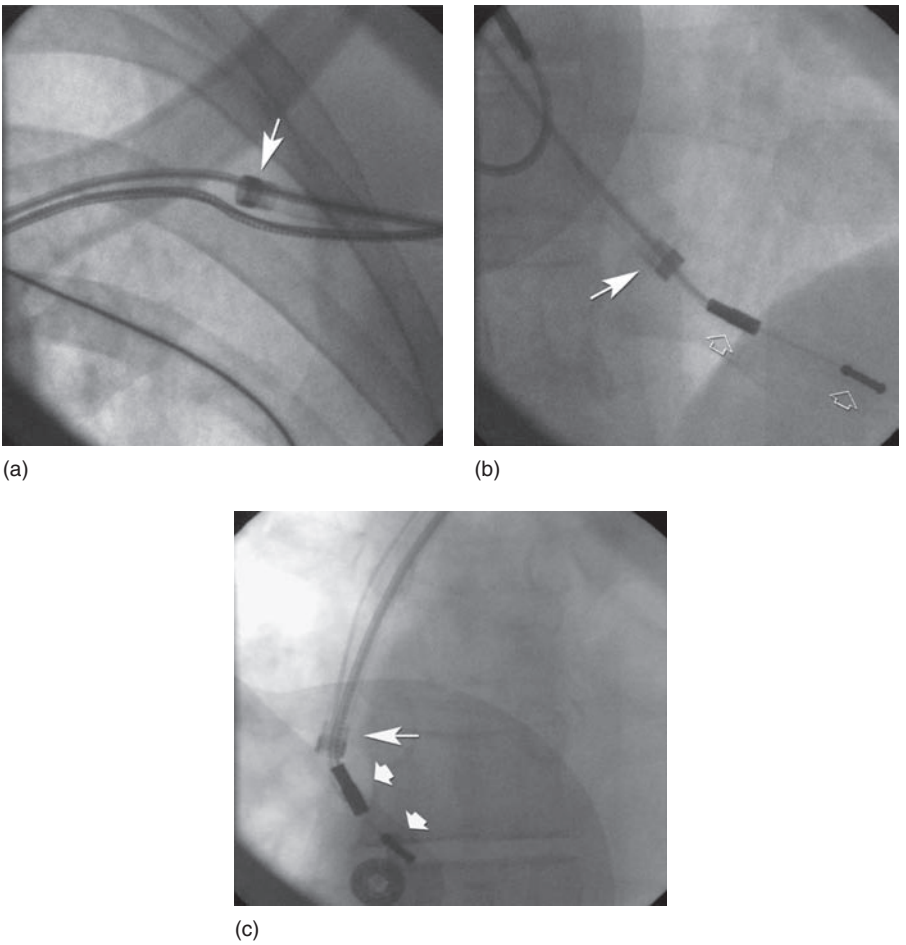

Figure 17.2 (a–c) Extraction of the old pacemaker leads within the left brachiocephalic vein using excimer laser sheath (long arrow). (Atrial lead, short solid arrow; ventricular lead, short open arrow.)

favorably to the laser sheath. We studied 450 consecutive lead extractions at our institution between November 1998 and November 2001 (Wilkoff BL, personal communication). Of these extractions, laser was used to extract 354 leads and electrosurgery was used to extract 96 leads. There were no complications in the electrosurgical group compared to two deaths in the laser group. Furthermore, procedure time was significantly lower in the electrosurgical group versus the laser (130 ± 49 min vs 158 ± 65 min, respectively, $p < 0.002$). Fluoroscopy time was also reduced (13.3 ± 10.6 min vs 17.1 ± 15.1 min respectively, $p < 0.05$). However, there was some selection bias in this series since the lead implant duration was significantly longer in the laser group compared to the electrosurgical group (8.2 ± 5.0 years versus 6.6 ± 4.4 years, $p < 0.005$). Regardless, it would seem that the electrosurgical sheath has comparable success rates to the laser.

Defibrillator lead extraction

The extraction of these leads challenges the increased amount of fibrous tissue surrounding the defibrillator coils, especially the proximal one located at the superior vena cava. The extraction of defibrillator leads can be accomplished using the same tools used for pacer leads with similar success rates.[15–17] In a series of 161 patients at the Cleveland Clinic, successful complete extraction of implantable defibrillator leads was achieved without major complication in 96.9% of patients.[18] Failure occurred in only three patients. Two patients had major complications including one death. According to the US lead extraction database, established in 1998, there are no major differences regarding extraction success and major complications compared with pacemaker lead extraction.

Coronary sinus lead extraction

Coronary sinus (CS) leads are typically non-active fixation, and non-tined thin-bodied leads; they are still capable of triggering significant fibrotic responses within the CS.[19] Similar to regular atrial or ventricular leads, CS leads implanted under 6 months may be extracted with simple traction. A small report on 14 patients showed 100% successful extraction without major complications and very short procedure and fluoroscopy times (13 min and 1.8 min, respectively).[20] However, more than one-third of these leads had been implanted for less than 6 months. Currently a 7 French electrosurgical dissection sheath (EDS) is available for extracting CS leads. A recent report by Burke et al showed the feasibility of CS lead extractions using a laser tool.[21] In their experience they were able to successfully extract the leads in six patients using laser sheaths, without procedural complications. Use of the laser in the smaller branch vessels of the cardiac veins is almost certain to cause problems, but is fine in the parts of the lead up to the CS os. However, further data regarding the risks and success of CS lead extraction will be required, especially as the number of these lead implants grows over the next few years. With the use of newer, thicker, bipolar CS leads, extraction may not be as simple and untraumatic as with the thin unipolar leads. The issues surrounding the extraction of these newer leads are yet to be understood.

PROCEDURE SUCCESS EVALUATION

According to the NASPE policy statement on device extractions,[6] the success of an extraction procedure could be evaluated from two different points of view:

1. Radiographically:
   a. Complete success (removal of all the lead material)
   b. Partial success (removal of all but a small portion of the lead)
   c. Failure (abandoned a significant length, more than 4 cm, of the lead).
2. Clinically:
   a. Success (achieved all the clinical goals of the procedure)
   b. Failure (unable to achieve all the clinical goals from the extraction).

These two different points of view may prompt the idea that in some cases the partial removal of a lead could be enough to be considered a ‘clinical success’

besides the fact that, from a radiographic point of view, the procedure should be called a 'partial success', and would be considered a significantly good endpoint to avoid any further unnecessary maneuvers that could eventually increase the complications rate without clinical benefit for the patient.

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Section VIII

Performing basic EP studies

18

Venous and arterial access, EP catheters, positioning of catheters

Chi Keong Ching, J David Burkhardt, Thomas Dresing, and Andrea Natale

Femoral artery and vein punctures • Femoral vein puncture • Femoral artery puncture • Subclavian vein puncture • Internal jugular vein puncture • Venous access during a procedure with aggressive anticoagulation or therapeutic INR • Standard catheter positions

FEMORAL ARTERY AND VEIN PUNCTURES

These vessels are common sites of entry for catheterization of right and left heart chambers for electrophysiologic recordings. The femoral artery typically begins in the midpoint of the inguinal ligament and ends at the junction of the middle and lower third of the thigh to become the popliteal artery. Its proximal course of about 4 cm lies within the femoral sheath and the arterial pulse can be felt at the inguinal skin crease. The femoral vein lies medial to the femoral artery, approximately one finger-breadth medial to the femoral artery. Adequate local anesthesia is given before vessel puncture to ensure patient comfort and cooperation.

FEMORAL VEIN PUNCTURE

The arterial course is outlined with three fingers while skin incisions are made medial to the arterial pulsation over the intended sites of entry. This small skin incision can be further enlarged by the use of a curved hemostat to prevent potential crimping of the intravascular sheath, Though the sheath can almost always be advanced over the guidewire safely and easily without having to first enlarge the skin defect. A Cook needle is then introduced through the skin incision and advanced along the anesthetized track at a 30–45 degree angle to the skin surface. Gentle suction is applied to the syringe as the needle is advanced until a clear flashback of non-pulsatile venous blood occurs. The syringe and the needle are depressed to be more parallel to the skin surface. The syringe is then detached and a J-tipped guide-wire is advanced into the hub of the needle and forward into

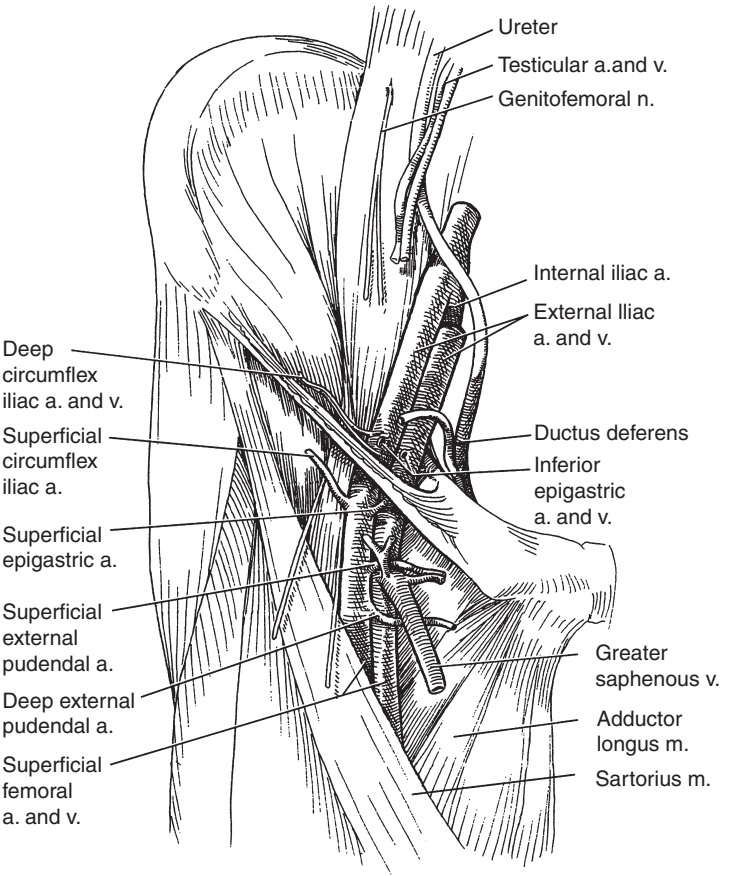


Figure 18.1 Relationship of the femoral vessels. Note the medial course of superficial and deep pudendal branches of the femoral artery. Published with the permission of valentine RJ. Anatomic exposures in vascular surgery. Philadelphia: Lippincott Williams & wilkins. 2003

the vessel without any resistance. If resistance is encountered, a downward depression of the needle hub to secure an intravascular position of the needle can be attempted. Otherwise the guidewire should be removed and a syringe re-attached and the whole assembly advanced or withdrawn slightly until a free flow of blood is encountered. If there is no free flow, the whole assembly is removed and pressure is held and landmarks rechecked before further venous punctures.

When the guidewire is successfully advanced intravascularly, the needle is removed and an intravascular sheath is then inserted over the guidewire until it protrudes from its proximal end. The whole assembly is then advanced with firm forward pressure and slight rotation. Once the sheath is intravascular and completely advanced, the guidewire and introducer can be removed and the side port flushed with heparinized saline. As illustrated in Figure 18.1, the intended site of entry should be within the femoral sheath. A lower site of entry may inadvertently puncture one of several branches of the femoral vein which traverse medially. The procedure can be repeated to accommodate up to three venous sheaths.

FEMORAL ARTERY PUNCTURE

Femoral artery puncture is performed lateral to the femoral vein puncture sites just below the femoral crease. With three fingers outlining the course of the femoral artery, the tip of an open lumen Cook needle is inserted at the site of maximal pulsation and carefully advanced. A pulsatile jet of flashback occurs when the needle enters the arterial lumen. With the left hand holding the hub steadily, a J-tipped guide-wire is then introduced through the needle into the arterial lumen and advanced into the lumen. With fluoroscopy, the guide-wire should be seen left of the vertebrae. If resistance is encountered or if the patient complains of any discomfort, the guidewire is likely to be within the subintimal wall of the artery. Other causes may be due to a kink in the intravascular sheath or tortuous vasculature. Alternatively a subintimal dissection may occur, in which case the needle is removed, a 5 French dilator is introduced over the wire and a small bolus of contrast agent is injected to verify the cause of obstruction. If arterial dissection is the cause, the whole assembly is removed and digital pressure is maintained for 5 to 10 minutes. If there is no dissection, other guide-wires may be tried. If resistance is encountered just beyond the tip of the needle, a downward depression of the needle hub should move the tip more intravascular and facilitate passage of the guide-wire. At all times, the backflow of blood must be pulsatile. When the guide-wire is adequately advanced without further resistance, the needle is withdrawn and the guide-wire wiped with wet gauzes. The desired intravascular sheath is then advanced over the guide-wire. The guide-wire is then removed and the side port of the sheath flushed with heparinized saline.

SUBCLAVIAN VEIN PUNCTURE

The left subclavian vein is the continuation of the axillary vein and extends from the outer border of the first rib to the sternal end of the clavicle. It lies posterior to the clavicle and often rests in a depression on the first rib and upon the pleura. The subclavian artery lies posterosuperior to the vein and is separated medially by the scalenus anterior. The site of puncture is immediately lateral to the ligament that joins the clavicle to the first rib which lies at the junction of the proximal two-thirds and distal one-third of the clavicle. Adequate anesthesia is given along the track of intended puncture. A Cook needle attached to a syringe is directed to the sternal notch, parallel to the clavicle. Gentle aspiration is performed as the needle is advanced slowly. A gush of dark venous blood without pulsatile flow indicates entry in the subclavian vein. The syringe is detached, the needle stabilized, and a guide-wire is advanced into the lumen without resistance. If resistance is encountered, the guide-wire is likely to be extravascular. The guide-wire should be visualized under fluoroscopy to ascertain its position and adjusted accordingly to direct it into the superior vena cava. If the guide-wire fails to advance at all, it should be withdrawn, the needle slightly pulled back or advanced to obtain a free flow of venous blood, and the wire re-advanced. With fluoroscopic guidance, the guide-wire should be advanced into the inferior vena cava, which lies to the right of the vertebrae, to ensure that the guide-wire has not inadvertently been introduced into the subclavian artery. The needle is then

removed and a desired intravascular sheath advanced over the guide-wire and the side port flushed with heparinized saline.

If pulsatile blood is aspirated, the needle has punctured the subclavian artery. The needle should be removed and digital pressure maintained for 5 to 10 minutes to allow proper hemostasis. A more medial site should be selected. If air is aspirated, the pleural space is entered and the puncture is too deep or too lateral. Other complications include hemothorax and subclavian arteriovenous fistula.

INTERNAL JUGULAR VEIN PUNCTURE

The internal jugular vein is located anterior and lateral to the carotid artery. It lies behind the clavicular head of the sternocleidomastoid muscle. The site of puncture is approximately at the level of the apex formed by both heads of the sternocleidomastoid muscle and medial to the lateral border of the clavicular head. The Trendelenberg position is helpful in distending the vein. The syringe and needle are directed lateral to the carotid artery. When a free flow of venous blood is encountered, the syringe is detached, the needle held firmly and a guidewire advanced. At all times the guidewire should be advanced without perceptive resistance. The needle is then removed and an intravascular sheath advanced as described previously. The complication of an internal jugular vein puncture includes carotid artery puncture with resultant hematoma and potential air embolism. Digital pressure should be maintained for 5 to 10 minutes in the event of inadvertent carotid artery puncture. Air embolism can be prevented by keeping the patient in the Trendelenberg position until the sheath is advanced. However, the risk of a pneumothorax is reduced.

VENOUS ACCESS DURING A PROCEDURE WITH AGGRESSIVE ANTICOAGULATION OR THERAPEUTIC INR

The Section of Electrophysiology and Pacing in The Cleveland Clinic often performs RF ablation in patients on warfarin with therapeutic international normalized ratio (INR). Additionally, intravenous infusion of heparin is given to maintain an activated clotting time (ACT) of 350 to 450 s for procedures that necessitate left atrial instrumentation. There is little margin for errors in obtaining venous access in these patients. An inadvertent arterial puncture may result in a large hematoma requiring early termination of the RF procedure. Therefore, venous access of the femoral veins is obtained with a modified Seldinger technique to avoid possible venous hematoma. An ultrasound-guided internal jugular vein puncture is performed to avoid inadvertent arterial puncture or through and through venous punctures. Standing at the head of the patient, an ultrasound probe is placed over the right side of the neck bordered by the two heads of the sternocleidomastoid (Figure 18.2). Two vascular structures are seen deep to it. Identification of the internal jugular vein can be easily made by gentle compression of the vessel (Figure 18.3). Thereafter the venous access to the internal jugular vein is performed using a modified Seldinger technique (Figure 18.4). Due care is

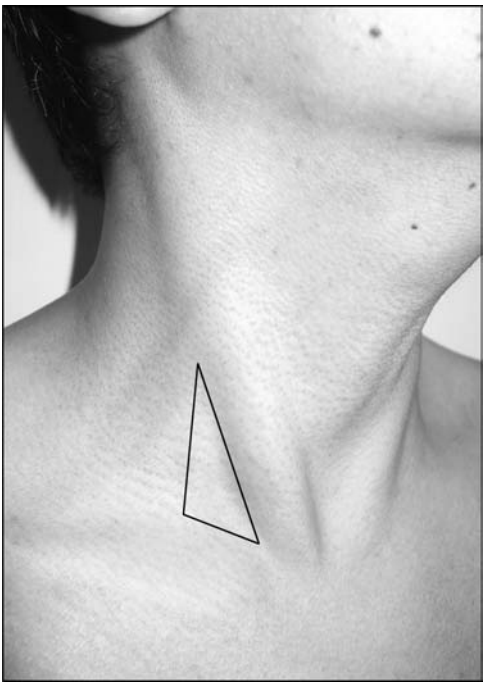
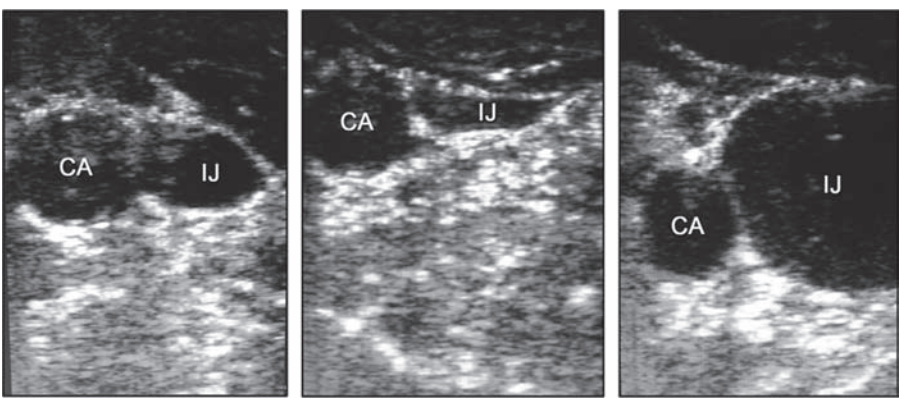


Figure 18.2 Surface anatomy of the neck. The two heads of the sternocleidomastoid muscle are depicted. Venous pucture is attempted between these two heads to avoid intramuscular anesthesia or an intramuscular route.



(a) (b) (c)

Figure 18.3 Ultrasound-guided internal jugular vein puncture. (a) The carotid artery is seen medial to the vein. (b) Gentle compression distinguishes the vein. (c) A Valsalva maneuver from the same patient distends the vein. IJ: internal jugular vein; CA: carotid artery. (See color plate section.)

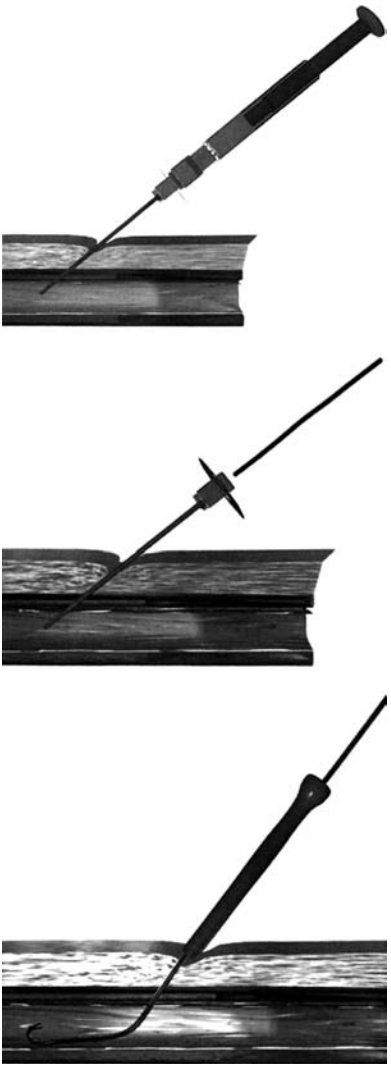


Figure 18.4 Modified Seldinger technique for venous cannulation. Published with permission from singer I. Interventional electrophysiology 2E. Philadelphia: Lippincott Williams and Wilkins, 2001.

given to avoid intramuscular anesthesia or the intramuscular route of venous access. Often an intramuscular hematoma ensues in these patients who are adequately anticoagulated. Alternatively, a catheter can be advanced from the femoral vein to the right internal jugular vein. With fluoroscopic guidance, venous access to the right internal jugular can then be performed, targeting the intravascular catheter. Thus far these measures have served their purpose and the complication rate of vascular access is comparable to patients who are not on anticoagulation. This approach can also be helpful in eliminating the risk of pneumothorax by obtaining access in the neck at a higher level.

STANDARD CATHETER POSITIONS

High right atrium

A fixed curve quadripolar catheter is advanced from the femoral vein and placed in contact with the right atrial wall. It should be at the lateral wall near the superior vena cava/right atrial junction.

Right ventricular apex

A fixed curve quadripolar catheter is advanced from the femoral vein and placed with the tip close to the right ventricular apex.

Coronary sinus

The coronary sinus allows recording of left atrial and ventricular electrograms. The availability of wide range of mutlti-polar catheters including steerable catheters makes venous access flexible. The catheter is advanced into the coronary sinus until the proximal electrode overlies the lateral border of the vertebrae in the posteroanterior projection.

His bundle

A quadripolar steerable catheter is usually used for His bundle recording. This can be advanced from the femoral vein to a superior position of the tricuspid annulus.

Other catheters

More specialized catheters are mentioned in the relevant sections of this book. The standard left anterior oblique and right anterior oblique views of these catheters are depicted in Figures 18.5 and 18.6.

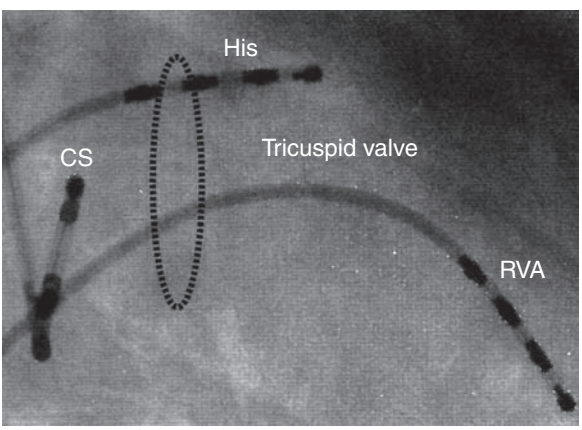


Figure 18.5 Right anterior oblique view of the His bundle catheter in relation to the tricuspid annulus. Right ventricular and coronary sinus catheters are shown. CS: coronary sinus; RVA: right ventricular apex.

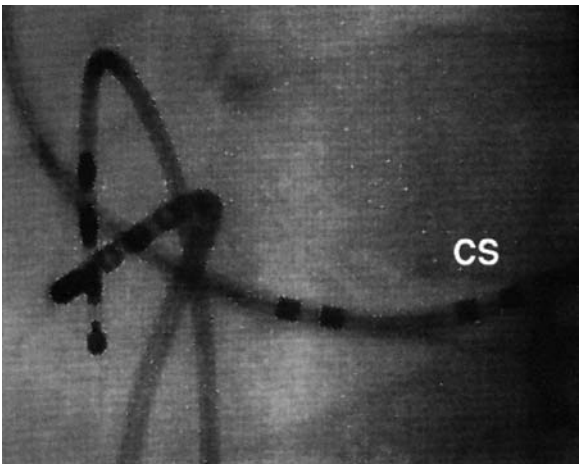


Figure 18.6 Left anterior oblique view of the coronary sinus catheter. CS: coronary sinus.

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19

Basic intervals and intracardiac ECGs

Claude S Elayi, J David Burkhardt, and Thomas Dresing

Intracardiac electrograms • Basic intervals

INTRACARDIAC ELECTROGRAMS

Intracardiac electrograms (IEGMs) and surface electrocardiograms (ECGs) both record cardiac electric activity. However, there are some differences that one must understand for appropriate interpretation of intracardiac electrograms. The surface electrocardiogram, which is recorded outside of the body on the surface, provides information about the electrical activity of the entire heart. Intracardiac electrograms are recorded inside the heart by intracardiac multi-polar catheters and display local electrical activity near the recording electrodes of the catheter (*near field*) as well as more remote significant cardiac electrical activity (*far field*) (Figure 19.1). The IEGMs are usually filtered differently from the ECG to minimize noise and interference. The paper recording speed is also generally faster than the standard 25 mm/s 12-lead ECG speed (100 or 200 mm/s more frequently). The intervals measured during an electrophysiology study are generally expressed in milliseconds (ms) rather than beats per minute (bpm) (Figure 19.2a and b). An exception to this rule is the term 'incremental atrial or ventricular pacing which refers to a rate in bpm instead of ms (see chapter 20). To obtain the cycle length in ms, the following formula is used:

Cycle length in ms = 60 000/rate in bpm

Conversely, the rate is obtained as the following:

Rate in bpm = 60 000/cycle length in ms

Thus, a rate of 60 bpm corresponds to a cycle length of 1000 ms, 100 bpm corresponds to 600 ms, 120 bpm to 500 ms, 150 bpm to 400 ms, 200 bpm to 300 ms, etc. As a result of this formula, heart rates in bpm and cycle length in ms have an inverse relationship. For instance, as the heart rate increases from 125 bpm to 150 bpm, the cycle length decreases from 500 to 400 ms.

During intracardiac recording, the screen of the monitor displays different channels which include a recording of the surface ECG and different intracardiac

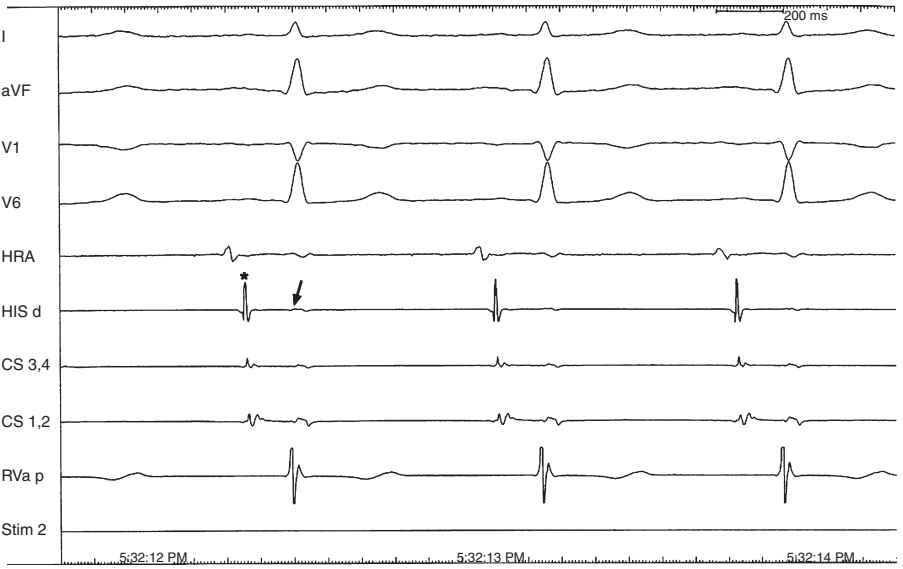

Figure 19.1 The His catheter is positioned in the right atrium on the lateral wall. The local atrial electrogram (near field) is easily identifiable (asterisk). The ventricular depolarization recorded on the same catheter is present but less obvious as it represents far field activity (arrow).

channels. In front of each channel, along the left margin of the screen, there is a label that allows orientation of the reader (Figure 19.2a). For instance, HRA, CS, or ABL refer respectively to the channel recording the high right atrium, the coronary sinus, or the ablation catheter. Moreover, the same label can be subdivided in different numbers, such as CS 1–2, 3–4, 5–6 … . The channel labeled CS 1–2 means that the EGM activity recorded represents the activity in the coronary sinus between poles 1 and 2 on the catheter. The catheters can have multiple poles. Pole 1 by convention is always the most distal, located at the tip of the catheter. As the pole number increases, the more proximal the pole will be located on the catheter.

Like surface electrograms, electrical potentials can be recorded between two electrodes within the heart (*bipolar*) or using one electrode in the heart (*unipolar*), the other being outside. The IEGMs recorded during electrophysiology studies and procedures are bipolar in general, but a unipolar recording is also sometimes useful. For instance, it can provide more precise mapping of the target area within the heart or can provide insight as to where the catheter is if the catheter's pressure against the wall is too great, causing a significant ST-segment elevation (this principle is applied to the pacemaker's and defibrillator's screw-in leads to verify good contact into the myocardium).

When interpreting the IEGMs, local atrial and ventricular activity should be identified by correlating the P-wave and QRS complex from the surface ECG. Some intracardiac signals are not seen on the ECG surface because their amplitude is too small (for instance, the His bundle electrogram). The relative size of the atrial and ventricular components depends on how the recording electrodes

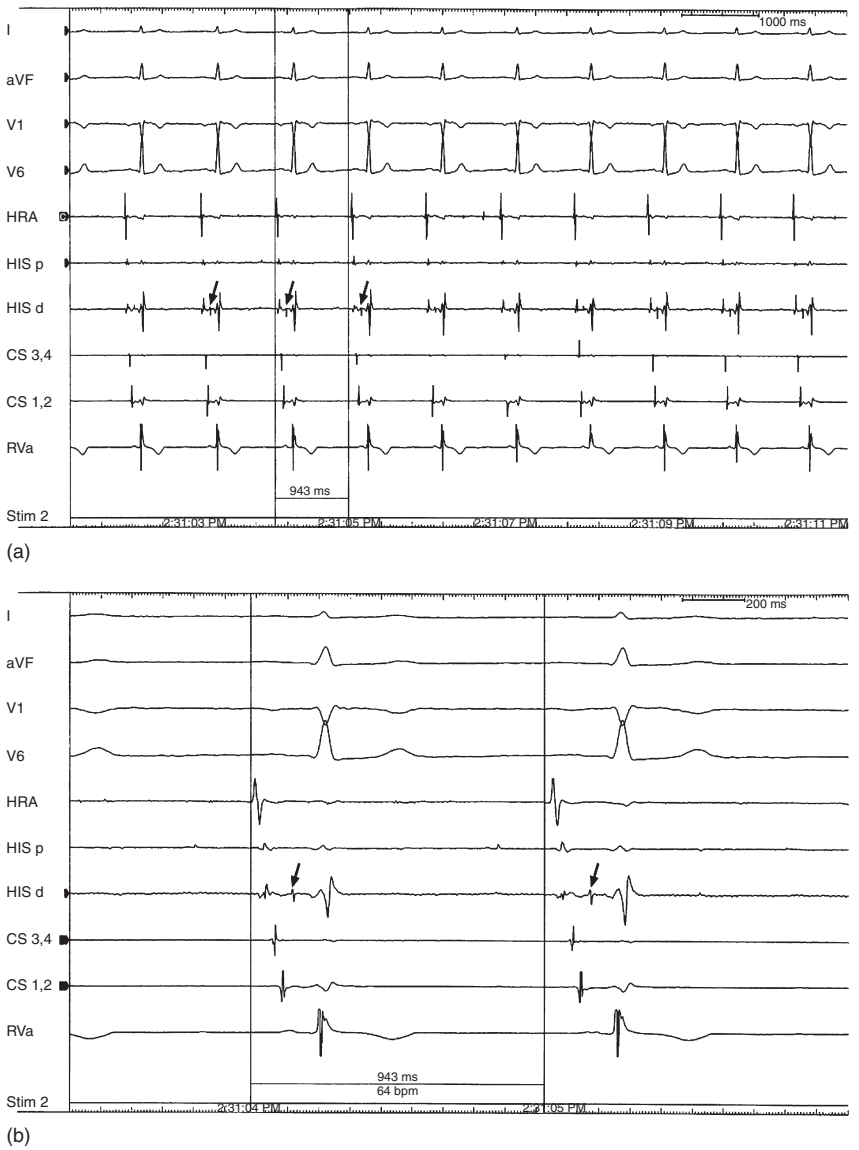

Figure 19.2 (a) This picture represents the monitor screen in the EP laboratory. The sinus cycle length is 943 ms. As labeled along the left margin, the channels represent respectively the surface ECG (4 channels), the high right atrium (HRA), the His (2 channels: His proximal and distal), the coronary sinus (CS channels) and the right ventricular apex (RVa). The paper speed recording is 25 mm/s; therefore, the IEGM intervals are more difficult to measure precisely than at 100 mm/s (see b). The His can be seen on the His distal (arrow). The small 'c' for 'clip' sometimes seen in the left margin between the labels and the channels mean that the IEGM amplitude is too high on a particular channel. The IEGMs are often clipped at a voltage level to avoid channels overlapping and to allow better interpretation of the IEGMs. (b) Same recording as (a) at 100 mm/s. The IEGM intervals can now be measured more accurately than at 25 mm/s. The His now appears better than at 25 mm/s. The sinus cycle length is expressed here in milliseconds (943 ms) and in beats per minute (43 bpm). Commonly, the cycle length is expressed only in milliseconds. Note that there is always a bar representing the scale in these pictures providing information about the paper speed (here upper right corner).

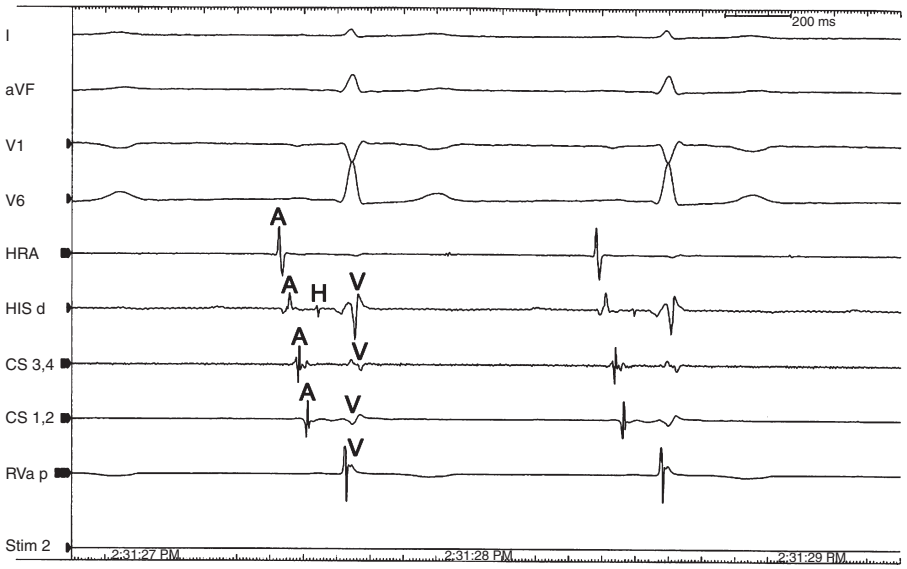

Figure 19.3 The HRA catheter is located in the right atrium and records only atrial activity. The His catheter at the tricuspid annulus level records atrial, His, and ventricle activities. The CS 1–2 and 3–4 are in the coronary sinus located around the mitral annulus at the junction between the left atrium and the left ventricle; the atrial and ventricular IEGM amplitudes are almost similar. The RVa catheter position at the right ventricular apex records only a ventricular electrogram.

are situated in the atrium or the ventricle. If the catheter is simultaneously close to the atrium and the ventricle (e.g. on the mitral or the tricuspid annulus), the atrial and ventricular EGM will have approximatively the same size (Figure 19.3). The atrioventricular ratio will increase/decrease if the catheter moves away from the annulus towards the atrium/ventricle. When the catheter is far from the atria (e.g. ventricular apex) or far from the ventricles (e.g. close to the sinus node), the EGM displays only local atrial or ventricular activity (Figure 19.3). When the catheter is placed close to the His bundle area, the EGM displays atrial, His bundle, and ventricular activities (Figure 19.3). If the catheter is placed outside of the heart (e.g. inferior vena cava), there are no cardiac signals recorded by the catheter.

A systematic and meticulous analysis of the IEGMs can provide several different types of information. Here are some examples:

- The amplitude of an IEGM: it must always be analyzed in perspective to the scale of the signal. A small signal can be recorded in a normal myocardium when the contact between the catheter and the tissue is not good or it can represent myocardial tissue with almost no activity (scar).
- The duration and relationship between different IEGMs (e.g. long HV or short HV, see Figure 19.4).
- The general morphology of the signal: for instance, a sharp potential in the pulmonary veins suggests a PV potential (Figure 19.5); a fragmented signal can represent an area of slow conduction; a double potential signal indicates a boundary into the myocardium.

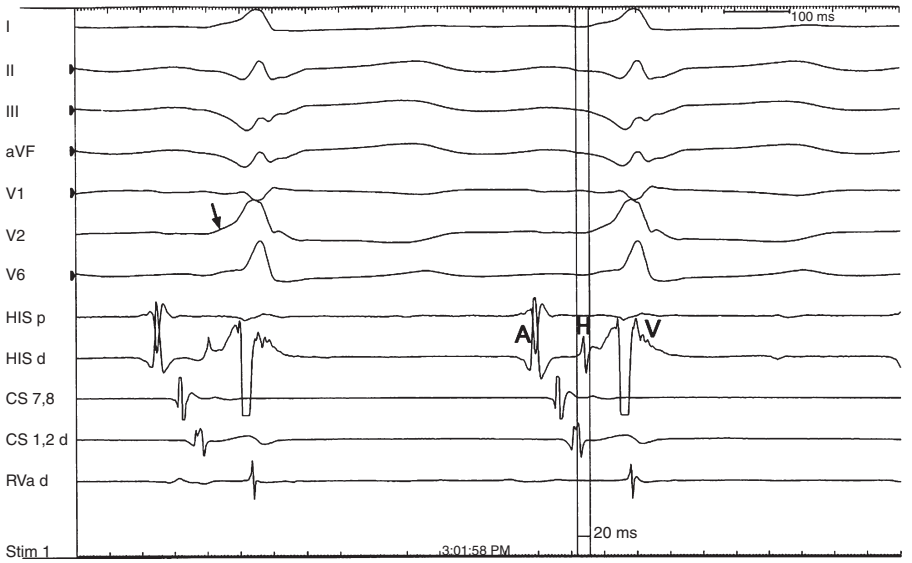

Figure 19.4 This figure illustrates the importance of the relation between the different IEGMs. The surface ECG recording displays a wide pre-excited QRS with a delta wave. The intracardiac recording at the level of the His displays a short HV interval (20 ms) on the His catheter because the ventricle has already been excited at the insertion of the accessory pathway.

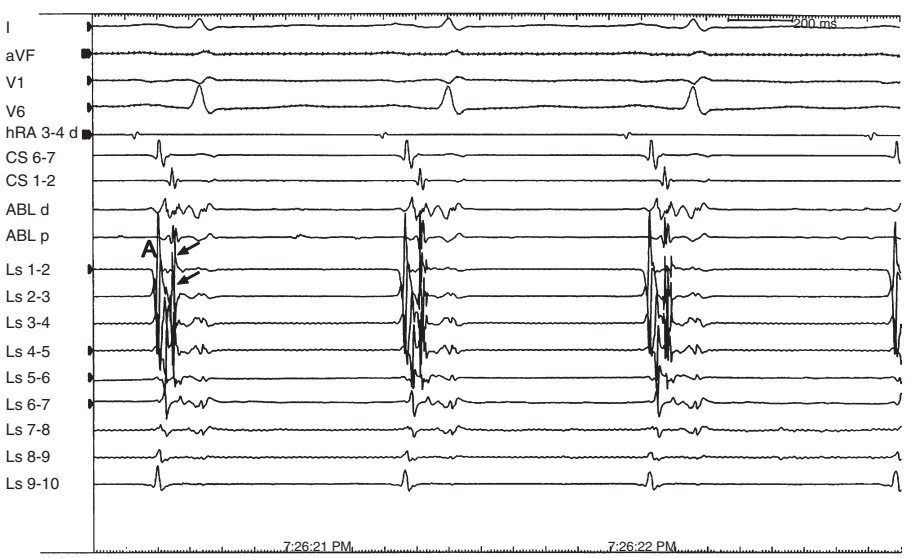

Figure 19.5 A circular decapolar ablation catheter called a 'lasso' is positioned at the entrance of the left superior pulmonary vein. On the recording, the left atrial activity is followed by a sharp potential (arrow) characteristic of the pulmonary vein potential.

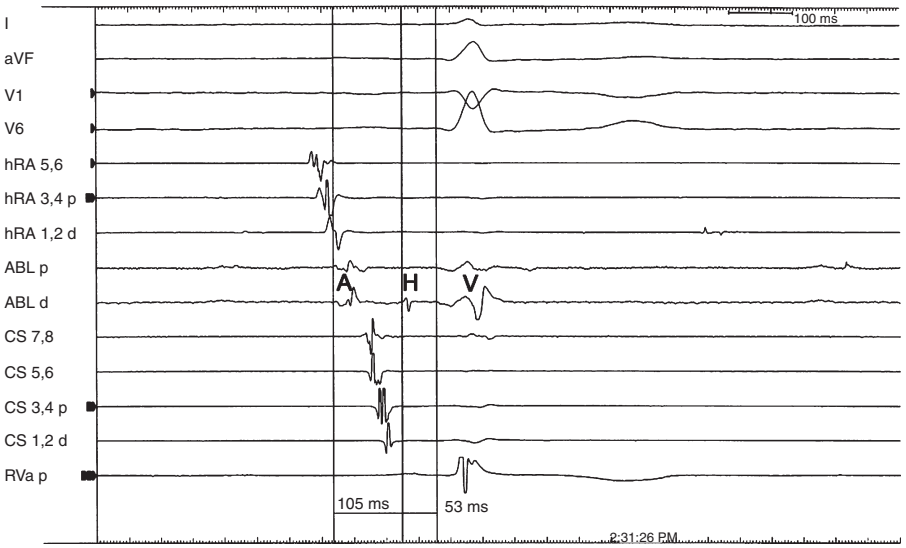

Figure 19.6 The speed recording is at 200 mm/s. The AH and HV intervals are always measured on the His catheter and are respectively 105 ms and 53 ms (normal values).

BASIC INTERVALS

On surface ECGs, the commonly measured intervals are PR, QRS, QT, atrial, and ventricular cycle length. A typical EP study also provides these data but, more importantly, the AH and the HV intervals. These two intervals are measured from the His bundle catheter recording (Figure 19.6).

The AH is the time measured from the beginning of the first major deflection (local atrial activation) to the beginning of the His bundle electrogram. This time estimates the conduction time across the AV node and is generally between 50 and 120 ms. It is highly dependent upon neurologic inputs (vagal and adrenergic tone) and medications. The HV interval starts at the onset of the His deflection to the earliest ventricular activation recorded either on the surface ECG or on the intracardiac electrogram. This represents the conduction time in the His system and the Purkinje fibers. It ranges generally from 35 to 55 ms. Grossly, a short HV interval suggests ventricular pre-excitation syndromes, whereas long HV delay reflects His-Purkinje system conduction disease.

Rarely, other intervals can be measured like the PA interval (earliest P-wave on the surface lead ECG to the earliest atrial intracardiac electrogram), the His bundle duration, and the right bundle to the ventricle duration.

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20

Basic EP study protocols

Claude S Elayi, Thomas Dresing, and J David Burkhardt

Generalities • Different methods of pacing • Other methods of pacing • Definition of the effective, relative, and functional refractory periods • Atrial pacing • Sinus node testing • Ventricular pacing • EPS example

GENERALITIES

The purpose of an EP study is to assess the dynamic electrophysiologic properties of the different atrial, AV node, HPS, and ventricular cells and eventually try to induce and analyze cardiac arrhythmias, with concomitant use of drugs if necessary (e.g., isoproterenol, adenosine, calcium, atropine, procainamide in the US, ajmaline in Europe, epinephrine, aminophylline).

During an EP study, multi-polar catheters are positioned in different areas of the heart. Most commonly, two or three catheters are placed, one in the ventricle (right ventricular apex and/or right ventricular outflow tracts), one at the His bundle level, and one in the coronary sinus and/or the right atrium. The electrodes of these catheters allow recording of intracardiac electrograms to measure baseline basic intervals and to entrain different areas in the heart by delivering some current to the myocardium (pacing). This energy delivery can be recorded as a sharp and high amplitude signal (spike) on intracardiac electrograms or on the ECG surface leads. If this impulse depolarizes the myocardium adjacent to the catheter and subsequently the rest of the heart, the impulse is capturing. Otherwise, the impulse is not capturing (Figure 20.1).

The pacing catheters are placed in a stable position to achieve continuous capture. The stimulus output generally has a pulse width of 2 ms and is set at twice the *diastolic threshold* (minimal energy to depolarize the myocardium).

A common terminology is used to describe the pacing stimuli and their subsequent intracardiac electrograms:

- S1: drive train pacing stimulus usually delivered in groups of 5–8 beats
- S2, S3, S4: respectively, a first, second, and third extrastimulus
- S1–S2, S2–S3, S3–S4: coupling intervals respectively between S1 and S2, S2 and S3, S3 and S4
- A1: atrial electrogram associated with S1 drive or spontaneous atrial beat

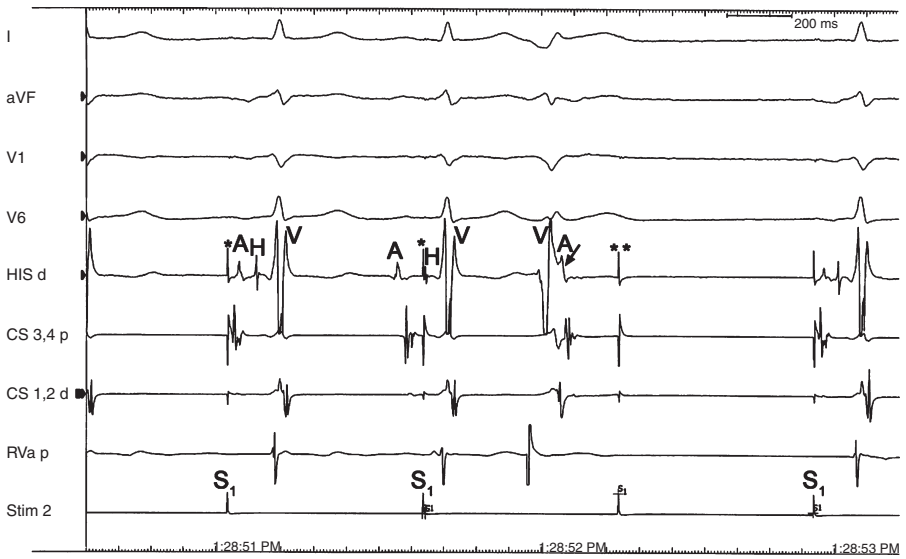

Figure 20.1 The atrium is paced from the coronary sinus with a 600 ms S1 drive train. For the first beat, the pacing spike (asterisk) is capturing the atrium with a His and a ventricular response. The second beat is a spontaneous atrial beat with a following atrial spike too early to capture the refractory atrium. The third beat is a spontaneous premature ventricular beat activating retrogradely the atrium (arrow). The next paced spike (two asterisks) is not capturing the atrium as it is still refractory from previous retrograde atrial depolarization. Note that the pacing spike is clearly displayed on the stimulation channel (lower channel labeled as 'Stim 2').

- A2, A3: atrial electrogram associated with respectively S2 and S3 or the first spontaneous atrial electrogram respectively after A1 or A2
- H1, H2, H3: His bundle electrogram associated respectively with A1, A2, and A3
- V1: ventricular electrogram associated with S1 or spontaneous ventricular beat
- V2, V3: ventricular electrogram associated with respectively S2 and S3 or the first spontaneous ventricular electrogram respectively after V1 and V2.

DIFFERENT METHODS OF PACING

Extrastimulus testing

Typically, a drive train of 6 to 8 paced beats S1 is performed in the heart structure (e.g. in the atrium) at a stable cycle length between 600 and 300 ms, followed by a premature beat S2 with a coupling interval starting from 500 to 400 ms. The drive train is repeated with a progressive decrease of the coupling interval by 10 to 20 ms until the structure becomes refractory and is no longer captured (effective refractory period of the structure). If needed, double (S2S3) or more extra stimuli can be delivered by repeating the same sequence with a S1 drive train sequence, an S1–S2 conducted beat (generally 10 ms above the S2 refractory period) and a decremental scanning interval of S3. The minimum-coupling

interval is commonly 200 ms because of the important risk of inducing arrhythmias with shorter coupling intervals.

Incremental pacing

Incremental pacing (e.g. in the atrium) begins at a stable cycle length slightly below that of the sinus rhythm. The pacing cycle length is then shortened by 10 to 50 ms, a few beats are observed at the new pacing cycle length and the cycle length is again decreased by the same amount. This sequence is repeated to achieve the goal of incremental pacing (e.g. determination of the Wenckebach's cycle length in the AV node). of note, the term 'incremental pacing' refers to a rate in beats per minute instead of a cycle length in ms.

OTHER METHODS OF PACING

- *Burst pacing:* delivering a set number of pulses at a constant cycle length per sequence. The sequence can be repeated at progressively shorter cycle lengths. This method can be used in sinus rhythm to try to induce an arrhythmia or during a tachycardia to penetrate the circuit's arrhythmia (*overdrive pacing*). In this latter case, burst pacing cycle length is initially slightly shorter than the tachycardia or at a programmed percentage of the cycle length of the detected tachycardia. *Ramp pacing* is almost the same feature, except that within a pacing sequence, each subsequent paced beat is decremented by a set amount (burst pacing is currently used in most of the defibrillators to try to terminate ventricular tachycardia before delivering a shock).
- *Long short pacing:* a sequence with alternatively a long interval between two-paced beats, followed by a short interval. It can be used to provoke arrhythmias or patterns of conduction block (e.g. to induce bundle branch re-entry).
- Pacing at a variable output*:* for example, para-Hisian pacing where the output is initially high enough to capture the His and the right ventricle and progressively decreased until the His is no longer captured.

DEFINITION OF THE EFFECTIVE, RELATIVE, AND FUNCTIONAL REFRACTORY PERIODS

These periods are measured during an S1 drive train and a progressive S2 decremental stimulus. When the refractory periods of a cardiac structure (e.g. the AV node) are measured, the input interval will be related to the upstream depolarized structure (right atrium) cycle length and the output to the downstream depolarized structure (His bundle) cycle length.

- *Relative refractory period (RRP):* longest input interval that results in conduction delay. The output interval starts to be longer than the input interval (e.g. for the AV node, when the A2H2 interval becomes longer than the A1H1 interval; see Figure 20.2).
- *Functional refractory period (FRP):* shortest output interval possible that can be elicited by any input interval (see Figure 20.3).
- *Effective refractory period (ERP):* longest input interval that fails to propagate, therefore no output (e.g. for the AV node, the longest A1A2 that fails to propagate to H2, see Figure 20.4).

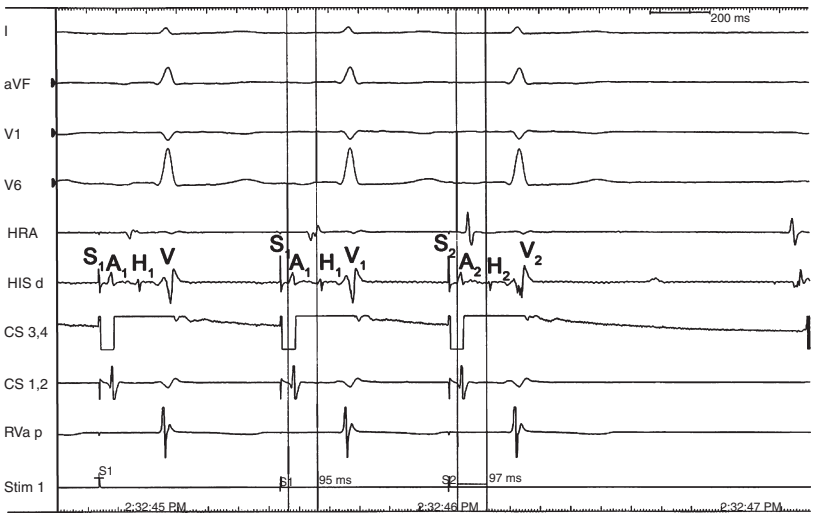

Figure 20.2 Relative refractory period. The atrium is paced from the coronary sinus with 8 beats stable 600 ms S1 drive train followed by a premature beat S2 with a coupling interval starting at 590 ms. Initially, the A1H1 and the A2H2 are equal (95 ms). The S2 coupling interval is reduced by 10 ms until 560 ms when the A2H2 starts to increase (97 ms) and becomes longer than the A1H1. With this 560 ms S2 coupling interval, the input (A1A2) starts to be longer than the output (H1H2); this represents the relative refractory period of the AV node.

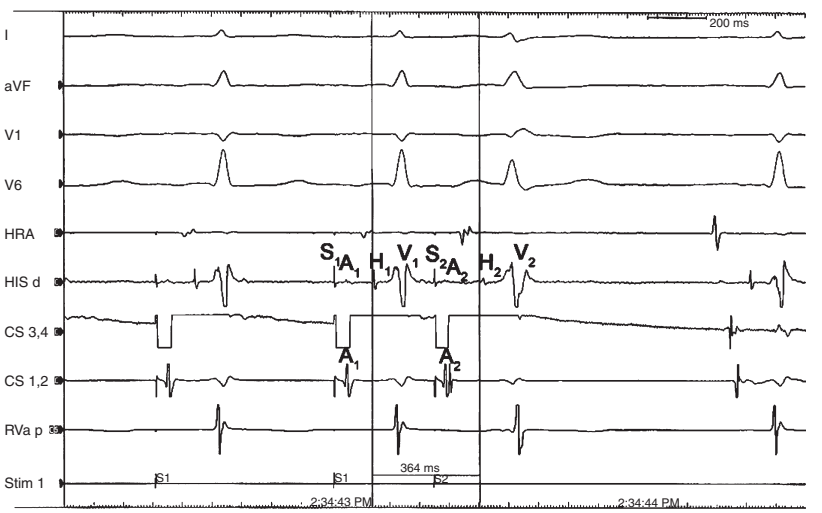

Figure 20.3 Functional refractory period (same patient as Figure 20.2). The S2 coupling interval is progressively decreased by 10 ms. A1A2 gradually decreases when A2H2 is increasing at the same time due to decremental properties in the AV node. The resultant H1 H2 tends to decrease until the shortest H1 H2 (364 ms) can be reached with an S2 coupling interval of 340 ms. For comparison, in Figure 20.2, at a coupling interval of 560 ms, the H1H2 interval is 562 ms. With further shortening of the coupling interval below 340 ms, H1H2 tends to increase. This 340 ms S2 coupling interval is the shortest output (H1H2) that can be generated by any input and represents the functional refractory period of the AV node.

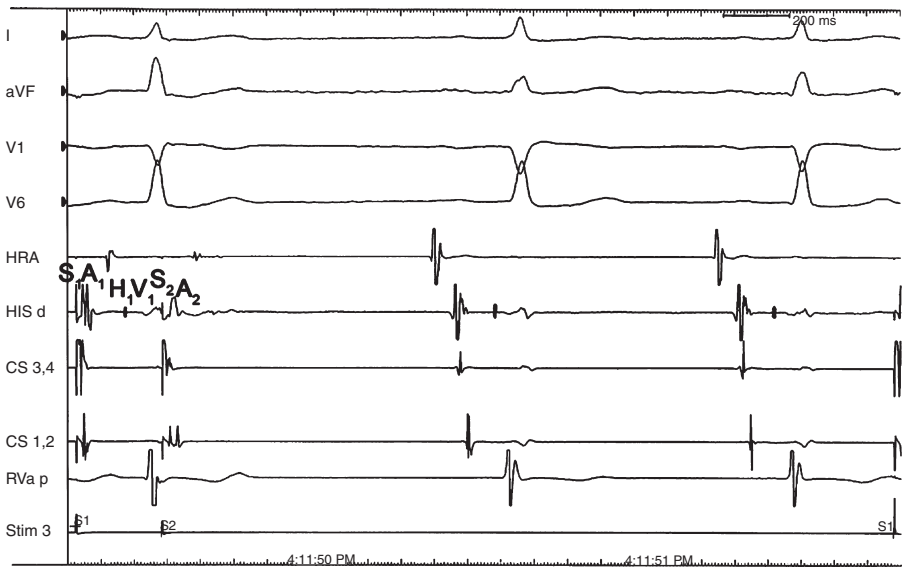

Figure 20.4 Effective refractory period (same patient as in Figures 20.2 and 20.3). When the S2 coupling interval is lowered to 260 ms there is a block in the AV node. The pacing spike captures the atrium, but does not conduct to the His and to the subsequent ventricle. This 260 ms S2 coupling interval represents the effective refractory period of the AV node.

ATRIAL PACING

Atrial extrastimulus testing

Atrial extrastimulus testing can determine the properties of the AV node (antegrade) and of the atrium.

By progressively shortening the S2 extrastimulus, the AV node RRP will be reached first when A2H2 begins to be longer than A1H1 (Figure 20.2). As the S2 atrial extrastimulus cycle length decreases, the conduction over the AV node (represented by the A2H2 interval) progressively increases, known as the *decremental conduction* over the AV node (Figure 20.2). An increase in the A2H2 by 50 ms or more is sometimes observed with a decrease of the atrial S2 extrastimulus by 10 ms. This A2H2 increase, also called a *jump*, is evidence of dual AV node physiology. Briefly, this means that antegrade conduction over the AV node has shifted from the usual fast pathway to a slow pathway. By further decreasing the S2 interval, the ERP of the AV node will be achieved when the atrium A2 is no longer followed by the His H2 (Figure 20.4). Finally, the S2 spike will no longer capture the atrium (atrial ERP, also called *atrial refractoriness*).

Atrial incremental pacing

The atrial cycle length is progressively shortened until the atrium does not conduct to the ventricle in a one to one relation. This cycle length is called the *AV node antegrade Wenckebach cycle length* (Figure 20.5).

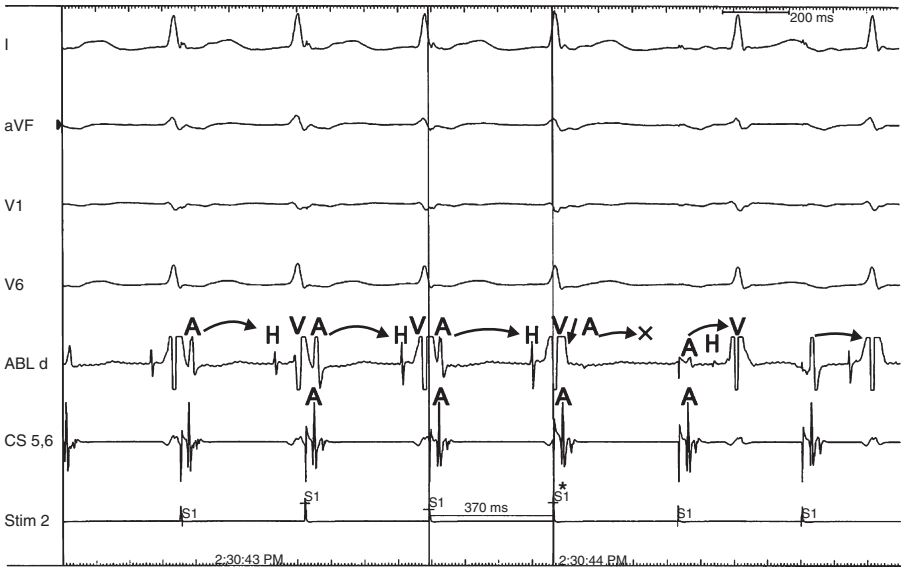

Figure 20.5 Incremental atrial pacing. The atrium is spaced with progressive incremental pacing (pacing spikes obvious on the lower stimulation channel labeled as 'Stim 2'). Each atrial spike is followed by atrial capture and subsequent His and ventricular capture (so-called one-to-one response to the ventricles) until the pacing spike (asterisk) does not capture the ventricle. This spike did capture the atrium (atrial activity clear on the CS 5,6), but with no subsequent His. Therefore, the block likely occurs in the AV node. The antegrade AV node Wenckebach cycle length is the time from the last paced beat conducted towards the ventricles to the first non-conducted beat to the ventricles (370 ms in this example).

SINUS NODE TESTING

Sinus cycle length is defined as the A to A interval in normal sinus rhythm. Sinus node function can be assessed by the sinus node recovery time (SNRT) (and its derivatives) and by the sino-atrial conduction time (SACT).

SNRT and its derivatives

- The SNRT represents the time needed for the sinus rhythm to resume after 30 s of atrial pacing faster than the sinus rhythm (atrial overdrive) at different cycle lengths (e.g. 700, 600, 500, and 400 ms). The SNRT is the interval recorded in the high right atrium from the last paced atrial electrogram to the first spontaneous atrial electrogram (Figure 20.6). A pause occurring after this first spontaneous sinus beat should be noted if longer than the SNRT (secondary pause). The SNRT in a patient is the longest time measured at any of the different pacing cycle lengths.
- The *corrected SNRT* is the difference between the SNRT and the spontaneous sinus cycle length prior to pacing. A normal value is less than 550 ms. (SNRT-SCL=CSNRT)
- The *total recovery time* is the interval from the last paced atrial electrogram until the sinus cycle length returns to the initial sinus node rate observed before atrial pacing. A normal value is less than 5 s.

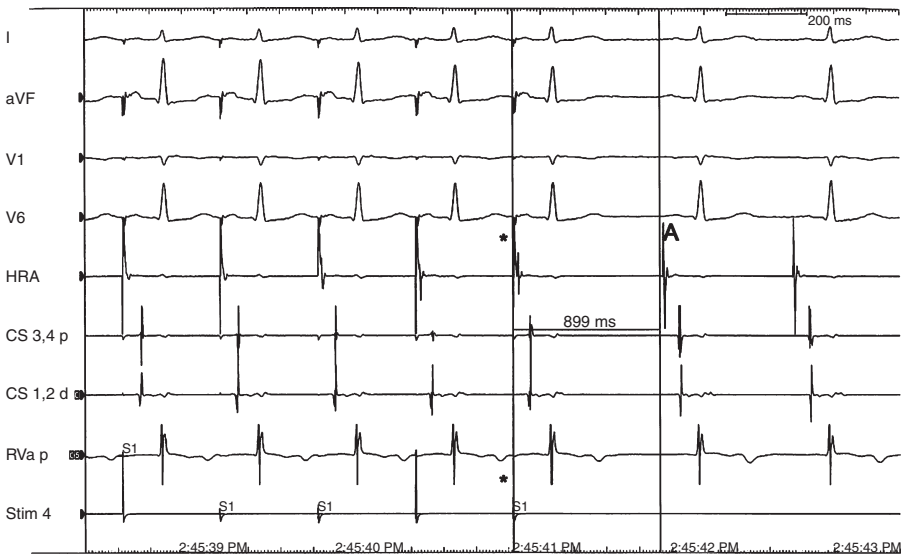

Figure 20.6 Sinus node recovery time (SNRT). After 30 s of atrial pacing at 600 ms in the high right atrium, there is a pause followed by sinus rhythm activity. The sinus node recovery time is measured in the high right atrium from the last paced spike (asterisk) to the first spontaneous atrial electrogram (899 ms, a normal value). This sequence was repeated at other pacing cycle length rates (e.g. 700, 500, 400 ms) but all SNRTs were shorter than 899 ms. In this patient, the SNRT is therefore 899 ms. The corrected SNRT is: SNRT−atrial spontaneous cycle length (so 899−800 = 99 ms, a normal value).

The SACT

- The SACT assesses if there is delayed conduction between the sinus node itself and the adjacent atrium in the high right atrium. It is more complex than SNRT calculation. Measurement of the SACT will not be detailed here because it is rarely used in clinical practice.

VENTRICULAR PACING

Ventricular extrastimulus testing (including ventricular programmed stimulation)

Ventricular extrastimulus testing can determine the properties of the AV node (retrograde) of the His-Purkinje system and of the ventricle myocardium.

Conventionally, the pacing catheter is positioned at the right ventricular apex for a basic EP study; at this site, the impulse generally invades retrogradely the distal His-Purkinje from the right bundle to the atrium through the AV node. During antegrade conduction (atrial pacing), the decremental pattern is mainly related to one structure: the AV node. During retrograde conduction (ventricular pacing), the decremental conduction can occur in two different structures: the His-Purkinje system and/or the AV node. This depends on the ventricular cycle

length and on the ventricular coupling interval. Indeed, to assess if a decremental pattern is mainly related to the His-Purkinje system (long retrograde VH interval) or the AV node (long retrograde HA interval), the His deflection needs to be clearly visualized on the IEGMs. However, the retrograde His is often not obvious (buried in the QRS). The interpretation of electrograms is therefore sometimes difficult during ventricular pacing. With further shorter coupling intervals, a marked delay between the pacing spike S2 and V2 (so called *latency*) is observed before the ventricular ERP is achieved (Figure 20.7).

Retrograde conduction to the atrium is present in 40 to 60% of the patients and can be variable. The retrograde VA conduction ranges usually from 200 to 400 ms. When present, the retrograde atrial activation through the AV node generally depolarizes the coronary sinus from the proximal part to the distal part and the right atrium from the low toward the high right atrium; the atrial activity close to the AV node is at least 20 to 30 ms earlier than the local high right atrium activity. This retrograde atrial activation sequence is called *concentric* (see Figure 20.8). On the contrary, there is *eccentric* retrograde atrial activation when an accessory pathway or an atrial tachycardia depolarizes the atrium in a different pattern.

Ventricular-programmed stimulation is a form of ventricular extrastimulus testing generally using several extrastimuli. This test can stratify the risk for sustained ventricular arrhythmias or can be used for the purposes of catheter mapping and ablation. For sustained ventricular arrhythmias risk stratification, a common protocol is pacing at two pacing sites (right ventricular apex and outflow tract),

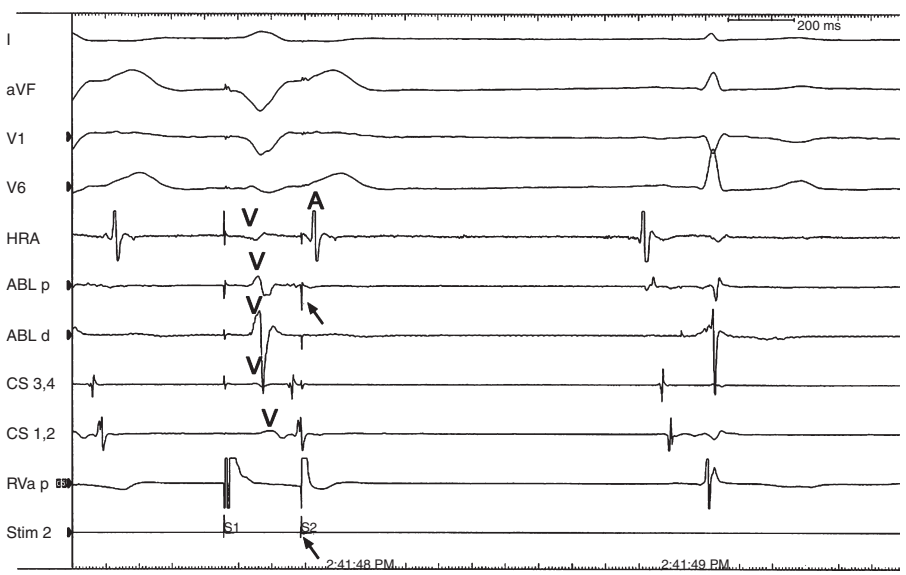

Figure 20.7 Ventricular effective refractory period. A drive train of six paced beats S1 (600 ms) is performed in the right ventricle (apex), followed by a premature beat S2 with a progressive decrease of the coupling interval by 10 ms until the ventricle becomes refractory. At a coupling interval of 230 ms, the ventricle is no longer captured following the pacing spike (arrow). The ventricular effective refractory period has been reached with an S2 ventricular coupling interval of 230 ms.

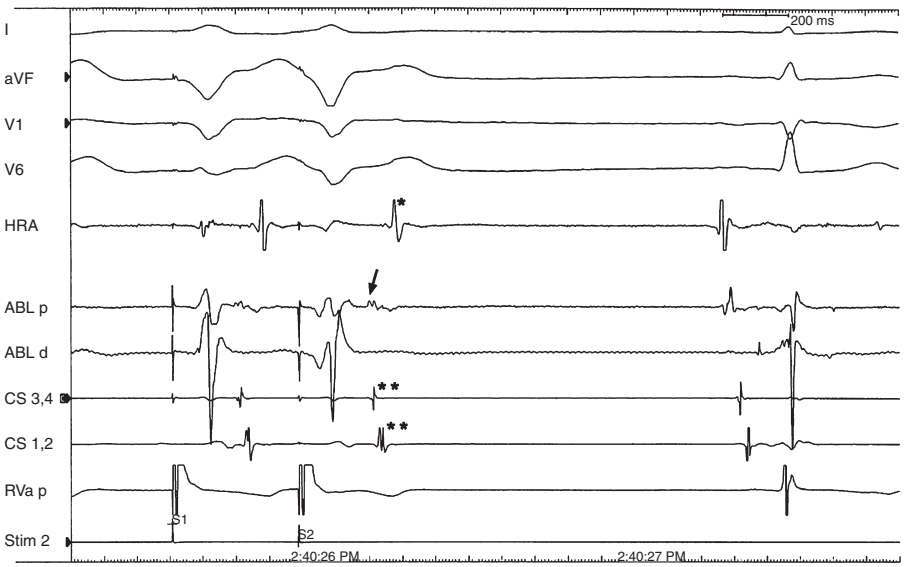

Figure 20.8 Concentric atrial activation during ventricular pacing. One catheter is at the high atrial atrium (HRA), one in the coronary sinus (CS), one at the level of the His (ABL), and one at the right ventricle apex (RVa). The earliest retrograde A is clearly on the His electrogram (arrow) and precedes the high right atrium (one asterisk) and the coronary sinus atrial electrograms (two asterisks). The coronary sinus is activated from the proximal CS (9–10) toward the distal CS (1–2). This sequence of retrograde activation is called concentric.

at two drive cycle lengths (8-beat drive trains S1 at 600 and 400 ms) and with three extrastimuli (decrementing by 10 ms until refractoriness of S2 then S3 and finally S_4). The ventricular-programmed stimulation is positive when ventricular arrhythmias are induced. The sensitivity and specificity of these studies depend on the subtype of the ventricular arrhythmia induced (monomorphic or polymorphic ventricular tachycardia, ventricular fibrillation) and on how aggressive the protocol was (see Figure 20.9).

Ventricular incremental pacing

When retrograde VA conduction is present, the ventricular cycle length is progressively shortened until the ventricle does not conduct to the atrium in a one-to-one relation. This cycle length is called the AV node retrograde Wenckebach cycle length (Figure 20.10). The classic pattern of Wenckebach is the most frequently observed with a progressive prolongation of the VA (decrement in the AV node) interval prior to block. The His-Purkinje system is more likely to adapt its refractoriness when the pacing cycle length increases progressively during incremental pacing than during extrastimulus testing.

EPS EXAMPLE

In summary, there is not a standard protocol for an EP study. Each laboratory has developed its own protocol and this varies in a lab depending of the goal of

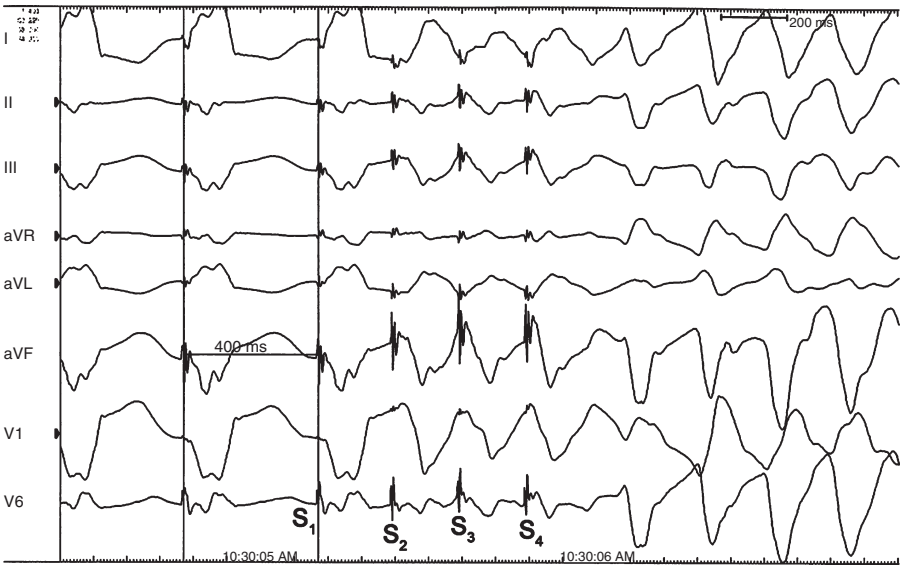

Figure 20.9 Ventricular programmed stimulation. The drive cycle length is here 400 ms at the right ventricular apex with 3 extrastimuli: S2, S3, and S4. The coupling intervals S1S2, S2S3, and S3S4 are respectively 210, 200, and 200 ms. A monomorphic ventricular tachycardia was induced with this protocol of stimulation.

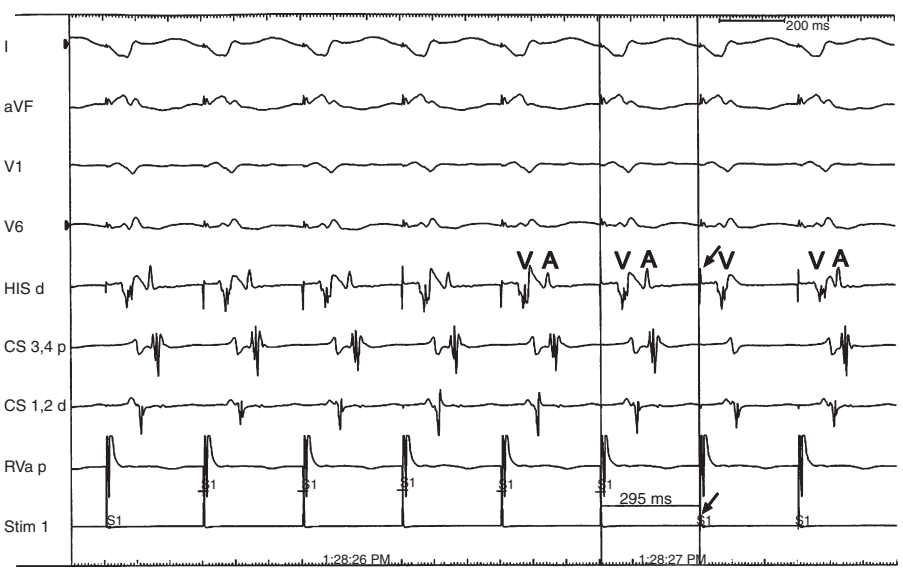

Figure 20.10 Incremental ventricular pacing. The ventricle is being paced with progressive incremental pacing. Each ventricular spike is followed by ventricular capture and subsequent retrograde His and atrial capture in a one-to-one response to atrium. The ventricular cycle length decreases until the spike labeled with an arrow is not followed by an atrial capture. The retrograde AV node Wenckebach cycle length is the time from the last paced conducted beat toward the atrium to the first paced non-conducted beat to the atrium (295 ms in this example).

the study. It is more likely to induce atrial arrhythmias and eventually atrial fibrillation when pacing is done in the atrium. Therefore, when the EPS is performed for atrial arrhythmias, ventricular stimulation is generally done first. Likewise, atrial stimulation is performed first when the EPS is done in the setting of ventricular arrhythmias.

A basic protocol could include:

- Measurement of basic intervals (cycle length, PA, AH, HV, QRS, QT).
- Determination of the SNRT after testing different basic cycle lengths (e.g. 700, 600, 500, and 400 ms).
- Incremental ventricular pacing down to the VA Wenckebach point if there is retrograde VA conduction.
- Ventricular extrastimulus testing down to ventricular refractoriness at two different basic cycle lengths (e.g. 600 and 400 ms).
- Incremental atrial pacing down to the AV Wenckebach point.
- Atrial extrastimulus testing at two different basic cycle lengths (e.g. 600 and 400 ms).

Multiple other maneuvers and drugs can be added, depending on the goal of the EPS study. (eg use of adenosine to block conduction in the AV node).

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21

Head-up tilt (HUT) table testing

Subramanya Prasad, David Burkhardt, and Thomas Dresing

Introduction/background • Test procedure/tilt testing protocols

INTRODUCTION/BACKGROUND

- HUT testing with or without adjunctive pharmacologic agents is the most commonly used test for syncope evaluation. Several studies have shown that the vasodepressor-cardioinhibitory response seen during a HUT test is comparable to spontaneous neurally mediated syncope (NMS).[1,2]
- In the young healthy individual or the elderly with syncope of unknown etiology, it is considered the gold standard test.[3,4]
  Throughout this chapter * denotes a Class I recommendation; # denotes a Class II recommendation and ^ denotes a Class III recommendation.
- The physiologic basis for HUT testing is discussed in detail under pathophysiology.
- Briefly, in healthy humans, orthostatic stress causes peripheral pooling of 500 to 1000 ml of blood, triggering arterial mechanoreceptors (major role) and thoracic wall and cardiac mechanoreceptors (minor role) to stimulate the vasomotor center (VMC) via vagal afferent C fibers.
- The VMC sends efferent vagal signals (cardioinhibitory) and neuroendocrine modulators causing reflex vasoconstriction of the splanchnic, musculo-cutaneous, and renal vascular beds, thus maintaining systemic arterial blood pressure during standing.
- In patients with NMS, these responses are deficient, resulting in syncope.

TEST PROCEDURE/TILT TESTING PROTOCOLS

Procedure

- The HUT is usually performed in an EP lab using a specialized tilt table (Figure 21.1). The recommendations for doing a HUT are listed in Table 21.1

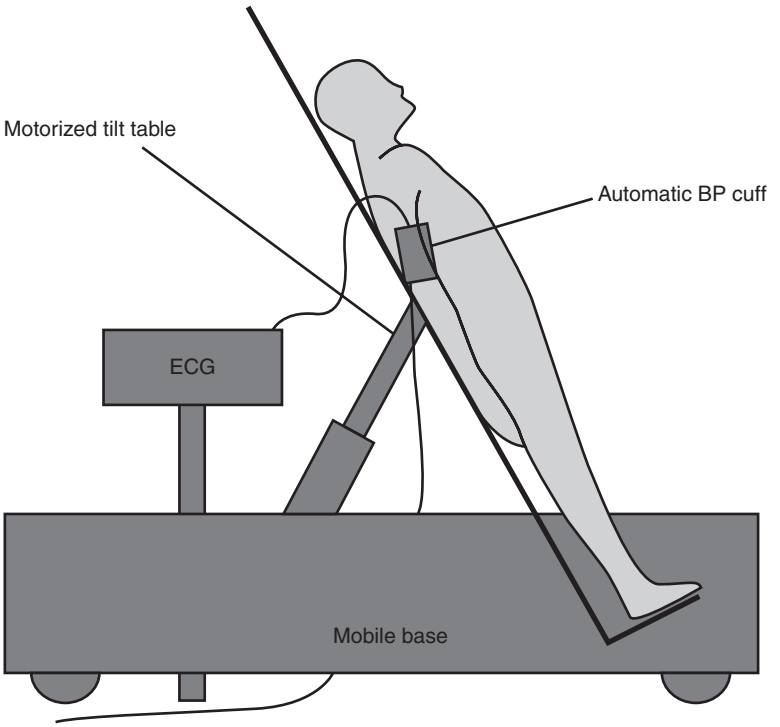

Figure 21.1 Tilt table.

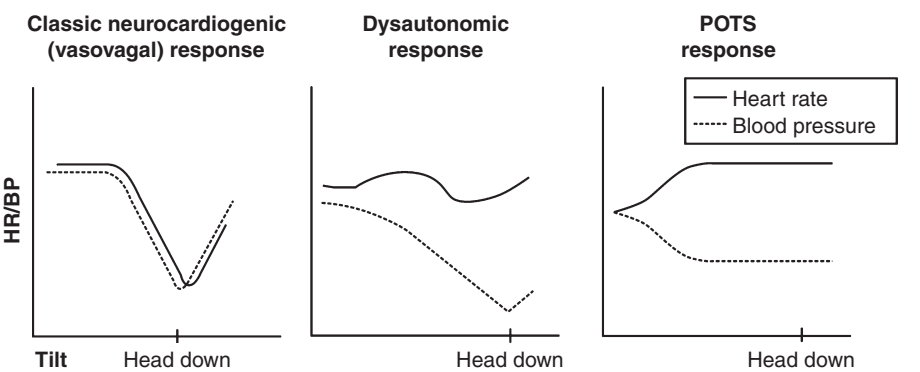

Figure 21.2 Cardiovascular changes produced by 60 degree tilt.

- HUT testing with or without pharmacologic provocation has been used to increase the sensitivity of HUT testing.
- The set-up of a HUT test is relatively simple. The HUT table is set up in a quiet room with minimal distractions.

Table 21.1 The various HUT protocols including methods, endpoints, response and interpretation

HUT protocol	Method	Endpoints	Response and diagnosis	Comments
HUT testing	*Supine pretilt phase of at least 5 min (without iv) and at least 20 min (with iv) *Tilt angle of 60–70 degrees with a passive phase of 20 min (minimum) and 45 min (maximum) Westminster protocol is the commonly preferred protocol (90% specificity) in the initial evaluation of syncope *Pharmacologic provocation using intravenous isoproterenol or sublingual nitroglycerin if passive phase is negative *Drug challenge phase duration of 15–20 min	*While most physicians consider steadily decreasing BP with symptoms as the endpoint, some prefer to terminate the test with occurrence of LOC[20] *In patients with structural heart disease, spontaneous syncope during HUT is diagnostic and requires no further testing	Three responses are seen 1. Cardioinhibitory (type 2) 2. Vasodepressor (type 3), and 3. Mixed (type 1). A typical vasovagal response starts invariably with Prodromal symptoms which precede VVR by 1 minute[21,22] The VVS usually lasts for <3 min[20] Marked hypotension is seen during the prodromal phase followed by bradycardia[20–22] While presyncope is seen with an SBP decrease of 90 mmHg, syncope is seen with an SBP decrease of 60 mmHg[21]	The sensitivity of HUT testing can be as high as 80% with a specificity of 70 to 86%, depending on the protocol and patient selection[7,8,23,24] Studies of HUT testing in syncopal patients by Fitzpatrick et al[5] in 1991 reported low positive response rates with angles <60 degrees By using >60 degree tilt for 45 min (based on a mean time to positive response of 24 +/− 10 min plus 2 SD) they reported a positive response rate of 75% (specificity 93%) Even among patients with syncope and a negative EPS, a positive HUT was shown in 75% of patients[5] The clinical response may be different from the response elicited during HUT,[25] which could explain the varied response to therapy Thus a negative HUT does not rule out NMS
Isoproterenol infusion	Single or escalating doses (1, 3, 5 μg/kg) of isoproterenol are infused at baseline to increase the HR (20–30% > baseline), followed by tilting for 20–30 min during isoproterenol infusion	The patient is returned to baseline if the test becomes positive or upon completion of the protocol	LOC with hypotension or loss of postural tone is considered a positive test Modest BP decrease with symptoms is non-specific	Studies by Almquist et al using single dose isoproterenol infusion during HUT increased the frequency of positive responses (56% vs 32%) and reduced the duration of HUT[13]

(Continued)

Table 21.1 (Continued)

HUT protocol	Method	Endpoints	Response and diagnosis	Comments
	For isuprenaline, an incremental infusion rate from 1–3 μg/min in order to increase average heart rate by about 20–25% over baseline, administered without returning the patient to supine position			In 1995, Natale et al using incremental low dose isoproterenol infusion during HUT, showed a 61% positive response rate (92% specificity)[27]
Nitrates	*Nitroglycerin by intravenous or sublingual route can be used for provocation of hypotension/syncope *For NTG, a fixed dose of 400 μg NTG administered sublingually, in the upright position	The patient is returned to baseline if the test becomes positive or upon completion of the protocol	LOC with hypotension or loss of postural tone is considered a positive test	In 1994 Raviele et al used iv nitroglycerin (NTG) infusion in unexplained syncopal patients showing a 53% positive response rate.[27] Later studies by Graham et al[28] and Raviele et al compared sublingual NTG to isoproterenol infusion showing similar positive response rates and specificity, with a better side-effect profile with NTG
Clomipramine	*A dose of 5 mg (1 mg/min iv) is given during the first 5 min of tilting. HUT is done for the next 15 min, or until syncope occurs	The patient is returned to baseline if the test becomes positive or upon completion of the protocol	LOC with hypotension or loss of postural tone is considered a positive test	A study of 55 patients with VVS showed more positive response rates (80% vs 53%) in the clomipramine group[29]

HUT with CSM	The CSM should be done in conjunction with HUT for 5–10 s in both supine and erect positions If asystole is seen, CSM is repeated after 1 mg atropine infusion	The procedure is considered positive if syncope is reproduced during or immediately after massage in the presence of asystole longer than 3 s and/or a fall in systolic blood pressure ≥50 mmHg	Three responses are seen 1. Cardioinhibitory (type 2) 2. Vasodepressor (type 3), and 3. Mixed (type 1). A positive response is diagnostic in the absence of any other competing diagnosis	Elderly patients undergoing CSM should be monitored for 2 hours postprocedure for neurologic events.[10] A study of elderly patients found a 0.28% incidence of neurologic events after CSM, although the events were transient and full recovery was the rule[10] In a study of 80 patients with unexplained syncope, a 9% positive response was seen during CSM during supine position, as opposed to 60% during a HUT, suggesting that 50% of patients with CSH are missed if CSM is done only in the supine position[30]
ATP infusion	# As proposed by Flammang,[18] 20 mg of ATP dissolved in 10 ml of saline is given as a rapid (< 2 s) bolus, followed by a 20 ml dextrose solution flush during ECG monitoring	The test is considered positive if a pause >10 s (even if interrupted by escape beats) is seen[19] Asystole lasting > 6 s, or AV block lasting >10 s is considered positive	ATP testing produces an abnormal response in some patients with unexplained syncope, but not in controls	ATP infusion is rarely used in the United States In a study of 316 patients with presyncope/syncope, using this protocol, 41% had a positive response. When they were followed for 50 months, patients with long pauses (>10 s) were more likely to have recurrent symptoms than those with <10 s pauses. The test was positive in 5% of controls[18] In two studies of unexplained syncope, ATP testing was abnormal in 28% and 41%[18,19] In a study of patients with syncope due to ECG documented pauses, ATP test reproduced AVB in 53% of patients with AV block but not sinus arrest.[19] These findings suggest that ATP testing may be useful in establishing intermittent AV block as the cause in patients with unexplained syncope

*Class I, #Class II, ^Class III.

- The table should have a foot board and safety restraints and be capable of passive swinging in a smooth yet rapid fashion, from 0 to 90 degrees within 10 s.
- Infusion pumps capable of giving iv fluids and medications (atropine) should be kept handy.
- The patient is usually advised to be in a fasting state (the rationale being to avoid postprandial splanchnic pooling, or vomiting during the procedure) for at least 2 hours prior to the procedure.
- After excluding orthostatic BP changes at baseline, and obtaining peripheral venous access, the patient should rest in the supine position for 20–45 minutes to decrease the likelihood of VVR due to venous cannulation.
- After obtaining supine heart rate (HR) and BP measurements for 3 to 5 minutes, HUT testing is performed between 60 and 90 degrees for 30 to 45 minutes.[5]
- Blood pressure, HR, and symptoms are recorded every minute along with continuous ECG monitoring, throughout the test. The possibility of profound asystole $>$ 10 s requires careful monitoring.
- Though continuous beat-to-beat arterial BP monitoring is the preferred method, most centers use intermittent sphygmomanometer measurements, especially in children.
- The patient is returned to baseline if the test becomes positive (LOC, unable to maintain posture with hypotension, or bradycardia) or upon completion of the protocol.

HUT testing protocols

- HUT testing with or without pharmacologic provocation has proved to be a useful tool for diagnosis of syncope.
- Though the Westminster protocol (non-pharmacologic) is most preferred, other protocols utilizing pharmacologic provocation with isoproterenol, nitroglycerin (NTG), and clomipramine (less commonly edrophonium and adenosine) have been used due to higher positivity rates. Table 21.1 lists the features of the various HUT protocols.
- Since the Westminster protocol is the most commonly used protocol it is discussed first in detail, followed by other specific protocols which are used less frequently.

Method

- The Westminster protocol (passive HUT at 60–70 degrees from 20 to 45 minutes) is the commonly preferred protocol in the initial evaluation of syncope.
- If the passive phase is negative, pharmacologic provocation using intravenous isoproterenol or sublingual NTG is performed.

Indications and contraindications

- * Unexplained single syncopal episode among patients with high-risk occupations or high risk of injury.

- * Recurrent episodes without structural heart disease, or with structural heart disease where other cardiac causes have been ruled out.
- * HUT testing is also indicated in patients with a negative EPS.
- # To detect an underlying vasodepressor component which could alter therapy.
- # To differentiate syncope with jerking movements from epilepsy.
- # Evaluation of recurrent unexplained falls.
- # Assessment of recurrent presyncope or dizziness.
- ^ A single episode without injury or not in a high-risk setting.
- ^ Clear diagnosis of VVS, where reproducing NMS would not alter treatment.
- HUT testing is contraindicated in patients who are orthostatic at baseline or in patients with near syncope without LOC.

Response interpretation and diagnosis

- Most patients show three clinical responses (types I, IIA, IIB, and III are based on Sutton et al[6]):
  - Cardioinhibitory (bradycardia or type 2)
  - Vasodepressor (hypotension or type 3)
  - Mixed (the most common or type 1)
- Cardioinhibitory type IIA: bradycardia without asystole, HR falls to a ventricular rate $<$40 beats per minute (bpm) for $>$10 s without asystole $>$3 s. Blood pressure falls before the onset of bradycardia.
- Cardioinhibitory type IIB: bradycardia with asystole, asystole occurs $>$3 s. Blood pressure falls with or before the onset of bradycardia.
- Vasodepressor type III: HR does not fall $>$10% from its peak at the onset of syncope with the following two exceptions:
  - Chronotropic incompetence: no HR increase during HUT ($<$10% pretilt rate)
  - POTS (postural tachycardia syndrome): an increase in HR $>$28 bpm compared to pretilt rate both at the onset of the upright position and throughout the tilt duration.
- Mixed type I: HR falls at the time of syncope but the ventricular rate does not fall $<$40 bpm, or falls to $<$40 bpm for $<$ 10 s with or without asystole $<$ 3 s. Blood pressure falls before the onset of bradycardia.

Response patterns during HUT (Figure 21.2)

- Based on the response of BP and HR during VVR, two patterns have been identified:
  - *Classic*: an initial rise in BP and HR (suggesting normal baroreflex function) is seen followed by VVR. Patients are younger, with h/o of several syncopal episodes starting early in life, and a lesser incidence of secondary trauma. They are thought to have a hyperactive ANS.
  - *Progressive*: the initial rise is absent. A steady decline in BP and HR is seen until the onset of VVR. Patients are predominantly old, with comorbidities, and have fewer syncopal episodes starting later in life. They are thought to have a hypoactive ANS.

Advantages and pitfalls

- HUT testing is a safe procedure with minimal complications. Most patients have symptoms ranging from nausea/vomiting to the effects of a syncopal episode reproduced by HUT testing.
- Asystole during VVS as long as 73 s has been reported.[7] A quick return of the table to the supine position and raising the legs is enough to restore consciousness in most patients.
- Rarely ventricular arrhythmias (especially with isoproterenol provocation) in patients with cardiac ischemia[8] and self-limited atrial fibrillation[9] have been reported. Hence isoproterenol provocation is contraindicated in patients with coronary artery disease.

HUT with carotid sinus massage

- Carotid sinus massage (CSM), when performed carefully, can provide a clinical diagnosis of carotid sinus syndrome. Similar to NMS, stimulation of the mechanoreceptors of the carotid sinus results in VMC-mediated parasympathetic and sympathetic responses.
- CSM should be performed preferably in conjunction with HUT in syncope due to unexplained cause, especially among patients $>$ 40 years because, in addition to an increased rate of positive responses, an additional vasodepressor component (usually seen in carotid sinus hypersensitivity [CSH]) can be identified.
- A CSM is contraindicated if (i) carotid bruit is present, (ii) CVA/TIA has occurred in the last 3 months, (iii) myocardial infarction within the last 6 months, and (iv) there is a history of VT or VF.[10]
- The CSM should be done as follows:
  - The carotid arteries should be palpated on both sides and auscultated for the presence of bruits (indicative of carotid disease)
  - If no bruits are heard, a vigorous and circular pressure is applied on the carotid artery anterior to the sternocleidomastoid at the level of the cricoid cartilage (carotid sinus) for 5–10 s in both supine and erect positions, with simultaneous electrocardiographic monitoring
  - If no response is seen on one side, CSM is repeated on the other side 1–2 minutes later
  - If a cardioinhibitory (asystolic) response is seen, the test is repeated after 1 mg atropine infusion, to look for an additional vasodepressor response.
- In the elderly CSM should be done cautiously. Elderly patients undergoing CSM should be monitored for 2 hours postprocedure for neurologic events.[10]

Isoproterenol infusion

- Most investigators will use isoproterenol (escalating doses) during a HUT, in patients with a negative HUT and a high index of suspicion of NMS. The use of pharmacologic provocation (isoproterenol) increases positive responses but reduces specificity.

- Isoproterenol infusion is contraindicated in patients with coronary artery disease to avoid provocation of serious arrhythmias or angina.[11]
- HUT with isoproterenol provocation can falsely raise sensitivity.[12]

NTG infusion

- NTG is a potent venodilator, which causes venous pooling, but spares the sympathetic compensatory responses to syncope. Thus it is particularly useful in duplicating the vasodepressor response.
- This is known as the Italian protocol.
- Though NTG infusion was used initially, recently many authors have used 400 μg of NTG sublingual spray after a 20 minute baseline phase.[13–15]
- It has a superior side-effect profile when compared to isoproterenol with comparable positivity rates.

Clomipramine protocol

- Clomipramine is a central serotonin reuptake inhibitor, leading to sympathetic withdrawal.

Adenosine triphosphate (ATP) infusion protocol

- ATP infusion causes endogenous release of adenosine causing AV nodal block, thought to be the triggering mechanism of syncope during spontaneous syncopal attacks and HUT testing.[16,17]
- Recently ATP infusion has been used as an adjunct to HUT testing in unexplained syncope.[18,19]
- Because ATP can induce bronchospasm and coronary spasm, it is contraindicated in patients with asthma and coronary artery disease.
- # ATP testing identifies a group of patients with unexplained syncope, with definite clinical features and benign prognosis, but a possible heterogeneous mechanism of syncope. Thus specific treatment should be postponed until a definite mechanism of syncope can be obtained.

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Section IX
Catheter ablation techniques

22

Ablation of SVT (AVNRT and AVRT)

Chi Keong Ching, Andrea Natale, Mauricio Arruda, and Patrick Tchou

Catheter ablation of AVNRT • Catheter ablation of AVRT

CATHETER ABLATION OF AVNRT

Fast pathway ablation

In the common form of typical AVNRT, anterograde conduction occurs through the slow AV nodal pathway, typically localized along the tricuspid annulus just anterior to the coronary sinus (CS) os, while retrograde conduction occurs through the fast pathway localized more superiorly along the mid to anterior part of the septum. Earlier attempts at ablation targeted the fast AV nodal pathway,[1,2] proved to be effective in 80–90% of patients. However, the risk of complete AV block ranged up to 22% due to its close proximity to the compact AV node.

The ablation catheter is positioned in the His region to record the maximum amplitude of the His bundle potential. The catheter is then withdrawn along the tendon of Tadaro until the His bundle potential just disappears (at most $<$0.1 mV) while a large atrial amplitude is recorded with an AV ratio of $>$1. The tendon is a structure that is approximated by a line extending from the proximal His bundle to the roof of the CS os. The endpoints are a prolongation of PR interval by about 50%, elimination or attenuation of the retrograde fast pathway, and non-inducibility of AVNRT.

Slow pathway ablation

There are two approaches to slow AV nodal pathway ablation. One is called an anatomic approach while the other uses electrogram characteristics to guide ablation. In reality, both approaches use electrogram guidance as well as anatomic landmarks.

Anatomic approach

This was first proposed by Jazayery et al[3] and ablation is performed using only anatomic landmarks. The triangle of Koch from the CS os to the His bundle is

divided into three regions called the posterior, mid, and anterior regions. Since the tricuspid valve, one of the borders of the triangle, is almost vertically oriented, these three zones can also be anatomically considered inferior, mid, and superior segments along the septal portion of the tricuspid valve. The ablation catheter is placed along the septal edge of the tricuspid annulus just anterior to the CS os (posterior zone) to obtain an AV ratio of 0.1 to 0.5. If AVNRT is still inducible, further RF ablation is applied adjacent to the previous site with a higher AV ratio. This slightly higher ratio moves the catheter slightly away from the tricuspid annulus so as to transect the tail of the AVN – the slow pathway. If unsuccessful, the catheter is moved toward the mid and superior positions. This approach achieves a success rate of 95–99% with an extremely low risk of AV block of 0.6–0.9%.

Electroanatomic approach

This electroanatomic approach utilizes both endocardial potentials and anatomic markers to guide RF ablation. Sun[4] described sharp atrial electrograms following a low amplitude atrial electrogram during sinus rhythm. This is recorded around the CS os, usually just anterior to it. Jais[5] described the potential recorded at the mid or posterior septum, anterior to the CS. The potential is variable, from sharp to slow with a common AV ratio of 0.5 to 0.7. Both of these potentials can be recorded simultaneously in the same patient: the sharp potential more inferiorly and the slow potential more superiorly. Occasionally, an overlapping zone near the CS os where both potentials can be recorded is present.

Catheter placement and electrophysiologic study

Generally a quadripolar catheter is positioned in the His bundle region, a second multi-polar catheter is placed in the CS, and a quadripolar catheter is placed at the right ventricular apex. The presence of a separate lateral right atrial catheter is desirable, but not necessary. The His bundle catheter or the RV catheter can be moved to the RA to define atrial activation sequences if needed.

The electrophysiology study is performed to document the fast pathway refractory period when possible, 1:1 AV conduction cycle lengths through the slow pathway, maximum AH intervals during 1:1 AV conduction, and inducibility of AVNRT. Isoproterenol, or atropine infusion, or both may be required if basal conditions are not yielding. The ablation catheter is withdrawn inferiorly from the His bundle region along the atrial edge of the tricuspid annulus. Positioning of the catheter at the slow pathway region can be performed in either the right atrial oblique (RAO) or left atrial oblique (LAO) view. In the LAO view, the septal position of the catheter can be readily appreciated. Deviations of the catheter to the right or into the CS os can be easily detected. However, the annular location of the catheter has to be assessed using the AV electrogram ratios. In the RAO view, the location of the catheter along the tricuspid annulus can be readily appreciated. However, the septal position of the catheter has to be guided by rotating the catheter until it touches the septum. An LAO view is used with the catheters placed in the His bundle region and curled down along the septal annulus towards the CS os. The most common area where a slow potential can

be recorded occurs in the inferior third of the axis from the His bundle to the CS os. The sharp potential described by Jackman[4] is usually recorded by moving the catheter slightly anteriorly from the CS os towards the tricuspid annulus. Frequently an overlapping zone with both sharp and slow potential exists anterior to the CS os.

To minimize the risk of AV block, it is best to start the RF application at a low power output such as 20–30 watts and a temperature setting of 50°C. The power and the temperature can be gradually increased during the RF application towards 50 watts and 60°C, while the occurrence of junctional rhythm is closely monitored. It is infrequent that temperatures above 60°C are needed. A slow junctional acceleration is usually seen when the slow pathway is heated. The cycle length of this junctional rhythm can be just above sinus rate to around 600 ms. Cycle lengths shorter than 500 ms should be a warning sign that the more distal portion of the AVN is being heated. Retrograde atrial conduction via the fast pathway should be closely monitored during this acceleration. Any evidence of retrograde block should prompt immediate termination of the RF application as this is another sign that the distal AV node may be affected by the RF. Absence of any junctional acceleration usually indicates that the ablation lesion was ineffective in eliminating the slow pathway. Electrical endpoints, including non-inducibility of AVNRT, increase in the AV nodal refractory period consistent with elimination of the slow pathway, an increase in the 1:1 AV nodal conduction cycle length, as well as a decrease in the maximum AH interval achieved during 1:1 AV conduction, are all signs of successful slow pathway ablation. Use of isoproterenol and/or atropine infusion may be necessary if those drugs were needed prior to ablation. At times, following ablation, a single AV nodal echo beat can still be induced with premature atrial stimulation. This may be an acceptable outcome if no AVNRT could be induced following isoproterenol challenge. Usually, when such an echo beat is still present in the absence of inducible AVNRT, the antegrade AV nodal slow pathway refractory period is longer and/or the longest achievable AH interval during premature atrial stimulation is shorter than before ablation. This indicates that modification of the slow pathway had occurred during ablation such that the longest conducting slow pathway fibers, those likely involved in the AVNRT, had been eliminated. Shorter conducting slow pathway fibers may still be present, but those are unable to sustain the AVNRT.

Complications

The dreaded complication in AV nodal pathway ablation is atrioventricular block, a complication seen at a much higher incidence in fast AV nodal pathway ablation. If present, atrioventricular block usually occurs immediately at the time of RF application. However, it may occur later, usually within the first 24 to 48 hours, although even late occurrences have been reported.[6]

Damage to the compact AV node or His bundle can occur if RF energy was delivered in anatomic sites near them. In such cases, positioning of the catheter at the slow pathway region is usually not very stable. Changes of position can occur readily with heart beat movement or with breathing. Thus, close monitoring of the catheter position during RF application is important in minimizing this complication.

The presence of a faster accelerated junctional tachycardia and/or retrograde block of junctional ectopy during RF application are markers predictive of complete permanent AV block.[7] Abrupt PR or AH interval lengthening during RF ablation should be a warning that the RF lesions are being applied closer to the fast pathway than the slow pathway. RF application should be stopped immediately.

Cryoablation

Although the risk of AV block is very low when the electroanatomic approach is adopted, it is nonetheless a severe and permanent complication. The use of cryoablation has been recently proposed. While cooling of the tissue would quickly result in cessation of function, the creation of permanent tissue ablation with cryoablation usually takes much longer application. Thus, it is recommended that these lesions be applied for up to 4 minutes. Close monitoring of the development of functional AV block during cooling usually provides adequate warning that an ablation site could result in permanent AV block. If ablation is stopped immediately upon detection of AV block, the block is totally reversible. Another advantage is the possibility of applying reversible cooling at $-30°C$, thereby allowing assessment of the functional effect of any prospective lesion before permanent damage is inflicted. However, close monitoring of AV block should still be performed during application of maximal cooling for the ablation. During cryoablation, no junctional rhythm is observed, unlike that of RF ablation. Below $-30°C$, the catheter is stuck to the atrial endocardium. This allows stimulation of the atrium to test the modification or disappearance of dual AV node physiology, non-inducibility of AVNRT, or interruption of the AVNRT due to slowing down followed by block of conduction over the slow pathway; or modification of the fast pathway ERP. If one or more of these criteria are met without changes in the basal AV conduction during ice mapping, then the temperature is lowered to $-75°C$ for 4 minutes, creating a permanent lesion.

While elimination of slow pathway conduction during cooling indicates that the catheter tip is near the slow pathway, it does not guarantee that the ablation will be successful. This is due to the large tissue temperature difference needed to interrupt function with cooling versus that needed to permanently kill the tissue. Another advantage of using cryoablation is the adhesion of the catheter tip to the atrial endocardium. This prevents any inadvertent catheter dislodgement during application. The disadvantage of this approach is that it frequently takes more time as the lesions have to be applied for up to 4 minutes at each location. Applying a second lesion at the successful site may add assurance that the tissue is permanently ablated. The lesion may also have to be applied at a location that appears closer to the compact AV node than during RF application. In most cases, these lesions have to be applied close enough to the compact node to note mild PR prolongation. The occurrence of marked PR prolongation or AV block should prompt immediate termination of the cryothermal application. While AV block and PR prolongation may persist for several seconds, and sometimes up to 30 seconds, it always reverses if the application is terminated promptly at the development of the block.

Conclusion

AVNRT can be cured with the ablation of either the fast or slow AV nodal pathway. The approach of choice would be to target the slow AV nodal pathway ablation. The techniques described for slow pathway ablation have a reasonably high percentage of success. There should be no immediate or late AV block if there is no impairment of either anterograde or retrograde conduction. However, a small percentage of late AV block has been seen with RF ablation. The recent use of cryoablation may further reduce the risk of this complication.

CATHETER ABLATION OF AVRT

Catheter placement and electrophysiologic study

Catheters are placed in the high right atrium, His bundle region, right ventricle, and coronary sinus. Programmed electrical stimulation is then performed to initiate SVT. The following electrophysiologic features are used to identify the anatomic site of an AP:

1. *Earliest ventricular and atrial potentials:* in manifest AP, the earliest local ventricular potential of pre-excited beats is mapped. Atrial pacing can be performed to enhance pre-excitation and the site of earliest ventricular excitation identifies the ventricular insertion site. In both concealed and manifest AP capable of retrograde conduction, the earliest local atrial potential during orthrodromic AVRT or ventricular stimulation identifies the atrial insertion site. Some cautions: the sites of shortest VA or AV intervals should not be confused with the site of earliest A or V activation. While the sites of accessory pathway insertion usually have short activation intervals, they may not be the shortest. The VA or AV interval is an activation interval and does not necessarily indicate conduction time. Caution should be utilized when mapping the earliest atrial activation during ventricular pacing. One must be aware that retrograde conduction can occur via both the accessory pathway and the AV node. For pathways near the septal regions, both of these two potential pathways could activate the atrium during ventricular pacing and therefore may be difficult to distinguish. Thus, mapping atrial activation during orthodromic tachycardia is the best way to confirm that the site of earliest atrial activation is the accessory pathway insertion site.
2. *Atrioventricular and ventriculoatrial interval:* local atrioventricular and ventriculoatrial intervals are close to each other at sites of earliest activation. These potentials are seen in bipolar recordings. The gain of the recordings should be adjusted such that the entire electrogram can be seen. The onset of the rapid deflection of the electrogram should be marked as the beginning of local activation at the catheter tip. At high gains, low amplitude low frequency signals can frequently be seen preceding the rapid component. These represent the far field approach of the wave front and should not be used to mark the local activation time. In unipolar recordings at sites of earliest ventricular activation, a QS morphology identifies the endocardial breakout of the pre-excited V electrogram.

3. *Atrioventricular pathway potential:* An AP potential can be recorded at times during anterograde and retrograde conduction. However, the AP potential is less frequently identified during retrograde conduction as this often superimposes onto the ventricular potential.

Ablation of left-sided free wall pathways

Either a retrograde aortic or a trans-septal approach can be adopted. In the retrograde aortic approach, the mapping catheter is advanced across the aortic valve by accessing the femoral artery. It can be placed just underneath the mitral valve on its ventricular aspect to map the ventricular insertion of the AP. At this position, the movement of the catheter tip is in concert with the ventricular motion. The atrial to ventricular (A/V) potential amplitude is less than 1. Alternatively, it can be further advanced across the mitral annulus to map the atrial insertion of the AP. At this position, the wagging motion of the catheter tip is dissociated from the ventricular motion. The A/V potential ratio is 1 or greater and increases as the catheter tip is advanced away from the annulus. In either approach, atrial potential amplitude beat to beat variation of less than 20% reflects catheter stability. In the transseptal antegrade approach, the intra-atrial septum is crossed to ablate the atrial insertion of the AP. Long directional sheaths can be used to offer greater catheter stability.

Left-sided APs can be ablated with a success rate of $>$95% and a low recurrence rate of $<$5%. Recurrence usually occurs early, within 1–2 weeks, but may occur as late as 6 months following ablation. In cases of early recurrence, a repeat ablation is not advisable until 6–8 weeks after the initial ablation as some pathways that were damaged by the initial ablation may eventually lose conduction. Risk of myocardial perforation of friable tissue created by the initial ablation is higher should repeat ablation be attempted soon. Additionally, the presence of edema, a reaction of the ablated tissue, may distort the local electrograms and impede energy delivery for efficient ablation.

Ablation of right-sided free wall accessory pathways

The initial success of right-sided AP is lower than that of left-sided AP. However, the complication risk is lower and myocardial perforation with cardiac tamponade is less common than left-sided ablation. Rare cases of paradoxical emboli through a patent foramen ovale and right coronary artery occlusion have been reported.[8]

The lower success rate can be attributable to the challenges associated with mapping right-sided accessory pathways:

1. *Difference in mitral and tricuspid annuli:* the tricuspid annulus is larger in size, averaging 11 cm in circumference.[9] The tricuspid valve is less of a complete fibrous ring and may have gaps where atrial or ventricular muscles are in continuity. Furthermore, right-sided APs often penetrate the annulus and may consist of a broad band of tissues. Though the prevalence of APs is lower in this region, multiple pathways are slightly more prevalent. Unlike the mitral annulus which can be marked by placing a catheter in the CS,

there is no analogous venous structure to mark the tricuspid annulus. If needed, a thin angioplasty wire or six French multi-electrode catheter can be placed in the right coronary artery to delineate the tricuspid annulus.

2. *Catheter stability:* it can be difficult to maintain catheter stability during ablation of right-sided APs. The lateral aspect of the tricuspid annulus has a large spatial excursion during ventricular systole. In addition, the approach to the tricuspid annulus from the inferior vena cava results in a more acute turn and the trans-septal approach to the mitral annulus. This more acute angle and the large movement of the lateral tricuspid annulus towards the RV apex during systole render catheter tip stability on the annulus more precarious. Long vascular sheaths with preformed curves that aim the catheter in the appropriate directions within the right atrium can improve the stability and facilitate appropriate delivery of RF energy on the atrial side of the annulus. An approach from the superior vena cava can be adopted for APs localized on the anterolateral aspect of the tricuspid annulus to provide better stability. Alternatively, a ventricular approach can offer much better stability during systole. However, a curved sheath and a smaller catheter curve may be needed to achieve a retroflexed contact at the ventricular end of the tricuspid annulus.

Ablation of septal accessory pathways

APs in this area are commonly classified as anteroseptal, mid-septal, and posteroseptal, as described in the early part of this chapter. Precise mapping and localization of all APs is mandatory to avoid impairment of AV nodal conduction during RF ablation. Understanding the anatomy of the conduction system in relationship to structures at the AV groove is critical for achieving successful ablation with minimal complication rates. As mentioned above, the AV node runs along the atrial edge of the tricuspid annulus in a cranial direction with a slight anterior tilt. At the central fibrous body, the compact node transition to the His bundle and crosses the tricuspid annulus. Just anterior and superior to the compact node is the membranous septum. The His bundle runs along the inferior border of the membranous septum along a ridge of ventricular myocardium. Thus, in anteroseptal accessory pathways there is always a small distance, no more than 5 mm, that separates the His bundle from the nearest myocardial connections to the tricuspid annulus. On the other hand, true septal pathways may have virtually no separation from the AV node.

Anteroseptal APs

These are classically defined as paraHissian or anteroseptal if the earliest AP activation site also shows a His potential. It is safest to ablate these pathways from the atrial side of the annulus as this position optimizes the distance from the His bundle and the AV node. Use of a sheath may help stabilize the catheter contact with the annular tissue. Optimally, RF energy should only be applied during narrow QRS rhythm in order to minimize the potential of ablating the normal conduction pathway. In cases where sinus rhythm is associated with marked pre-excitation, initial RF lesions may need to be applied to during orthodromic tachycardia.

Application of RF energy should be in a graded manner, paying close attention to onset of rapid junctional tachycardia, indicating heating of the compact AV node, or the development of right bundle branch block, indicating heating of the right-sided surface of the His bundle. When applying energy during orthodromic tachycardia, block in the AP is associated with sudden slowing of the rhythm to sinus rhythm. This may cause the catheter to dislodge. The map location of the catheter tip may also change significantly due to changes in cycle lengths. Thus, atrial pacing at a rate similar to the tachycardia may need to be instituted immediately to maintain contact and to assess stability of catheter tip location. A slow accelerated junctional rhythm can be seen at times due to the proximity of RF application to the compact AV node. This indicates that there is mild heating of the AV node tissue. However, more rapid junctional acceleration should prompt immediate cessation of RF application, similar to the approach during slow pathway ablation. Cryoablation has also been utilized in this region. Its advantages and disadvantages are similar to those in ablation of AVNRT.

Midseptal APs

The AP potential can be recorded in an area along the tricuspid annulus defined by the His bundle anteriorly and coronary sinus ostium posteriorly, either on the right or left side of the atrial septum. Care should be taken in mapping either side as the AV node is in close proximity to the atrial insertion site, especially in the mid-septal location. Application of RF energy is best directed on the ventricular side of the annulus, aiming to ablate the ventricular insertion, as the AV node is on the atrial side. This would minimize the chance of causing damage to the AV node. In left-sided midseptal APs, catheters are positioned at the His bundle and coronary sinus to mark the area. The ablation catheter is then moved along the mitral or tricuspid annulus bounded by these two catheters. Electroanatomic mapping systems should be used whenever available to facilitate accurate location of these pathways.

Posteroseptal APs

Posteroseptal APs traverse the pyramidal space posterior to the septum. This region of the cardiac anatomy is complex and understanding the relationships of the mitral and tricuspid annular regions to the CS and the basal LV septum is crucial to locating the accessory pathway properly. The septal and inferior portions of the tricuspid annulus, the triangle of Koch, the anterior superior regions of the proximal CS abutting the mitral annulus, and the proximal CS venous branches should all be carefully mapped to reveal the atrial and ventricular connections of the AP. Left-sided mapping of the atrial septum and ventricular side along the mitral annulus should be considered. The right posteroseptal AP inserts along the tricuspid annulus in the vicinity of the CS ostium. The left posteroseptal AP may be located at a subepicardial site around the proximal CS or the middle cardiac vein. In such instances, the ablation catheter may be advanced into the CS to search for early activation sites or an AP potential to target RF application. At other times, the left posteroseptal AP may be located at a subendocardial site along the posteromedial aspect of the mitral annulus. The ventricular end of this

location can also be approached from the retrograde direction. The septal portion of the mitral annulus is directly inferior to the aortic outflow and can best be reached by clocking the catheter tip from a mid-ventricular septal position while holding a gentle curve. Again, application of RF lesions in these areas, especially in the mid-septal region, should be done during narrow QRS antegrade conduction whenever possible to minimize inadvertent ablation of the normal conduction pathway. Cryoablation, of course, can also be used if available. The use of cryoablation may be particularly desirable in the smaller venous branches originating from the proximal CS as it has greater safety in minimizing potential damage to the nearby arteries.

Ablation of epicardial atrioventricular pathways

The incidence of epicardial AP is approximately 0.5% of patients referred for RF ablation of AP. In right-sided epicardial AP, small or no AP potentials can be recorded. A thin multi-polar catheter can be placed in the right coronary artery for epicardial mapping. Endocardial ablation can be guided by both location and recordings from the epicardial electrode. Because the right atrium and the right ventricle are relatively thin, transmural ablation is usually feasible from an endocardial approach. However, there are rare instances where the pathway connects from the right atrial appendage to the epicardial ventricular surface somewhat removed from the annulus. If this site has heavy endocardial trebeculations, transmural ablation may not be achieved. A transcutaneous epicardial approach for ablation has been described[10] and can be used in these rare instances. Ablation of accessory pathways along the annulus from an epicardial approach may be difficult as it could be hindered by the close proximity of the right coronary artery. The presence of epicardial fatty tissue around the AV groove also limits RF ablation efficacy.

A left-sided epicardial AP is characterized by a large AP potential along the CS or its tributaries. These pathways typically connect to the epicardial ventricular surface. Ablation can be successfully and safely achieved by delivering RF applications within the CS or its tributaries.[11] Cryoablation via a CS approach may also be used in these circumstances. It has a lesser propensity to cause venous stenosis and has a lower risk of damaging the nearby arteries that frequently travel close to the veins. In rare circumstances, there may be AP connections from the left atrial appendage to the LV epicardial surface. These may need an epicardial approach to achieve successful ablation.

Ablation of atrioventricular pathways with slow decremental conduction

These AP variants were originally described as nodoventricular or Mahaim pathways. Clinically, these arrhythmias exhibit a wide QRS tachycardia, usually with a left bundle branch block pattern. While other potential connections have been postulated, the vast majority of these pathways are atriofascicular or atrioventricular in nature, with slow decremental conduction characteristics suggestive of a node-like property.[12] The ventricular insertion sites of atrioventricular and atriofascicular fibers can be localized by mapping the local AP potential. Early ventricular

activation may not reveal the true site of accessory pathway in the atriofascicular variety. A His-like potential can frequently be identified in these cases just under the anterolateral portion of the tricuspid annulus. Distal connection to the myocardium may occur via the Purkinje fibers or possibly even directly into the right bundle, yielding rapid retrograde conduction into the conduction system. Mechanical block of the AP by catheter manipulation can occur during manipulation of the catheter tip on either side of the tricuspid annulus. Pace mapping on the atrial side of the tricuspid annulus can facilitate identifying the atrial end of the pathway. The shortest stimulus to QRS or RV interval of maximally pre-excited beats during atrial pacing should identify the atrial end of the pathway. Since these pathways typically show no retrograde conduction, retrograde activation mapping is of no use to identify the atrial insertion. Once a site has been identified, RF ablation can be delivered during pre-excited SVT or during atrial pacing with maximal pre-excitation. If successful, the SVT will terminate. In many cases, pre-excited accelerated rhythms occur during RF ablation due to heating of excitable node-like fibers. Left-sided decremental accessory pathways can also occur, but are much less frequently seen than the right-sided variety. Ablation can be approached in the same manner, but using left-sided approaches on the ventricular side of the mitral annulus.

True nodal ventricular conduction is indeed rare. These pathways have been suggested in reports where ablation of the slow AV nodal pathway had eliminated a pre-excited decremental AV conduction.[13] In some instances, the earliest ventricular activation of pre-excited beats was recorded at the ventricular aspect of the annulus, suggesting a ventricular insertion rather than a fascicular insertion site. Given these observations, it is not clear if these fibers originate from the AV node or course the annulus in close proximity to the AV node. When these occur, distinguishing these pathways from septal accessory pathways with decremental conduction can be difficult.

Ablation of permanent junctional reciprocating tachycardia (PJRT)

PJRT is characterized by sustained tachycardia (>12 h/day) with a narrow QRS complex. This tachycardia commonly appears in infants and children and may persist into adulthood. It is usually refractory to drug therapy and is frequently not associated with clinical symptoms. However, it can cause tachycardia-mediated cardiomyopathy. Studies indicate that a concealed AP with slow and decremental retrograde conduction properties is involved in the initiation and maintenance of orthodromic AVRT. Occasionally anterograde conduction can be seen with variable pre-excitation.[14] The AP is usually localized to the septal tricuspid annulus close to or just inside the CS os in 80% of cases, and along the posterior right or left free wall in the remaining cases.

Conclusion

Catheter ablation of AP has been a preferred therapy given its low procedural risk and its excellent success rate. However, a clear understanding of the anatomy at the various sites of ablation is important in generating successful outcomes and

minimizing risks. Careful mapping of APs with modern mapping equipment can be very useful, especially in complex anatomic areas of the heart. Use of alternative energy sources to RF may enhance the safety of these procedures in special circumstances. In addition, percutaneous epicardial access may allow ablation of pathways that are inaccessible from the endocardial side. This approach may spare surgical ablation in such an unusual circumstance.

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23

Management and ablation of atrial flutter

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Ablation of cavotricuspid isthmus (CTI)-dependent atrial flutters • Atypical RA flutter • Left atrial flutter

The effect of atrial flutter (AFL) on the hemodynamic status of the patient is a key determinant of the management strategy as to whether an immediate cardioversion or pharmacologic therapy should be attempted. AFL carries a moderate risk of systemic thromboembolism and thus effective therapy is of great importance. The 2003 ACC/AHA/ESC practice guidelines for the management of supraventricular arrhythmias provide recommendations on how to manage AFL in its acute and chronic states[1,2] (Figure 23.1).

Acute treatment: acute therapy is recommended in patients who are hemodynamically unstable or highly symptomatic.[3] The following are the therapeutic options that are available for the acute treatment of AFL:

- *Direct Current Cardioversion* is associated with success rates greater than 90%. Biphasic shocks as low as 25 J are effective in flutter conversion.
- *Overdrive termination*: overdrive pacing can terminate AFL in 80% of cases by pacing the atria at rates that are faster than the flutter cycle length, thus producing block in both directions. It is a very useful bedside maneuver in post-open-heart patients with epicardial wires. Occasionally attempts at overdrive termination may result in severe sinus node related bradycardia or degeneration to AF. In patients with a pacemaker or an implantable cardioverter defibrillation (ICD), overdrive pacing at a CL slightly faster than the tachycardia cycle length (CL) or a 50 Hz burst pacing in the atrium can be used.
- *Chemical cardioversion:* prolonging the refractory period without slowing the conduction velocity in the tachycardia circuit facilitates pharmacologic termination of the flutter.[4–6] Class III drugs like sotalol, dofetilide, amiodarone, and ibutilide are more effective than class Ic drugs.[3,7,8] All the patients should have telemonitoring and serial ECG and electrolyte levels. Torsades may occur in 1–4% of patients and is related to dose and the presence of underlying cardiac and renal abnormalities.[9]

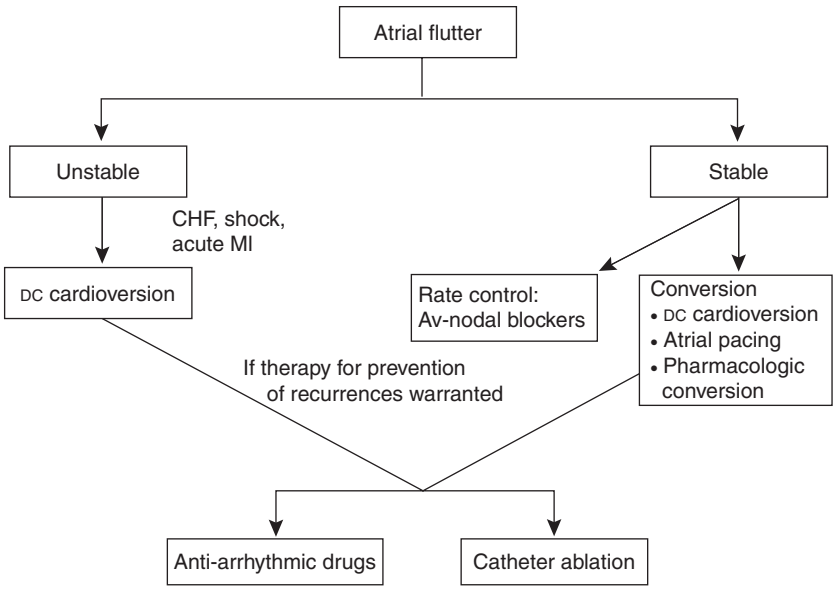


Figure 23.1 The 2003 ACC/AHA/HRS guidelines for the management of AFL. Published with permission from the AHA.

- *Rate control:* AV nodal blocking agents like beta-blockers, calcium-channel blockers, and digoxin can also be used in an acute state for rate control in the absence of hemodynamic compromise.

Chronic management: in the absence of acute hemodynamic compromise the management strategy could be:

- *Rate control with anticoagulation* using AV nodal blockers and chronic anticoagulation on warfarin.
- *Rhythm control* can be accomplished with classes Ia, Ic, or III anti-arrhythmic agents with or without direct current cardioversion. Class Ia and Ic drugs prevent recurrences by affecting the initiating atrial premature beats.[3] Class III drugs prevent maintenance of the arrhythmia by prolonging the wavelength (product of conduction velocity and duration of refractory period) of the circulating impulse. Class I drugs may decrease the flutter rate resulting in 1:1 AV nodal conduction manifesting in much faster ventricular rate. And marked QRS widening associated with class Ic drugs may make these fast 1:1 flutters look like ventricular tachycardia. Marked QRS widening with increasing ventricular rate varies by individual and an exercise test after initiating therapy is advisable. If QRS widens with increasing ventricular rates the class Ic drug should be either discontinued or an AV node blocking drug should be added to decrease the ventricular response.[3]

Catheter ablation: the ability to identify the macrore-entrant circuit of the flutter by endocardial activation mapping and pacing paved the way for a more invasive and curative therapeutic option in the form of ablation.[10] Catheter ablation

started as a high-energy endocardial DC shock that quickly evolved to a more precise local ablation using RF energy.[11–13] Various other energy sources are being tried to accomplish the ablation of the critical isthmus in the circuit with conduction block as the endpoint. Our group has shown the superiority of catheter ablation as the first-line therapy in patients with AFL compared to anti-arrhythmic drugs.[14] Catheter ablation was not only highly successful with a better quality of life, but was also associated with lower rates of hospitalization and degeneration to AF. With current technology, RF ablation of the flutter circuits is safe and curative with >90% long-term success rate.

Anticoagulation in AFL: there are no prospective randomized studies that looked at the thromboembolism rates in paroxysmal and permanent flutter and the role of anticoagulation therapy in these patients. Anticoagulation therapy should be considered in AFL patients because of the frequent asymptomatic paroxysms, the associated cardiovascular abnormalities that favor systemic thromboembolism, frequent degeneration of AFL to AF, and atrial stunning after conversion of AFL by pace termination or electrical shock.[15] Thromboembolic prophylaxis should be used for chronic AFL in the same manner as that used for atrial fibrillation. Cardioversion and catheter ablation should only be performed in patients who have an INR ranging between 2 and 3, and in those who have been in AFL for less than 48 hours, or those who have no clots on transesophageal echocardiography (TEE). After successful catheter ablation, warfarin can be stopped 4–6 weeks later if sinus rhythm is still present without continued indication for anticoagulation.[1,3]

Introduction to catheter ablation: a thorough understanding of the atrial anatomy is the key to success.[16] It is important to identify the functional and anatomic barriers that are essential for flutter propagation and perpetuation. Ablating the isthmus that is necessary for the integrity of the circuit can successfully treat most macro re-entrant atrial arrhythmias like atrial flutters.[17–19] The line of ablation should join one fixed barrier to the other fixed barrier through the isthmus. A history of prior cardiac surgery or atrial fibrillation ablation should make the operator consider atypical flutters as part of the differential diagnosis.

ABLATION OF CAVOTRICUSPID ISTHMUS (CTI)-DEPENDENT ATRIAL FLUTTERS

The typical counterclockwise, typical clockwise, and lower loop flutters can be successfully treated with CTI ablation. Similarly, targeting the CTI can also ablate one of the two loops in double loop re-entry flutters that are seen in patients with atriotomies.[20]

Anatomy

The CTI extends in an anterolateral to posteromedial direction in the lower part of the RA; the tricuspid annulus anteriorly, the CS medially (septal), the IVC/Eustachian ridge posteriorly, and the lower end of the crista laterally form the boundaries of the CTI.[21,22] The dimensions of the CTI are variable, ranging from a few mm up to 3 cm in width and >1 cm in thickness. The septal end of the isthmus is relatively narrow compared to the lateral end.

Lab set-up

CTI ablation can be successfully performed using a simplified approach with an ablation catheter and a quadripolar pacing catheter that can be moved to different locations in the RA. With this approach no detailed atrial mapping can be performed but the participation of the isthmus in the perpetuation of the flutter can be established based on entrainment. An empiric CTI ablation in atypical flutters should not be done if it is not part of the circuit. A 20-pole halo catheter that spans the septum, anterior wall, and the CTI along with a separate CS catheter is the popular set-up that is well described. Others have used a single non-steerable multi-polar reference catheter with 8–12 electrode pairs that span the RA septum and anterior wall as a reference and pacing catheter.[20] A 20-pole (10 distal and 10 proximal poles with a 2 mm electrode separation) steerable catheter can also be used to span the posterolateral wall, the CTI, and the CS. With growing clinical experience operators have modified this procedure to their personal choice. A three-dimensional (3D) mapping system (CARTO or NavX) can also be used for additional guidance to map the flutter and establish the propagation.[23–26] A 3D mapping system is also helpful in delineating the anatomic landmarks and guiding the lesion set. Most of the experience in ablation has been with RF energy. However, there are some emerging data on the successful use of cryoablation (9 French, 8 mm cryocatheter) for isthmus ablation.[27–29] Experience with 4 mm and 8 mm tip, non-irrigated, closed irrigation, and open irrigation ablation catheters has been reported. Occasionally, the reach of the ablation catheter to the anterior end of the isthmus at the tricuspid annulus is insufficient. In these situations, the operator should promptly exchange for a long sheath that facilitates better access and stability to the entire breadth of the isthmus.

Ablation

CTI-dependent flutter ablation has evolved to become a more anatomically oriented procedure.[30] CTI ablation can be performed either in flutter or during normal sinus rhythm. For patients who come in persistent flutter, entrainment should be attempted at the lateral end, in the isthmus, and the septal end to confirm the participation of the CTI in the circuit. In about 17% of patients there may be some evidence of slow conduction across the CTI manifested by double potentials when the ablation catheter is swept from the septal to the lateral end. An electroanatomic map of the flutter can be created using either CARTO or NavX for additional guidance. A linear set of lesions spanning the breadth of the isthmus can be created either with a succession of point-by-point applications keeping the catheter stable during each application or by continuous application while dragging the ablation catheter from the annulus to the IVC. There is some debate regarding the precise location (septal vs lateral) of the ablation line. The site is really selected mostly based on the ease of catheter manipulation, stability, reach across the entire width of the isthmus, and avoiding any very high voltage areas that may indicate large, thick pectinate muscles. Both the lateral line and the septal line have similar efficacy.[31,32] We typically tend to use the mid-line of the isthmus as our target line of lesions. This fluoroscopically equates to 6 o'clock position on the TA in LAO 45. Start at the TA end of the isthmus with local EGM

showing a small A and a large V. A maximum curve on the ablation catheter is often necessary to reach this point. Manipulation in the RAO position may help in reaching the TA. A long preshaped guiding sheath may help in easy manipulation and better stability. When electroanatomic mapping is used, the ablation points are tagged for a better visual understanding of the line of lesions. The catheter tip temperatures may not reflect the tissue temperature because of the high flow in this region. The target temperatures and power are different for different ablation catheters. With every successful lesion the local EGM decreases in voltage with fragmentation. Forty-five to sixty seconds is required for longer lesions. In this fashion, the ablation catheter is drawn from the TA towards the IVC, until a sharp atrial EGM is seen at the proximal electrode recordings which will become the next ablation point. As the catheter approaches the IVC, the hard curve should be slightly released so that the tip rests on the isthmus. When pulled down with a tight curve the catheter tip has a potential to flip and fall into the IVC. Often times, the IVC end of the CTI has low voltage electrograms and is a common site for conduction gaps. Care should be taken to extend the lesion set all the way up to the IVC. If a reference catheter is present on either side of the isthmus, comparison of local and reference EGM timing helps to assess the isthmus conduction (Figure 23.2). The reference catheters that traverse the isthmus can create some difficulty in the manipulation of the ablation catheter and prevent adequate tissue contact. The operator should attempt to come underneath the reference catheter in those situations. At this point gain up the recording EGMs on the ablation tip and check for conduction gaps along the ablation line.[33] Tachycardia termination when ablated in flutter is only a proof of its isthmus dependency and is not suggestive of a complete conduction block. Isthmus conduction persists after the termination of the tachycardia or may recur within minutes after a transient block.[34] Pacing on either side of the isthmus may easily demonstrate persistent CTI conduction (Figure 23.3). Conduction slowing in the isthmus often occurs prior to block. If ablation is stopped at this point with the resolution of edema, there will be some recovery and a high risk of recurrence of atrial flutter.

Confirmation of conduction block

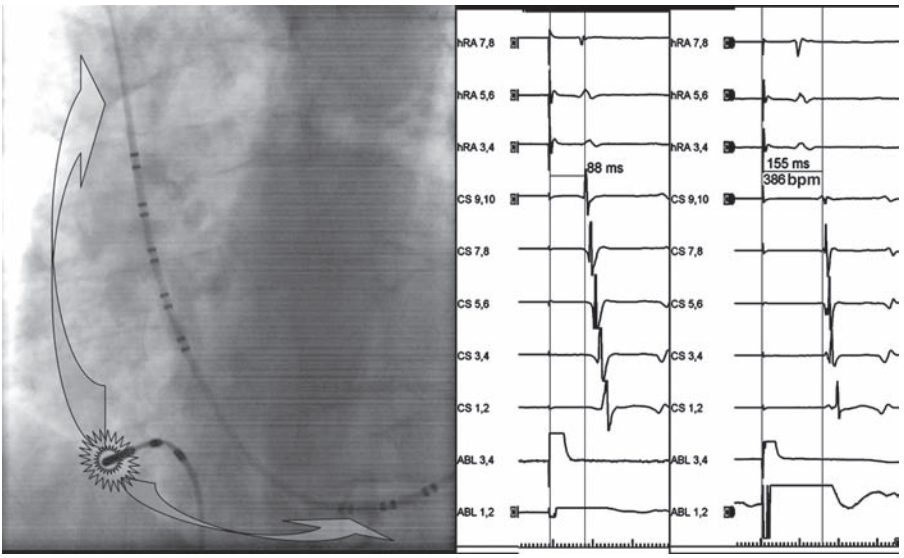
Confirmation of conduction block depends on assessing conduction of stimulated wavefronts from one side of the ablation line to the opposite side. The following markers of conduction block can be used to confirm conduction block across the CTI.

Change in activation sequence

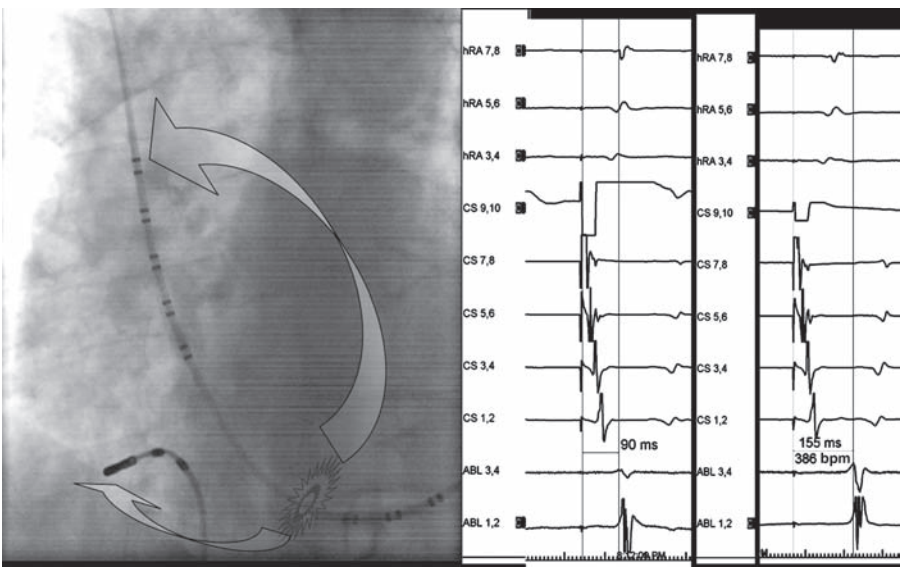
This is one of the first indicators of conduction block.[33,35] Prior to ablation activation of RA is ascending while pacing either the low anterior or low septal wall, but with CTI conduction block this activation sequence is reversed. Sequence reversal alone may not distinguish block from slowed conduction.

Increase in transisthmus conduction time (bidirectional block)

This is confirmed by pacing on one side of the CTI and measuring the conduction time to the opposite side (Figure 23.4). If a CS catheter is in place, pace from



(a)



(b)

Figure 23.2 Assessment of conduction times to evaluate isthmus block. (a) Before isthmus ablation when pacing from the CS os, activation proceeds in 2 directions, up the septum, and along the isthmus to the lateral isthmus (ablation catheter location). The measured conduction time to the ablation catheter is below 100 ms. After isthmus ablation, activation time measured from the ablation catheter increases to 150 ms, where activation of the low lateral wall only occurs after the high right atrial activation, i.e. counterclockwise activation, indicating unidirectional block. Bidirectional can only be confirmed when pacing from the ablation catheter as seen in (b), and conduction time to the CS os increases to more than 110 ms.

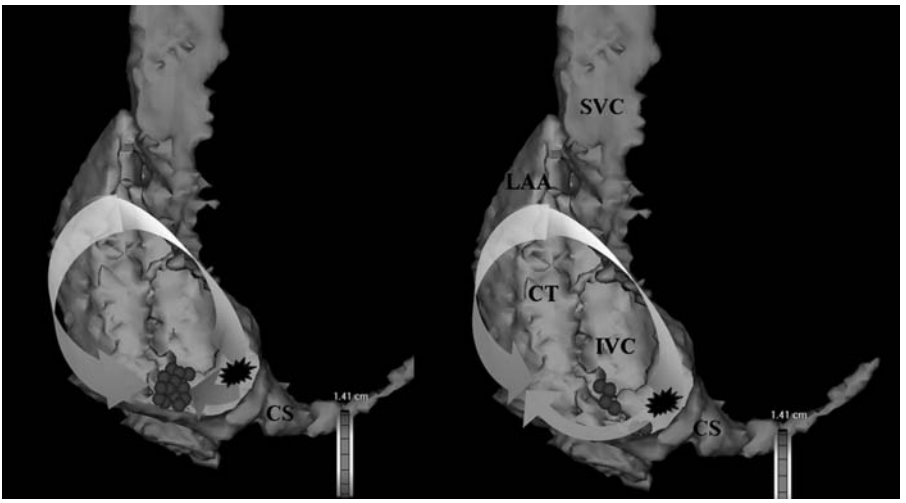


Figure 23.3 CT image of the right atrium 'clipped' in LAO view. The right image shows the activation sequence after partial isthmus ablation with the presence of a gap. The left image shows complete unidirectional block. (See color plate section.)

the proximal CS electrodes and record local EGM on the ablation catheter placed at the lateral end of the CTI (approximately 7 o'clock on the TA in LAO) and repeat *vice versa* by pacing at the lateral end and recording from the proximal CS.[36,37] A conduction block is confirmed if the conduction time from one end to the other is at least twice the conduction time prior to the ablation. There is no definite number that confirms conduction block. A 50% increase in transisthmus conduction time from baseline is known to be 80% specific for CTI block.[38] However, bidirectional conduction times of $>$130 ms are typically considered to be indicative of conduction block. One caveat to this marker is that conduction across the posterior right atrium through the crista terminalis can falsely suggest conduction through the isthmus when block is present (crista shunt) (Figure 23.5).[35,39] The presence of crista shunt can be identified by creating a detailed RA activation map, although time consuming, while pacing from the CS. Pacing posterior to the CS on the posterior wall shortens the conduction time to the lateral end of CTI. It would lengthen it if the line of block were incomplete.

Double potentials

Double electrograms separated by an isoelectric baseline (100–110 ms, 100% positive predictive value) along the whole ablation line. Each electrogram reflects activation on either side of the line of block.[40] Often times it is hard to interpret these potentials and they may reflect local conduction disturbances caused by RF applications. After completion of the ablation line, when checking the line for block, an inadequate separation between the two potentials is suggestive of conduction gap (Figure 23.6).

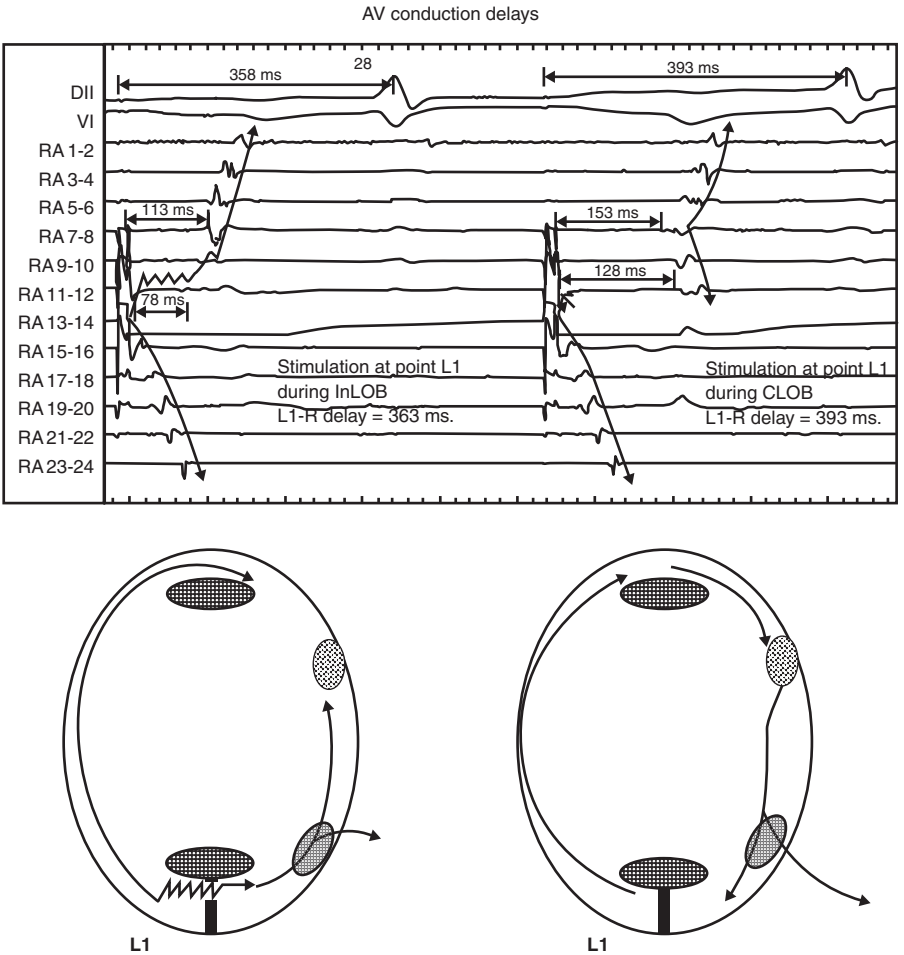


Figure 23.4 Diagrammatic representation of activation through the cavotricuspid isthmus (CTI) during L1 pacing site (dipole 13–14) when in line of block (LOB) (left panel) and after clob-directional (CLOB) (right panel), during RF application, assessed by direct electrogram recording on the 24-pole mapping catheter. When in LOB and pacing at site L1, activation proceeds through the CTI and ascends up the septum to the atrioventricular node. After CLOB, a direct assessment by the 24-pole mapping catheter documents activation detouring around the tricuspid annulus and descending down the septum to the AV node and the coronary sinus ostium. Published with permission of Laurent G et al.[45]

Differential pacing

This is a helpful technique to delineate the origin of the double potentials to the CTI. When the pacing site is moved a little bit further from the line of block, then the conduction time from the pacing site to the potential generated by the wavefront activates the distal side of the line becomes shorter and that to the proximal side becomes a little bit longer, and the opposite occurs if there is still conduction through the isthmus[41] (Figure 23.7).

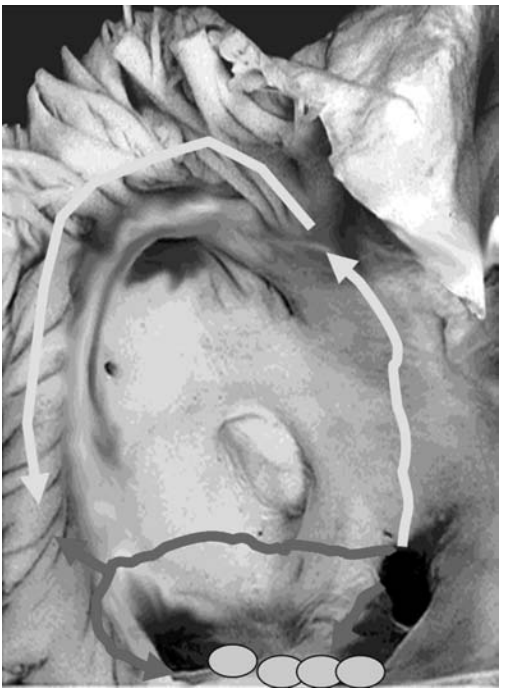


Figure 23.5 *Crista 'shunt'.* Diagrammatic depiction of the CTI and posterior atrial wall, showing that despite absence of conduction along the CTI when pacing from the CS os, yet still the conduction time to low lateral wall may be short, suggesting passage of the conduction wave through the crista along the posterior wall. (See color plate section.)

Reversal of EGM polarity on the opposite side of the ablation line from the pacing site

Unipolar EGMs change from biphasic (conduction through isthmus) to positive monophasic (end of activation at the opposite side of line of block)[42] (Figure 23.8). Occurrence of conduction block is also associated with changes in the bipolar EGM configuration.[43]

Change in P-wave morphology

A consistent change in P-wave morphology from negative to positive when pacing lateral to the ablation line is a good indicator of conduction block. P-wave morphology during pacing is mostly determined by the direction of septal activation than by the RA lateral wall. With a conducting isthmus the septum is activated caudocranially, resulting in a negative P-wave, whereas the septal activation changes to craniocaudal direction with positive P-waves in the presence of conduction block.[44]

Changes in AV conduction delay during septal and lateral RA pacing

Assuming that the cardiac chambers are within reasonable limits, and in the absence of AV nodal conduction delays, this is a simple tool for confirming CTI block.

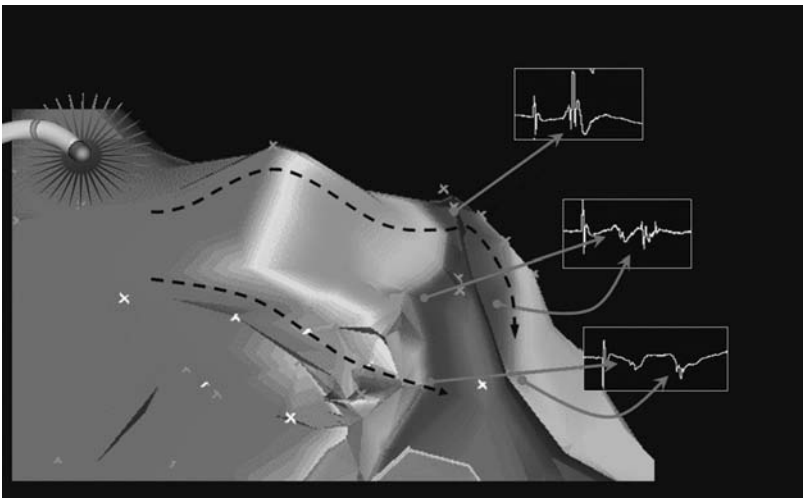


Figure 23.6 Gap along the ablated isthmus. Electroanatomic map of the CTI while pacing from the lateral wall. Widely split double potentials are seen at one end of the line and as the catheter is moved along the line the distance between the double potentials decreases, indicating the area of gap. (See color plate section.)

While pacing from the lateral end of the CTI, the time interval from the pacing spike to the QRS complex will be significantly longer in the presence of a complete line of block than when there are conduction gaps. This is explained by the time it takes for the impulse to travel along the lateral wall and activate the ventricles through AV node. On the contrary, the activation time with septal pacing is not much different before and after CTI block.[45]

Changes in atrial activation sequence with RV pacing

Occasionally the pacing artifacts can obscure the EGMs on the CTI when tested from either side of the line of block. Also pacing may not be possible due to electrode saturation. In those cases a change in atrial activation sequence along with a widely separated double potential on the CTI is a reliable marker of conduction block.[46]

Ablation catheter choice

There is a large body of data on the efficacy of the conventional 4 mm catheter for CTI ablation. Compared to the standard 4 mm electrode, irrigated/cooled electrodes decrease the number of lesions required for block and decrease fluoroscopy time.[47,48] Ablation catheters with an 8 mm tip have a similar efficacy to the cooled electrode. Coole 8-mm tip delivers more power and produces deeper lesions.[49] Although not compared directly, acute and short term results are better with an 8 mm tip (Freezer Max, Cryo cath) than with a 6 mm (Cryo cor) cryoablation catheter.[27,28,50,51]

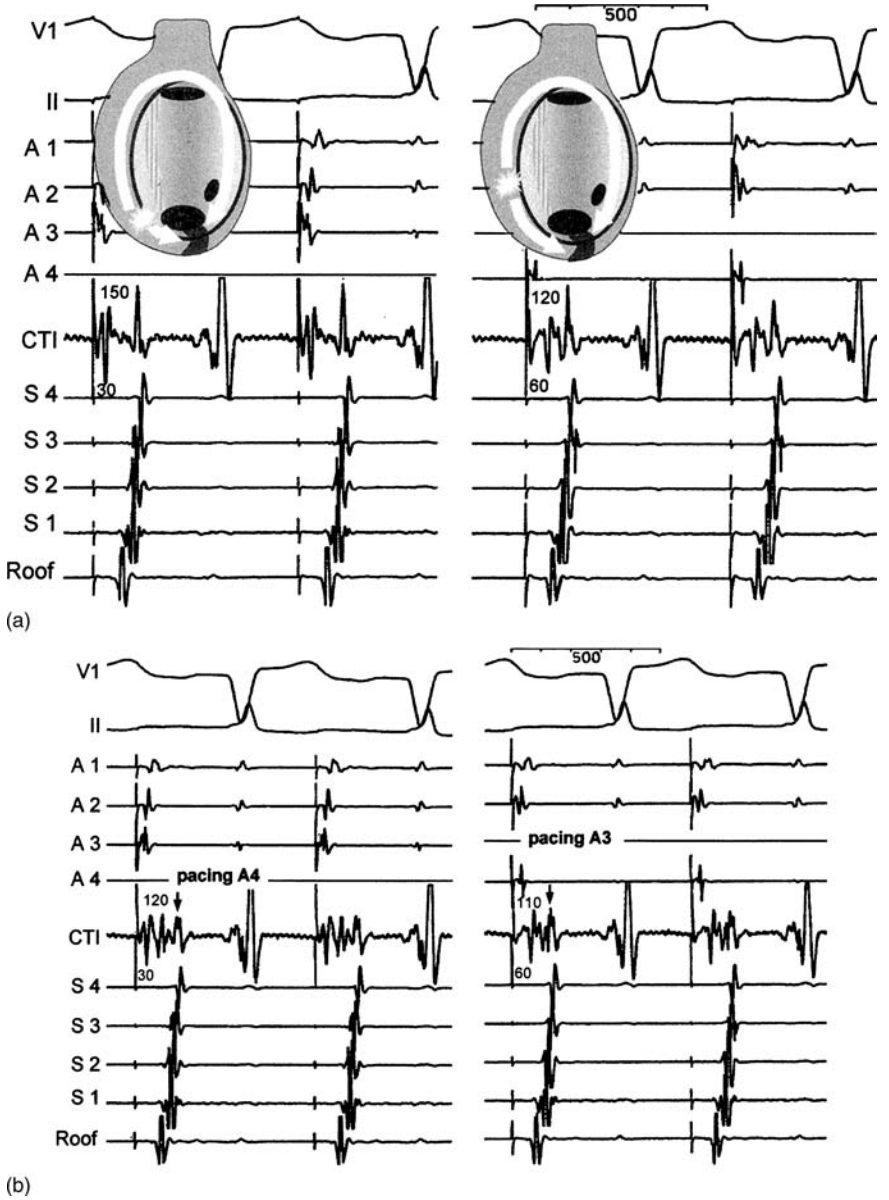


Figure 23.7 Differential pacing (anterior RA) confirming double potentials as a sign of counterclockwise isthmus block. Cavotricuspid isthmus (CTI) reveals a double electrogram with stimulus-to-spike intervals of 30 s and 150 ms pacing low anterior wall (left panel), 60 and 120 ms when pacing 1.5 cm higher (right panel). These tracings depict activation explaining interval changes. (b) Pacing at the low anterior wall (left panel). The CTI EGM shows 3 components with stimulus-to-spike intervals of 30 to the first and 120 ms to the last EGM. Pacing at 1.5 cm higher (right panel), the first spike interval doubles to 60 ms and the last interval decreases to 110 ms, while the middle spike interval most likely merges with the last spike. The first two spikes result from blocked counterclockwise activation and the last spike is from blocked clockwise activation. Published with permission from Cosio FG, Nunez A, Goicolea A. Catheter ablation of arrhythmias. Futura publishing company, Inc. Armonk, NY, 2002

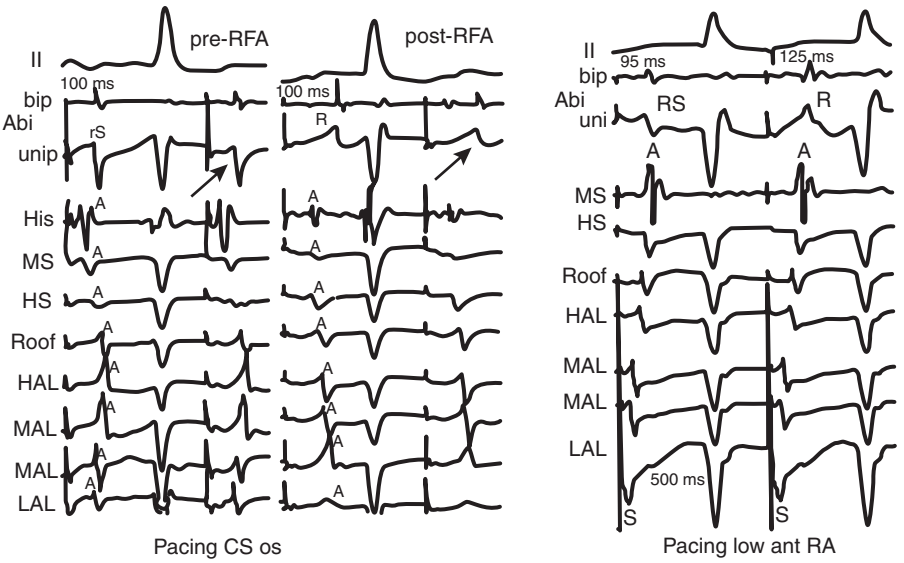


Figure 23.8 Change in the electrogram configuration at the opposite site of the ablation site is seen during pacing after occurrence of isthmus block. The left panel depicts recordings prior to and postablation during pacing from the coronary sinus (CS). The right panel shows changes during intermittent block while pacing at the low anterior wall. On the left panel, note the change of the unipolar electrogram from biphasic to positive (arrows), coinciding with changes in the bipolar electrogram and anterolateral wall activation. On the right panel, there is a change in unipolar and bipolar electrogram configuration at the isthmus, however no change in septal activation is seen. Published with permission from Cosio FG, Nunez A, Goicolea A. Catheter ablation of arrhythmias. Futura publishing company, Inc. Armonk, NY, 2002

Success rates

Among commonly used ablation catheters, the externally irrigated catheter has a higher efficacy for rapid achievement of CTI block. The externally irrigated catheter is known to accomplish CTI block more frequently with fewer RF applications of shorter duration compared to the internally cooled tip catheter and 8 mm tip catheters, the difference being significant compared with internally cooled ablation. The acute success rate at intervention was 87%. Follow-up data from 39 acutely successful patients showed 27 (69%) without conduction recurrence on repeat EPS at 3 months, and none (0%) had symptom recurrence.[28,50]

ATYPICAL RA FLUTTER

Diagnosis

The diagnosis of the atypical RA flutter is made by excluding the involvement of CTI as part of the flutter circuit:

- Presence of bidirectional CTI activation causing collision at the site by the two activating wavefronts coming from the lateral and septal ends rules out the CTI being part of the circuit.

- Proof of CTI conduction block as discussed in the previous section with an ongoing flutter activating the rest of the RA is a definite indication of an atypical flutter.
- Rule out the participation of CS or LA in the circuit through entrainment mapping at these sites.
- Documentation of activation throughout the full re-entry CL in the RA.
- Pseudo atypical flutter – counterclockwise or clockwise CTI dependent flutters with atypical ECG findings should also be ruled out.[52]

Anatomy

A central barrier, either fixed or functional, is key for maintaining re-entry. Crista terminalis, SVC, IVC, and scars from previous atriotomies and natural scars creates a substrate for the flutter to circulate around. A routine anatomic ablation may not be feasible because of the multiple possible circuits that can sustain the atypical flutters. So mapping the entire RA is necessary to determine the precise flutter circuit and define the isthmus that is amenable for ablation. A 3D map provides a good anatomic correlate to electrical activation of the flutter circuit. Atrial flutters encountered in post-ASD repair patients serve as a good learning model in understanding the primary circuits that are formed around the atriotomy scars and secondary circuits that form around the tricuspid valve.[52] Atriotomy scars that are long, vertical (or $<45°$), anteriorly placed, and incomplete at the level of the IVC are more predisposed to peri atriotomy re-entry. Whereas atriotomy scars that are short (<2 cm), transverse, posteriorly placed, and complete scars that extend to the IVC are prone to peri tricuspid re-entry and are less conducive for peri atriotomy reentry.[52,53] RA volume and TV perimeter were not found to be predictors of re-entry. Peri crista re-entry and other small, functional circuits in various parts of the RA are the other forms of atypical flutters on the right side.[54] Occasionally, more circumscribed re-entry circuits have been mapped to the RA free wall without any surgical scar.[55] These circuits may be localized within the SVC or use the pectinate muscle as a central barrier. To summarize, the non-CTI-dependent RA flutters can be mostly classified as:

- Free wall atriotomy flutters – single and dual loop re-entry, peri atriotomy and intra atriotomy re-entry
- Peri SVC and peri crista terminalis re-entry
- Small re-entry circuits – RA free wall and SVC re-entry.

Catheter ablation

The mapping strategy depends on the presence, inducibility, and sustainability of the flutter that is being evaluated.

- If the arrhythmia is stable enough then a 3D map can be created using CARTO or NavX systems. Occasionally double or multiple re-entry is characterized by the presence of more than one activation front that meets the criteria of the clinical flutter with a similar CL. Sometimes bystander activation may confuse

the circuit. High-density mapping and entrainment mapping of the region in question will help in appreciating two separate waves of collision.[56]

- In general, barriers that are keys for stable re-entry and large areas devoid of electrical activity can be mapped easily provided good catheter contact is confirmed. However, narrow lines of block that are thinner than the recording field are hard to map. Maximizing conduction delay by pacing at different sites and mapping during more than one form of activation can help.[52]
- Variations in the tachycardia features may tend to confuse the operator. A variation in ECG morphology without a change in CL is usually suggestive of alternation of multiple loops due to block in one of the loops, or change in bystander activation, or activation of the same circuit in the opposite direction.[56,57] A significant change in the right atrial activation is suggestive of circuit transformation or activation in the opposite direction of the same. Variations in activation pathways resulting from circuit transformation or simply changes in conduction time may manifest as changes in tachycardia CL. Often times, these changes in activation may not cause any surface ECG changes due to the distance from recording electrodes or insufficient electrically active tissue.
- Once the circuit is defined by electroanatomic mapping, the narrowest, safest, and the most stable portion of the isthmus should be ablated. Collateral damage to the nearest structures including the SA node, AV node, and phrenic nerve is important to remember. Catheter stability and the width of the isthmus are major factors that influence the duration and success of the procedure.
- Sometimes the clinical flutter is not easily inducible or sustainable for complete mapping. If the circuit around a peri atriotomy scar is identified then an empiric ablation of both the isthmuses – CTI and the lower end of the scar to the IVC – may be performed.
- Most of the clinical experience for atypical RA flutters has been with RF and there are not sufficient data with cryo energy.
- Although non-inducibility is a useful parameter, complete stable conduction block within the re-entry path is the definite endpoint for ablation. Non-inducibility could also be due to delay in conduction or changes in autonomic tone and cannot be used as an endpoint if the arrhythmia was not inducible to start with or if it was mechanically terminated.

LEFT ATRIAL FLUTTER

Diagnosis

Left atrial flutters almost always are secondary to an underlying structural heart disease.[58–60] Dilated or hypertrophic cardiomyopathy, mitral valve disease with regurgitation or stenosis, LA surgical scars, and more recently LA ablation for AF ablation are the most common predisposing factors for LA flutters. A history of successful typical flutter ablation in the past suggests the possibility of an atypical flutter.[61–63] The RA and LA flutter can be differentiated using various criteria:

- Left atrial flutter must be considered in all patients with an atrial tachycardia having ECG morphology not characteristic of typical atrial flutter. The flutter wave usually has a positive deflection in lead V1, although this positivity may be significantly reduced when the V1 electrode is misplaced (typically too

high) or is masked by a negative T-wave in lead V1. Low voltage flutter waves in a VL and I associated with a positive P-wave in V1 are also suggestive of left atrial flutter.[59,60] Uncommonly, left atrial flutter presents with negative deflections in the inferior leads suggestive of typical atrial flutter. At times, differentiation of the RA or LA origin based on surface ECG morphology alone could be difficult.

- An invasive EP study becomes necessary when the origin of the flutter is not clear based on the history and surface ECG. Entrainment mapping at the high right atrium, right free wall, and the CTI typically helps to rule out the RA flutters. Typical findings include a gradient of postpacing intervals that is longest in the right atrial free wall and significantly shorter in the mid and distal coronary sinus.[59] Septal pacing may capture the LA and may not help the differentiation. Coronary sinus activation sequences are usually of limited value in the diagnosis of left atrial flutter.
- Larger spontaneous right atrial CL variations with concomitant variations of less than 20 ms in the LA (as shown by the CS recordings) can be seen with flutters of LA origin.[59] There could be rare instances where the RA is electrically isolated from the LA due to extensive scarring from previous surgeries.
- A quick recording of activation times from 10 different points in the RA with a fixed reference in the CS can help to determine if the flutter is right-sided or not. If $<$50% of the tachycardia CL is recorded among these 10 points, the RA origin can be ruled out.[59] Rarely, a small re-entry circuit in the RA or a slowly conducting bystander zone with activation times equal to that of LA can confuse the picture.

Anatomy

Similar to the RA there are functional and fixed barriers even in the LA that form the center of the re-entrant circuits. Mitral annulus and pulmonary vein (PV) ostia form the natural barriers. Scars from previous surgery, ablation, or atrial remodeling may be present in any part of the LA. The LA scars that form the re-entrant circuits were mostly localized to the posterior wall (50%), septum (25%), and the roof (25%) from the Bordeaux experience.[59] A wide variety of linear scars from various AF ablation techniques may be encountered as a part of the flutter circuit. The most common flutter circuits that have been described are:

- Peri mitral re-entry
- Peri pulmonary vein ostial re-entry
- Double loop re-entry involving both the mitral valve and the PV antra
- Peri atriotomy re-entry
- Small regional re-entry anywhere in the LA
- Incomplete linear RF scar related re-entry circuits.

Catheter ablation

Ablation of LA flutter using conventional mapping can be difficult. Electroanatomic mapping using 3D systems like CARTO or NavX is of benefit in properly corroborating the electrical activation in relevance to the anatomy. Once an

RA flutter is ruled out, the operator should proceed with trans-septal puncture. As described elsewhere in this book, the intracardiac echocardiography guided fluoroscopic approach has significantly simplified the trans-septal access. Intravenous heparin is used for anticoagulation, targeting activated clotting times of 350–400 s.

- Based on the available clinical evidence the LA scar or electrically silent area is defined as amplitude of atrial potential <0.05 mV and absence of capture at 20 mA. The mapping strategy depends upon the presence or inducibility of left atrial flutter and its stability. A quick activation map (80 to 120 points) of the LA should be created.
- A single-loop tachycardia with a fixed barrier as its core typically remains stable and unchanged during catheter manipulation and may be difficult to pace terminate, whereas mechanical 'bump' termination (without extrasystoles) that renders the arrhythmia non-inducible suggests a relatively fragile isthmus.
- In patients without inducible arrhythmia, sinus rhythm mapping can allow identification of fixed barriers. Detailed high-density mapping of the whole chamber may be necessary, but the culprit isthmus still can be completely concealed by activation that is parallel (as opposed to orthogonal) to the line(s) of block forming the isthmus.
- The complete re-entrant circuit can be defined as the spatially shortest route of unidirectional activation encompassing the complete tachycardia cycle length in terms of activation timing and returning to the site of earliest activation. The accuracy of activation mapping depends upon the determination of local activation times. Unlike single-component electrograms, multi-component electrograms require careful analysis because they reflect multiple asynchronous local activations within a small area.
- Multiple re-entrant loops are frequently present during left atrial flutter; therefore, multiple isthmuses are available as targets for ablation. The recognition of multiple isthmuses and the choice of a particular isthmus for ablation are difficult, if not impossible, without a 3D mapping system.
- For peri mitral re-entry, lesions from any one of the inferior pulmonary veins to the posterior mitral annulus are the shortest lesions that, if complete, would successfully eliminate re-entry, unless the central obstacle (e.g., scar on the roof associated with mitral regurgitation) extends over to the anterior or posterior LA wall. Lesions from the right inferior pulmonary vein ostium down to the mitral annulus are difficult to render transmural and complete because of connections between the coronary sinus and the right and left atria. Medial ablation lines connecting the right-sided PVs to the mitral annulus may create significant activation delay of the lateral LA during sinus rhythm, resulting in deleterious hemodynamic effects on the atrioventricular synchrony. So whenever possible, a lateral ablation line from the left-sided PVs to the mitral annulus is preferable (Figure 23.9).
- In patients who have undergone an operative intervention to the left atrium, a surgical incision placed in the Waterstone groove leaves a scar that can be easily extended down to the anterior mitral annulus and requires much less ablation.[60] However, completing this lesion delays activation of the left atrial appendage and may diminish efficiency of left atrial contraction.
- In postoperative or postcatheter ablation left atrial flutter, the arrhythmia often is dependent upon a discrete gap in an ablation lesion, and a 'focal'

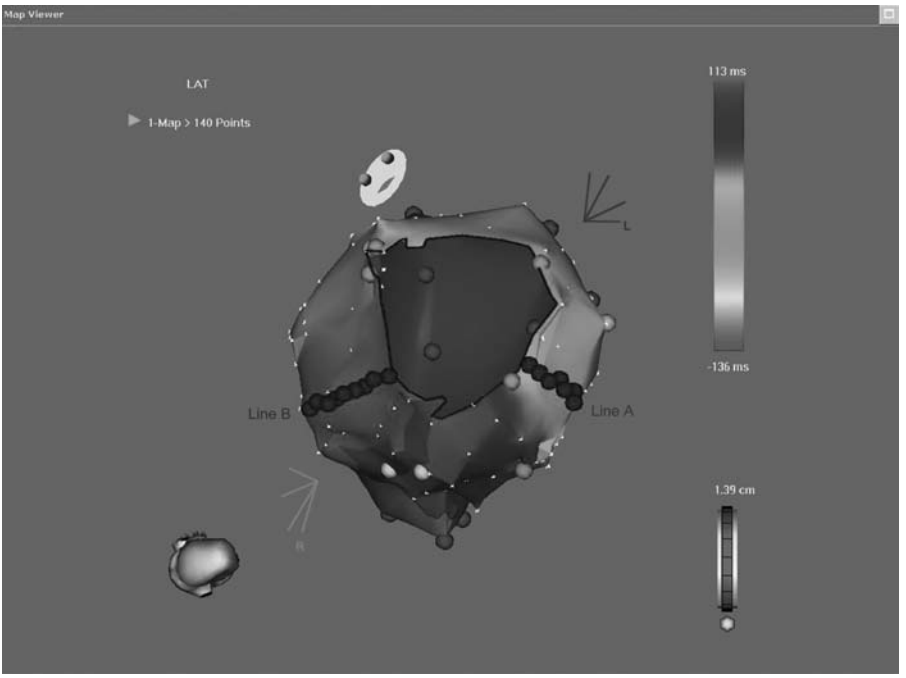


Figure 23.9 Electroanatomic map of the LA during flutter. Activation sequence shows a flutter circuit circulating around the mitral annulus. Ablation lesions were placed at the left (left inferior pulmonary vein and mitral annulus). However, when flutter persisted another line was created at the right mitral isthmus which terminated the flutter. (See color plate section.)

ablation lesion is sufficient to block this isthmus and eliminate the tachycardia. This process is much easier than creating a complete transmural lesion across a wide isthmus. Unless high-density mapping is performed, the focal nature of the isthmus may not be appreciated.

- For patients with multiple and/or unstable left atrial flutter, creating a catheter-based mini-maze is one solution. This technique consists of creating two complete linear lesions: one extending across the posterior left atrium from the right to the left pulmonary vein ostia and another from the left inferior pulmonary veins down to the mitral annulus.
- In patients with variable CL $>$ 10%, creation of a complete activation map of reasonable confidence may not be feasible.[59] Intravenous anti-arrhythmic drugs may be used to stabilize the arrhythmia. A voltage map of the LA in sinus rhythm may help to identify the scar zones (electrically silent areas). Linear lesions connecting scar to the nearest anatomic barrier (mitral valve) may be created.
- If the arrhythmia is too variable it should be considered as atrial fibrillation. Reassess if the PV antra are electrically isolated and additional lesions along the thick muscular portion of the septum, roof, and the inferior PV gutters could be placed to aid in substrate modification.
- In rare situations, a part of the CL in the LA activation map could be missed despite a high-density map and good PPI intervals. This part of the circuit

could be epicardial in location and mapping followed by ablation in the CS may terminate the flutter and create complete conduction block in the circuit.

Catheter choice

Although conventional RF catheters could be used for the left atrial flutters, in our experience open irrigation tip catheters have been more efficacious. Similar experience was published by the Bordeaux group.[59] Low flow and thick atrial tissues are common variables in patients with structural heart disease. Open-tip irrigation catheters with a smaller distal electrode not only offer higher mapping resolution, but also keep the electrode and tissue interface cooler, reducing the likelihood of char generation and systemic embolization.[64]

Safety and success

The potential complications are very similar to AF ablation. The success rates for LA flutter ablation in experienced institutions have been more than 70%.

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24

Ablation of atrial fibrillation

Oussama Wazni, Mohamed Kanj, Patrick Tchou, Mauricio Arruda, and Andrea Natale

INTRODUCTION

- Atrial fibrillation (AF) is one of the 21st century epidemics.
- AF triggers often originate from the thoracic veins.
- AF ablation aims to electrically 'disconnect' the pulmonary veins (PVs) from the rest of the left atrium by ablating around the origin of the veins, which include the PVs, the superior vena cava (SVC), and the ligament of Marshall together with the coronary sinus.
- Presently there are at least four techniques of AF ablation:
  1. The Cleveland Clinic approach targets electrical isolation of the entire PV antra as the endpoint. This is achieved by a circular mapping technique with the use of intracardiac echocardiography for guidance (Figures 24.1 and 24.2).
  2. An anatomic approach, guided by navigation systems (CARTO, Navx, LocaLisa). Radio-frequency (RF) is delivered outside the PV ostia with a variety of additional ablation lesions. With this approach the endpoint is not isolation but reduction of the local electrogram.
  3. Isolation guided by angiography: in this approach ablation is limited to the tubular part of the veins. Additional linear lesions on the left atrial roof and the isthmus between the left inferior PV and the mitral annulus are created.
  4. Ablation of fragmented electrogram approach: in this case lesions are delivered in the right and left atria at sites where the local electrogram is fragmented.

PATIENT SELECTION AND PREPROCEDURE MANAGEMENT

1. Only symptomatic patients who have failed at least one anti-arrhythmic drug are considered for the procedure.

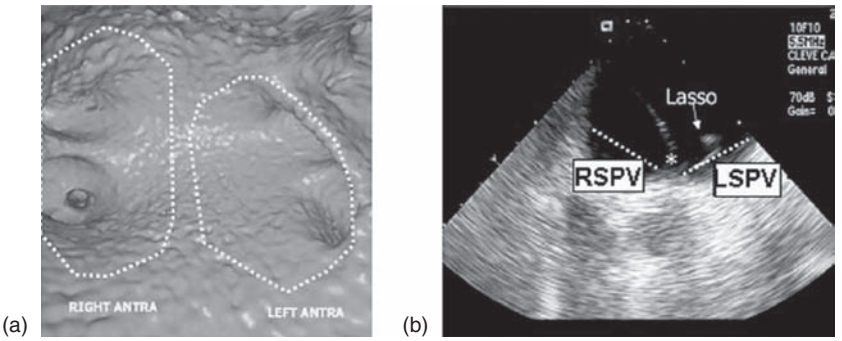


Figure 24.1 Anatomic definition of pulmonary vein ostium and antrum using three-dimensional CT imaging (a) and ICE (b). Note that the right and left pulmonary vein antra include the posterior wall of the left atrium. (See color plate section.)

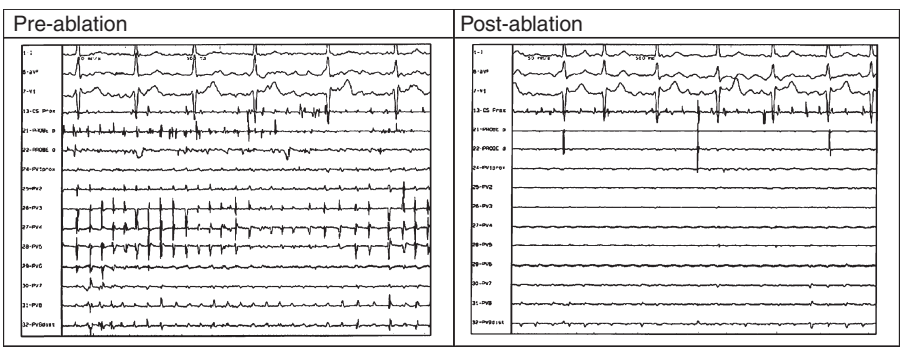


Figure 24.2 Circular mapping catheter recording.

2. Anti-arrhythmic medications are stopped 4–5 half-lives prior to procedure, except amiodarone, which is stopped 4–5 months prior to the procedure.
3. Warfarin may be discontinued 2 days prior to the procedure depending on the physician preference and the individual risk of thromboembolism.
4. Transesophageal echocardiography is performed in patients with subtherapeutic international normalized ratio (INR) who have AF on the day of the procedure.

PROCEDURE

Access

1. Light sedation is achieved with fentanyl and midazolam. Deep sedation is avoided because it interferes with neurologic checks and may cause deep breathing that in turn affects catheter manipulation and position.

2. Groin access: two 8 French sheaths in the right femoral vein and one 11 French sheath in the left femoral vein. Great care should be taken to avoid the femoral artery as this is a frequent cause of large hematomas due to high levels of anticoagulation. If the artery is inadvertently punctured the needle should be withdrawn and continuous manual pressure applied for at least 5 minutes. An 8 French sheath is also placed in the right jugular vein using fluoroscopic or ultrasound guidance.
3. A multi-polar mapping catheter is placed in the coronary sinus via the right internal jugular vein sheath to record right atrial and coronary sinus electrograms. This catheter is used for differential pacing which helps distinguish between PV and LA appendage potentials.
4. A 10 French phased-array intravascular ultrasound catheter is then placed in the right atrium to assist with performing trans-septal punctures, guiding catheter location, and manipulation within the left atrium, as well as monitoring for cardiac complications and microbubble formation.
5. Left atrial catheterization is then performed through two trans-septal punctures at the mid-posterior septum using a Mullen's and an SR0 sheath. Heparin boluses are given prior to first and second trans-septal puncture, followed by continuous infusion to achieve an activated clotting time (ACT) $>$350 s (Figure 24.3).

Ablation (Figure 24.4)

The endpoint of the procedure is electrical isolation of all PV antra. Entry block is present when no PV potentials could be recorded along the antrum or inside the vein by the circular mapping catheter. Electrical dissociation of the PV from the left atrium confirms exit block as well.

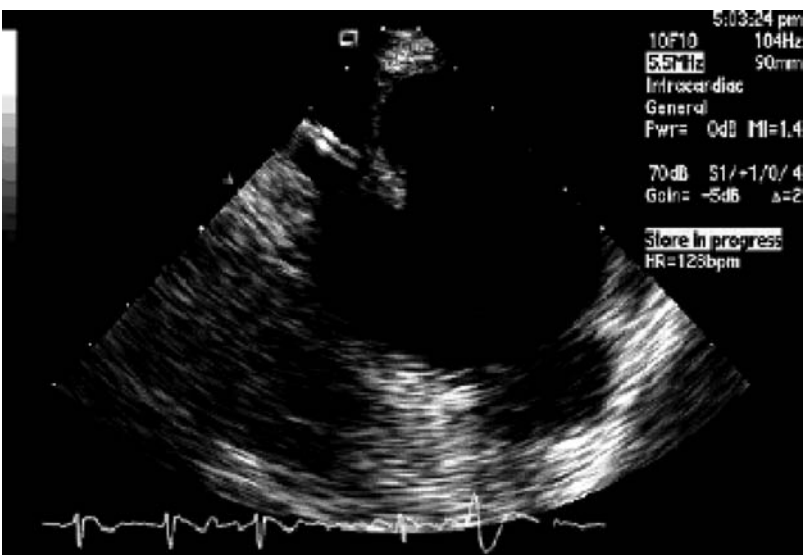
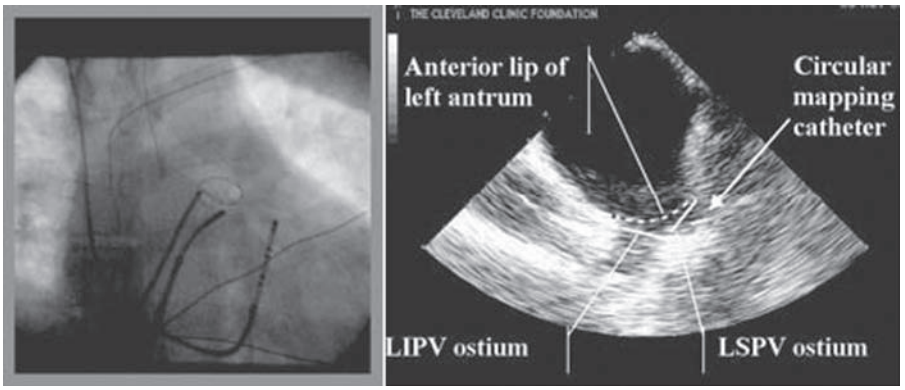
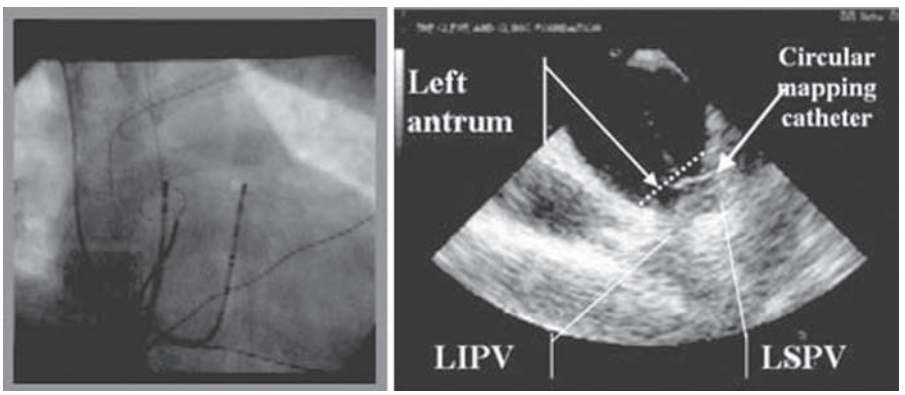


Figure 24.3 Intracardiac echo image of trans-septal puncture.



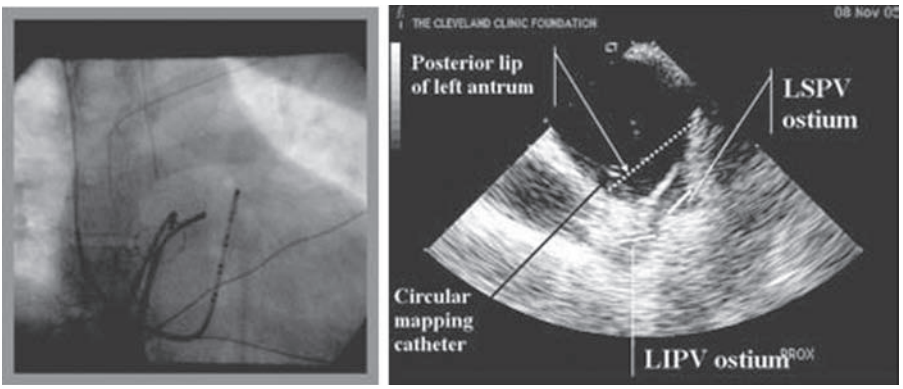
(a)



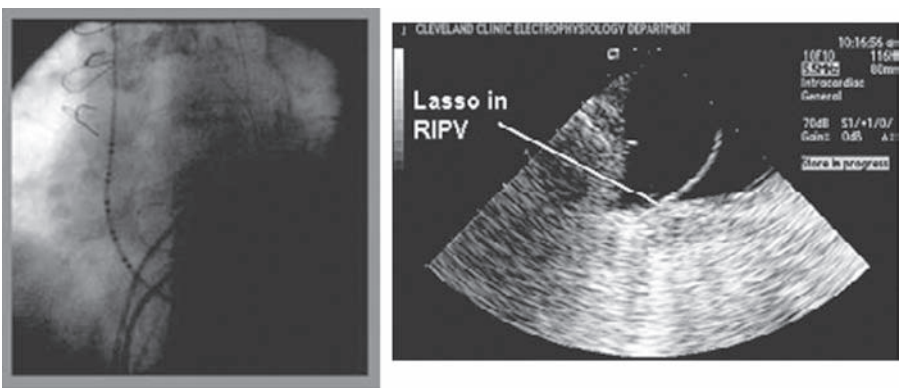
(b)

Figure 24.4 Fluoroscopic and corresponding ICE images of circular mapping catheter positioning: (a–c) Circular mapping catheter manipulation in the left PV antrum. (d–f) Circular mapping catheter manipulation in the lower portion of the right PV antrum. (g,h) Relationship between the left and right PV antrum with respect to the roof and the posterior walls of the left atrium. (i) SVC–right atrium junction which is at the level of the pulmonary artery.

1. A 10-pole, 20 mm diameter circular mapping catheter (Lasso), is introduced through the Mullen's sheath and an 8 mm tip or an open irrigation ablation catheter is introduced through the SR0 sheath. A J-curve ablation catheter may be used instead of an F-curve in cases of severe left atrial enlargement or in case of an anterior trans-septal puncture.
2. For patients presenting in sinus rhythm, isolation is usually performed in the following order: left superior, left inferior, right superior, and lastly right inferior PVs.
3. The circular mapping catheter is positioned at the PVA–LA junction defined by ICE. Potentials seen from depolarization of the PVA–LA junction fascicles are identified on the recordings.
4. RF ablation is performed wherever PV potentials are recorded on the mapping catheter sites around the PV antra.



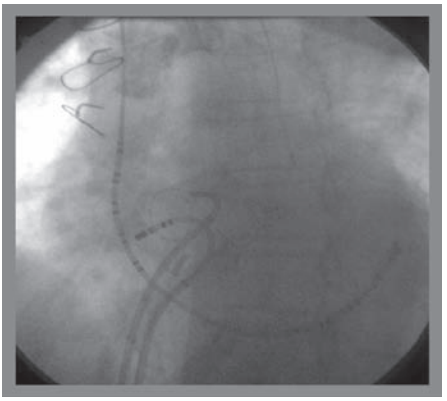
(c)



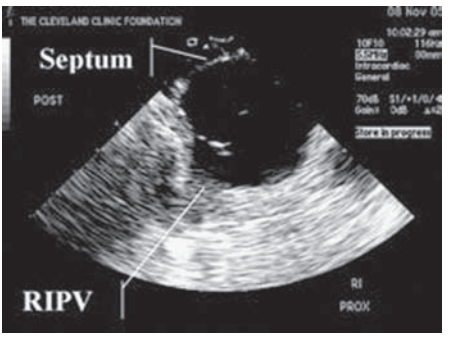
(d)

Figure 24.4 (Continued).

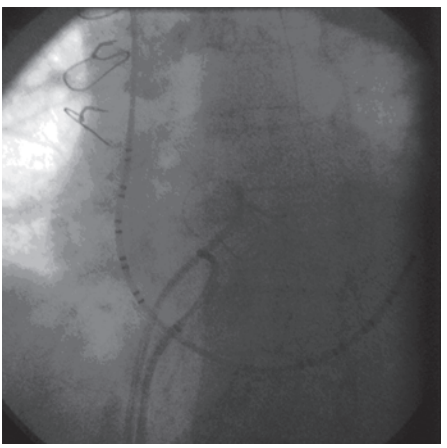
5. RF energy is usually set at 30 W and 55°C and the power titrated up to a maximum of 70 W by increments of 5 W every few seconds while monitoring for microbubbles. Upon the detection of microbubbles, the power is titrated down. If a sudden shower of bubbles is seen, the power is turned off.
6. With the open-irrigation catheter a temperature of 45°C and maximum power of 50 W is used. During ablation with the open-irrigation catheter an esophageal temperature probe is inserted to help with power titration during posterior wall ablation. Each ablation treatment has the endpoint of local potential elimination.
7. The ablation catheter is then moved to the next position on the circular mapping catheter. The PV potentials on the circular mapping catheter that define part of the PVA are ablated. Multiple movements of the circular mapping catheter around the PV antrum are needed. To cut on fluoroscopy time we use ICE, ablation artifact, and occasionally a 3D mapping system (CARTO, Navix) to assist with monitoring catheter position.



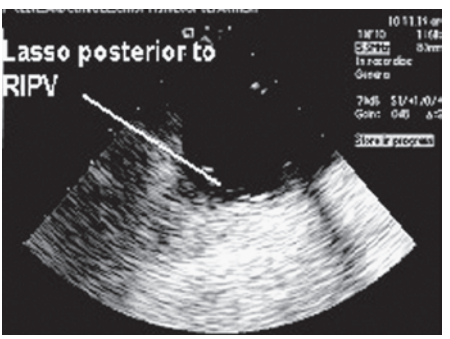
(e1)



(e2)



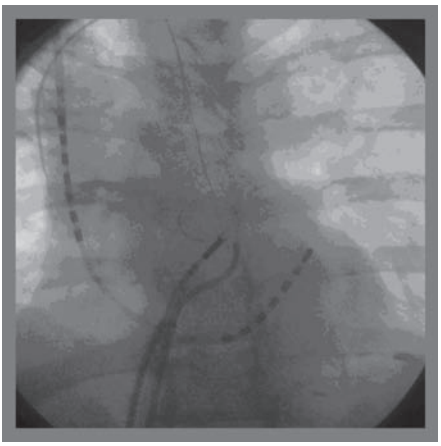
(f1)



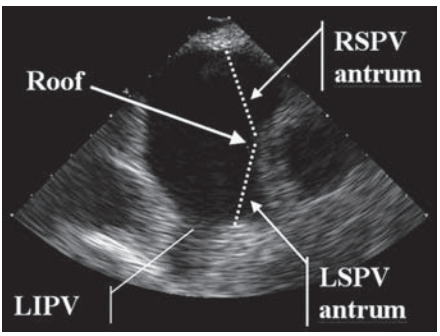
(f2)

Figure 24.4 (Continued).

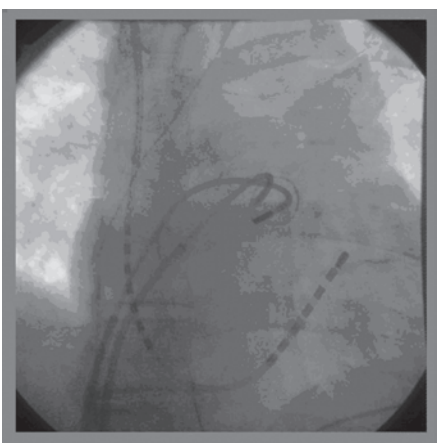
8. In patients who present in AF there are two strategies that could be employed.
   a. DC cardioversion can be performed and the ablation can be carried out as above.
   b. Ablation can commence in AF as described above with the addition of more ablation targets such as the atrial septum, the mitral annulus, and inside the coronary sinus. This strategy can result in conversion to sinus rhythm, more organized AF, or atypical AFL. AFL can then be mapped and ablated. If, however, the patient continues to be in AF or atypical AFL even after extensive mapping and ablation, DC cardioversion is performed.
9. All four PV antra are then extensively remapped with the circular mapping catheter to check for any persisting PV potentials, and, if necessary, further ablation is performed to eliminate these.



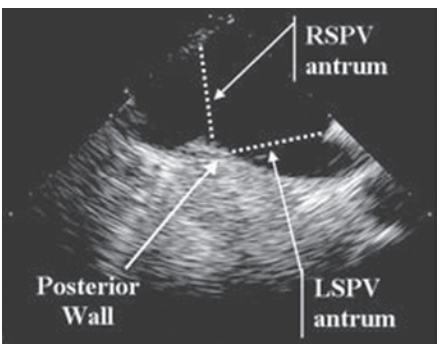
(g1)



(g2)



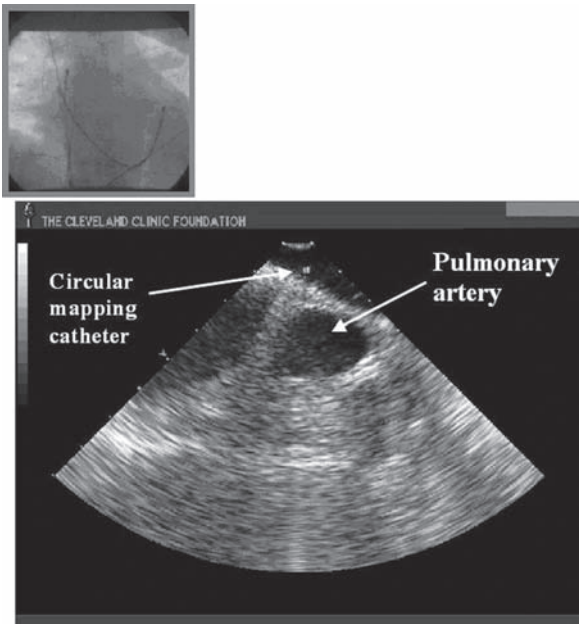
(h1)



(h2)

Figure 24.4 (Continued).

10. Heparin is stopped and catheters and sheaths are pulled back into the right atrium.
11. The circular mapping catheter, guided by ICE, is positioned at the superior vena cava (SVC)–right atrial junction, which is marked by the lower border of the pulmonary artery.
12. Isolation of the SVC is then performed at this level. High voltage pacing (at least 30 mA) is used to check for phrenic nerve stimulation prior to isolating the lateral portion of the SVC. SVC isolation is avoided in patients with newly implanted pacemakers or defibrillators.
13. Protamine 10–15 mg intravenously is then given if ACT $>$ 350 and venous sheaths are pulled once ACT$<$ 300.
14. Neurologic checks are performed intermittently during the procedure, at the end of the procedure, and the following day just before discharge.



(i)

Figure 24.4 (Continued).

POSTPROCEDURE CARE AND FOLLOW-UP

Warfarin therapy is either not discontinued prior to ablation or is restarted on the evening of the procedure and maintained for at least 5–6 months with a target INR of 2–3. Low molecular weight heparin is often given in high-risk patients until INR is therapeutic. Warfarin is continued indefinitely if patients experience recurrence of AF or if there is significant (≥70%) PV stenosis on CT scan 3 months postablation. Anti-arrhythmics are continued for a 2 month period. Episodes of AF in the first 2 months are not considered procedure failures and are usually treated by DCCV.

Patients are monitored with a 24 hour Holter recording before discharge. Upon discharge an event recorder is used to monitor events during the first 5 months. During the monitoring period, patients are asked to record when they experience symptoms as well as at regular intervals, even if asymptomatic. Additional event recorder monitoring is obtained beyond the 5 month period to confirm freedom from AF. Additionally, a 48 hour Holter recording is performed at 3, 6, 9, and 12 months postablation.

FUTURE DIRECTIONS

Newer technologic advances on the horizon will make the procedure easier and safer. These include real-time 3D CT combined with a variety of balloon systems, and robotic and stereotactically guided ablations.

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25

Ablation of normal heart ventricular tachycardia

Mohamed Kanj, Mauricio Arruda, Andrea Natale, and Patrick Tchou

Structurally normal heart • Classifications • Diagnosis • Indication for ablative procedure • Anatomy of outflow region • Access • Patient scrubbing • Catheter choice • Induction • Mapping • Suspect epicardial origin if • Catheter treatment of normal heart ventricular tachycardias • Idiopathic LV tachycardia

STRUCTURALLY NORMAL HEART

- Normal myocardial perfusion
- Normal myocardial structure
- Normal myocardial function
- However, normal heart ventricular tachycardia can occur in patients with known heart disease.

CLASSIFICATIONS

- Outflow ventricular tachycardia
  - Cusp tachycardia
  - Right ventricular outflow ventricular tachycardia.
- Inflow ventricular tachycardia
  - Tricuspid valve ventricular tachycardia (Figure 25.1)
  - Mitral valve ventricular tachycardia
- Idiopathic left ventricular tachycardia
- Epicardial LV tachycardias
- Miscellaneous forms (other sites both in the right and left ventricles).

DIAGNOSIS

- Based on ECG
  - AV dissociation
  - Capture or fusion beats

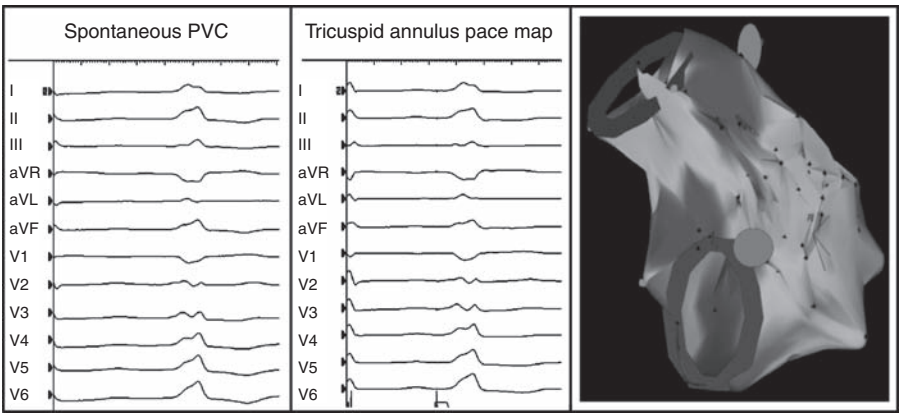


Figure 25.1 Premature ventricular complex originating from the tricuspid valve. (a) 12-lead ECG of the PVC. (b) Near perfect pace mapping along the antero-superior aspect of the tricuspid valve. (c) CARTO image showing site of perfect pace map and successful ablation. (See color plate section.)

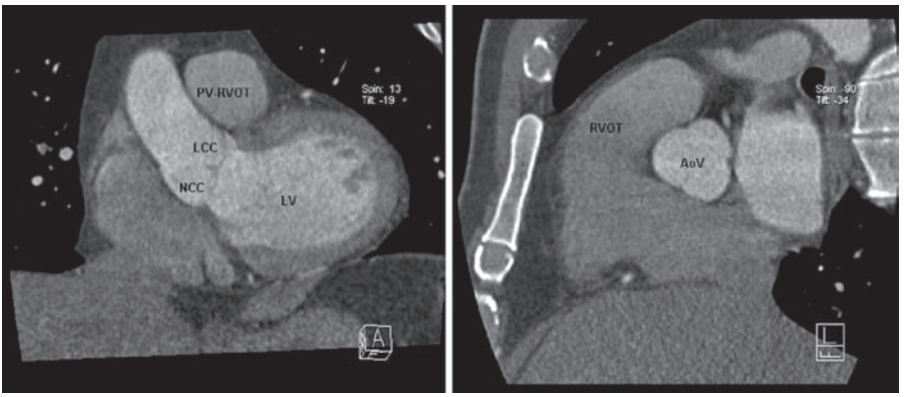
  - Brugada criteria
  - Important to recognize the origin of the tachycardia
- Rule out supraventricular tachycardia with aberrancy or antidromic atrioventricular reciprocating tachycardia, especially if AV dissociation is not present
- LBBB with inferior axis favors outflow tachycardias (OTs)
  - Early precordial transition favors LVOT
  - Late precordial transition favors RVOT
- RBBB favors LV tachycardia (ILVT).

INDICATION FOR ABLATIVE PROCEDURE

- Symptoms despite medical therapy
- Patient's preference
- Regression of LV dysfunction.

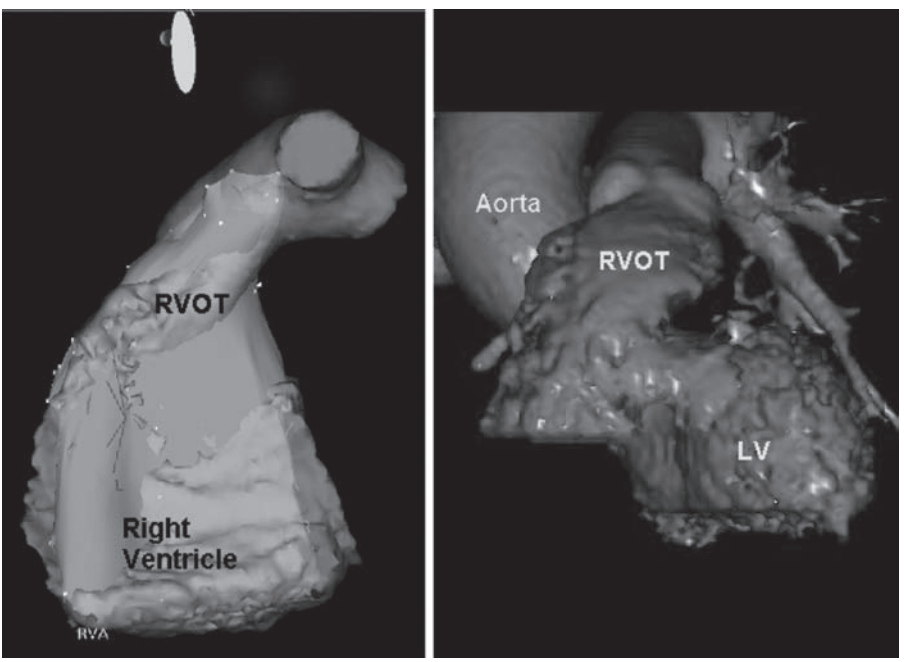
ANATOMY OF OUTFLOW REGION

- Aortic valve (AoV) is caudal and posterior to the pulmonary valve (PV) and they lay in perpendicular planes (Figure 25.2).
- At the PV region, the right ventricular outflow is pointing posteriorly and superiorly. Thus, its anterior portion is superior to its posterior portion (Figure 25.3). The valve ring can be readily identified on an electrogram (EGM) map. EGM amplitudes drop off rapidly as one crosses the PV into the main pulmonary artery trunk.
- The LV outflow, at the aortic valve, points laterally to the right and superiorly with some anterior tilt (Figure 25.4a).



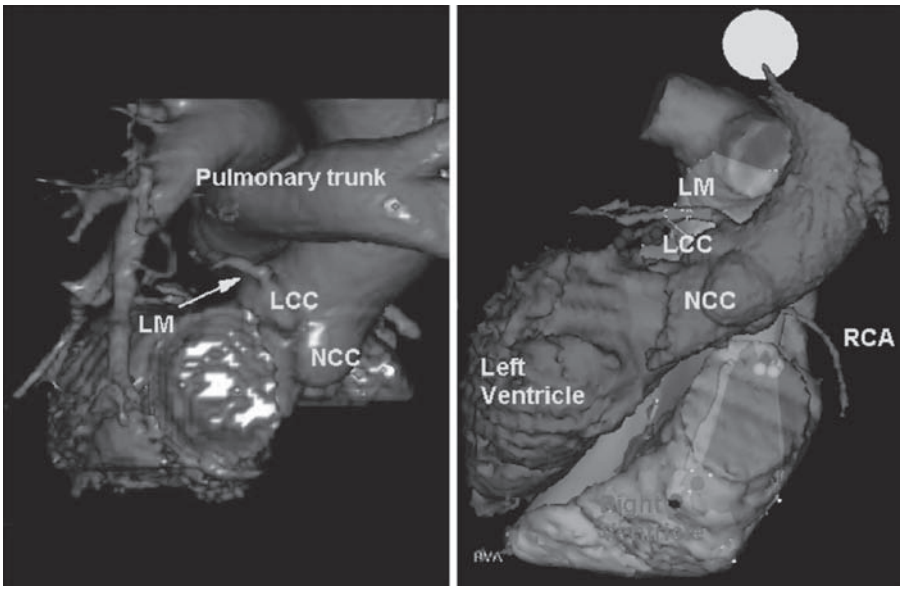
(a) (b)

Figure 25.2 Cardiac CT scan with image cuts through the (a) pulmonary valve plane and (b) through the aortic valve plane. Note that the planes of the aortic and pulmonary valves are perpendicular.



(a) (b)

Figure 25.3 (a) Left lateral view of CARTO-Merge and (b) antero-posterior projection of 3D reconstruction of the heart showing the posterior superior course of the RVOT. (See color plate section.)



(a) (b)

Figure 25.4 (a) PA view of the heart model generated by 3D reconstruction of cardiac CT. (b) PA CARTO-Merge view of the heart showing the RVOT in relation to the left main (LM) and the right coronary artery (RCA). (See color plate section.)

- The left atrial appendage covers the left coronary cusp (LCC) and the right atrial appendage covers the right coronary cusp (RCC). The non-coronary cusp (NCC) lies against the interatrial septum (Figure 25.2a). Pacing in the NCC often results in atrial capture.
- Caution during ablation (Figure 25.4b):
  - Left posterior portion of RVOT is close to the left main (LM) coronary artery
  - Right posterior portion of RVOT is close to the right coronary artery (RCA)
  - Right coronary cusp (RCC) lays against the interventricular septum in close proximity to the His bundle
- Adjacent structures: In case of failed ablation move to the adjacent structure:
  - Inferior portion of the RVOT lies anterior to the LCC and RCC
  - Aorto-mitral continuity covers the LCC.

ACCESS

- A venous access for an RV catheter used for programmed stimulation
- A venous or arterial access for mapping ablation catheter depending on tachycardia origin (RV, LV). Side port of the atrial sheath should be used for continuous pressure monitoring.

PATIENT SCRUBBING

- Both groin areas
- Subxyphoid area for epicardial access or for emergency pericardiocentesis.

CATHETER CHOICE

- RF energy is preferable
- Mapping and ablation can be performed using a 4 mm, 8 mm, or 3.5 mm irrigation catheter. The latter has the advantages of higher resolution of EGM recording and good energy delivery
- Occasionally a cryocatheter may be needed in case of:
  - RV inflow tachycardia originating close to the right bundle
  - LV septum near the His bundle
  - Catheter stability is an issue.

INDUCTION

- No induction is needed if frequent PVC with same morphology
- Ventricular or atrial programmed stimulation (burst, train with extrastimuli, long short stimulation)
- Isoproterenol infusion:
  - Induction during infusion: exercise-induced VT
  - Induction during washout: repetitive monomorphic VT
- Calcium (2 g of calcium chloride or calcium gluconate)
- Caffeine or aminophylline infusion
- Change sedation level
- Phenylephrine infusion with or without a small dose of isoproterenol.

MAPPING

- Used to define origin of tachycardia prior to ablation
- Two types: activation and pace mapping
- Activation mapping:
  - Facilitated by the use of electroanatomic mapping systems (CARTO, NAVX)
  - Define all the borders of the site of earliest local activation
  - Perform high resolution mapping at the site of earliest local activation
  - Beware of catheter-induced PVCs
  - Always pace map at the site of earliest activation prior to ablation to distinguish the breakout site from sites near it
- Pace mapping:
  - Often more predictable for tachycardia origin site than activation mapping
  - Helpful if difficult to induce ventricular ectopy or tachycardia
  - Should be performed at the tachycardia cycle length or PVC coupling interval to control for rate-related QRS changes due to rate-related change in cardiac position
  - Should be performed at the lowest energy output possible. However, aortic cusp tachycardia usually requires high output pacing
  - Keep in mind that 12-lead in the lab may be different from standard 12-lead ECG due to lead position. So one should always have a 12-lead in-lab ECG of the PVC/ventricular tachycardia.

SUSPECT EPICARDIAL ORIGIN IF

- Pacing at the earliest activation site results in an imperfect pace map
- Far field signal at the earliest activation site

- Slow initial activation due to time to propagate to endocardial Purkinje structures
- Endocardial ablation may still be successful, especially with an 8 mm or an irrigation catheter, if not then map epicardium using:
  - A small (4 French or less) multi-polar mapping catheter (Cardima) through the coronary arteries or veins (Figure 25.5a)
  - Standard epicardial access (Figure 25.5b).

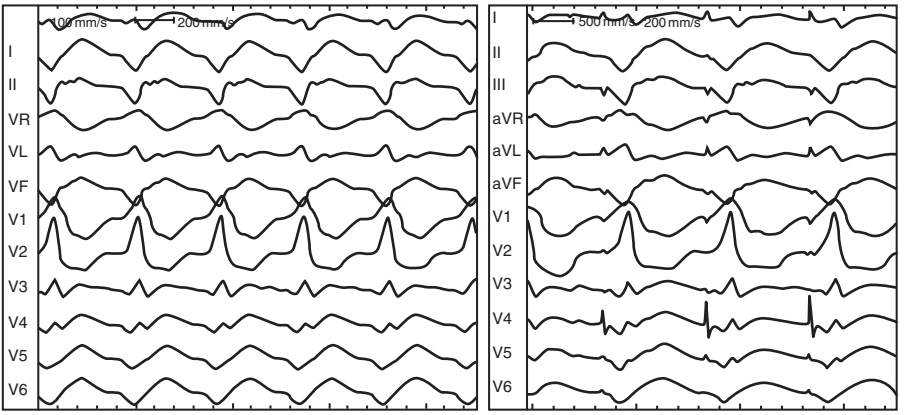
CATHETER TREATMENT OF NORMAL HEART VENTRICULAR TACHYCARDIAS

RVOT

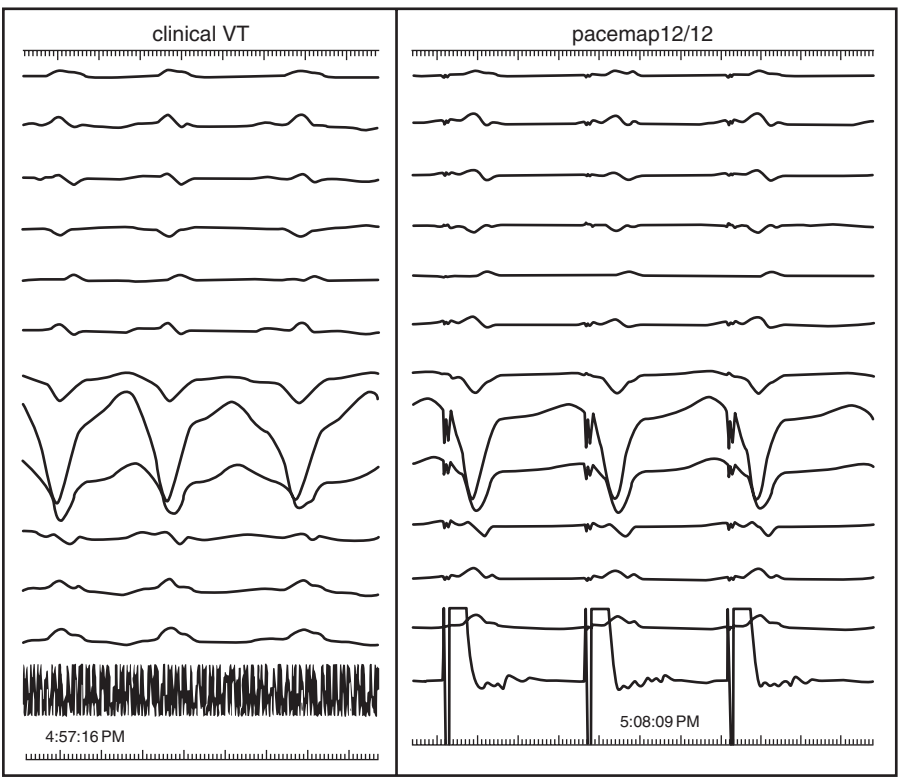
- Catheter mapping (Figure 25.6):
  - The free wall is 2–3 mm thick and could perforate during mapping
    - always retract the catheter from the myocardium prior to changing catheter position
    - start mapping from high to low to minimize pushing while advancing the catheter. Be aware of contact with RV wall
- Catheter ablation at the site of:
  - $\geq$ 11/12 pace map
  - Earliest site EGM:
    - bipolar: $>$ –30 ms prior to QRS
    - unipolar: sharp negative deflection
  - Often automaticity resulting in rapid ventricular tachycardia is seen during early seconds of ablation
- Caution: inferoseptal and posterior portions of RVOT are in close proximity to LM/LAD and RCA respectively
- Think aortic cusp tachycardia if failed ablation in the RVOT and the earliest activation is in the infero-septum.

LVOT (Figure 25.7a):

- Coronary cusp tachycardia and aorto-mitral continuity tachycardia
- Heparin infusion to achieve an ACT of 300–350 s
- Catheter mapping (Figure 25.7b):
  - Retro-aortic approach
  - The tachycardia is epicardial in origin (cusps are fibrous structures)[1]
  - Activation mapping (Figure 25.7c–e):
    - farfield local EGM
    - two-component EGM (local and farfield)
    - earlier activation using epicardial mapping
  - Pace mapping (Figure 25.8):
    - is more accurate than activation mapping
    - needs high output to capture
    - fine movement in cusp results in significant change in pace map due to diverging coarse of fibers in the cusp region
  - LCC cannulation: in the LAO projection, advance catheter with a slight bend on its tip



(a)



(b)

Figure 25.5 (a) Epicardial pace mapping from a Cardima TM catheter placed in the posterior coronary vein resulted in a near perfect pace map. Ablation from this site resulted in termination of tachycardia. (b) Epicardial pace mapping using a catheter placed after pericardial access resulted in a near perfect pace map from the lateral left ventricular wall.

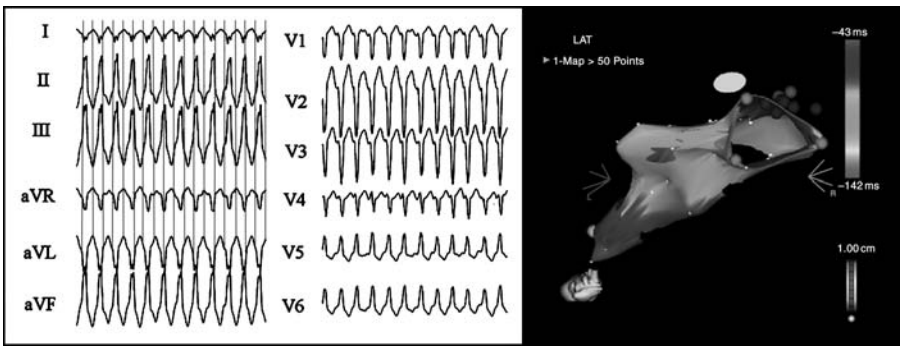


Figure 25.6 12-lead ECG and activation map using CARTO of the RVOT tachycardia. (See color plate section.)

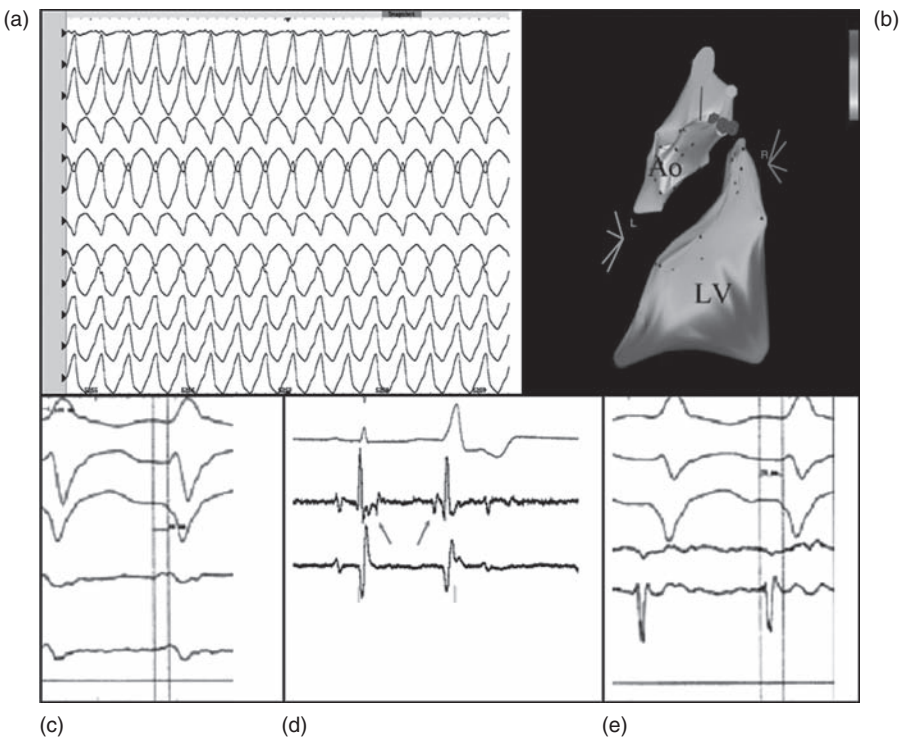


Figure 25.7 Left coronary cusp tachycardia. (a) 12-lead ECG during tachycardia. (b) Activation map using CARTO with earliest activation in the left coronary cusp. Ablation at this site resulted in termination of the tachycardia. Activation mapping of a left cusp ventricular tachycardia from a different patient with LCC ventricular tachycardia showing (c) far-field signal, (d) two-component EGM, and (e) earlier activation epicardially. (See color plate section.)

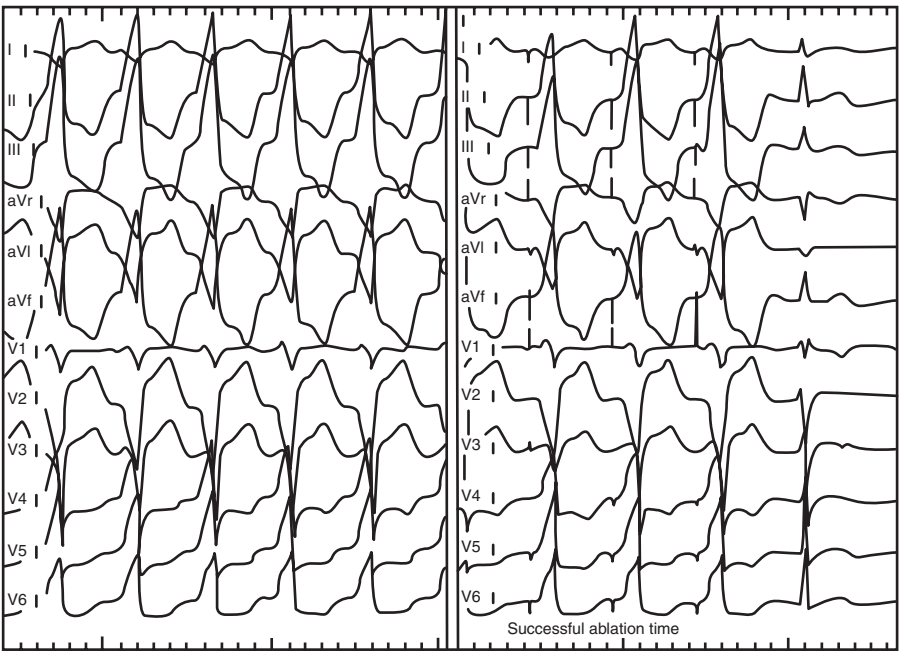


Figure 25.8 Pace mapping from the LCC resulted in a near perfect pace map. Ablation at the site resulted in termination of the tachycardia.

- RCC cannulation: rotate the catheter clockwise in the aortic root while advancing it
- Catheter movement can be done under additional intracardiac ultrasound guidance through a probe placed in the right atrium (Figure 25.9):
  - avoid risks associated with coronary angiography
  - live monitoring of catheter position
  - spatial information about location of catheter with respect to coronary ostia
  - monitor lesion formation and complications
- Catheter movements should be careful to avoid dissection and coronary spasm

- Catheter ablation:
  - $\geq$ 11/12 pace map
  - Earliest site EGM:
    - less accurate than pace mapping; used if failure to capture
    - bipolar: $>$ –30 ms prior to QRS
    - unipolar: sharp negative deflection
  - Avoid ablation in proximity to coronary ostium of less than 5 mm
  - Despite it being an epicardial tachycardia, the preferred method of ablation remains endocardial:
    - epicardial pace mapping will result in atrial pacing due to its proximity to LAA
    - site is close to epicardial coronary arteries

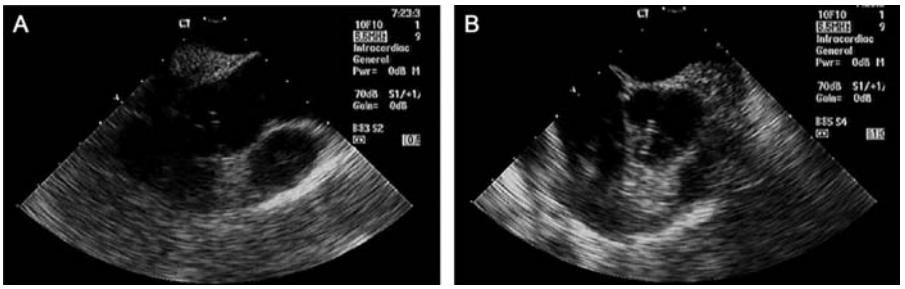


Figure 25.9 Intracardiac echocardiographic images obtained using ICE probe positioned in the right atrium.

- Caution:
  - beware of coronary ostium (either with angiography or with intracardiac echocardiography)
  - avoid excessive pressure that may result in vascular or valvular injury
  - the His bundle is just under the RCC/NCC junction.

IDIOPATHIC LV TACHYCARDIA

- Access: retroaortic unless there is a history of aortic disease (dissection, dilation, severe atheroma, and mechanical valve) then trans-septal approach
- Mechanism:
  - Re-entry (Figure 25.10)
  - Antegrade limb: verapamil-sensitive, slowly conducting, node-like fibers with decremental properties that insert into the His-Purkinje system:[2]
    - posterior fascicle:
      - more common
      - RBBB morphology with superior axis

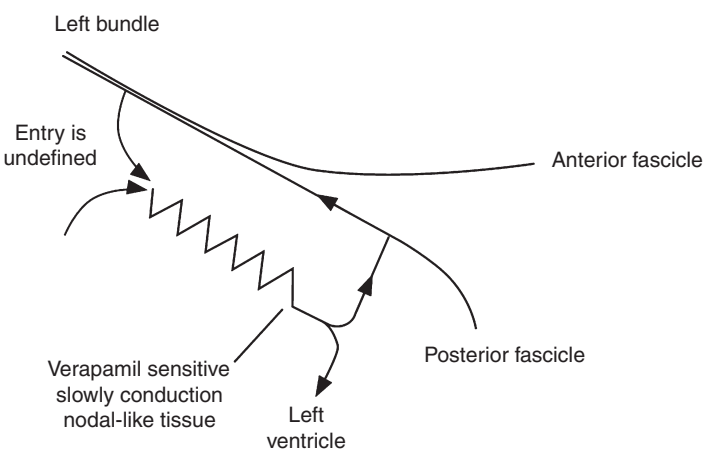


Figure 25.10 Diagram showing proposed mechanism of idiopathic left ventricular tachycardia.

        - anterior fascicle:
            - RBBB morphology with inferior axis
    - Retrograde limb: undefined yet. It could be the left ventricular His-Purkinje system or left ventricular myocardium
- Induction:
    - Atrial or ventricular programmed stimulation
    - Adrenergic-dependent
- Diagnosis: fascicular Purkinje potential earlier than His and local ventricular potentials
- Catheter mapping:
    - Left posterior fascicle: along the inferior mid-septum
    - Left anterior fascicle: along superior mid-septum
    - Mapping early ventricular activation might be misleading and often reveals early apical activation due to propagation of the impulse through the Purkinje fibers
    - Concealed entrainment from pacing near the exit site
    - Pace mapping may not be ideal since pacing generally captures the myocardium rather than just the Purkinje fibers that propagate the re-entrant impulse to the myocardium
- Catheter ablation (Figure 25.11):
    - Ventricular exit site: early presystolic Purkinje potential
    - Distal anterograde limb: distal diastolic potential
    - Distal areas with concealed entrainment
    - Anatomic linear ablation of the involved fascicle

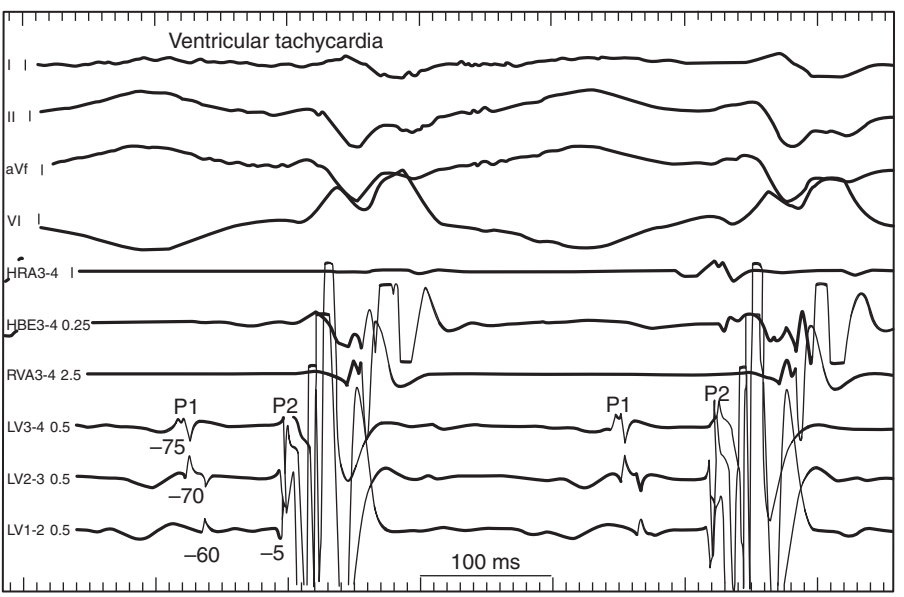


Figure 25.11 Successful catheter ablation site showing diastolic potential (P1) and presystolic Purkinje potential (P2).

- Caution:
  - Avoid brisk catheter movements which can easily traumatize the antegrade limb
  - Avoid ablating very proximally to avoid permanent LBBB.

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2. Nogami A, Naito S, Tada H et al. Demonstration of diastolic and presystolic Purkinje potentials as critical potentials in a macroreentry circuit of verapamil-sensitive idiopathic left ventricular tachycardia. J Am Coll Cardiol 2000; 36(3): 811–23.

26

Catheter ablation of ventricular fibrillation and polymorphic ventricular tachycardia

Timothy Mahoney, Mauricio Arruda, Andrea Natale, Patrick Tchou, and Robert Schweikert

INTRODUCTION

Sudden cardiac death (SCD) remains the leading cause of death in the United States and industrialized world. The majority of sudden cardiac death is caused by ventricular fibrillation (VF) associated with structural and ischemic heart disease. Over the last decade, much time and research has been devoted to the development of implantable cardioverter defibrillators (ICDs). After several multi-center trials demonstrated survival benefit in populations resuscitated from SCD, initial application of this technology centered on secondary prevention.[1–3] Indication for ICD implantation expanded further after benefit was demonstrated in populations with ischemic and non-ischemic cardiomyopathy who had ICDs placed for primary prophylaxis.[4–6] The recent increase in ICD use has been demonstrated to be cost effective,[7] but ICDs remain a large concern from an economic standpoint. Estimates reflect that with current inclusion criteria, approximately 500 000 Medicare beneficiaries now qualify for ICDs.[7]

ICD therapy centers on the treatment of ventricular arrhythmias post initiation. ICD therapies do not address prevention of VF or represent a curative therapy. Though demonstrating improvements in mortality, ICDs have not impacted the disease process and may have increased morbidity through the application of cardioversion. Though ICDs are making an impact on survival, they do not abolish lethal ventricular arrhythmias and are not without their own set of psychosocial and economic dilemmas.

Recent insights have changed our understanding of VF and polymorphic ventricular tachycardia. Application of this understanding to the development of

successful catheter ablation strategies has brought hope that a cure for SCD may one day become a reality for some patients. Though experiences with VF and polymorphic VT ablation are limited, early success holds much promise.

CATHETER ABLATION OF VF: BASIC PRINCIPLES

Ventricular fibrillation represents the final common pathway for SCD and thus is an attractive target for ablation.[8,9] Several recent case reports and series have described the successful application of catheter-based ablation therapies to treat both persistent and recurrent VF in ischemic and structurally normal hearts.[10–16]

To begin to consider catheter ablation a reality, a fundamental understanding of the mechanisms of VF is needed. These mechanisms, once understood, must demonstrate a source of initiation that would readily lend itself to extinction with catheter ablation (i.e. one or a few foci). Several theories on the origins of VF have been proposed. Early models considered VF to represent several independently operating foci of electrical activity. If this hypothesis were correct, the number of foci involved in a single form of VF would be too numerous to isolate and ablate.

New theories on the origins of the electrical triggers of VF question preconceived ideas on VF initiation. These theories propose VF could be initiated by just one or two ventricular premature beats (VPBs).[17,18] Mathematic and computer models have demonstrated how two independent foci (or rotors) could explain the electrocardiographic and physiologic mechanisms of VF. In 1994, Winfree discovered 'the electrocardiogram of two … separately pinned rotors would qualitatively resemble torsades de pointes, a polymorphic re-entrant tachycardia responsible for syncope in patients'.[19] Further investigation demonstrated how a single rotor (or wave) could be the source of VF.[17] This single wave interacts with fixed anatomic obstacles and gives rise to multiple wavelets which are self-contained and result in VF. This theory has come to be known as 'the single wavelet hypothesis' (Figure 26.1).

The single wavelet hypothesis demonstrates a mechanism of VF initiation that can allow the realistic application of catheter-based ablation strategies to eliminate foci which are the origin of VF. Several other possible mechanisms also explain how a single focus can lead to VF. For example, a VPB can occur that uses myocardial tissue (i.e. scar, Purkinje network, myocardial cells) as a focus of re-entry to perpetuate VF. Another hypothesis describes how, after depolarization, VPBs can occur in the cardiac vulnerable period (R on T) leading to VF. All these mechanisms have one unifying theme: a single focus or wavelet as the root cause for VF.

Identification of the source of the wavelet makes catheter ablation a reality. In most cases of VF ablation to date, a single focus, mainly a single VPB, has been isolated as the cause of the majority of VF. Many studies have demonstrated that there are surprisingly few sources of VPBs and that specific types of myocardial tissue serve as substrates for these VPBs. In particular, the Purkinje system has been implicated as a possible source of the majority of VPBs that initiate VF[15] (Figure 26.2). Non-Purkinje, myocardial sources of VPBs have also been identified as triggers, but are less frequently involved. Based upon electromorphologic parameters of VPBs preceding VF episodes, ablative therapies target the suspected VPBs in the hope of curing recurrent VF.

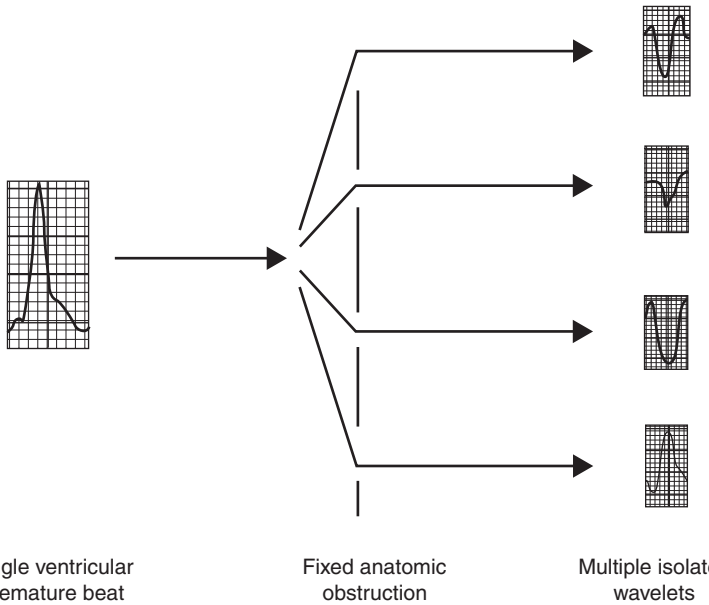

Figure 26.1 Single wavelet hypothesis of ventricular fibrillation. A single premature beat encounters a fixed obstruction (i.e. scar) with dispersion of multiple wavelets of electrical activity, resulting in ventricular fibrillation on 12-lead ECG.

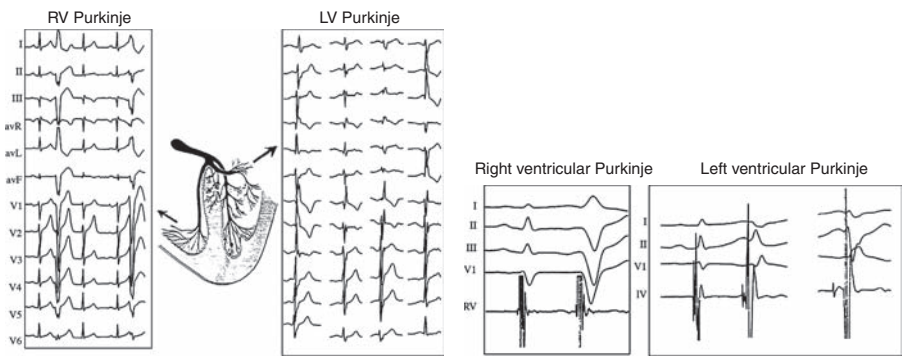

Figure 26.2 Left panels depicts 12-lead ECG tracings demonstrating ectopic beats generated from the right and left Purkinje network. Ectopic beats from the right Purkinje network typically demonstrate left bundle branch pattern in V1 and are wide. Left ventricular Purkinje beats are usually narrow and can have a left–right or intermediate axis. Right panels depict mapping of Purkinje generated beats during spontaneous ectopy at EP study. In this example the RV Purkinje beat precedes the ventricular electrogram by 10 ms. There are two examples of LV Purkinje potentials of 30 and 65 ms prior to surface ventricular electrogram. Typically, the delay between right ventricular Purkinje beats and the surface electrogram is less than that on the left. From Weerasooriya et al.[20]

The following is a discussion of methods and experiences using catheter ablative strategies in various types of VF and in polymorphic ventricular tachycardia.

CATHETER ABLATION OF IDIOPATHIC VF

Though the majority of VF occurs in structurally abnormal hearts, there is a subset of individuals resuscitated from SCD with no ischemic or structural heart disease. These patients represent the largest population of those who have responded to ablative therapies.

In the largest series on the application of ablative strategies for idiopathic VF, Haïssaguerre et al[10] reviewed their experience with 27 patients at six centers. Patients were deemed to have 'idiopathic VF' after exhaustive clinical and electrocardiographic work-ups. All patients underwent EP study and had triggers of VPBs localized to the site of earliest activation. The assumption was made that any initial sharp potential preceding the VPB complex noted on surface ECG by $<$15 ms represented either a peripheral or proximal Purkinje muscle component. Absence of a preceding, early sharp potential indicated ventricular muscle as the source of ectopy. The site of earliest electrical activity (either myocardial or Purkinje) was targeted for radiofrequency ablation (Figure 26.3). Premature beats

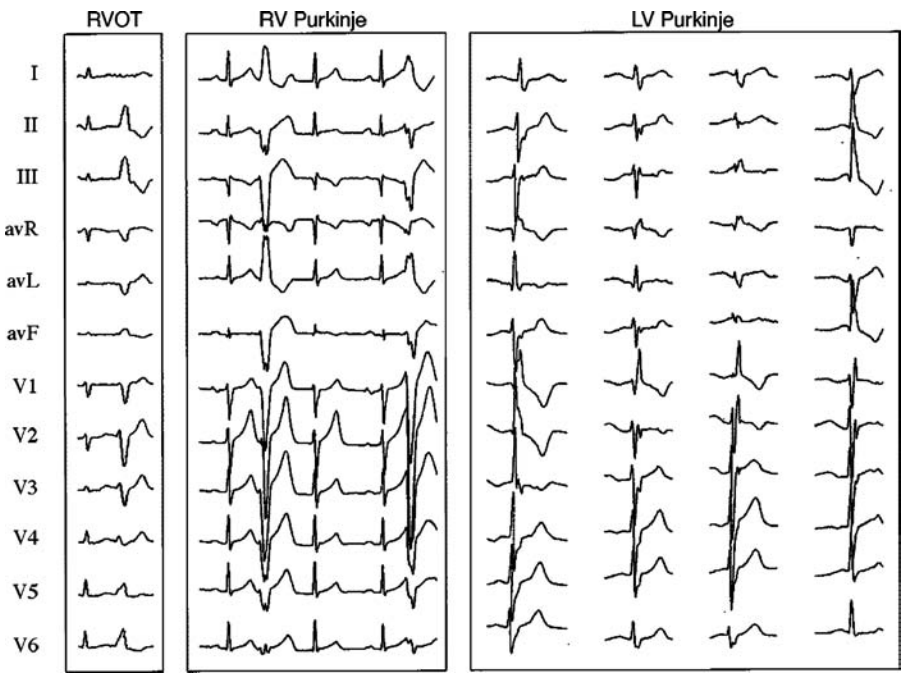

Figure 26.3 Morphology of premature beats. Left panel demonstrates morphology of premature beats from RVOT. Middle panel demonstrates morphology of premature beats from the mid-anterior right ventricular Purkinje system. Right panel demonstrates four different premature beats from the LV Purkinje system. From Haïssaguerre et al.[10]

were observed in 24 patients, with only 4 beats originating from ventricular muscle cells in the RVOT. The remaining 20 patients had earliest activation from the Purkinje system (RV in 7, LV in 9, and both in 4). The other 3 patients who had no premature beats were considered to have Purkinje beats based on identical characteristics of beats on 12-lead ECG.

The foci of premature beats were ablated after isolation using two to four multi-polar catheters, with ECG revealing abolition of local Purkinje potential or VPB (Figure 26.4). Patients who had complete elimination of premature activity were followed off anti-arrhythmic drugs for recurrence of ventricular tachyarrhythmias. Three patients had late recurrence of VPBs, with two of them having recurrence of VF and shocks. One of these recurrences had an episode of polymorphic VT leading to syncope. In the other 24 of 27 patients, there was no sudden death, syncope, or recurrence of VF.

This study showed the promise of a possible pathway to a 'cure'. Several other case reports and series have noted similar success using techniques isolating the earliest site of activation of ventricular premature beats.[11,12] Various methods, including non-contact mapping,[12] have been used with similar success to isolate and ablate these early foci. At this point, though early experiences are promising, success rates are not close to an acceptable level that would obviate the need for ICDs. The hope is with continued refinement and experience, the procedure will eventually join or even replace anti-arrhythmic medications and ICDs in the armamentarium of treatments of idiopathic ventricular fibrillation.

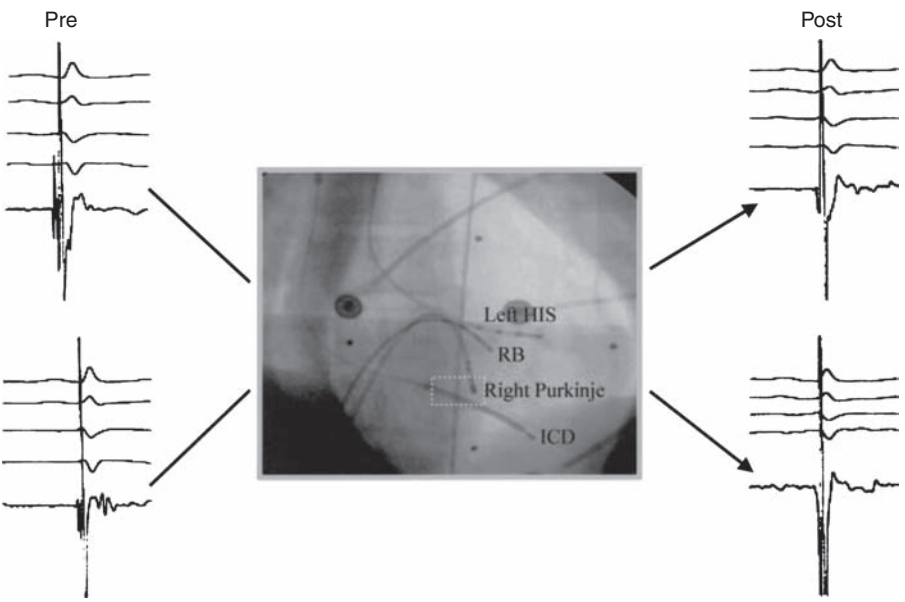

Figure 26.4 Middle, anterior-posterior radiographic image showing ablation in RV; right bundle (RB) and left-sided His recordings. Panels demonstrate recording before (left) and after (right) delivery of RF ablation. From Haïssaguerre et al.[10]

CATHETER ABLATION OF ISCHEMIC VF AND POLYMORPHIC VT

Ventricular fibrillation is most commonly associated with ischemic cardiomyopathies. VF poses a risk in both the acute setting of myocardial infarction and in the natural history of chronic ischemic disease. The mechanism of VF in ischemia has long been considered scar-related. Further understanding into the mechanisms of this scar-related phenomenon has helped make ablation a reality. Once again, the Purkinje fibers and their unique characteristics play an important role in the initiation of ventricular fibrillation in the ischemic heart. The resilience of the Purkinje system has been demonstrated in its ability to survive post-transmural myocardial infarction.[21] At EP study, Purkinje potentials have been demonstrated in peri-infarct zones and have been implicated as early triggers of VF storms post-MI.[13] To date, experience in ischemic VF ablation has been limited, but success has been demonstrated in both early post-MI and in polymorphic VT/VF storms associated with chronic ischemia.[13,14]

Catheter ablation of VF storms and polymorphic VT post acute MI

Ventricular fibrillation and tachycardia are both well-known sequelae of myocardial infarction and are associated with increased mortality. The incidence of ventricular arrhythmias associated with acute MI has been reported to be 10.2%, with 3.5% developing VT, 4.1% VF, and 2.7% both VF and VT.[15] The current treatment of these lethal arrhythmias has been based on recurrent DC cardioversion (DCCV) and anti-arrhythmic drug therapy. Though these therapies are somewhat effective in protecting patients from SCD, they are not without their own set of complications and limitations. The possibility of using catheter ablation to eliminate these arrhythmias has been raised with some skepticism, but if possible could alleviate the risk of SCD without exposing patients to the risk of DCCV and drug therapy.

There has been limited experience peri MI with ablation of drug resistant electrical storm. Bänsch attempted ablation in a series of patients with acute MI, depressed EF, and drug refractory electrical storm despite successful revascularization.[14] In this limited study (4 patients), LV mapping was performed and VPBs that triggered ventricular arrhythmias were ablated. At follow-up, all patients were free of ventricular arrhythmias. The importance of this study was that the investigators were able to demonstrate that like patients with no apparent heart disease, patients with VF peri MI could be successfully treated with elimination of VPBs.

Ablation has also been used to a very limited extent in patients with polymorphic VT in the setting of acute MI. Szumowski performed ablation on 5 patients with recurrent polymorphic VT despite revascularization and medical therapy.[16] Using electroanatomic and pace mapping techniques, origins of VPBs were isolated. Initiating VPBs were found to occur along the scar border zone. Elimination of these foci successfully treated the arrhythmias. None of the patients had defibrillator therapies postprocedure.

The limitations of ablation for arrhythmias peri MI are that only a small subset is at risk for recurrent arrhythmias and the experience to date is limited. At this

time, identifying the population at risk prior to first episode is impossible and the tedious and difficult nature of the procedure makes VT/VF ablation an unlikely candidate to be used for primary prophylaxis. As a result, ablation to this point can only be used as a 'bail out therapy'. Though a decrease in recurrence has been demonstrated, it is yet to be seen whether the application of ablation to this population will impact on morbidity and mortality.

Catheter ablation of VF storms in chronic ischemic heart disease

VF associated with chronic ischemia most reflects the substrate for which the majority of ICDs are implanted, i.e. patients post-MI who meet MADIT I and/or II criteria. These patients are an ever expanding population of individuals with prior history of MI and reduced ejection fraction who are at risk for SCD. The ventricles after myocardial infarction undergo extensive cardiac remodeling that results in necrotic myocardial scar that is primed for microreentry. Given the often heterogeneous nature of scar tissue, the ability to isolate single foci in ischemic myocardium has been looked upon with some skepticism. However, several clinical studies have demonstrated that few foci in the peri infarct area are responsible and this has allowed the development of possible curative therapy for the majority of those at risk for SCD.

The experience to date with ablation of VF storms in chronic ischemic heart disease has been promising. In the largest series so far, our center investigated the origins of VF storms and the efficacy of medical therapy and catheter-based ablation in patients with chronic ischemic heart disease.[13] This study looked at 29 patients greater than 6 months post-MI with documented VF storm. Twenty-one patients were treated successfully with medical therapy (heart failure medications and anti-arrhythmics); the other eight patients with refractory VF underwent ablation. EP studies revealed that VF episodes were preceded by isolated VPBs. Like VPBs seen in idiopathic VF, these VPBs were preceded by Purkinje like potentials (PLPs). Successful ablation was performed via elimination of documented PLPs that preceded VPBs that induced fibrillation. All potentials were noted to be around the scar border zone, which was identified by voltage mapping which isolated areas of low voltage consistent with scar (Figure 26.5). In patients whose VPBs were not mappable, mapping of the scar border zone and ablation of PLPs around the zone successfully eliminated VF. Only one recurrence of VF was documented at 10 $\pm$ 6 months of follow-up.

Our center demonstrated that catheter ablation was a potentially applicable therapy for chronic ischemic VF and elucidated some important principles about the potential targets for therapy. The idea that ischemic VF is a scar-related phenomenon is reinforced. However, *in vivo*, ischemic VF is actually triggered by single or very few areas of isolated electrical activity. These areas can be isolated and targeted for ablation. However, many refinements in the procedure and larger trials looking at efficacy are needed. One still unanswered question is whether isolation and ablation of each focus are necessary, or whether a simple anatomic method of isolating the scar border zone can effectively terminate sources of VF. Another yet unanswered question is whether ablation can be successful in patients with no history of prior VF episodes. To date, no case studies have been

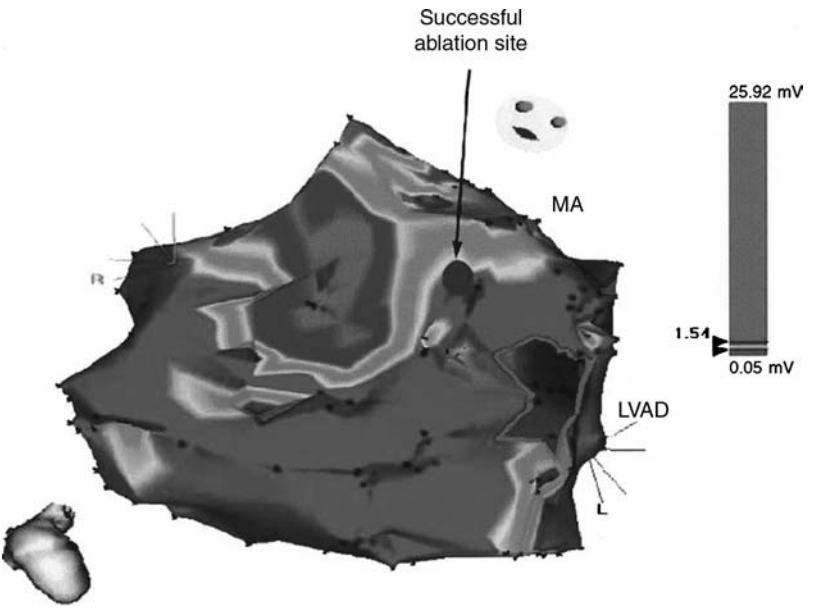

Figure 26.5 Three-dimensional CARTO map of LV in patient with VF storm ablation. Red regions represent scar, green and blue represent abnormal tissue in scar border zone, purple indicates normal voltage (>1.5 mV). Red circle denotes area where PVCs with Purkinje like potentials were mapped and successfully ablated. From Marrouche.[13] (See color plate section.)

reported on the application of ablation for primary prophylaxis in ischemic VF/VT, i.e. in patients meeting MADIT II criteria.

CATHETER ABLATION OF VENTRICULAR FIBRILLATION ASSOCIATED WITH LONG QT AND BRUGADA SYNDROME

Catheter ablation in the Brugada syndrome

The Brugada syndrome is a condition associated with abnormal sodium channel function leading to a peculiar ECG pattern and elevated risk of sudden cardiac death. Diagnostic criteria, and medical and device therapy are discussed elsewhere. To date, the hallmark of therapy has been ICD implantation for the prevention of sudden cardiac death in high-risk individuals. However, new enthusiasm has arisen for the possible application of ablation to treat patients with recurrent arrhythmias.

Several case series have been performed establishing the feasibility of the procedure in Brugada patients. Similar to other forms of VF/polymorphic VT, ablation foci have been established to arise from the Purkinje fibers.[22] However, in Brugada syndrome foci frequently arise from the ventricular muscle of the RVOT. Success rates have been promising, though experiences are limited.

Catheter ablation in the long QT syndrome

The long QT syndrome is a condition which is characterized by two, mainly inherited, forms of abnormal myocardial repolarization which are associated with an elevated risk of sudden cardiac death. Similar to Brugada syndrome, the experience with ablation has been limited. However, early work to date has demonstrated the feasibility of ablation, and foci arising from both the RVOT and Purkinje system.

SUMMARY AND CONCLUSIONS

In summary catheter ablation has shown much promise for patients with medically refactory VF/polymorphic VT in a variety of arrhythmic substrates, including normal hearts, channelopathies, and cardiomyopathies. However, proof of concept has been validated with preliminary experience at several centers. Over the next decade, more work needs to be done both in refining the procedure and in validating outcomes. Initially, such an approach may be offered to patients who have failed medical therapy and in particular are experiencing frequent ICD therapies. However, the use of catheter ablation as first-line therapy may become a reality for some types of ventricular arrhythmia substrates. For those with cardiomyopathy and an indication for an ICD, catheter ablation may not replace the need for an ICD in the absence of a randomized clinical trial. However, catheter ablation may result in improvement in quality of life and other psychosocial factors by reducing the frequency of painful ICD shocks. There has also been no experience with catheter ablation as primary prophylaxis in patients with depressed EF. This is the largest population at risk for sudden cardiac death and the population in which ablation may eventually have the largest impact.

In summary, catheter ablation has shown much promise for patients medically refractory for VF/polymorphic VT in a variety of arrhythmia substrates, including normal hearts, channelopathies, and cardiomyopathies. However, widespread application of this approach, particularly as a first-line therapy, is limited due to the lack of randomized trials. Furthermore, this type of catheter ablation is complex and may be quite challenging without the most advanced computerized technology; therefore the procedure has been reserved for use in a few experienced centers.

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27

Mapping and catheter ablation of postmyocardial infarction ventricular tachycardia: a substrate-based approach

Mauricio Arruda, Marketa Kozeluhova, Tamer Fahmy, Dimpi Patel, and Luigi Di Biase

Assessment prior to mapping and ablation procedure • Regionalizing the 'exit site of origin' of VT • Scarred-substrate modification: an alternative ablative approach • Epicardial mapping and ablation of post-MI VT: an adjunctive percutaneous approach • Mapping systems • Energy source for ablation

The management of ventricular tachycardia (VT) associated with prior myocardial infarction (MI) remains a major challenge despite the technologic advances over the past decade. Sustained VT may present in up to 20% of patients with history of a prior MI[1] and may account for up to 80% of sudden cardiac death (SCD) cases in the United States. The Multicenter Automatic Defibrillator Implantation Trial-II (MADIT-II) has shown that patients with prior MI and significant decreased left ventricular ejection fraction (EF) have increased mortality rates and that the implantation of an ICD can improve life expectancy in this patient population.[2]

Despite the favorable outcomes shown by ICD clinical trials, the prevalence of VT and its overwhelming morbidity remain unaffected. This arrhythmia is often refractory to anti-arrhythmic drugs and/or antitachycardia pacing. Therefore additional non-pharmacologic therapeutic approaches are highly desirable in the management of post-MI VT.

Percutaneous radiofrequency (RF) catheter ablation is an alternative approach and often performed as an adjunct therapy for post-MI patients presenting with refractory scar-related VT. The current strategies utilized for mapping and ablation of post-MI VT will be summarized below.

ASSESSMENT PRIOR TO MAPPING AND ABLATION PROCEDURE

- Obtain detailed history and physical examination.
- Assess history of bleeding or clotting disorders or use of anticoagulants.

- Investigate and treat ongoing myocardial ischemia and define infarct location.
- Review medications including anti-arrhythmic drugs.
- Obtain imaging studies to assess left ventricle (LV) function and to exclude intracardiac thrombus.
- Analyze the 12-lead ECG of clinical VT and ICD/PM electrograms of all documented events.

Strategies for mapping and ablation of post-MI VT

Advances in electrophysiologic techniques for mapping and ablation of post-MI scar-related VT have favorably impacted the management of this arrhythmia. The conventional approach for post-MI VT ablation utilizes ventricular activation mapping and entrainment maneuvers during VT to identify and guide RF delivery at critical components of the VT circuit. Such an approach is technically challenging and applicable only to sustained, stable, and hemodynamically tolerated VT. Selected cases performed by experienced investigators may achieve 70–75% long-term success.[3–5]

Substrate delineation in sinus rhythm can be obtained by detailed bipolar voltage mapping. It may precisely identify the scar, its border, and associated isthmus or channels possibly containing the critical component of the VT re-entrant circuit.[6] Substrate delineation and its modification by ablative techniques may improve long-term success. It has become an integral approach as indicated in our suggested algorithm for mapping and ablation of post-MI VT (Figure 27.1).

Substrate delineation by left ventricular bipolar voltage mapping is initially performed during sinus rhythm. Standard voltage criteria to discriminate normal from scarred myocardium have been demonstrated and widely utilized clinically.[7,8] Typically the electroanatomic mapping system (Carto – Biosense Webster) is used. The voltage amplitude (mV) of each bipolar EGM acquired at multiple sites in the LV (normal and scarred myocardium) is displayed as voltage mapping according to the following color code:

Viable myocardium	$\geqslant$1.5 mV	Purple
Dense scar	$\leqslant$0.5 mV	Red
Scar border zone	0.5–1.5 mV	Color range

The acquisition of a high resolution mapping allows detailed delineation of the scar, particularly at its borders and areas exhibiting relatively high voltage surrounded by low voltage scarred tissue, typically representing channels or isthmus that often participate as the critical component of the tachycardia re-entrant circuit.[9] During substrate mapping in sinus rhythm, sites exhibiting *double and/or late potentials* should be tagged on the map. These sites, representing slowly conducting tissue, may be later incorporated into the ablation strategy.

REGIONALIZING THE 'EXIT SITE OF ORIGIN' OF VT

The 12-lead ECG and imaging studies provide an approximate size and location of the scar resulting from a myocardial infarction. To further identify the *VT site of*

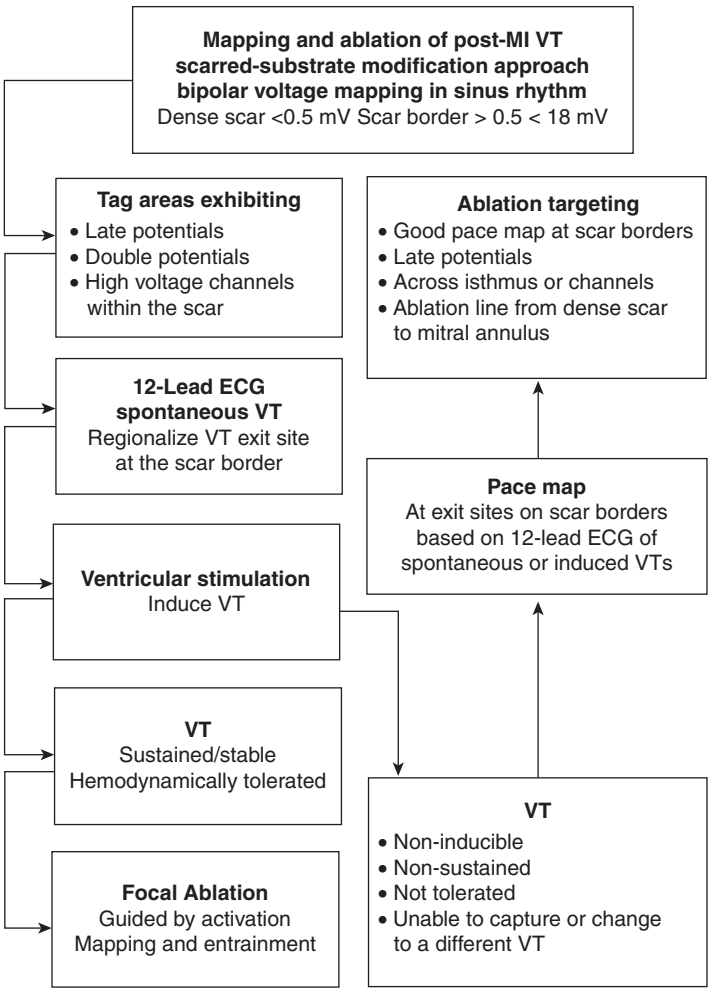

Figure 27.1 Stepwise algorithm for scarred-substrate delineation and modification in patients presenting for ablation of postmyocardial infarction ventricular tachycardia.

origin, a detailed analysis of the 12-lead ECG during VT may localize the region harboring the breakthrough or *exit site* of the tachycardia re-entrant circuit, virtually always in the LV.

Typically, LBBB indicates *septal exit sites* and RBBB *free-wall exit sites*; the frontal plane leads distinguish between *inferior and superior exit sites*; RBBB with rightward axis correlates with *lateral free-wall exit sites*; and the horizontal plane differentiates between *basal and apical exit sites*, as shown in the Figure 27.2.

Mapping and ablation of hemodynamically tolerated VT

Patients presenting with spontaneous or induced VT that is tolerated, easily reproducible by ventricular stimulation, and stable during pacing maneuvers

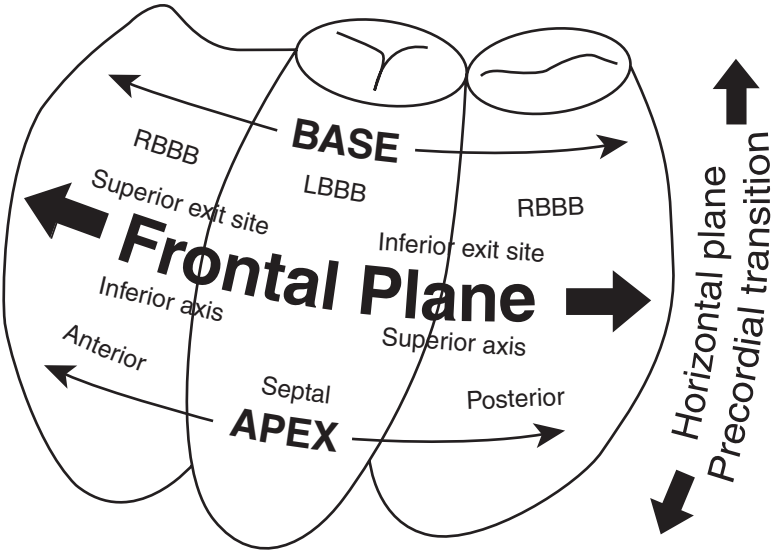

Figure 27.2 Diagrammatic representation of the left ventricle exhibiting the stepwise 12-lead ECG analysis for regionalizing the *exit site of origin* of VT.

should be categorized as having a mappable VT. The initial mapping and ablation strategy will target the critical component of the re-entrant circuit utilizing the elegantly described *activation mapping and entrainment* techniques.[9,10]

The scarred substrate resulting from myocardial infarction is often complex, largely subendocardial but potentially three-dimensional (3D), containing intramural and subepicardial extensions. The VT circuit is typically macrore-entrant with its entrance and mid-isthmus embedded inside of the scar and its exit at the scar border with the viable myocardium. Since the re-entrant circuit may not be limited to the subendocardium, activation mapping of the entire circuit is often not feasible. The re-entry paths are determined by dense scar tissue or valvular structures, functional block of excitation, or collisions of wavefronts creating inner and outer loops. Typically during endocardial bipolar mapping, recordings from a common pathway or from a zone of slow conduction exhibit low amplitude, fractionated (mid-diastolic or presystolic) potentials.

The scarred substrate may harbor the so-called *electrically unexcitable scar* (EUS), which is defined by sites exhibiting a pacing threshold $>$ 10 mA at 2 ms.[11]

Entrainment mapping

Sites exhibiting fragmented, mid-diastolic, or presystolic potentials obtained during activation mapping could actually represent a critical component or simply adjacent bystanders. Entrainment, defined as continuous resetting of the re-entry circuit, is a pacing technique that validates such recordings.

Pacing, at the lowest possible output, 10–20 ms faster than the VT cycle length (CL), captures the underlying myocardium during its excitable gap.

Local depolarization propagates in the same direction (orthodromic) and in the opposite direction (antidromic) of the re-entry circuit. The antidromic collides with the returning orthodromic wavefront. Capture with minimum fusion, undetectable on the surface ECG (reproducing the VT morphology), renders the maneuver as *concealed entrainment*, or *entrainment with concealed fusion*, or *exact entrainment.* A representative case is shown in Figure 27.3.

Entrainment mapping criteria

The *critical site for re-entry maintenance* fulfills all the following entrainment criteria:

1. Diastolic potential in VT (mid-diastolic or presystolic activity)
2. Paced QRS = VT QRS (12-lead ECG)
3. Stimulus to QRS interval = electrogram (diastolic potential) to QRS interval
4. Postpacing interval (PPI – last stimulus to local diastolic potential) = VT cycle length.

Adjacent bystander sites are commonly found in the scarred substrate. They are identified as diastolic potentials generated by surviving tissue connected but not critical to the re-entrant circuit. Pacing may show cancelled entrainment and identical intervals *except for a prolonged postpacing interval* (PPI), the hallmark of bystander potentials.

Limitation of entrainment mapping

1. Broad VT isthmus
2. Intramural or epicardial VT isthmus
3. Inadequate RF lesion formation (limited by catheter stability, scarred tissue)
4. Anti-arrhythmic drugs enhance slow conduction, resulting in a falsely prolonged stimulus to QRS and postpacing intervals.

SCARRED-SUBSTRATE MODIFICATION: AN ALTERNATIVE ABLATIVE APPROACH

Indications

- Failed ablation guided by activation mapping/entrainment
- Unable to capture during entrainment/pace map
- Pace-induced VT morphology change or multiple VTs
- Non-inducible, non-sustained or not tolerated VTs.

Stepwise strategy (Figures 27.1, 27.3–27.5)

1. Delineate the substrate by bipolar voltage mapping in sinus rhythm.
2. Pace map at multiple sites at the scar border
   - Analyze the 12-lead ECG of all spontaneous or induced VTs
   - Select the pacing sites according to the ECG criteria to locate the VT exit site.

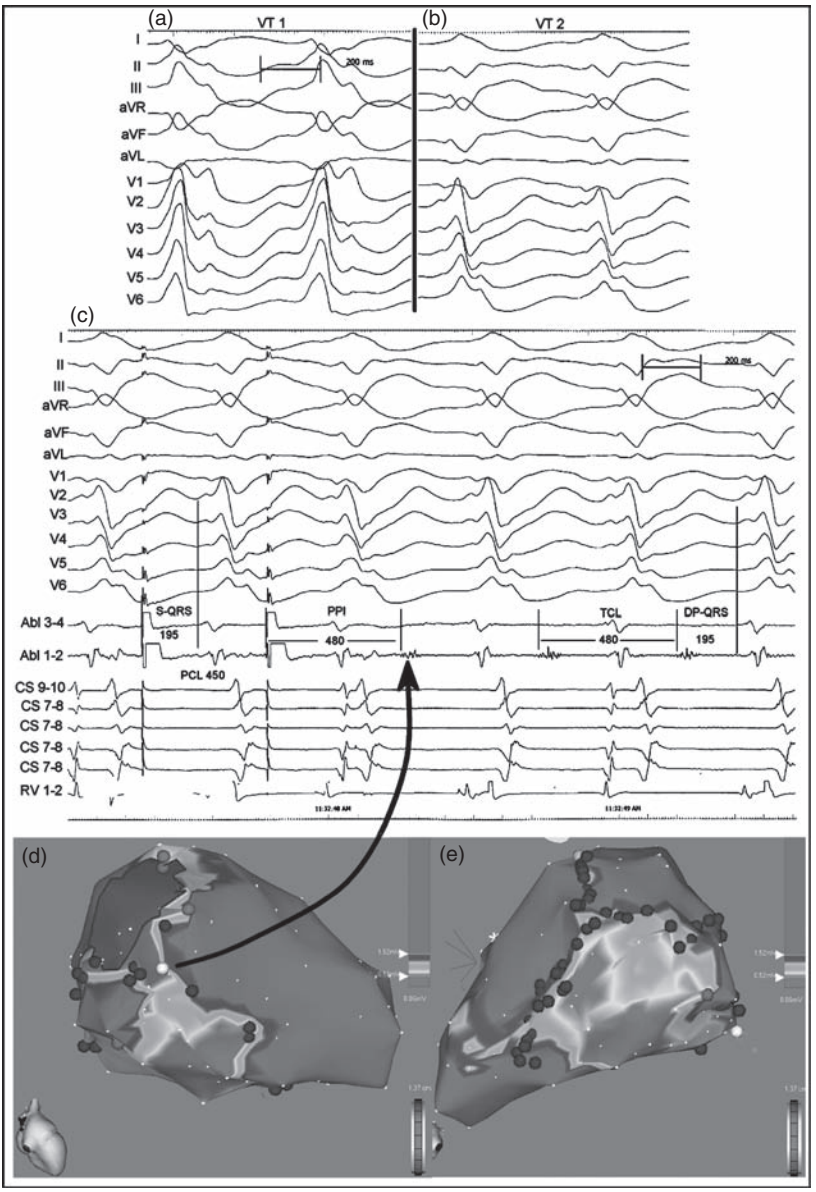

Figure 27.3 (a, b) 12-lead ECG morphologies of two induced VTs (VT2 clinical tachycardia). (c) Entrainment mapping of VT2. Note the mid-diastolic potential (MDP, arrow), recorded 195 ms before the onset of the QRS, was captured with the same stimulus to QRS (S-QRS) interval and 12-lead ECG morphology as the VT. The postpacing interval (PPI) was identical to the tachycardia cycle length (TCL), rendering this site a critical component of the VT re-entrant circuit. RF current delivery at this site terminated the VT which could no longer be re-induced. (d, e) Bipolar voltage LV mapping in sinus rhythm. Note the presence of significant scarring extending from the infero-septum to the postero-lateral LV. The white tag on the septal border of the scar (d) indicates the recording site of MDP and successful ablation. Additional RF was delivered (red tags) to connect the scar to the mitral annulus (MA). (e) The postero-lateral aspect of the scar. RF was delivered along the scar border all the way to the MA. VT 1: non-sustained, single induction. Following substrate modification no VTs could be induced. (See color plate section.)

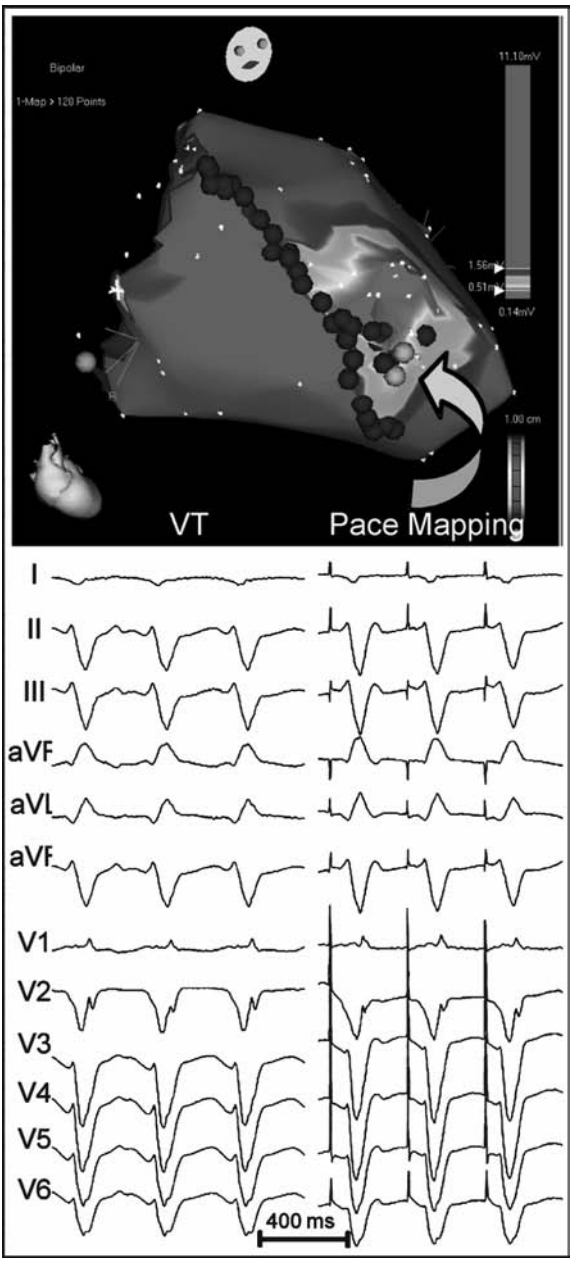

Figure 27.4 Top panel: voltage mapping in sinus rhythm showing a discrete antero-septal scar. Lower panel: 12-lead ECG morphology of VT (left) and during pace mapping (right) from a site near the scar border (golden tags, arrow) on the voltage map. Since the VT was not stable, ablation (red tags) target the site of near identical pace mapping. Scar substrate modification was achieved by ablation along the scar border from its apical aspect to the mitral annulus. This approach rendered the patient non-inducible. (See color plate section.)

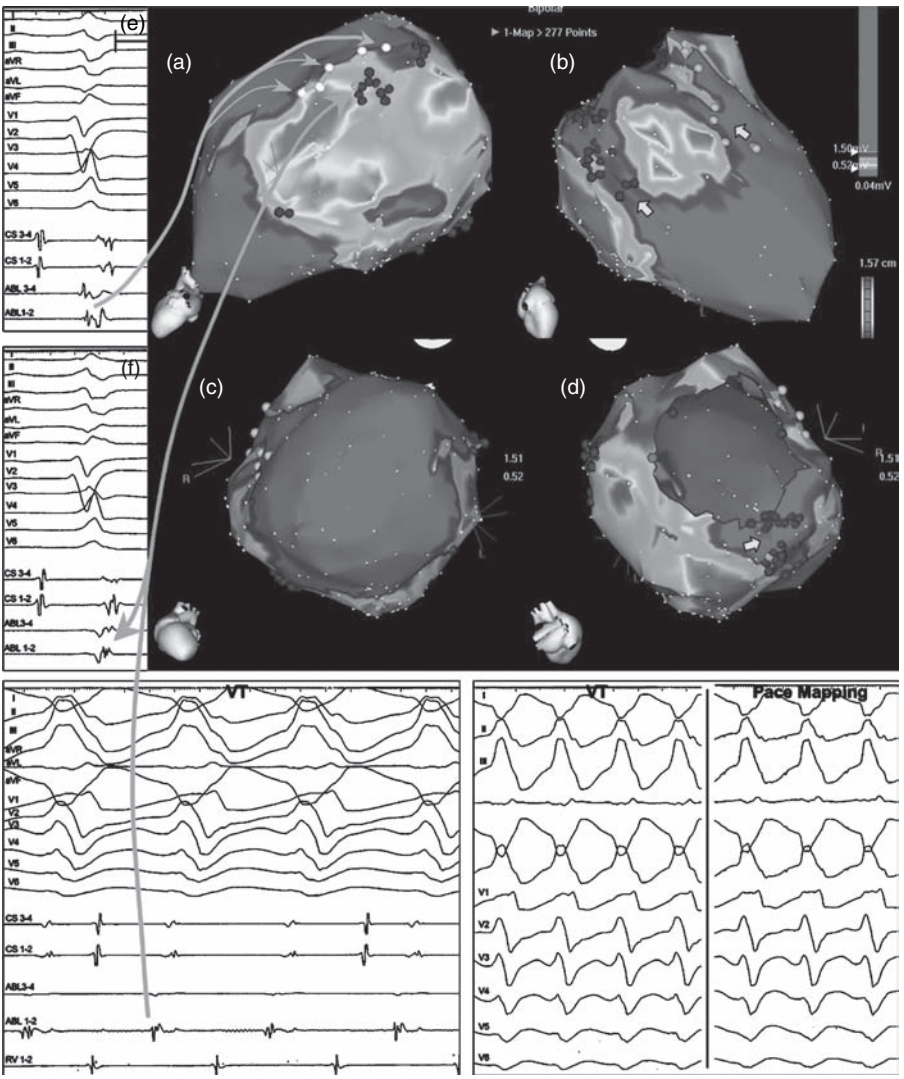

Figure 27.5 (a–d) Voltage mapping of the LV in sinus rhythm shown in the postero-lateral, septal, apical, and basal views, respectively. Note the extensive scarring and a residual channel approaching the infero-septal mitral annulus (yellow arrow, b, d). Sites exhibiting double (DP, e) or late potentials (LPs) during voltage mapping were tagged white (a). Note LPs in the coronary sinus recordings at the same region. The clinical VT was induced (bottom left). VT mapping, targeting the areas with DP, identified presystolic activation (green tag, a). Recordings at that site, upon VT termination, showed DP (f). Pace mapping at the same site (bottom right) reproduced the VT morphology. RF was delivered at that site (red tags), towards the mitral anulus and along the infero-septal isthmus (yellow arrow, b, d). No VTs could be re-induced. Golden tags (b, c, d) were sites with Purkinje potentials (posterior fascicle). (See color plate section.)

3. Ablation – empiric substrate modification by targeting sites exhibiting:
   - Good pace map on 12-lead ECG
   - Late potentials in sinus rhythm
   - Channels or isthmus on the scarred substrate
     linear lesions across these sites containing residual strands of myocardium
   - Isthmus between the dense *scar and the mitral annulus*
     empiric linear lesion to intercept *mitral isthmus dependent VT*.[12]

EPICARDIAL MAPPING AND ABLATION OF POST-MI VT: AN ADJUNCTIVE PERCUTANEOUS APPROACH

The well established 3D aspect of the scarred substrate, potentially containing intramural and subepicardial extensions as the critical components of the re-entrant circuit, may result in unsuccessful ablation via an endocardial approach.

Electrocardiographic predictors of VT with epicardial site of origin[13]

1. Pseudo-delta wave pattern
2. Prolonged intrinsicoid deflection time
3. Short RS interval
4. Long QRS complex duration.

As an alternative to endocardial mapping, two percutaneous approaches may be used to epicardial mapping and ablation of post-MI VT:

1. *Coronary venous approach*: coursing in the subepicardium, the coronary veins may be catheterized via the coronary sinus with multi-electrode micro-catheters.[14,15] Epicardial coronary venous mapping is obtained at sites beneath the epicardial fat that can be quite extensive. It has the advantage of being relatively less invasive allowing mapping in close proximity to the heart, but is limited by the anatomical distribution of the coronary veins and their proximity to adjacent coronary arteries. In addition, distal venous ablation is limited by catheter technology.
2. *The percutaneous subxiphoid approach* allows free pericardial space mapping and ablation using conventional catheters.[16,17] Pericardial access is obtained by a fluoroscopy-guided, over-the-wire placement of a sheath into the pericardial space using a subxiphoid transthoracic apical pericardial puncture. A representative case is shown in Figure 27.6.

Indications

- Failed endocardial approach
- Presence of LV thrombus
- Prosthetic aortic and/or mitral valves.

Limitations

- Coronary artery injury (during access and/or ablation)
- Pericardial adhesions from previous cardiac surgery or pericarditis
- Epicardial fat tissue (precludes contact to the myocardium)

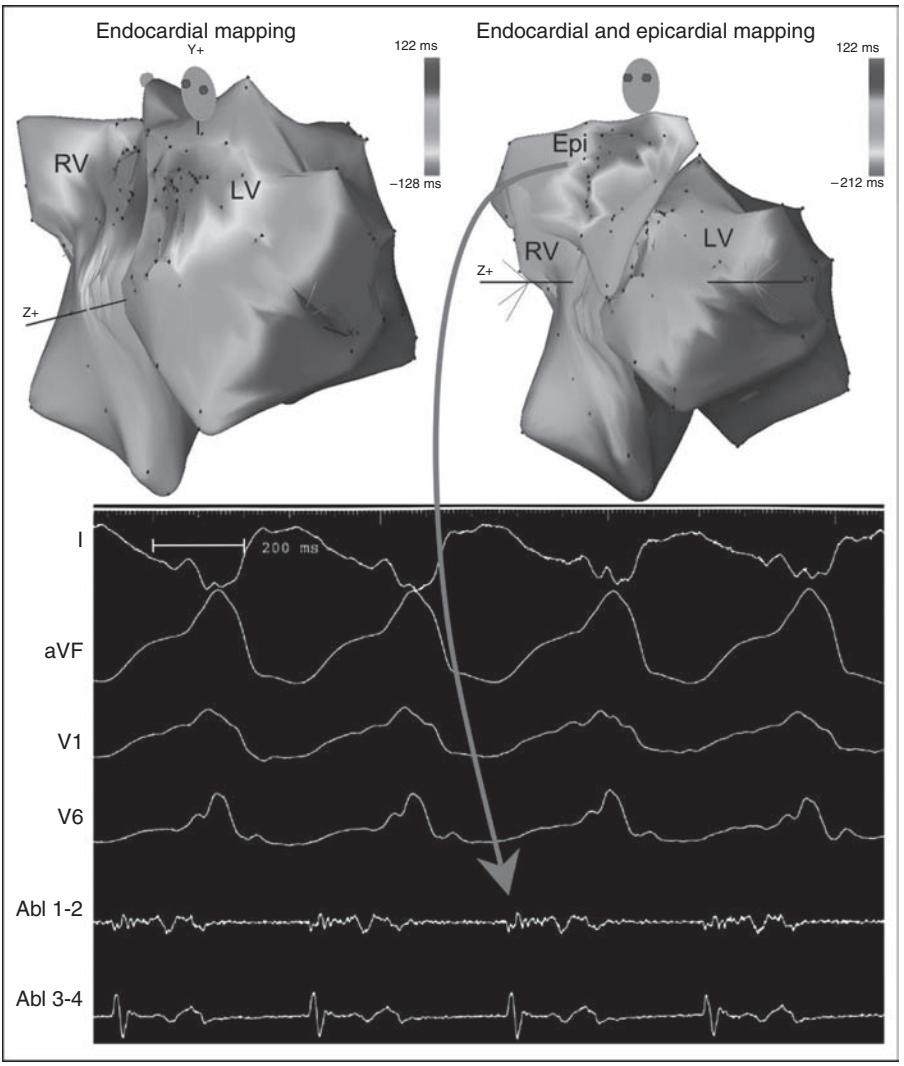

Figure 27.6 Top left panel: VT mapping showing equally earliest activation at the antero-septal aspect of both right and left ventricles. There was no significant scar during voltage mapping. Presystolic and mid-diastolic potentials (bottom panel) could only be recorded during epicardial mapping (top right panel). The VT was successfully ablated from the epicardium. (See color plate section.)

- Cardiac perforation
- Position of the left atrial appendage
- Phrenic nerve injury by ablation
- Mid-myocardial VT circuit.

MAPPING SYSTEMS

The mapping systems currently available (Carto – Biosense-Webster; EnSite NaviX – St Jude Medical) allow 3D display of cardiac maps. The ability to

superimpose the voltage, activation, and propagation maps enhances the likelihood of successful ablation, particularly in the settings of post-MI VT. The EnSite – Non-contact mapping system has been successfully used to guide ablation of *not tolerated* VT.[18] Segmented 3D CT and MR imaging have been integrated with EP mapping systems to enhance anatomic accuracy. This investigational technology and its value for mapping and ablation of cardiac arrhythmias have been evaluated clinically.

ENERGY SOURCE FOR ABLATION

Radiofrequency energy (RF) is the most common energy source used for ablation of cardiac arrhythmias. RF is typically delivered via a 4 or 8 mm platinum tip electrode. Thermometry (temperature control RF delivery mode) has virtually eliminated the unwanted char and thrombus formation at the electrode–tissue interface. Although safer, thermometry-guided ablation (particularly with a 4 mm tip electrode) is limited by lower RF power delivery and consequently relatively small lesion sizes. The 'cool-tip electrode catheter' is an alternative to thermometry-guided ablation. The *open irrigation saline cooled-tip electrod*e catheter (Biosense-Webster) has been widely used clinically.[19] It allows high RF energy delivery, resulting in larger lesions. It requires great caution when setting the RF generator for *maximum power*, which should be individualized for specific arrhythmias and ablation sites. In addition to careful power titration, application times may be reduced in the attempt to avoid intramyocardial steam formation and the so-called 'POP phenomenon', which could result in cardiac perforation.

Alternative energy sources[20–23] and technologies for ablation of cardiac arrhythmias are currently under investigation and include *ultrasound*,[24–26] *cryothermy*,[23,27] *laser*,[28,29] and microwave.[30,31]

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Arrhythmogenic right ventricular dysplasia

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INTRODUCTION

Arrhythmogenic right ventricular dysplasia (ARVD) is a progressive, genetically determined heart muscle disease, that is characterized by structural and functional abnormalities involving mostly the right ventricle (RV) and at a later stage may affect the left ventricle as well.[1] Pathologically there is RV myocardial atrophy, and fibrofatty replacement, which clinically leads to RV functional deterioration and electrical instability that may predispose to life-threatening ventricular arrhythmia, heart failure, and sudden death.[2]

The disease was first described by Guy Fontaine et al in 1977,[3] while the clinical features of the disease were first reported in 24 French patients by Marcus et al in 1982.[4] Ever since these first reports, much effort has been made to reveal the enigma of ARVD, yet still there are many unanswered questions, starting from the natural history and up to the optimum management of different patients.

EPIDEMIOLOGY

The incidence of ARVD is not exactly known, however its prevalence in the general population has been estimated to be 1:5000 to 1:10 000.[5]

ARVD is an important cause of sudden cardiac death (SCD) in young adults below the age of 35 years. In the United States it accounts for 5% of SCD in this population, while in Veneto, in northeast Italy, it accounts for 11% of overall cases, and 22% in athletes.[6,7] Similarly, it has been reported to account for 3–10% of unexplained SCD in patients less than 65 years.[8] Moreover, it was also found to be present in 36% of sudden unexpected postoperative deaths.[8a]

NATURAL HISTORY

There is little information regarding the clinical course of ARVD in patients having overt disease with significant ventricular arrhythmia, and even less is known in

asymptomatic family members. It has been proposed that ARVD passes into four phases, where a patient may be accidentally discovered in any phase:[6]

1. *The concealed phase:* characterized by subtle RV structural changes with or without ventricular arrhythmias. Sudden death may occasionally be the first manifestation of the disease.
2. *Overt arrhythmia phase:* in which symptomatic ventricular arrhythmias may be associated with overt structural and functional RV abnormalities.
3. *Global RV dysfunction phase:* due to progression of the RV muscle disease with preserved LV function.
4. *Biventricular failure phase:* with significant LV involvement. In such case, the disease mimics dilated cardiomyopathy with its related complications.

The annual mortality rate from ARVD is 2.8%, which can be decreased by medical therapy to 1%.[9] Sudden cardiac death accounts for one-third of the cases, whereas heart failure is the cause of death in the remaining two-thirds.[8]

PATHOLOGIC CHARACTERISTICS

The typical pattern of ARVD consists of replacement of the mid-mural and/or external layers of the RV myocardium, and to a much lesser extent, that of the LV, by fatty tissue and fibrosis mingled with normal tissue.[2] The process begins at the *epicardium* and spreads gradually through the myocardium towards the endocardium.

Grossly, there is dilatation of the RV, being covered by fatty tissue. The most commonly affected areas in the RV are the *infundibulum*, *apex,* and the *inferoposterior (subtricuspid)* areas (*the triangle of dysplasia*) (Figure 28.1). The septum is seldom affected, and later the LV may be affected. On cut section, the thinness of the myocardium is striking, and major fat infiltration is seen in the subepicardial region.[10]

Histologically, persistent strands of cardiomyocytes bordered or embedded in a variable extent of fibrous tissue are seen inside the fat, where only the subepicardial layers are spared. In contrast, the trabeculae carne of the apex and the right side of the septum are sometimes hypertrophied. Aneurysmal dilatation is sometimes present at the apex, the subtricuspid area, and in severe forms the infundibulum. Inflammatory cells may be seen in a large number of cases.[2] The left ventricle has been found to be affected in up to 76% of cases.[11]

Another form has been described, the purely fatty type, in which fat, intermixed with cardiomyocytes can be observed, with no evidence of fibrosis, inflammatory infiltrates, or LV involvement.[12] However, this type may either represent an early stage or a separate entity from ARVD, and has recently been called 'fat dissociation syndrome'.[13]

ETIOPATHOGENESIS

Little is known about the exact etiologic factors, and the mechanism of development of ARVD, however several theories have been postulated, in which the genetic basis may play a major role.

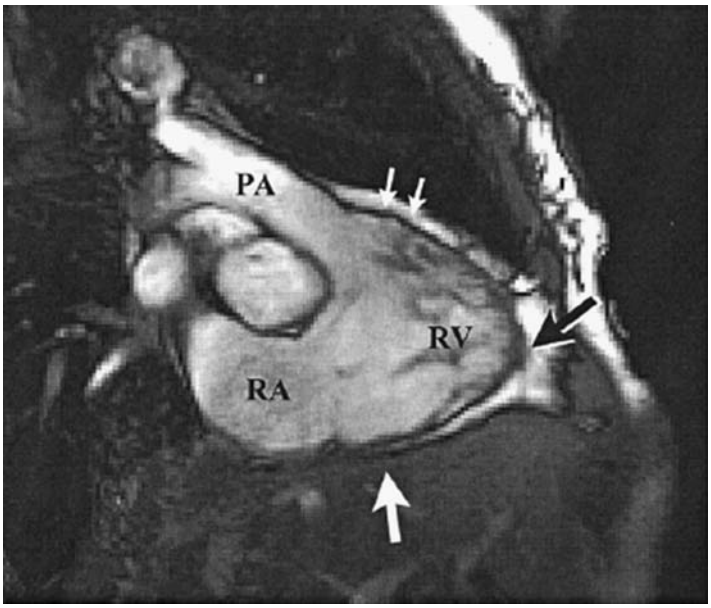

Figure 28.1 MRI image in the oblique sagittal plane showing the *triangle of dysplasia*, which is constituted by the inferior subtricuspid area (thick white arrow), RV apex (black arrow), and RV infundibulum (thin white arrows). RA, right atrium; PA, pulmonary artery.

Genetic basis

- A familial history of ARVD is present in 30–50% of cases, where the most common pattern of inheritance is autosomal dominant, although an autosomal recessive pattern has also been reported with the rare entity named as Naxos disease, seen only in the Greek island of Naxos, having additional cutaneous manifestation, palmoplantar keratoderma, and wooly hair.[14]
- Nine different forms of ARVD have been described, and are genetically classified based on different loci mapped on different chromosomes. Among them, mutations in five different genes have so far been implicated in the pathogenesis of ARVD:[9,15]
  - Three genes; desmoplakin, plakoglobulin, and plakophyllin, encoding the desmosomal proteins responsible for cell adherence and integrity.[16]
  - Transforming growth factor β, which is also involved with desmosomal proteins, (TGFβ-3), but its major role is in its involvement in tissue repair with fibrosis.
  - A gene encoding the ryanodine receptors, the RyR2 gene, responsible for maintaining calcium homeostasis. Intracellular calcium imbalance has been implicated in delayed afterdepolarization and triggered activity, causing catecholaminergic polymorphic VT (CPVT).[9]

Theories of pathogenesis

The exact pathogenesis of ARVD has not yet been elucidated; however three theories have been postulated:

1. *The dystrophic theory:* is based on the mutation of genes encoding desmosomal proteins and cell integrity. Impaired desmosomal function,

when subjected to mechanical stress, causes myocyte detachment and cell death, explaining its occurrence in athletes. This also explains the predilection of the thinnest portions of the RV, *the triangle of dysplasia*, early in the disease, as well as restriction of LV involvement to the thin posterolateral wall, sparing the thicker septum. In addition, the heterogeneous distribution of mechanical stress on the ventricle accounts for the regional disease expression and aneurysm formation.[17]

2. *The apoptotic theory:* programmed cell death has been found to occur in 35% of cases, especially those with acute symptoms early in the disease process.[18,19] Apoptosis is not only automatically triggered by the 'internal clock', but may be also triggered by intracellular calcium imbalance caused by genetic RyR2 abnormalities, or by T-lymphocytes, induced by viral and other inflammatory conditions.[2]
3. *The inflammatory theory:* this is supported by the presence of the inflammatory infiltrates as well as the isolation of Coxsackie virus from cases of ARVD with evidence of myocarditis.[20] The fibrofatty replacement is viewed as a healing phenomenon.[21] This hypothesis is not against family occurrence, as genetic predisposition to viral infection triggering an immune response and affecting the RV has been shown in animals.[22]

In fact there is no clear distinction between the genetic and the acquired theories, and probably a mixture of both may be incriminated together in the disease occurrence.

CLINICAL PRESENTATION

- Usually presents at adolescence, but intrauterine cases have been reported.[23]
- Males are more commonly affected than females in a ratio of 2.7:1.[21]
- The frequency of symptom occurrence is as follows:[8]
  - Palpitations 67%
  - Syncope 32%
  - Atypical chest pain 27%
  - Dyspnea 11%
  - Asymptomatic, especially in family members.

Signs

- RV failure 6%
- Sudden cardiac death 30%
- Arrhythmic presentation:
  - Ventricular arrhythmias: it occurs in 50% of cases. Any form of ventricular arrhythmias can occur having LBBB morphology with a superior axis, although RBBB VT has also been reported in sporadic cases.[24]
  - Supraventricular arrhythmias: may be present in 25% of cases. In a decreasing frequency, atrial fibrillation, atrial tachycardia, and atrial flutter may occur.

DIAGNOSIS

Diagnostic criteria

Diagnostic criteria were proposed by the Task Force from the European Society of Cardiology and International Federation of Cardiology (ESC) in 1994 (Table 28.1).[25]

Table 28.1 Diagnostic criteria for ARVD

Criterion	Major	Minor
Family history (FH)	Confirmed by biopsy or autopsy	FH of sudden death <35 years FH based on clinical diagnosis
ECG	Epsilon wave	Late potentials on signal average ECG
Depolarization/conduction abnormalities	Localized QRSd >110 in V1, V2, or V3	-
Repolarization abnormalities	-	Inverted T-wave in the right precordial leads above 12 years with no RBBB
Arrhythmias	-	LBBB VT on ECG, Holter, exercise test Frequent PVCs (>1000/24 h on Holter)
Tissue characterization	Fibrofatty replacement in endomyocardial biopsy	-
Structural or functional abnormalities	Severe global RV dilatation and dysfunction Localized RV aneurysm/ severe segmental dilatation	Mild global RV dilatation and dysfunction Mild segmental dilatation

For diagnosis of ARVD one must have 2 major, 1 major and 2 minor, or 4 minor criteria present.

Diagnostic tools

Electrocardiogram

May be normal in 40–50% of patients at the initial presentation, however by 6 years virtually all patients may be having one or more of the following criteria:[26]

- *Complete or incomplete RBBB* (in 14–18%); epicardial mapping suggests that this pattern is due to parietal block in the terminal Purkinje system rather than to bundle disease.[26]
- *Epsilon wave:* a distinct wave appearing just beyond the QRS in V1 (in 30% of cases); it is caused by delayed activation of parts of the RV (Figure 28.2).
- *Prolonged QRS duration:*
  - In V1–V3 >110 ms in 50% of localized, and 78% of diffuse ARVD[27]
  - QRSd in V1–V3 exceeds V6 by >25 ms (parietal block)
  - V1 + V2 + V3/V4 + V5 + V6 ≥ 1.2.
- *T-wave inversion in V1–V3* (in 55–85%), the extent of right precordial lead inversion relates to the degree of RV involvement; however it is not specific for ARVD.
- *QRS dispersion ≥40 ms*: it was found as an independent predictor of SCD, as well as VT induction at EPS.[27,28]
- *QT dispersion ≥65 ms* may be found in up to 50% of cases.
- *Delayed S-wave upstroke in V1–V3 ≥55 ms* has been found to be a specific marker, and may be present in 95% of cases. A delay of more than 70 ms was also shown to be an independent predictor of VT induction at EPS[27] This criterion is still currently not included in the Task Force criteria (Figure 28.3).

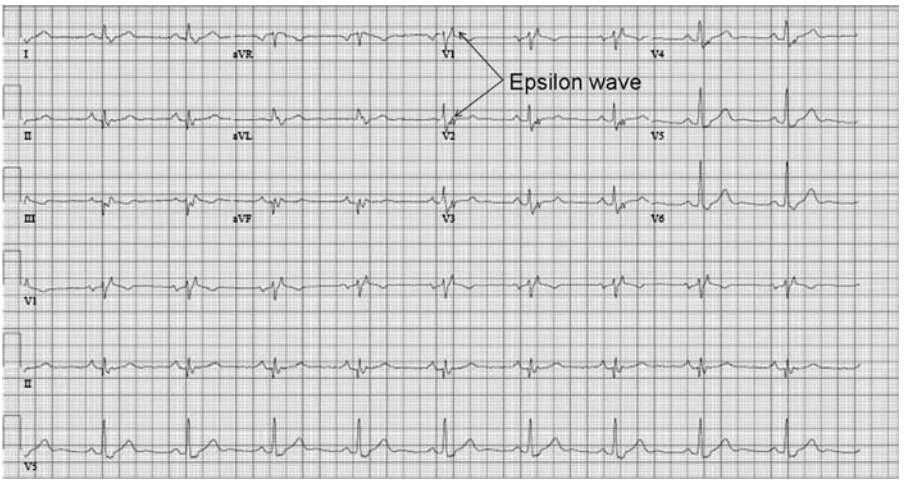

Figure 28.2 Epsilon wave in ARVD patients. It is reproducible and appears mostly in V1 and V2.

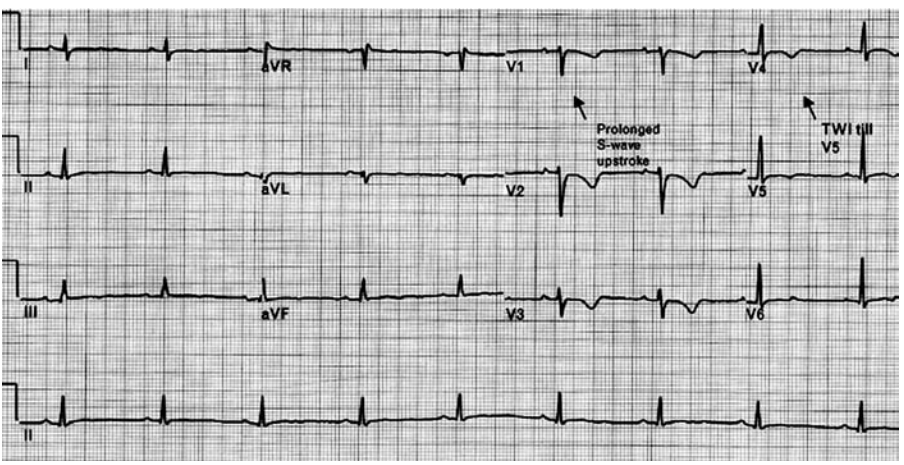

Figure 28.3 Resting ECG of a patient with ARVD. There is T-wave inversion in anterior leads reaching up to V5. Also note delay in S-wave in V1–V3. Reproduced with permission from Nasir et al, 2004.

ECG evolution: consistent with the progressive nature of the disease, the majority of patients may demonstrate progression of some ECG features. In one study the following was found over time:[29]

- Prolongation of S-wave upstroke ≥ 10 ms in 69%
- QRS prolongation ≥ 10 ms in 66%
- New T-wave inversion in ≥ one precordial lead in 37%
- New bundle branch block in 11%.

Echocardiography

The following structural and functional changes may be seen:

- RV dilatation especially in the RVOT long axis $>$ 30 mm.
- RV dysfunction can be evaluated by fractional area change (FAC) $<$ 32%, or evidence of segmental wall motion abnormalities.
- Dilatation of the RV wall correlates with the severity of the disease:[23]
  - Mild having RV EDV $<$75 ml/m^2 with localized akinesia/dyskinesia
  - Moderate 75–120 ml/m^2 with localized akinesia/dyskinesia
  - Severe $>$120 ml/m^2 with widespread akinesia/dyskinesia.
- Morphologic abnormalities may be also seen including:[30]
  - Trabecular derangement in 54%
  - Hyprerreflective moderator band in 34%
  - Sacculations in 17%.

Scintigraphic studies

- Radionuclide ventriculography can detect regional and global dysfunction with very high specificity.
- MIBG has been used to demonstrate regional sympathetic denervation in the RV wall, one of the theories of arrythmogenesis in ARVD.[31]

Magnetic resonance

- The diagnosis of ARVD by MRI is highly dependent on the technique used and the radiologist's experience. Currently the development of ECG gating, the breath holding technique, as well as the black blood, double-inversion recovery fast spin echo (DIR FSE) technique has significantly reduced motion artifacts and improved tissue resolution.[32]
- The use of selective fat suppression provides more accurate evidence of fat infiltration due to high contrast between the epicardial fat and the RV myocardium (Figure 28.4).[32]
- MRI can detect both morphologic and functional abnormalities, including intramyocardial fat, wall thinning, trabecular disarray, RV regional and global dilatation, and dysfunction.
- Being not included in the current Task Force criteria, the mere finding of fat by non-invasive techniques should not be considered as evidence of ARVD. In normal individuals it is abundant near the apex and the AV groove, and may be present in up to 50% in old age.[12,33] However, other morphologic criteria should be present to raise the suspicion for ARVD. In a recent report more than 70% of patients diagnosed only on the basis of MRI were wrongly diagnosed.[34]
- Unfortunately, MRI cannot be used in a large sector of patients due to implanted cardiac device interference. In such cases multi-slice CT scan is a promising technique that may have a major role in the diagnosis of ARVD, awaiting controlled studies for its validation.

RV angiography

Cine ventriculography has been considered the gold standard method for diagnosis of ARVD, however being an invasive procedure hinders its routine use

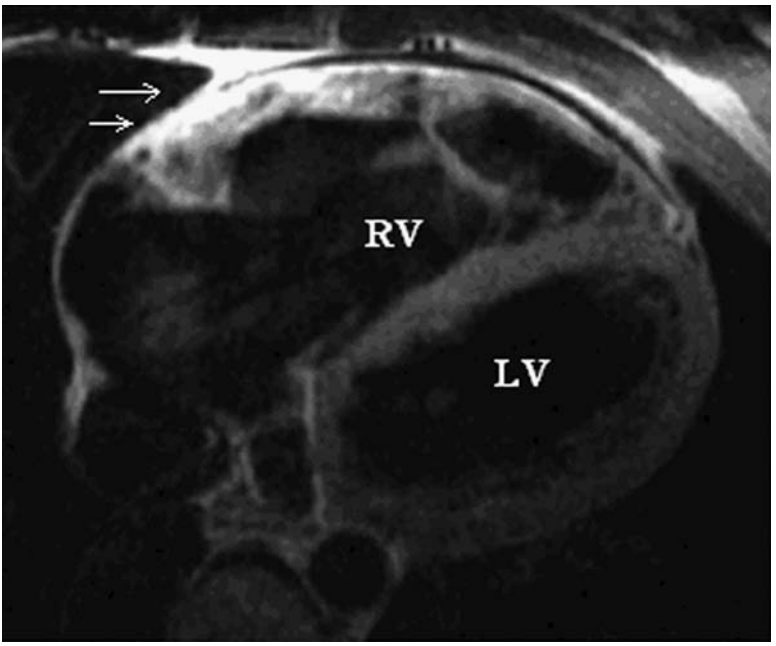

Figure 28.4 MRI of an ARVD patient. As shown there is RV dilatation as well as high signal intensity (fat) at the free wall.

in screening and follow-up. It should be done in two standard views (30° RAO and 60° LAO). Special care should be given as PVCs may affect the accuracy of the diagnosis. The following abnormalities may be seen:[10]

- Infundibular aneurysms
- Hypertrophic trabeculae (>4 mm thick) separated by deep fissures[35]
- Round areas of negative contrast in the trabecular zone, and moderator band
- Wall bulging at the apex, multiple outpouching at the inferior wall, and diastolic bulging of the subtricuspid area
- Tricuspid valve prolapse
- In diffuse cases there is global dilatation and reduced contractility.

Endomyocardial biopsy

- It is not commonly performed as it lacks sensitivity. The site of biopsy is usually the RV septum, an area that is uncommonly affected by the disease process; however, biopsy may be also important to exclude other diseases such as sarcoidosis.
- Biopsy of the free wall or the junction of the apex and the free wall has a sensitivity of 67% and a specificity of 92% if it shows more than 3% fat tissue and more than 40% fibrosis.[36] However, this area is at risk of perforation in ARVD.

MANAGEMENT

General recommendations

- Avoidance of competitive sports or any exercise that would cause symptoms, as presyncope or palpitation.[37] Mechanically stressed ventricles are not only at risk of different forms of arrhythmias, but of acceleration of the disease process as well.
- The major goal of therapy is prevention of sudden death (ICD), suppression of arrhythmias (AAD, catheter ablation), and standard therapy for heart failure in cases progressing to right or biventricular failure.[5]

Treatment strategies

- Patients at high risk for lethal arrhythmia and SCD include those with:
  - Severe RV dysfunction
  - LV involvement
  - History of aborted SCD, or syncope
  - Family history
  - ECG abnormalities, mainly QRS dispersion, delayed S upstroke, and epsilon wave (or late potentials in SAECG).[8]
- To date, due to heterogeneity of the disease and the limited data on risk stratification, there are no guidelines for the management of different forms of ARVD. The following strategy has been proposed (Figure 28.5).

Treatment modalities

1. *Anti-arrhythmic drugs:* in the largest study on acute and long-term efficacy of AAD on ARVD, sotalol (in doses upto 640 mg in selected patients) was found to be the most effective in patients with inducible or non-inducible VT.[38]
   - Sotalol – 68% in inducible, 83% in non-inducible
   - Amiodarone 15% in inducible, 25% in non-inducible, reported to have a higher success rate in other studies

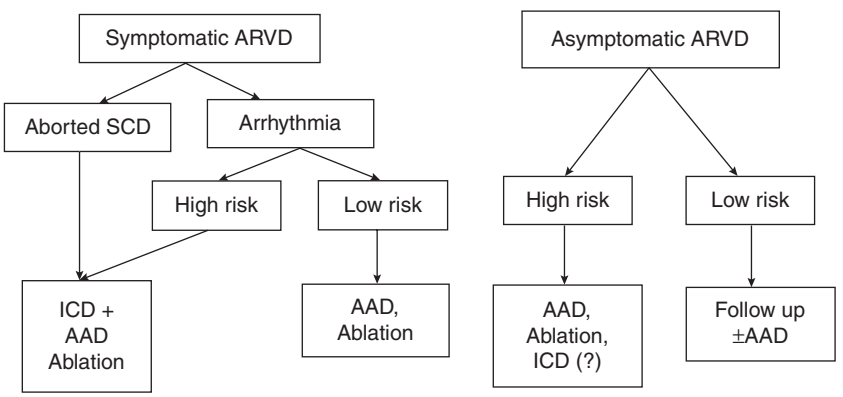

Figure 28.5 Proposed approach for ARVD patients. Modified from Wichter et al. Arrhythmogenic right ventricular cardiomyopathy antiarrhythmic drugs, catheter ablation, or ICD? Herz 2005, with permission.

- β-Blockers and verapamil were both ineffective in inducible VT, but had an efficacy of 29 and 50%, respectively, in non-inducible VT. β-Blockers may be required for patients with catecholaminergic VT.

2. *ICD therapy:*
   - According to the recommendations of the Task Force of the European Society of Cardiology (ESC) in 2001, ICD is considered as a class I indication for secondary prevention and a class IIa indication for primary prevention.[39]
   - It has been shown that the majority of patients receive appropriate ICD therapy (48–78% in different reports) and it has been life saving in a large number of cases (24–50%).[40–42] Even in studies where primary prevention was the main indication (73% of cases), appropriate therapy was given in 70%, and life saving ones in 30%.[42]
   - Due to structural abnormalities of the RV, and the progressive nature of the disease, special considerations should be given during implantation of the RV lead. Myocardial atrophy and fibrosis may interfere with the sensing and pacing threshold as well as the defibrillation threshold, and hence appropriate therapy.[43]
3. *Ablation therapy:*
   a. Indications of ablation:
      - Single morphology monomorphic VT (ablation may be curative)
      - Frequent ICD shocks
      - Frequent recurrences of drug-refractory or incessant VT.

   Although the ESC guidelines in 2001 do not support ablation of VT, the recent advances in ablation with the use of electroanatomic mapping systems have significantly improved the acute and long-term results.[39]

   b. Arrhythmogenic substrate and arrhythmia mechanism:
      - Re-entry is the main mechanism of VT in ARVD. Strands of healthy myocardium arranged in parallel layers, separated/bordered by fibro-fatty tissue, provide the substrate for the re-entrant mechanism with the anatomic barrier and the zone of slow conduction.[1]
      - Another possible mechanism that has been postulated is vortex-like re-entry (phase II re-entry). Re-entry may occur between the M cells in the midmural layer and the adjacent healthy cells having different action potential duration. This may be the cause of polymorphic VT and SCD occurring at night.
      - The least likely mechanism is enhanced automaticity occurring during exercise. Inflamatory cells present in the acute phase are also known to cause triggered activity.

   c. Electrophysiologic characteristics:

   During EP study the following characteristics may be observed:
      - Arrhythmia is induced and terminated by programmed stimulation or burst pacing. In most cases, can be entrained as ischemic VT.
      - Delayed fractionated potentials could be detected indicating zones of slow conduction.
      - There are areas of increased pacing threshold indicating fibrofatty tissues.
      - Stimulus to QRS is increased, reaching up to 80 ms in some areas.[1]

   d. Electroanatomic mapping:
      - Areas of dysplasia can be identified and quantified by electroanatomic mapping techniques; by mapping the RV in SR they appear as

contiguous low voltage areas (<0.5 mV), with long potential duration (70 ms)[44] (Figure 28.6); these criteria have been found to be significantly different than healthy individuals or those with RVOT tachycardia.[45]

- The areas of dysplasia have been mainly found under the tricuspid valve, the anterolateral wall, and under the pulmonary valve, as well as the apex. The septum was found to be affected in one report.[24]
- Unlike ischemic VT there is steep transition of voltage between the diseased area and the healthy myocardium with a very narrow border zone.[44]

e. Ablation strategy. A suggested ablation strategy is shown in Figure 28.7 (the algorithm):
   - A voltage map of the RV is first created in sinus rhythm, with adjustment of the scar settings to <0.5 as scar, >1.5 as healthy.
   - *If the tachycardia is unstable or hemodynamically intolerable*, pace mapping is performed to regionalize the possible exits.
   - Short lines of ablation (2-8cms) are created by sequential point by point lesion, and designed to:
     - Partially encircle the proposed exit region of the scar.
     - Connect the scar to an anatomic barrier (tricuspid valve) (Figure 28.8).
     - Connect two adjacent scars together.
   - *If the tachycardia is stable and well tolerated*, entrainment mapping is performed to identify a possible isthmus, for shorter ablation lines.

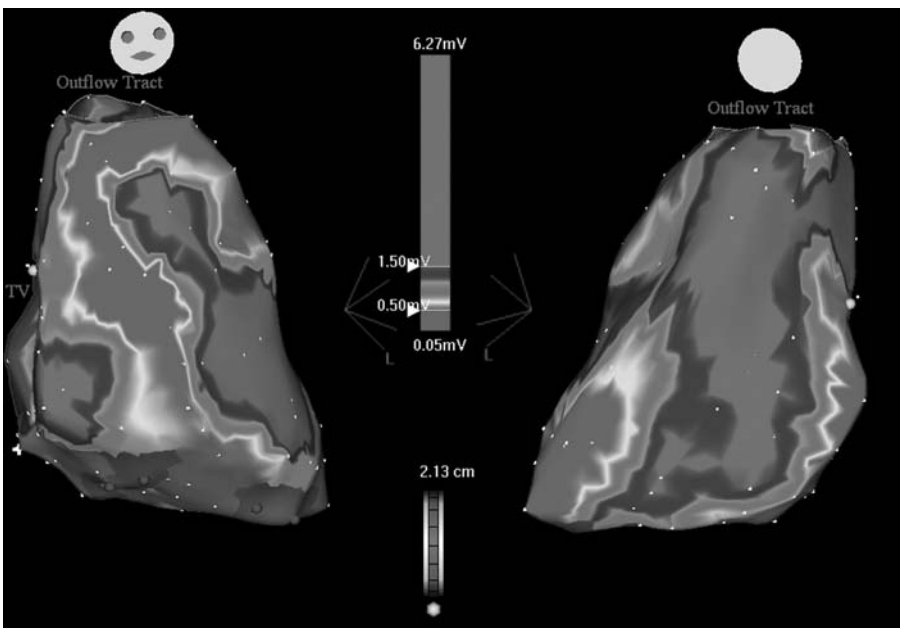

Figure 28.6 Electroanatomical map of the RV, in a patient with ARVD, in AP (left panel) and PA (right panel) views. Regions in red represent the scar (bipolar voltage <0.5mv), while purple regions are normal myocardium (>1.5 mv). Low voltage areas are mainly seen below the tricuspid valve and inferior wall, as well as areas in the anterolateral wall. Dense scar areas (<0.1 mv) on the inferior wall are tagged in grey color. Note that the septum seen in PA view is least affected. (See color plate section.)

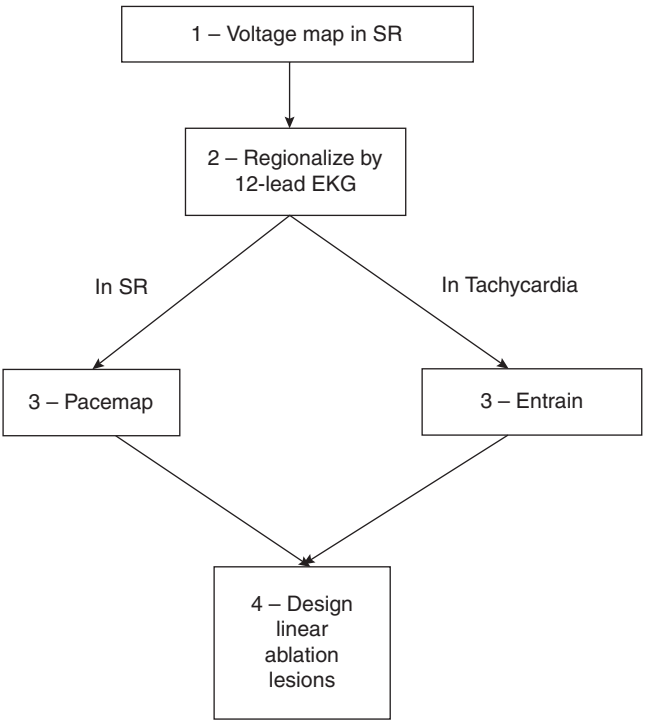

Figure 28.7 Suggested ablation strategy for ARVD patients.

- Focal ablation has been successfully attempted in some reports; however even for those tachycardias which seem to be focal, re-entry is the most likely mechanism, being either micro-reentrant or occurring between epicardial and midmyocardial layers, with a break-through in the endocardium.[24,45]
- Epicardial ablation has rarely been resorted to;[24] this is possibly because epicardial circuits may be accessed through the thin RV wall at the affected area.
- Ablation catheters used may be deflectable 8 or 4 mm, however cooled-tip ablation is only used with caution, especially in the anterolateral wall, for fear of perforation.[45]
- Linear ablation lesions are created by sequential point lesions under CARTO guidance. Radiofrequency energy is applied in every point for 60–120, with a power output of 30 W titrated to 50 W with a maximum temperature of 60°C.

ABLATION OUTCOME

Earlier reports prior to electroanatomic mapping have shown poor results; in one series the success rates for 50 patients were 32, 45, and 66% in one to three

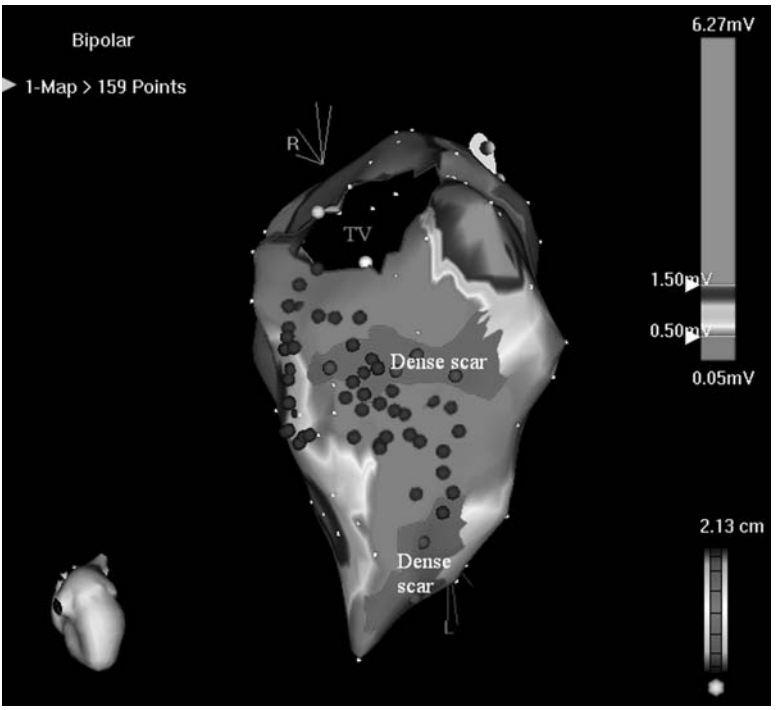

Figure 28.8 Caudal view of the RV inferior wall, showing the ablation strategy adopted in a patient with ARVD. Lines are created to connect the two dense scar areas, as well as to connect the scar with the Tricuspid valve abolishing all tachycardias. (See color plate section.)

ablation sessions.[46] However, recent results show higher success rates up to 90% after a mean follow-up of 27 months, while other reports still show a high late recurrence of up to 46% after 3 years, indicating the progressive nature of the disease.[24]

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29

Ventricular arrhythmias in idiopathic dilated cardiomyopathy

Tamer Fahmy, Oussama Wazni, Patrick Tchou, Mauricio Arruda, and Andrea Natale

INTRODUCTION

Ventricular arrhythmia is commonly encountered in patients with dilated cardiomyopathy (IDCM) occurring in 60–87% of patients.[1] Its incidence increases with left ventricular (LV) function deterioration. Moreover; it accounts for 8–50% of cardiac death in that subset of patients. Besides the conventional therapy for LV dysfunction, management of ventricular arrhythmia requires a hybrid therapy of anti-arrhythmic drugs, implantable defibrillators, and ablation therapy.[2]

SPONTANEOUS AND INDUCED VENTRICULAR ARRHYTHMIAS

- Complex ventricular arrhythmias have been reported to occur in up to 60% of patients with dilated cardiomyopathy, where non-sustained VT (NSVT) occurs in around 50% of them; most of these patients are usually asymptomatic.[3,4] Meanwhile, in 40% of patients presenting with syncope, monomorphic or polymorphic VT (SMVT) were reported to be the cause.[5,6]
- On the other hand the inducibility of sustained monomorphic VT by programmed electrical stimulation is infrequent, and the induction of different forms of arrhythmic presentation is dependent on the spontaneous arrhythmia presentation (Table 29.1).
- Most importantly, the risk of sudden death and occurrence of spontaneous VT persists despite absence of inducible arrhythmias. This confirms the limited prognostic utility of EP studies and highlights the need for ICD in those patients.

MECHANISMS OF VT

Based on the mechanism of induction and termination, together with the response to pacing on EP studies, the underlying mechanism of VT may be:[7,8]

Table 29.1 Types of arrhythmias induced in patients with different arrhythmia presentation

Presentation	Induced arrhythmia		
	NSVT (%)	PMVT/VF (%)	SMVT (%)
NSVT	40	0–30	0–15
Cardiac arrest	20	30	10–15
SMVT			75–100

- Re-entry (73%) located within:
  - The myocardium
  - His-Purkinje system (HPS):
    - bundle branch re-entry (BBR)
    - interfascicular re-entry.
- Focal (27%):
  - Triggered activity (most probable)
  - Abnormal automaticity.

ARRHYTHMIA SUBSTRATE AND ARRHYTHMOGENESIS

1. Re-entrant tachycardia:
   a. Myocardial
      The three prerequisites for re-entrant tachycardia, the anatomic barrier, slow conduction, and unidirectional block, are; usually present in patients with IDCM.
      - *the anatomic barrier*: endocardial plaques and patchy myocardial fibrosis have been reported in patients with IDCM;[9,10] tachycardia circulates around these barriers in the myocardium or epicardium
      - *slow conduction*: much like in patients with ischemic VT, the presence of strands of surviving myocardium among areas of fibrosis forms the basis of slow conduction[7,8]
      - *unidirectional block*; this is facilitated by the dispersion of refractoriness among different areas caused by the variable myocardial content of norepinephrine.[7]

   b. HPS
      - the most common form is BBR, however the fascicles may be also involved (interfascicular, or focal fascicular) (Figures 29.1–29.3)
      - it usually occurs in patients having a diseased conduction system (long PR, IVCD, or LBBB), which is seen in 50% of patients with IDCM
      - slow trans-septal conduction may also be involved in the mechanism (Figure 29.4); this is caused by ventricular dilatation and myocardial disarray seen in those patients[7,11]
      - although its occurrence is infrequent, BBR is important to recognize, since ablation of one of the bundles is usually curative.[12,13]
2. Focal tachycardia:
   - Both early and late afterdepolarization have been incriminated in the genesis of VT, especially NSVT.[7]
   - Early afterdepolarization is facilitated by conditions that prolong the duration of action potential and refractoriness. This is usually seen in hypertrophied and failing myocardium.

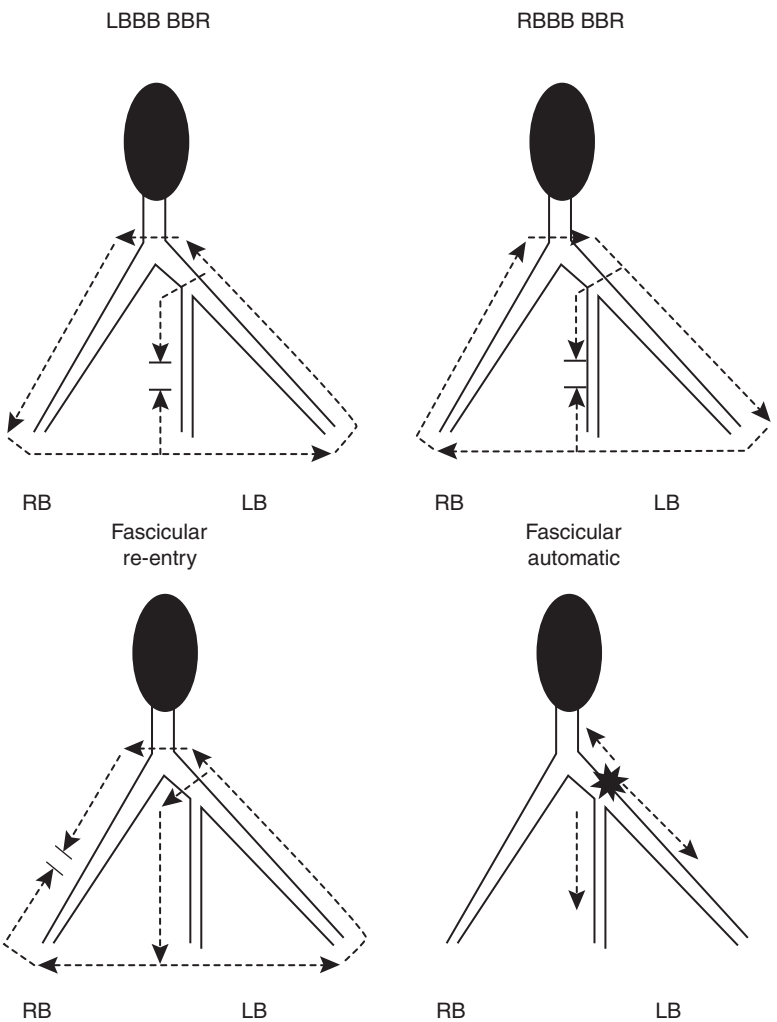


Figure 29.1 Schematic diagram showing the different re-entrant circuits that could occur in the His-Purkinje system. LBBB, left bundle branch block; RBBB, right bundle branch block. Reproduced from reference 12 with permission.

- Late afterdepolarization occurs due to intracellular calcium overload, which is commonly seen in the hypertrophied cardiomyocytes.

Other factors that may contribute to arrhythmogenesis in IDCM include:

- Electrolyte imbalance; both hypokalemia and hypomagnesemia are common in these patients due to concurrent diuretic usage.
- High levels of circulating catecholamines, and increased sympathetic tone.
- The pro-arrhythmic effects of drugs used in the management of these patients, including anti-arrhythmic drugs, digoxin, and phosphodiesterase inhibitors.

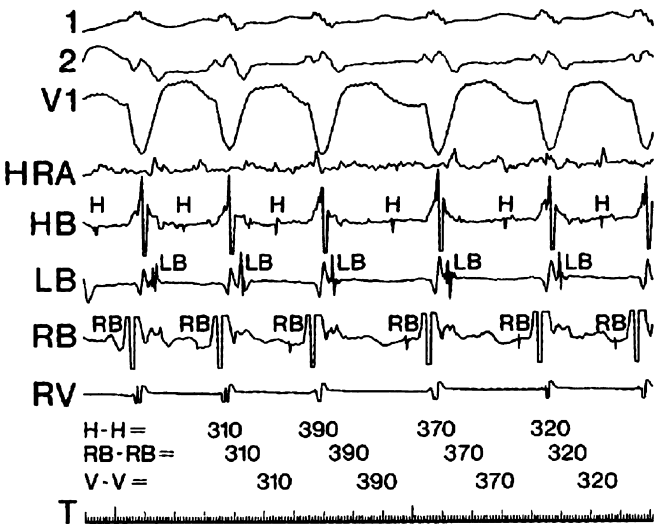


Figure 29.2 Bundle branch re-entrant tachycardia. From top to bottom are 3 surface ECG leads, intracardiac recordings of the high right atrium (HRA), His bundle (HB), left bundle branch (LB), right bundle branch (RB), and right ventricular apex (RV). The tachycardia has LBBB morphology; the activation wavefront passes through the RB, RV apex, retrogradely through the left bundle, and back to the His. Note that variations of the H-H are followed by variations in the V-V. Atrial fibrillation is also seen. Reproduced from reference 13 with permission.

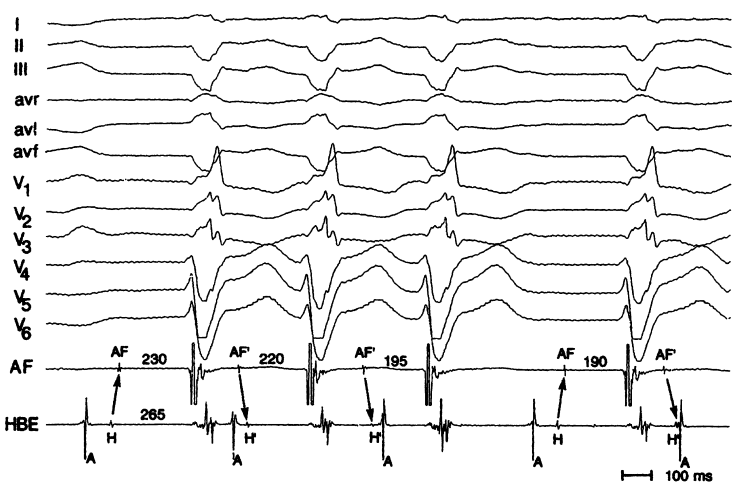


Figure 29.3 Interfascicular tachycardia. From top to bottom are 12 surface ECG leads, left ventricular catheter recording from the anterior fascicle (AF), and His bundle recording. The first beat shows left anterior hemiblock distal to the recording site and antegrade conduction over the posterior fascicle, followed by retrograde conduction again over the anterior fascicle, then the His with reversal of activation sequence in the second and third beats. Reproduced from reference 12 with permission.

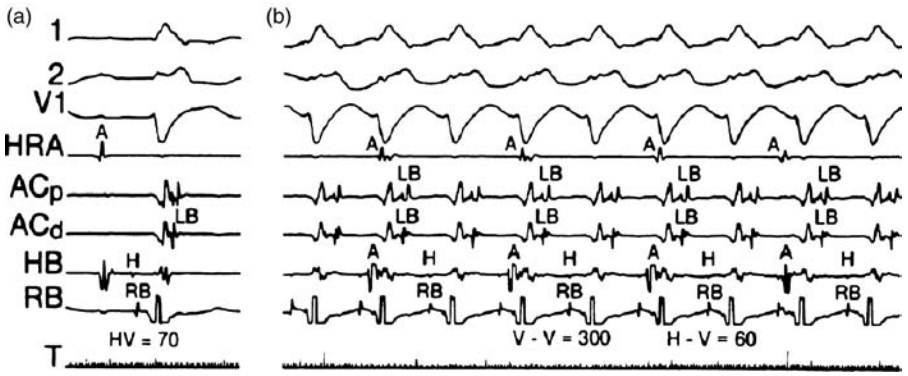


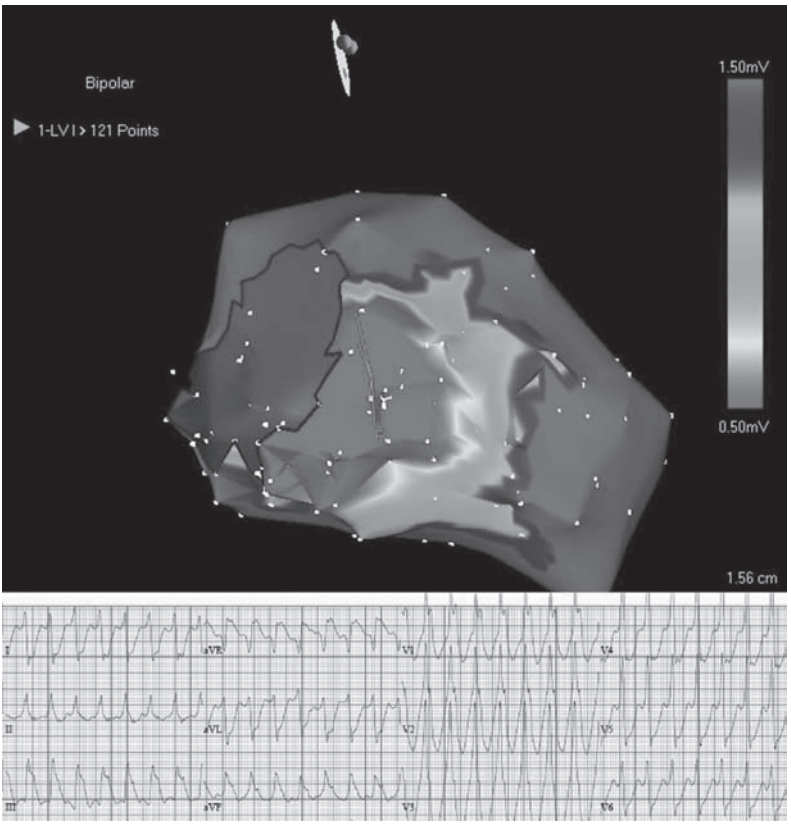
Figure 29.4 Bundle branch re-entry with trans-septal activation. From top to bottom are 3 surface ECG leads, intracardiac recordings of the high right atrium (HRA), ablation catheter at the left bundle branch area (ACp and ACd), His bundle region (HBE), and mid-septum recording the right bundle potential (RB). Panel (a) is in sinus rhythm showing LBBB morphology, with HV prolongation and retrograde activation of the LB. Panel (b) shows tachycardia having the same morphology as that in sinus rhythm, with retrograde activation of the LB. The tachycardia was terminated by ablation of the LB. Reproduced from reference 13 with permission.

- The concurrent occurrence of myocardial ischemia due to possible coronary embolization from atrial or ventricular sources.

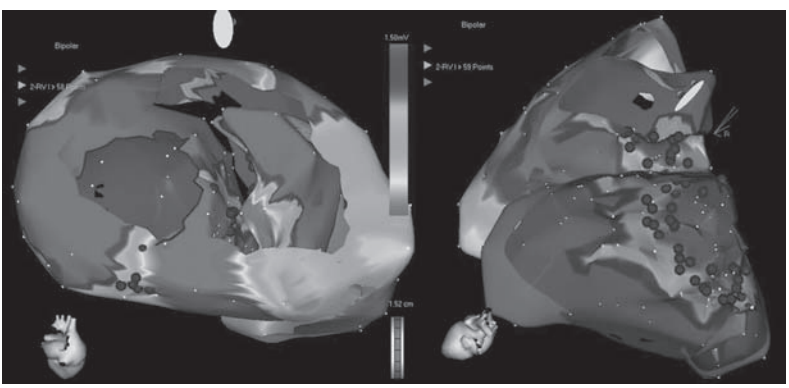
ELECTROANATOMIC MAPPING AND ELECTROPHYSIOLOGIC CHARACTERISTICS

- Low voltage areas (<1.5 mV) are mainly seen at the base, particularly perivalvular.[8] This has been observed by both endocardial and epicardial mapping. These areas correlate well with the site of origin of VT[1] (Figure 29.5).
- In the vast majority of patients, the abnormal electrograms constitute less than 25% of the total LV, although it ranges from 6 to 48% of the LV endocardium.
- The area of scar (<0.5 mV) has generally been reported to account for less than one-third of the low voltage areas, although it may not be observed at all.
- Fractionated and late electrograms are usually seen within the low voltage areas.
- Bundle branch re-entry is characterized by:[14,15]
  - Most commonly the activation goes down the RB, and up the LB, giving an LBBB morphology with fast initial forces and a left superior axis.[16]
  - His bundle (H) and bundle branch (B) potentials may be seen preceding the ventricular activation.
  - A long HV interval that is equal to or greater than that during sinus rhythm (>80 ms).
  - Changes in tachycardia cycle length are preceded by a similar H-H or B-B variation.
  - Captured beats, if present, can only have the same morphology as the tachycardia.
  - BBR tachycardia can be confirmed by entrainment from the RV apex.[16]

This tachycardia may be poorly tolerated and degenerates easily to VF.



(a)



(b)

Figure 29.5 (a) Voltage map of the LV showing a scar area near the septal mitral annulus. A 12-lead ECG showing one morphology of his tachycardia is seen, suggesting that its exit is at the upper lateral border of the scar area. (b) As shown on the left panel, further mapping in the right ventricle revealed a scarred area at the septal side of the tricuspid valve as well as the outflow tract. A low voltage epicardial area corresponds to the underlying endocardial scar. The right panel is a clipped image of both ventricles to show the endocardial ablation areas surrounding the scar, and terminating all tachycardias. (See color plate section.)

SUBSTRATE AND VT MAPPING

Different mapping techniques may be used to identify the target ablation site.[17–20]

1. Substrate mapping:
   This is performed to characterize the different possible substrates for VT according to the endocardial EGM voltage.
   a. Voltage mapping
      - it is usually done during sinus, or paced rhythm in pacemaker-dependent patients; both the LV and the RV should be mapped
      - bipolar EGMs are recorded from different ventricular sites using the electroanatomic mapping system; a 3D shell of the whole ventricle is formed, depicting various EGM voltages in different color codes (red being the lowest voltage, and purple the highest)
      - the color scale is further adjusted to display the different areas as follows:
        - healthy endocardium >1.5 mV (or 1.8 to adjust for ventricular hypertrophy if present)
        - scarred myocardium <0.5 mV
        - border zone between 0.5 and 1.5 mV
        - dense scar (below 0.1 mV) can be tagged

      NB; the size of each of these areas will depend on the density of mapping of the area.
      - During the mapping procedure, sites showing late or fractionated EGMs should be tagged for later reference.
2. Tachycardia mapping
   Different techniques have been described. The use of each will depend on the tachycardia stability and hemodynamic tolerance.
   a. Pace mapping
      - this is specifically performed for unstable tachycardias or may be done to confirm the exit site after mapping of stable tachycardias
      - pacing is done at the same cycle length of the clinical tachycardia, or as the coupling interval of mapped PVCs; pacing threshold should be double the diastolic threshold, and should not increase more than 10 mV with a 2 ms duration to avoid the virtual electrode effect by capturing the healthy myocardium away from the pacing site
      - pacing is started at the border zone of regions likely to be near the circuit exit, as expected by the surface ECG during tachycardia
      - if the pace map reproduces the exact (12/12) morphology as the mapped tachycardia, the area is tagged as a potential ablation target
      - areas with long stimulus–QRS (>40 ms) duration are typically indicative of slow conduction areas, and hence a possible isthmus

      If a stable monomorphic tachycardia is induced, the following two techniques may be further done.
   b. Activation mapping
      - mapping during tachycardia performed at the expected area, pursuing the earliest presystolic activation site; this can also be done in cases of frequent monomorphic PVCs; acceptable sites should measure $>$ 40 ms pre-QRS
   c. Entrainment mapping
      - pacing is initiated at a cycle length only 20–30 ms shorter than the TCL, and at a maximum threshold of 10 mV and 2 ms duration.

Faster rates or higher amplitudes may be associated with QRS fusion, and hence false negative results. This may be due to escape of the antidromic pacing wave front through a different exit, and activation of the nearby myocardium giving a different QRS morphology that fuses with the original tachycardia wavefront

- a pacing site within the tachycardia circuit should have the following characteristics:
  - concealed entrainment with no change of tachycardia morphology
  - a postpacing interval (PPI) approximating that of the TCL (<30 ms)
  - if the pacing site is within the tachycardia isthmus, the following may be met:
    - a long S-QRS (>40 ms), i.e. slow conduction area
    - if a diastolic potential could be identified during tachycardia, the S-QRS should be equal to EGM-QRS
    - it has also been suggested that the relation of the S-QRS duration to the TCL may identify the catheter location within the isthmus. <30% of the TCL-near the exit site, 30–70%-within the isthmus, and >70%-at the circuit cinletorina bystander loop

ABLATION STRATEGY

Different strategies are adopted for different ablation types of tachycardias; a five-stepped algorithmic approach is suggested in Figure 29.6.

- *Focal tachycardia*: focal ablation is applied at the site of earliest activation on the electroanatomic map with a perfect pace map and a presystolic electrogram activity >40 ms.
- *BBR tachycardia*: one of the bundle branches, mostly the RB, is targeted for ablation. The RB potential is pursued at the mid-septum. Ablation may be complicated by infranodal block and permanent pacing may be required (Figure 29.6).
- Myocardial re-entry:
  - In stable tachycardias; short lines of ablation are created targeting the isthmus, after its identification by entrainment and pace mapping.
  - In unstable tachycardias; after substrate mapping and identification of the probable site, ablation lines are designed as follows:
    - connecting two scars
    - connecting a scar to an anatomic barrier (valve)
    - partially encircling the possible exit.
- *Epicardial ablation*:
  - Many studies have demonstrated the efficacy of epicardial ablation in recurrent cases. It has also been proved successful as an adjuvant strategy to the endocardial approach in the primary setting in many cases.[20–23]
  - The pericardial space is usually accessed via the subxiphoid approach, much like pericardiocentesis.
  - Low voltage areas are usually larger than the corresponding endocardial areas.

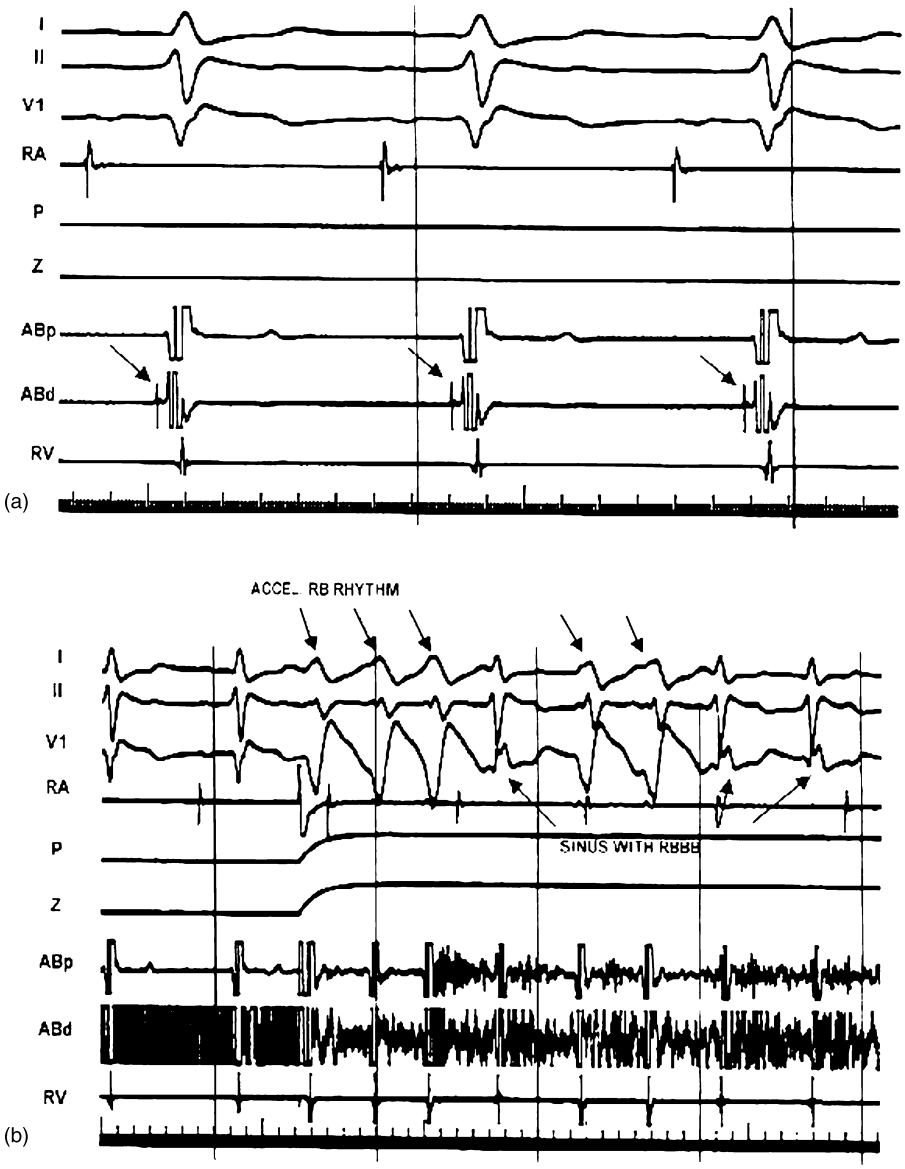


Figure 29.6 Electrogram recording during right bundle ablation. (a) Recording of a right bundle potential used to guide delivery of ablative energy. There should be little or no atrial electrogram at the recording site to assure a distal right bundle site of ablation. A more proximal ablative lesion could potentially cause complete His bundle block. (b) Initiation of radiofrequency energy delivery to ablate the right bundle. An accelerated right bundle rhythm can sometimes be seen at the initiation of energy delivery. Right bundle branch block is seen soon thereafter. Reproduced from reference 12 with permission.

- During catheter manipulation or ablation epicardially, it is imperative to avoid injury of important epicardial structures as the coronary arteries, and the phrenic nerve. While the catheter is kept at the ablation site, coronary angiography could estimate distance to the nearest coronary artery. Meanwhile, high output pacing with no phrenic nerve capture, is an important tool to verify the safety of the phrenic nerve during ablation. Cryoblation may have a lower risk of inducing coronary artery lesions.[24] Phrenic nerve injury, with subsequent diaphragmatic paralysis, is usually a temporary self limited condition that usually resolves within 6 months.[25]
- Due to the presence of fat, cooled-tip ablation may yield better results by preventing overheating and hence reaching a higher power.

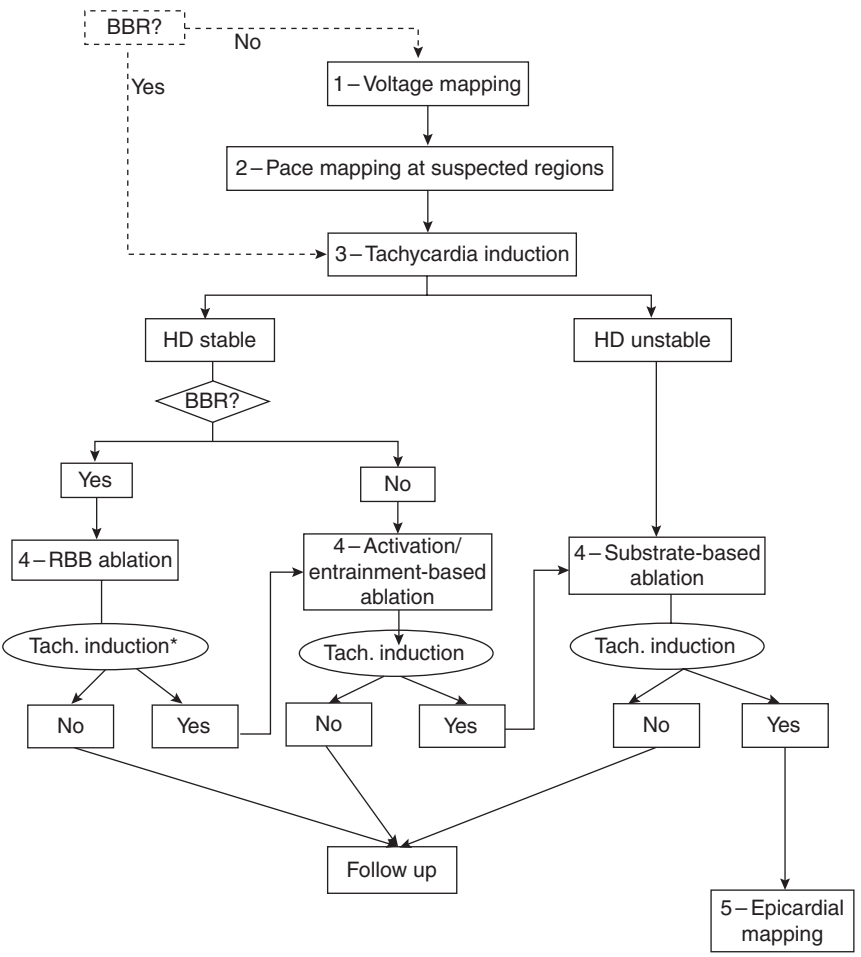


Figure 29.7 Stepwise approach for the ablation strategy in patients with dilated cardiomyopathy. *Another form of tachycardia appearing after RBB ablation.

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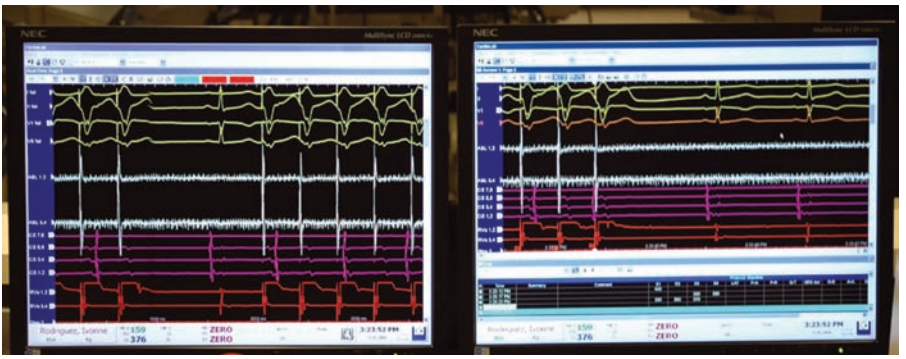


Figure 3.3 The page displayed during studies typically shows several intracardiac electrograms with 3 to 4 surface ECG leads which allows for axis determination, activation timing, and P/QRS morphology.

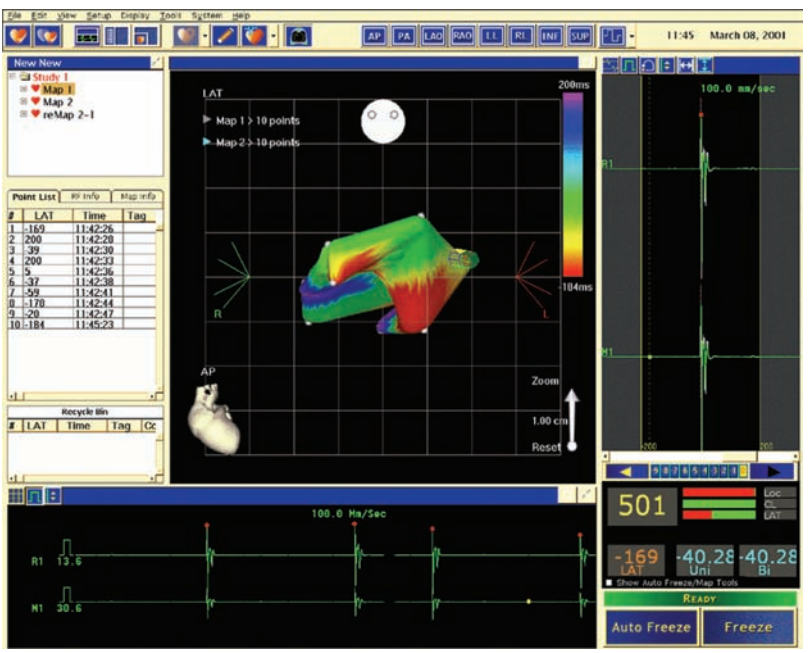
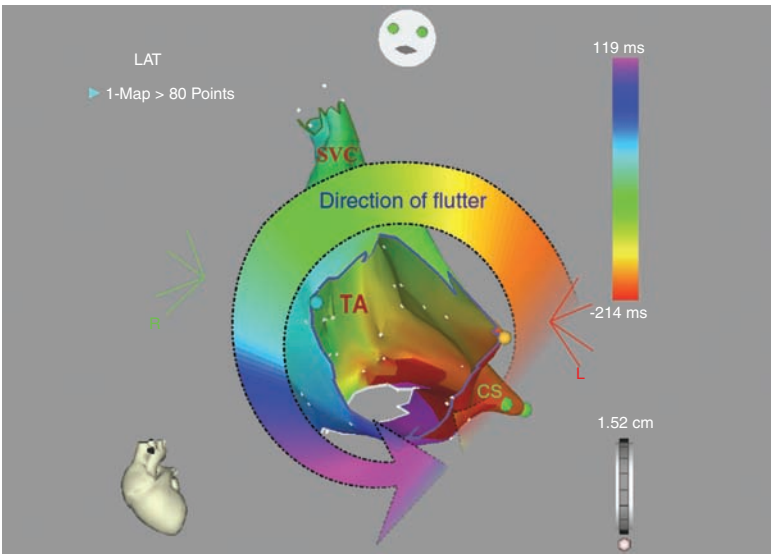
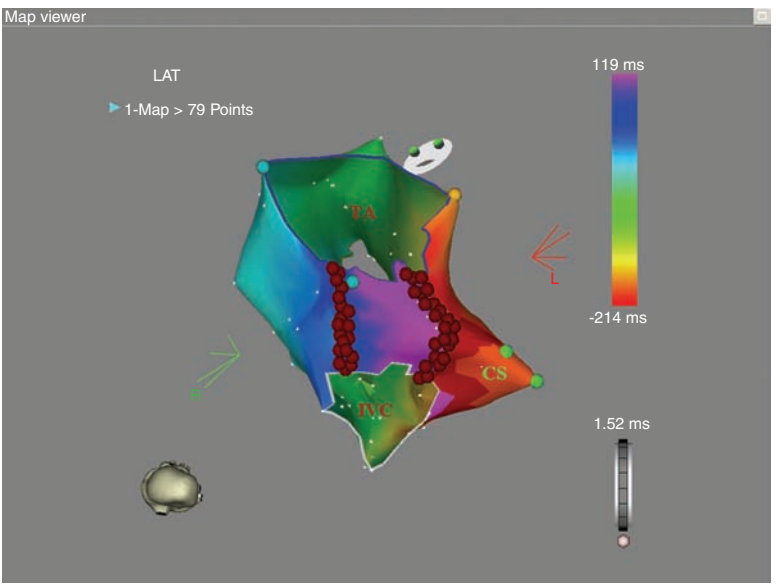


Figure 3.6 With a magnetic field sensor in its tip that is referenced to an externally located patch on the patient, the catheter can be displayed and recorded in three dimensions with intracardiac electrograms.



(a)



(b)

Figure 8.6 Electroanatomic activation map of the right atrium during flutter. (a) In the AP view, the activation wave is seen propagating up the septum and down the lateral wall, where 'early meets late' at the inferior wall (CCW direction). (b) Inferior view of the right atrium showing the CT isthmus. Two ablation lines are designed to encompass the broad CTI; line A joins the Tricuspid annulus to the CS os and further down to the IVC (septal isthmus), while line B joins the lateral tricuspid annulus to the IVC (lateral annulus).

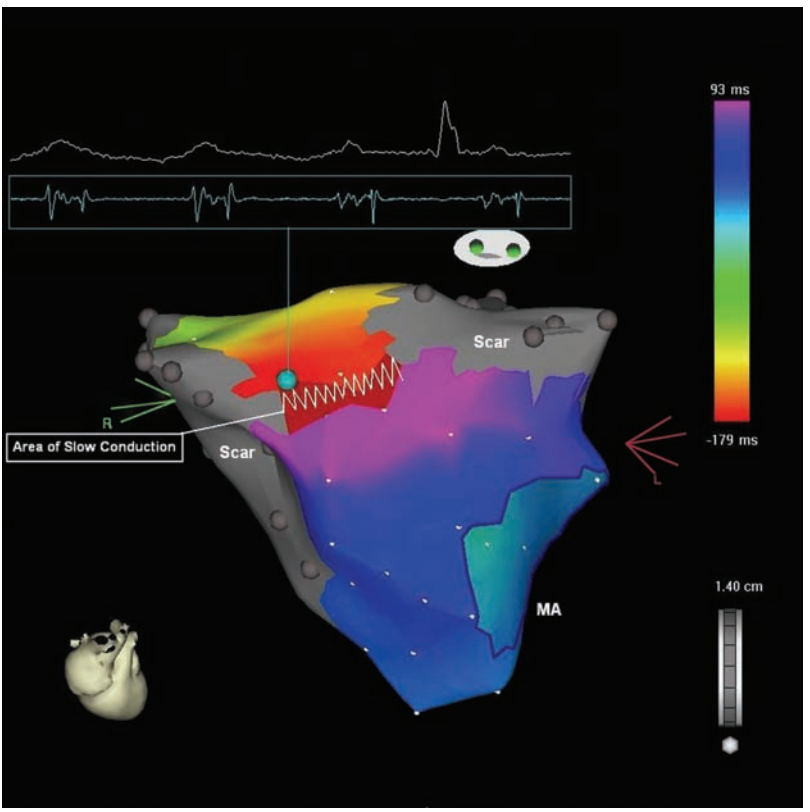


Figure 8.8 Electroanatomic map of the left atrium in a previously ablated patient. Two scars at the location of the PVs on both sides provide anatomic obstacles around which a flutter propagates. The flutter activation wave is seen traveling down the posterior wall, around the mitral annulus, and up the anterior wall. An area of slow conduction is shown between the two scars anteriorly where fractionated potentials are recorded. MA, mitral annulus.

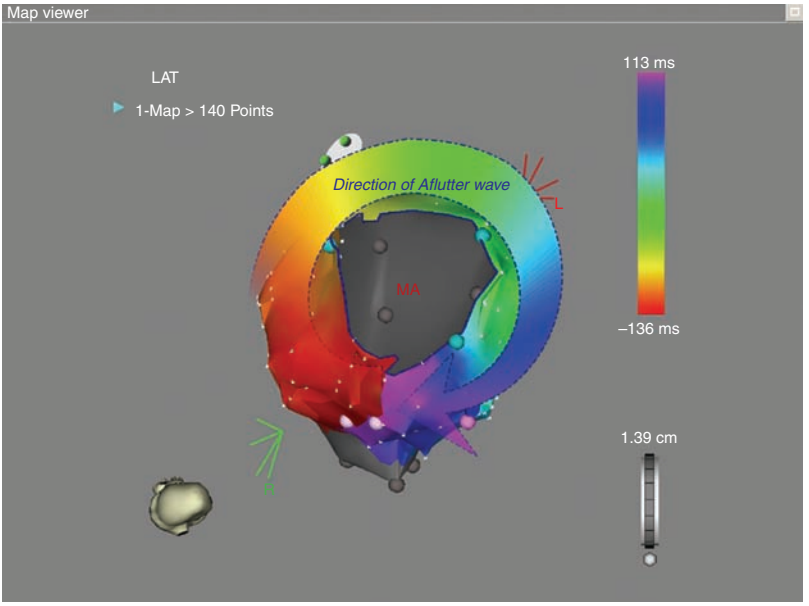


Figure 8.10 Electroanatomic map of the left atrium. Sequential activation around the mitral annulus in a clockwise fashion.

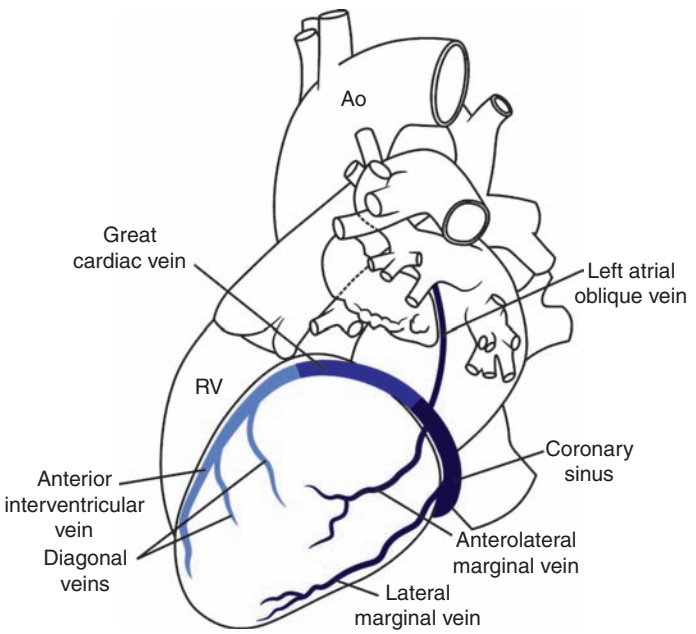


Figure 16.2 Anatomy of the coronary veins.

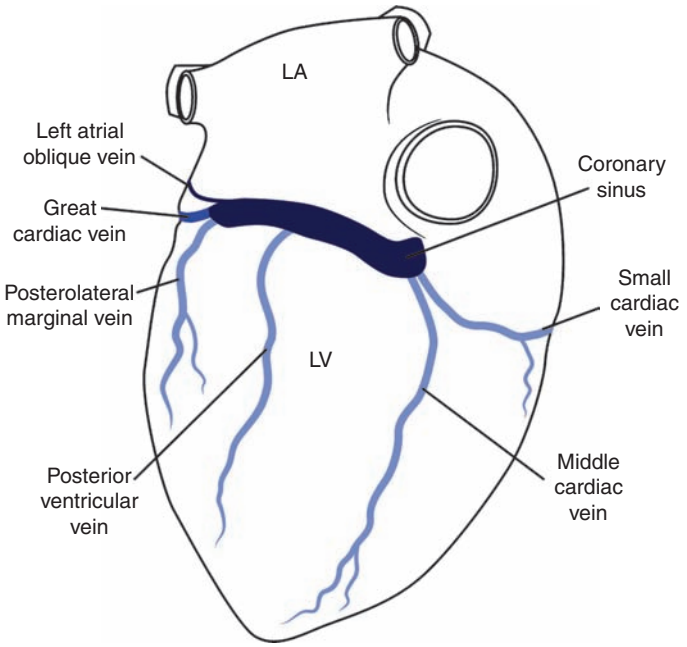
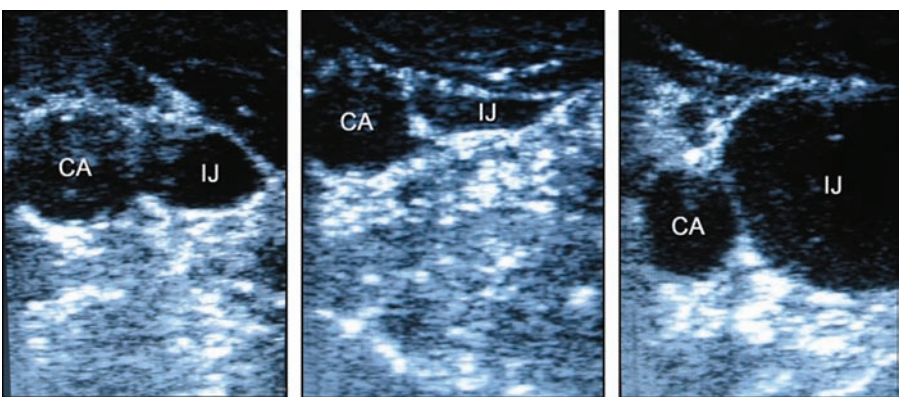


Figure 16.4 Anatomy of the coronary sinus including the posterior interventricular vein or middle cardiac vein and posterior ventricular vein.



(a) (b) (c)

Figure 18.3 Ultrasound-guided internal jugular vein puncture. (a) The carotid artery is seen medial to the vein. (b) Gentle compression distinguishes the vein. (c) A Valsalva maneuver from the same patient distends the vein. IJ: internal jugular vein; CA: carotid artery.

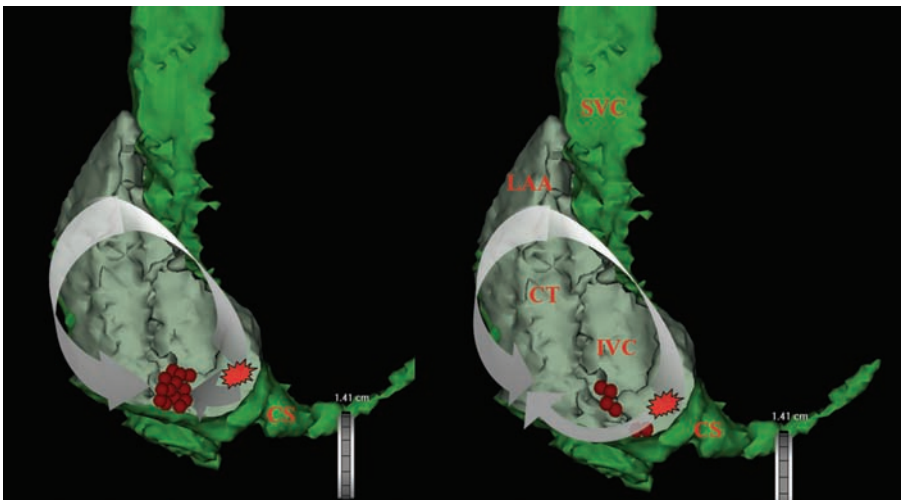


Figure 23.3 CT image of the right atrium clipped in LAO view. The right image shows the activation sequence after partial isthmus ablation with the presence of a gap. The left image shows complete unidirectional block.

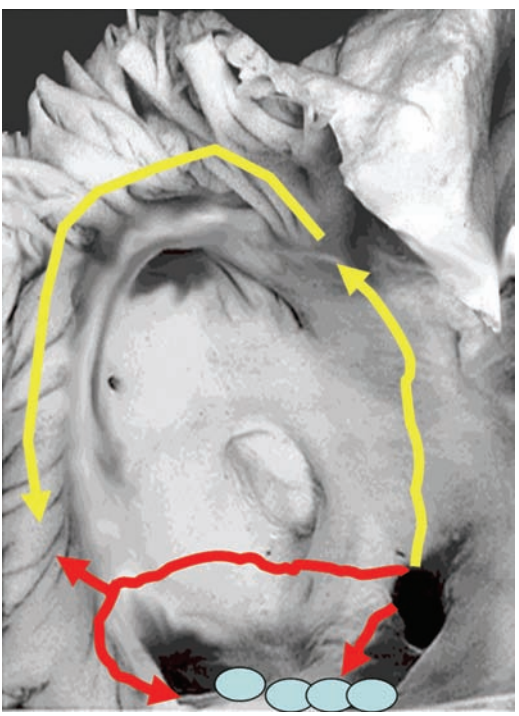


Figure 23.5 *Crista 'shunt'*. Diagrammatic depiction of the CTI and posterior atrial wall, showing that despite absence of conduction along the CTI when pacing from the CS os, yet still the conduction time to low lateral wall may be short, suggesting passage of conduction wave through the crista along the posterior wall.

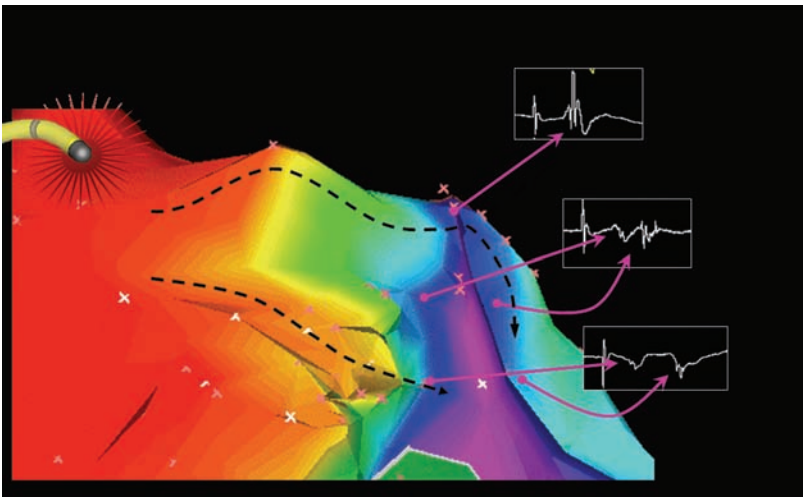


Figure 23.6 Gap along the ablated isthmus. Electroanatomic map of the CTI while pacing from the lateral wall. Widely split double potentials are seen at one end of the line and as the catheter is moved along the line the distance between the double potentials decreases, indicating the area of gap.

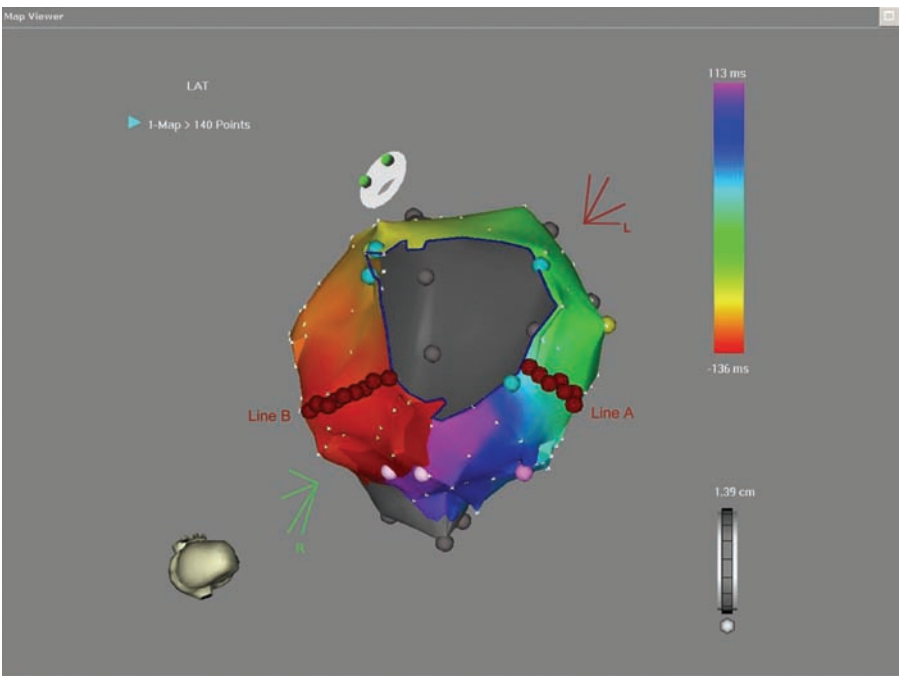
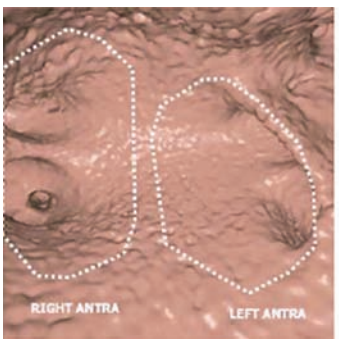
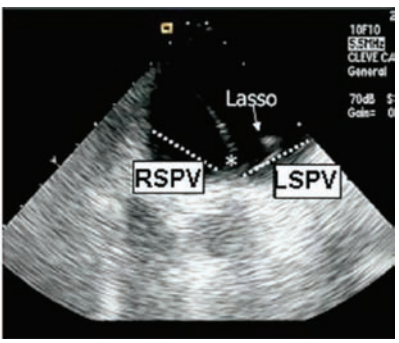


Figure 23.9 Electroanatomic map of the LA during flutter. Activation sequence shows a flutter circuit circulating around the mitral annulus. Ablation lesions were placed at the left (left inferior pulmonary vein and mitral annulus). However, when flutter persisted another line was created at the right mitral isthmus which terminated the flutter.

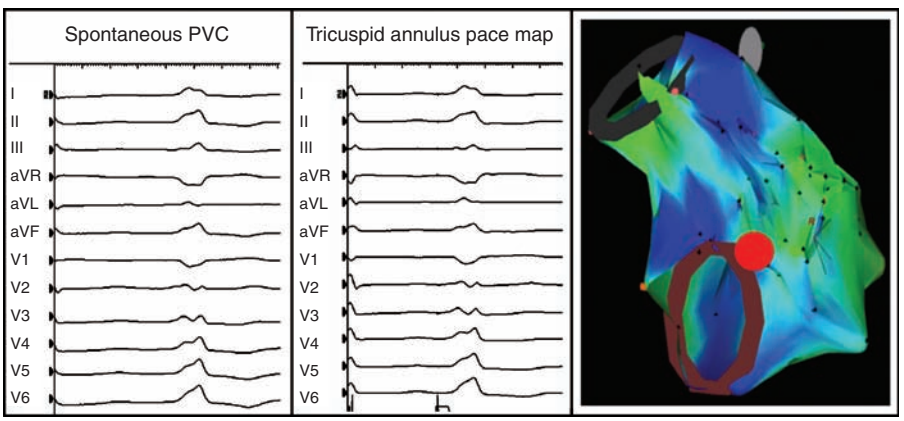


(a)



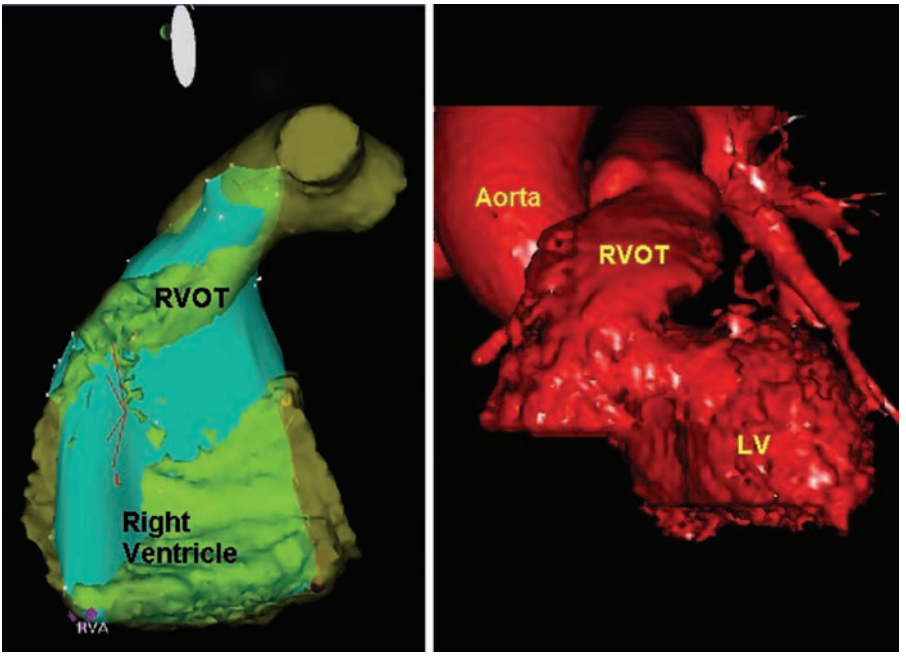
(b)

Figure 24.1 Anatomic definition of pulmonary vein ostium and antrum using three-dimensional CT imaging (a) and ICE (b). Note that the right and left pulmonary vein antra include the posterior wall of the left atrium.



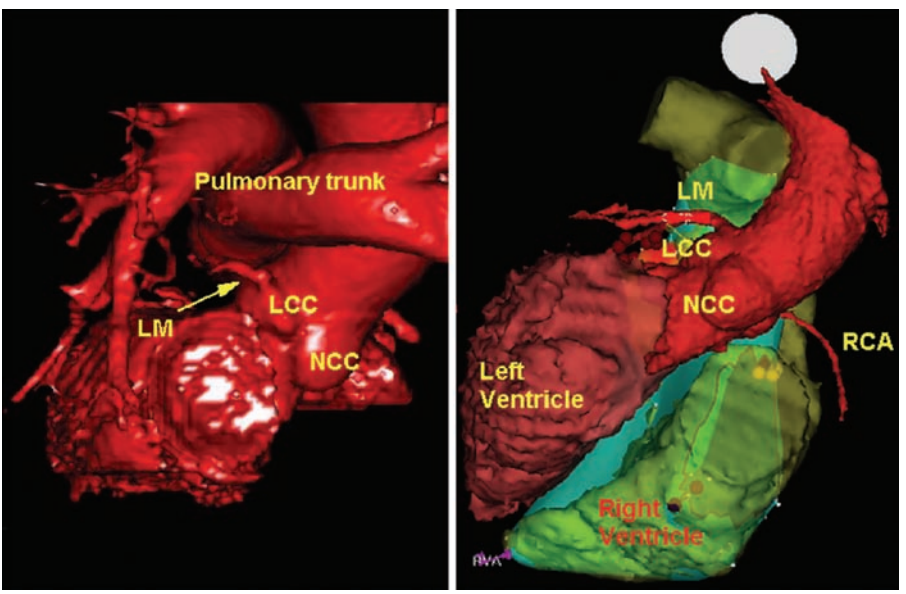
(a) (b) (c)

Figure 25.1 Premature ventricular complex originating from the tricuspid valve. (a) 12-lead ECG of the PVC. (b) Near perfect pace mapping along the anterosuperior aspect of the tricuspid valve. (c) CARTO image showing site of perfect pace map and successful ablation.



(a) (b)

Figure 25.3 **(a)** Left lateral view of CARTO-Merge and (b) antero-posterior projection of 3D reconstruction of the heart showing the posterior superior course of the RVOT.



(a) (b)

Figure 25.4 (a) PA view of the heart model generated by 3D reconstruction of cardiac CT. (b) PA CARTO-Merge view of the heart showing the RVOT in relation to the left main (LM) and the right coronary artery (RCA).

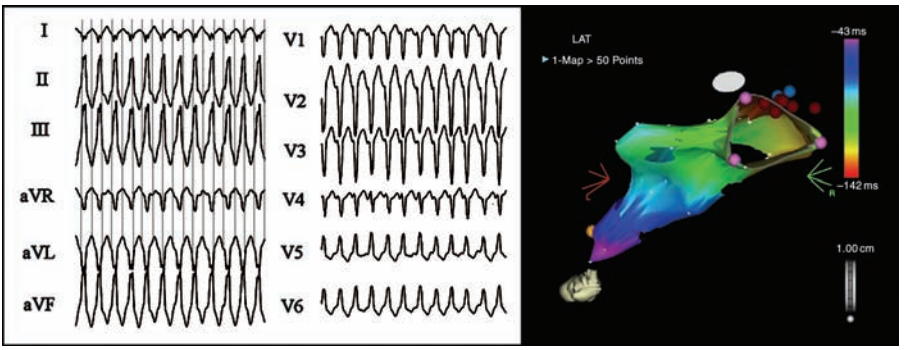


Figure 25.6 12-lead ECG and activation map using CARTO of the RVOT tachycardia.

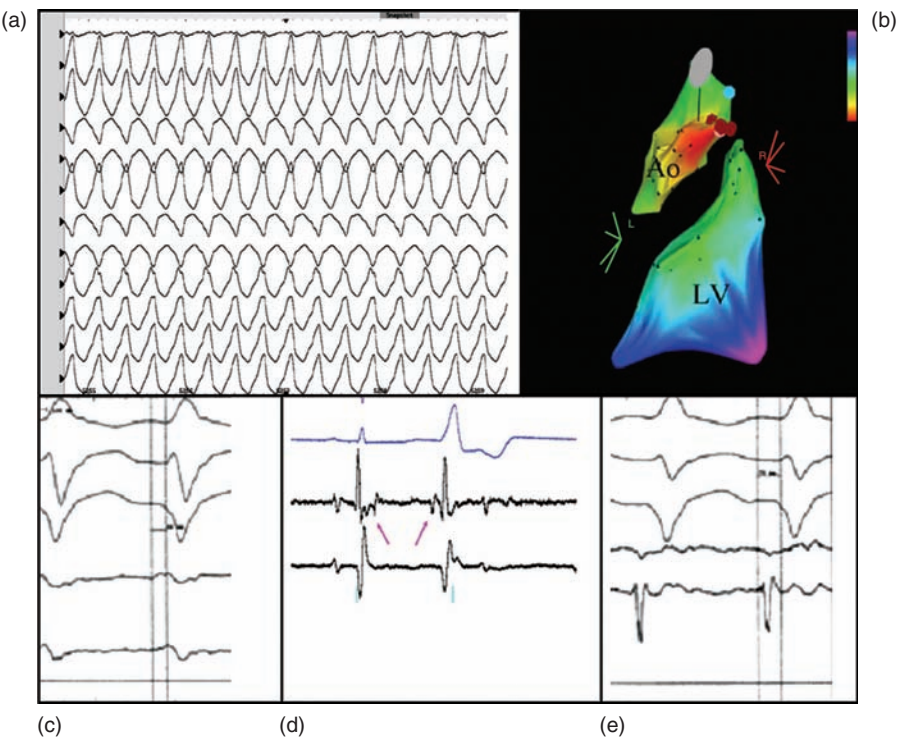


Figure 25.7 Left coronary cusp tachycardia. (a) 12-lead ECG during tachycardia. (b) Activation map using CARTO with earliest activation in the left coronary cusp. Ablation at this site resulted in termination of the tachycardia. Activation mapping of a left cusp ventricular tachycardia from a different patient with LCC ventricular tachycardia showing (c) far-field signal, (d) two-component EGM, and (e) earlier activation epicardially.

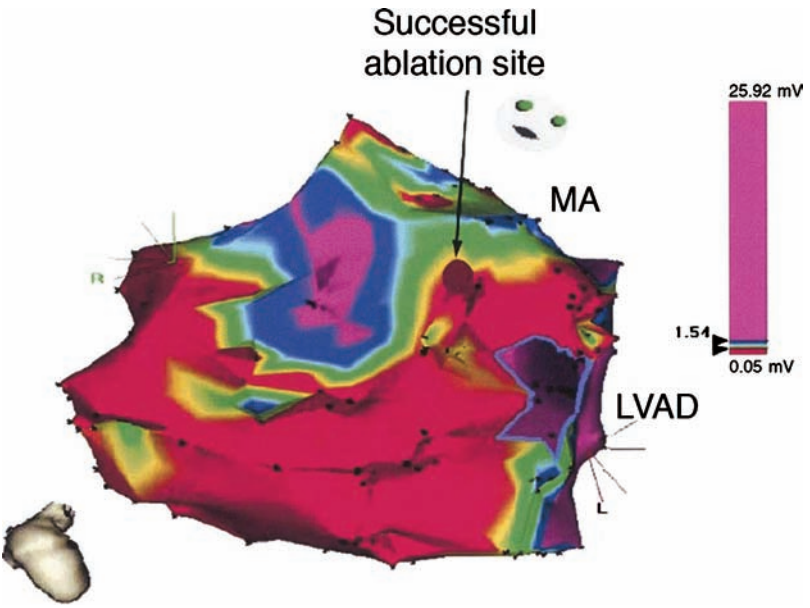


Figure 26.5 Three-dimensional CARTO map of LV in patient with VF storm ablation. Red regions represent scar, green and blue represent abnormal tissue in scar border zone, purple indicates normal voltage (>1.5 mV). Red circle denotes area where PVCs with Purkinje like potentials were mapped and successfully ablated. From Marrouche.[13]

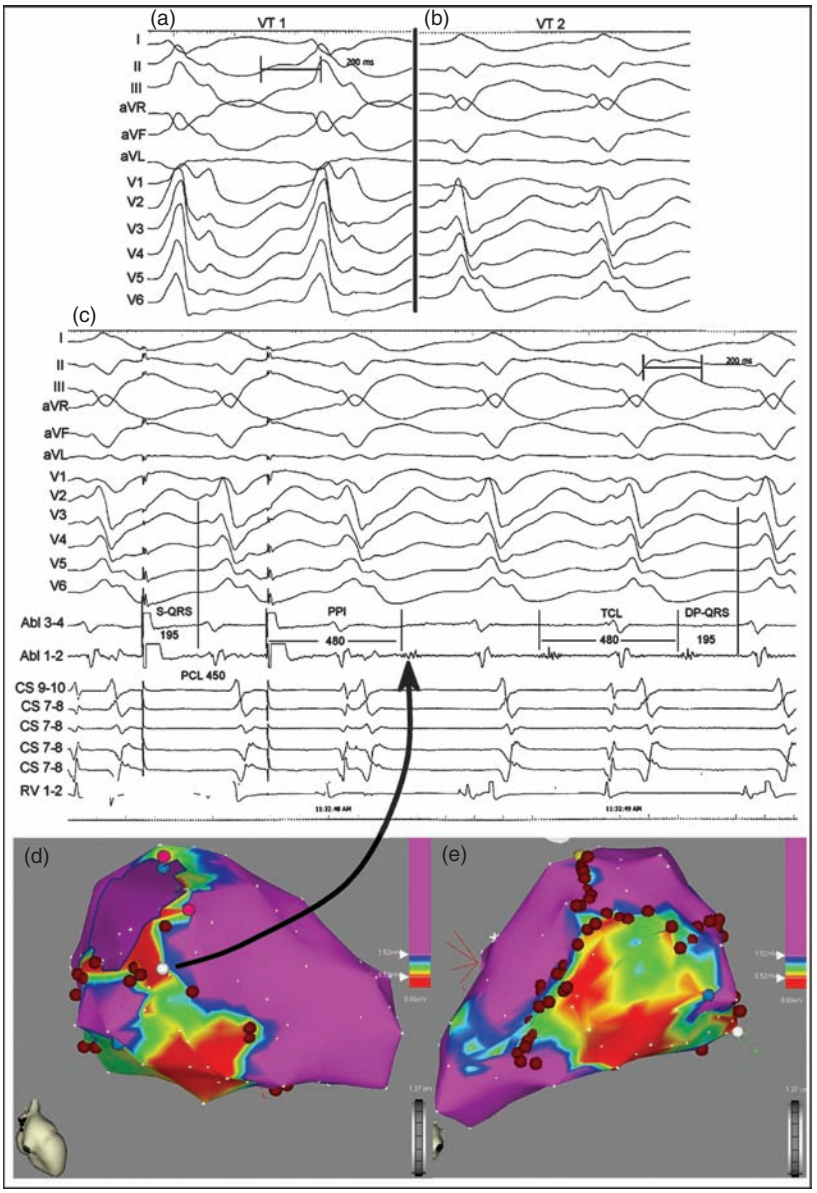


Figure 27.3 (a, b) 12-lead ECG morphologies of two induced VTs (VT2 clinical tachycardia). (c) Entrainment mapping of VT2. Note the mid-diastolic potential (MDP, arrow), recorded 195 ms before the onset of the QRS, was captured with the same stimulus to QRS (S-QRS) interval and 12-lead ECG morphology as the VT. The postpacing interval (PPI) was identical to the tachycardia cycle length (TCL), rendering this site a critical component of the VT re-entrant circuit. RF current delivery at this site terminated the VT which could no longer be re-induced. (d, e) Bipolar voltage LV mapping in sinus rhythm. Note the presence of significant scarring extending from the infero-septum to the postero-lateral LV. The white tag on the septal border of the scar (d) indicates the recording site of MDP and successful ablation. Additional RF was delivered (red tags) to connect the scar to the mitral annulus (MA). (e) The postero-lateral aspect of the scar. RF was delivered along the scar border all the way to the MA. VT 1: non-sustained, single induction. Following substrate modification no VTs could be induced.

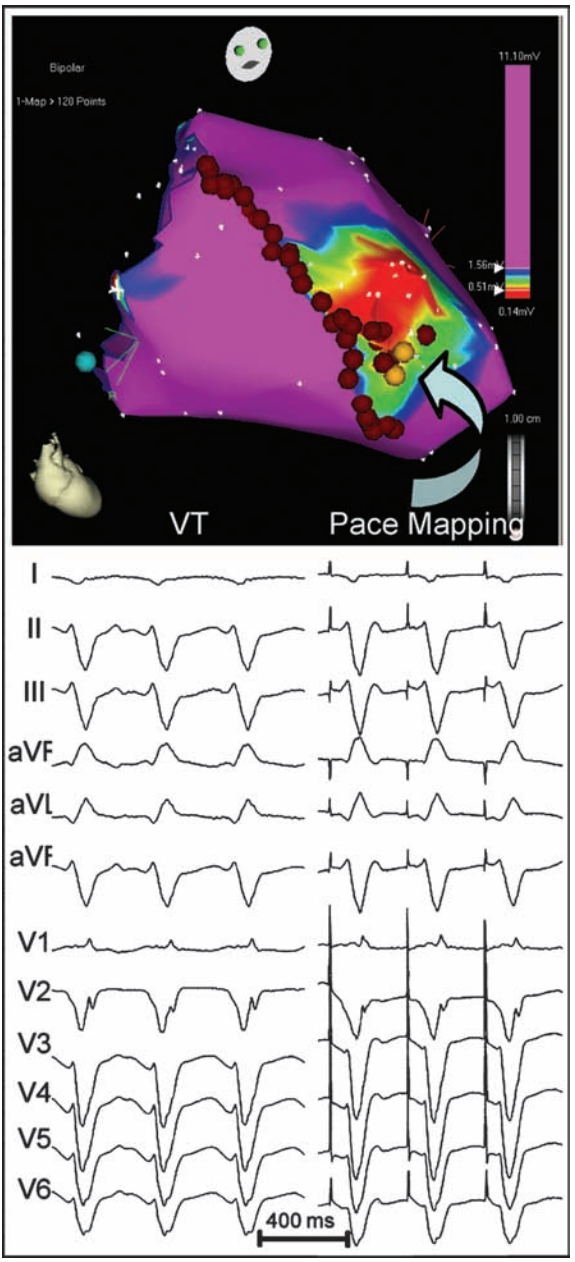


Figure 27.4 Top panel: voltage mapping in sinus rhythm showing a discrete antero-septal scar. Lower panel: 12-lead ECG morphology of VT (left) and during pace mapping (right) from a site near the scar border (golden tags, arrow) on the voltage map. Since the VT was not stable, ablation (red tags) target the site of near identical pace mapping. Scar substrate modification was achieved by ablation along the scar border from its apical aspect to the mitral annulus. This approach rendered the patient non-inducible.

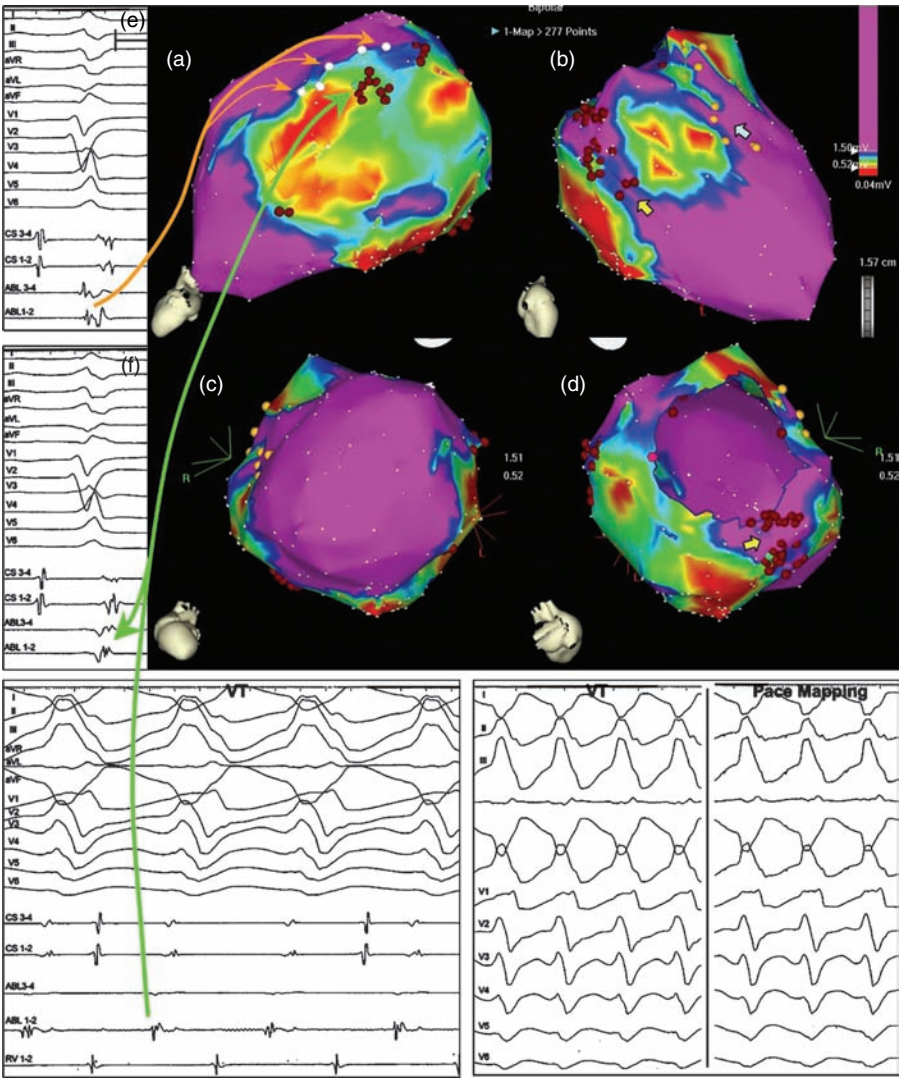


Figure 27.5 (a–d) Voltage mapping of the LV in sinus rhythm shown in the postero-lateral, septal, apical, and basal views, respectively. Note the extensive scarring and a residual channel approaching the infero-septal mitral annulus (yellow arrow, b, d). Sites exhibiting double (DP, e) or late potentials (LPs) during voltage mapping were tagged white (a). Note LPs in the coronary sinus recordings at the same region. The clinical VT was induced (bottom left). VT mapping, targeting the areas with DP, identified presystolic activation (green tag, a). Recordings at that site, upon VT termination, showed DP (f). Pace mapping at the same site (bottom right) reproduced the VT morphology. RF was delivered at that site (red tags), towards the mitral anulus and along the infero-septal isthmus (yellow arrow, b, d). No VTs could be re-induced. Golden tags (b, c, d) were sites with Purkinje potentials (posterior fascicle).

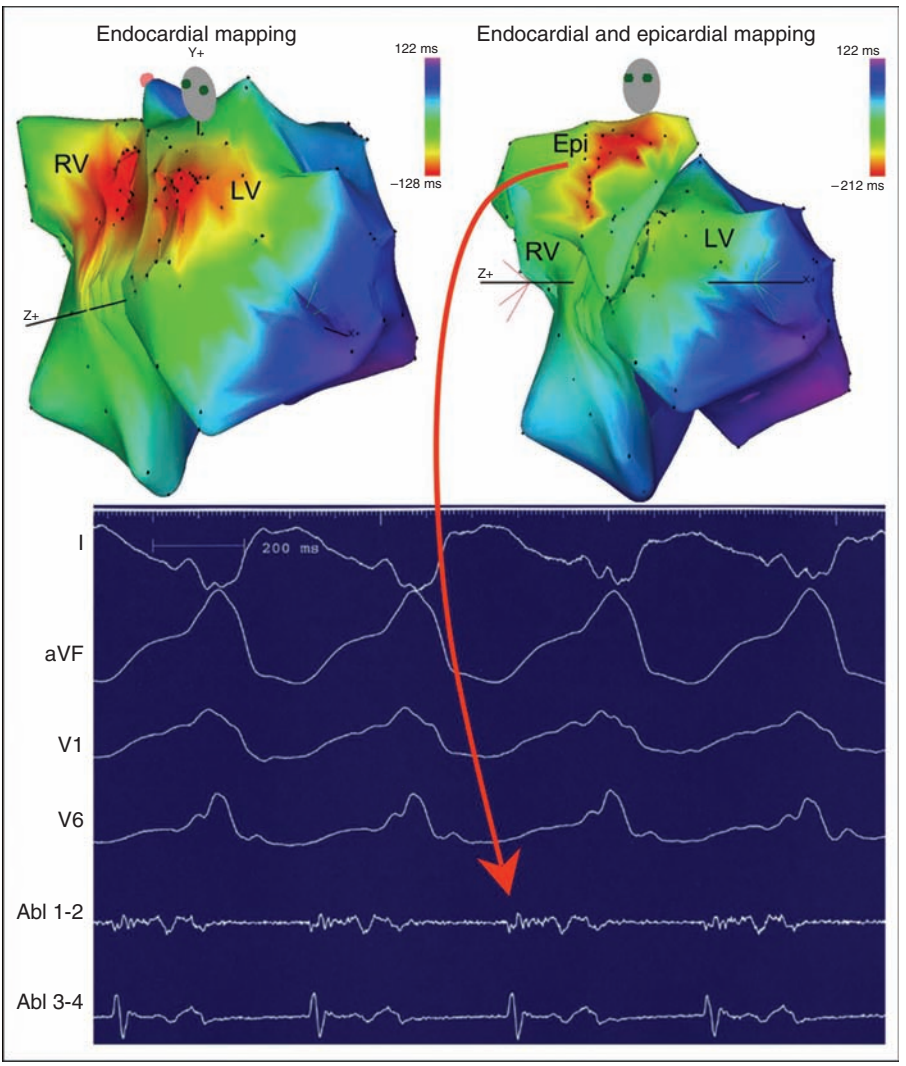


Figure 27.6 Top left panel: VT mapping showing equally earliest activation at the antero-septal aspect of both right and left ventricles. There was no significant scar during voltage mapping. Presystolic and mid diastolic potentials (bottom panel) could only be recorded during epicardial mapping (top right panel). The VT was successfully ablated from the epicardium.

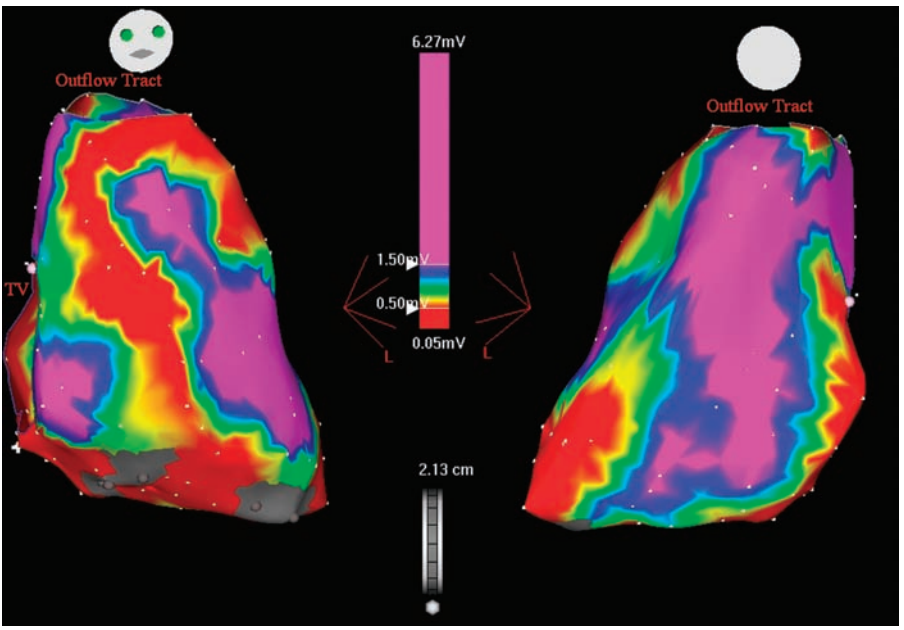


Figure 28.6 Electroanatomical map of the RV, in a patient with ARVD, in AP (left panel) and PA (right panel) views. Regions in red represent the scar (bipolar voltage $<$ 0.5mv, while purple regions are normal myocardium ($>$ 1.5 mv). Low voltage areas are seen mainly seen below the tricuspid valve and inferior wall, as well as areas in the anterolateral wall. Dense scar areas ($<$ 0.1 mv) on the inferior wall are tagged in grey color. Note that the septum seen in PA view is least affected.

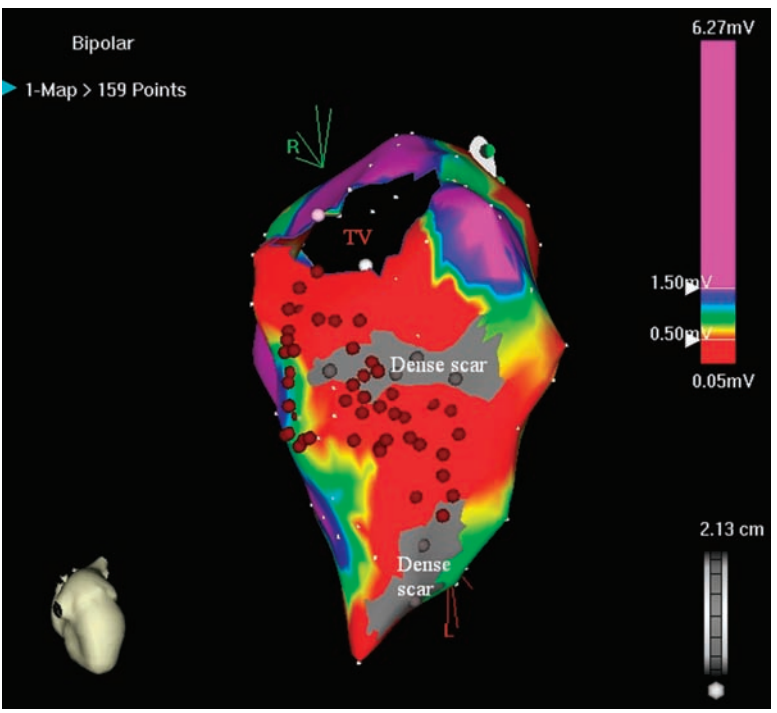
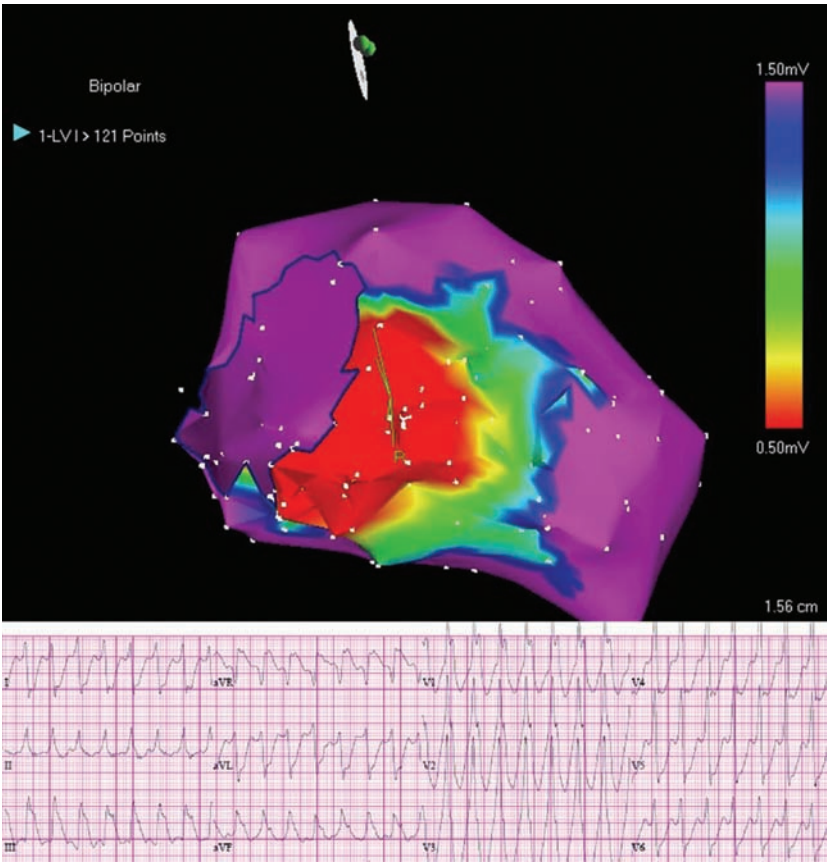
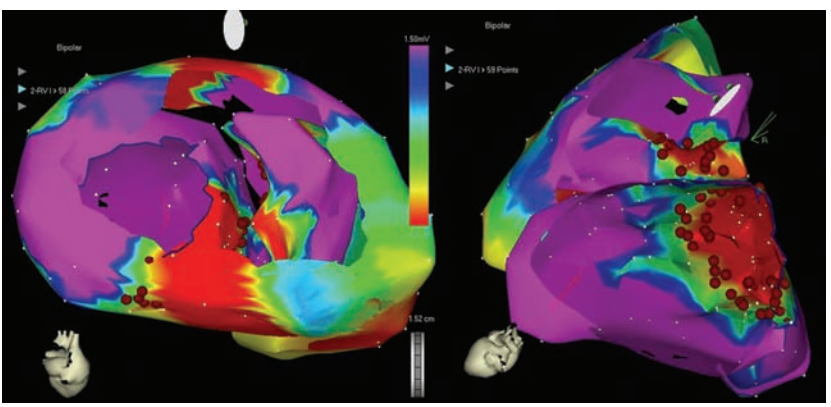


Figure 28.8 Caudal view of the RV inferior wall, showing the ablation strategy adopted in a patient with ARVD. Lines are created to connect the two dense scar areas, as well as to connect the scar with the Tricuspid valve abolishing all tachycardias.



(a)



(b)

Figure 29.6: (a) Voltage map of the LV showing a scar area near the septal mitral annulus. A 12-lead ECG showing one morphology of His tachycardia is seen, suggesting that its exit is at the upper border of the scar area. (b) As shown on the left panel, further mapping in the right ventricle revealed a scarred area at the septal side of the tricuspid valve as well as the outflow tract. A low voltage epicardial area corresponds to the underlying endocardial scar. The right panel is a clipped image of both ventricles to show the endocardial ablation areas surrounding the scar, and terminating all tachycardias.

Cardiac Electrophysiology

HANDBOOK OF

The first practical, user-friendly guide to the theory and practice of a routinely used technique, this new manual provides the specialist in training with a thorough grounding in the equipment, procedures and clinical findings with which clinicians need to be familiar.

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- a review of the main kinds of arrhythmia, with illustrations of typical ECG findings supported where appropriate by correlative imaging
- the principal diagnostic and therapeutic procedures, including implantation of pacemakers, resynchronization therapy, use and placement of catheters and ablation techniques.

Providing practical guidance on clinical applications, and illustrated with numerous graphics, checklists and flowcharts to enable readers to locate information quickly and easily, Handbook of Cardiac Electrophysiology is an accessible resource covering a widespread, but complex technology, and a must-have for the cardiac specialist in training.

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