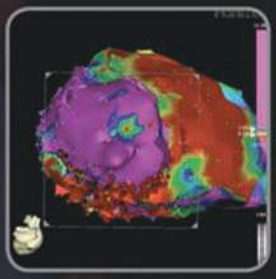
Ventricular Tachycardia/ Fibrillation Ablation



The state of the Art based on the VeniceChart International Consensus Document

Andrea Natale and Antonio Raviele

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THE STATE OF THE ART BASED ON THE VENICECHART INTERNATIONAL CONSENSUS DOCUMENT

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Preface

Sustained ventricular arrhythmias—ventricular tachycardia (VT) and ventricular fibrillation (VF)—are an important cause of morbidity and sudden death, especially in patients with structural heart disease. Therapeutic options for the treatment of these arrhythmias include antiarrhythmic drugs, implantable cardioverter defibrillators (ICDs), and surgical and catheter ablations. Antiarrhythmic drugs have disappointing efficacy and adverse side effects that may outweigh the benefits. ICDs effectively terminate VT/VF episodes and represent the mainstay therapy to prevent sudden death. However, ICD shocks are painful, reduce the quality of life, predict increased risk of death and heart failure. Catheter ablation, as therapeutic option for ventricular arrhythmias, has been first proposed in 1983. Since then, significant developments in ablation and mapping technologies have been made. The most relevant developments include the use of radiofrequency energy, introduction of steerable, large-tip, and irrigated catheters, activation and entrainment mapping, electroanatomic mapping with the possibility of performing substrate-based ablation during sinus rhythm, multielectrode mapping with the possibility of ablating hemodynamically unstable VT, and epicardial mapping and ablation. All these advances have contributed to improved outcomes and to a substantial expansion in the indications of catheter ablation of ventricular arrhythmias. Moreover, they have generated the need to standardize the different aspects of the procedure.

Inspired by this need, the organizers of VeniceArrhythmias 2009 have assembled world-recognized experts in the field of ventricular arrhythmias to develop an international consensus document on VT/VF ablation. In the present book, the work produced by the VeniceChart members is presented in detail. Practically, all the issues concerning VT/VF ablation are extensively treated in the 14 different chapters. The results are outstanding and the book may be considered a comprehensive and up-to-date overview of the topic. We are confident that the text will provide a highly valuable source of information not only for researchers and specialists in electrophysiology, but also for general cardiologists, internists, fellows in cardiology, and medical students.

We are deeply indebted to several colleagues who have contributed to the realization of the volume. Their names are reported in the list of contributors. Without their enthusiasm and personal effort, this book would not have been possible. We have also to recognize the professionalism of Kate Newell, Senior Development Editor of Wiley-Blackwell Publishing, who took care of the editorial aspects of the book. Furthermore, we wish to thank

Rita Reggiani, Raffaella Pieri, Angela Giacomello, and all the staff of Adria Congrex for their invaluable assistance. We also acknowledge the important contribution of our colleagues at the Ospedale dell'Angelo, Venice-Mestre, Italy, as well as at the Texas Cardiac Arrhythmia Institute, Austin, USA. In particular, we thank Aldo Bonso, David J. Burkhardt, Andrea Corrado, Antonio Rossillo, Javier E. Sánchez, and Sakis Themistoclakis. Finally, we could not have accomplished the goal of realizing this book without the constant support of our families. Our deepest appreciation and gratitude go to our wives, Carmen and Marina, for their patience, personal sacrifice, and continuous encouragement.

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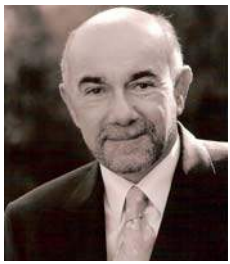

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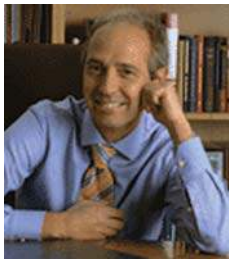

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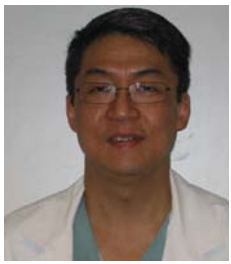

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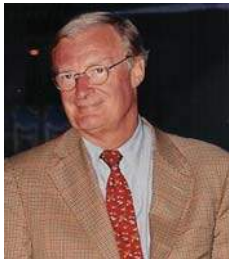

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CHAPTER 1

Epidemiology, Classification, and Clinical Impact of Ventricular Tachycardia/Ventricular Fibrillation

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Epidemiology of ventricular tachycardia and ventricular fibrillation

Ventricular arrhythmias can occur in both normal subjects as well as subjects with structural heart disease and can range from nonsustained brief runs of ventricular tachycardia (VT), to sustained VT or ventricular fibrillation (VF). The true incidence of ventricular arrhythmias in the overall population is not entirely known, as they may be nonsustained or asymptomatic. In addition, the inability to sample the electrocardiogram (ECG) continuously may limit the ability to determine a true incidence and the technique used to record the ECG may influence the results of epidemiological studies. Nonetheless, studies have examined ECG recordings in a variety of populations [1–6]. In healthy military recruits, premature ventricular contractions (PVCs) were seen on a standard 12-lead ECG in 0.8%; the rate was lower in younger individuals, and up to 2.2% in individuals over the age of 50 [1]. Another study examined middle-age men who underwent a 6-h cardiac monitor for ventricular arrhythmias. In this study there was a 62% incidence of asymptomatic PVCs; the incidence of PVCs was higher in patients with known or suspected heart disease [7]. Several studies have also examined the PVCs and

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nonsustained VT induced during exercise (or during recovery from exercise) and correlated this with an increased risk of mortality [5,6].

Ventricular arrhythmias can also manifest as sudden cardiac death (SCD) both in the normal population as well as in the population of individuals with structural heart disease. SCD is the most common manifestation of VF. It is worth noting that while the majority of SCD is because of ventricular arrhythmias, bradycardia and pulseless electrical activity play a minor role in SCD [8]. It is estimated that the incidence of SCD in the USA is between 200,000 and 400,000 deaths per year [9]. High-risk groups such as patients with left ventricular dysfunction may have a higher overall risk of SCD, but only represent a small proportion of patients with SCD [8]. The majority of SCD occurs in individuals with no known heart disease [8]. However, there is some uncertainty in the true estimate of SCD in the population. The wide range of estimates of SCD may be related to inclusion criteria used in individual studies. In addition, the definition of SCD has varied in some studies from 1 h or less to death that occurs within 24 h [10,11]. Death certificate data that have been used in some studies may also be limited [12,13]. An important problem is that in most studies nonwitnessed sudden deaths are not included. The incidence of SCD in the general population varies widely, ranging from 53 to 100 per 100,000 individuals, and may account for 5.6–18.5% of overall deaths [14]. The contribution of patients who may be at high risk for SCD, such as those with left ventricular dysfunction, to the overall incidence is not clearly known. A recent study by Stecker *et al.* [15] evaluated all cases of SCD in a large community cohort to determine the left ventricular ejection fraction (LVEF) among patients who had it measured prior to the SCD. In this study, 714 individuals (of the total population of 660,486) had SCD over a 2-year period. The LVEF was known in 121 individuals. Only 36 patients (30%) had a severely reduced ejection fraction, and 58 (48%) had a normal ejection fraction [15]. In addition, patients with a normal ejection fraction had a significantly lower incidence of prior coronary artery disease [15]. In higher-risk population, such as those with a prior myocardial infarction, the risk of ventricular arrhythmias is associated with the level of left ventricular dysfunction. A study that evaluated the home use of automated external defibrillators for sudden cardiac arrest demonstrated that in patients with prior myocardial infarction and an LVEF above 35%, the annual risk of SCD because of ventricular arrhythmias was less than 1% per year [16]. The risk of ventricular arrhythmias and SCD seems to be the highest during the first month after myocardial infarction, in particular among patients with lower ejection fractions and those with frequent ventricular premature complexes (VPCs) [17–21].

Risk factors

The most common etiology for SCD is coronary artery disease. Therefore, risk factors for coronary artery disease are also felt to be risk factors for SCD. The risk of SCD increases with advancing age [22]. Estimates from

the Framingham Study show a peak risk in men aged 55–64 years [22]. In Multnomah County, Oregon, only 25% of all SCD occurred at an age less than 65 years [14]. In women, a similar increase in incidence with age is seen. In the Nurses Health Study, the risk of SCD increased markedly with advancing age [23]. Gender differences are also seen with SCD occurring more commonly in men. This is likely related to the higher incidence of coronary artery disease in men as compared to premenopausal women [14,22]. The presence of coronary heart disease risk factors in women strongly predicts the risk of SCD [23]. Population studies have also identified an increased risk of SCD among first-degree relatives of SCD victims [24–26]. In the Paris Prospective Study, 7746 men were followed for an average of 23 years; 1.5% died suddenly, accounting for 19.6% of cardiovascular deaths. Parental history of SCD was an independent predictor of SCD in the offspring. When both parents were affected, the risk increased by 80% [27]. Race has also been implicated as a risk factor for SCD, with African-Americans having a higher incidence of SCD [28–30]. In a large study of SCD in Chicago, African-Americans were found to have a higher incidence of SCD as compared to Caucasians [28]. It is unclear if these racial disparities are the result of genetic differences, differences in the access to care, or differences in the environment. SCD has also been linked to cigarette smoking, obesity, and significant psychological stress [23,31–34].

Trends over time

Over the past several decades, there has been a clear decrease in the incidence of ventricular arrhythmias causing SCD [35–37]. Data from the Framingham Study reveal that the age-adjusted risk of SCD has decreased by 49% during 1990–1999 as compared to the years 1950–1969 [35]. This is undoubtedly because of improved treatment of coronary artery disease [38–41]. In particular, the introduction of medications such as beta-blockers and angiotensin-converting enzyme inhibitors has decreased the incidence of ventricular arrhythmias in high-risk populations [40,41]. Other therapies such as statins have been shown to decrease overall mortality, but not the incidence of VT/VF in a population of patients with left ventricular dysfunction [42,43].

While the overall incidence of SCD as a result of ventricular arrhythmias seems to be decreasing in the population of patients with coronary disease, there appears to be no significant change in the risk of SCD because of ventricular arrhythmias among patients with nonischemic heart disease. In a population-based study in Rochester, Minnesota, between 1991 and 2004, the incidence of SCD in individuals with ischemic heart disease decreased from 134 per 100,000 between years 1991 and 1994 to 55 per 100,000 between years 2000 and 2004. In contrast, in individuals with no ischemic heart disease the incidence increased over the same period of time from 21 per 100,000 to 29 per 100,000 [36].

A better understanding of risk factors for ventricular arrhythmias and SCD may help lead to improved prevention strategies.

Classification of ventricular tachycardia and ventricular fibrillation

Impulse formation (enhanced automaticity, triggered activity) and impulse conduction (reentry) are the mechanisms for isolated VPCs or nonsustained or sustained VT. Automaticity is the property of spontaneous phase 4 activity and is not seen in normal working myocardial fibers. Although automaticity is a normal property of Purkinje fibers, it is usually manifested as an escape rhythm. Enhanced automaticity from these normal fibers may be produced by catecholamines. Automaticity from *damaged* Purkinje fibers or ventricular muscle has been suggested as a mechanism for some catecholamine-sensitive VPCs or VTs [44]. The extent of damage produces depolarization that can lead to either Na- or Ca-dependent automaticity. Such rhythms can neither be initiated nor be terminated by programmed stimulation.

Triggered activity arises from oscillations in membrane potential during (early afterdepolarizations) or following (delayed afterdepolarizations) an action potential [45]. Experimental evidence implicates early afterdepolarizations in the initiation of VPCs and polymorphic tachycardias in the long QT syndromes. Delayed afterdepolarizations can be caused by intracellular calcium overload, which activates the Na^{+}/Ca^{++} exchanger resulting in the transient inward current, Iti. Factors that increase intracellular calcium include increases in heart rate, beta-adrenergic stimulation, and digitalis. Beta-adrenergic effects are mediated through a cAMP-induced increase in intracellular calcium, and are antagonized by adenosine, which effects a decrease in cAMP. This mechanism often results in isolated VPCs (e.g., RVOT) or repetitive runs of VT [43,46].

Reentry requires (1) two or more potential pathways of activation; (2) unidirectional conduction block in one (or more); (3) slow conduction to allow the initial site of block time to recover and be re-excited to complete a reentrant circuit. Unidirectional conduction block may occur after a properly timed extra-beat or enhanced sinus rate, and is probably functional rather than fixed in most instances [47,48]. However, regions of conduction block can be anatomically fixed such that they are present during tachycardia and sinus rhythm; dense, non-excitable fibrosis or valve annuli create these types of anatomic boundaries for reentry [49]. Slow conduction may be caused by a decrease in sodium channel activity, but most importantly zigzag conduction is produced by separation of myocytes by fibrosis and connexin disarray [50].

Classification according to the duration of ventricular arrhythmias

Ventricular premature complexes are isolated complexes originating from the His-Purkinje system (HPS) or ventricular myocardium. When arising proximally in the HPS (i.e., close to the His bundle), the complexes look

more like aberrancy, and when they arise distally, they look more ventricular (i.e., wider, atypical patterns for aberration). VPCs may occur as isolated phenomena or appear in bigeminal or other patterns. If they appear at a multiple of cycle lengths, they are said to be parasystolic; such rhythms are because of an automatic focus. Very shortly coupled VPCs (on ascending limb of the T wave) can initiate VF in otherwise healthy people and is one type of idiopathic VF [51,52].

Ventricular tachycardia (VT) is a term applied to ≥3 consecutive QRS complexes at a rate greater than 100 beats per minute (bpm).

Nonsustained VT terminates spontaneously within 30 s.

Sustained VT is defined as continuous VT lasting for ≥30 s or that requires an intervention for termination (such as cardioversion).

Classification according to QRS morphologies

Monomorphic VT has a similar QRS configuration from beat to beat. Some variability in QRS morphology at initiation is not uncommon, followed by stabilization of the QRS morphology. Right bundle branch block (RBBB)- and left bundle branch block (LBBB)-like VT configurations are terms used to describe the dominant deflection in V1, with a dominant R wave described as "RBBB-like" and a dominant S wave as "LBBB-like" configuration [53]. This terminology is potentially misleading, as the VT may not show features characteristic of the same bundle branch block-like morphology in other leads. While virtually all VT (or VPCs) with a "RBBB"-like pattern arise in the left ventricle only, VTs (or VPCs) with "LBBB"-like morphology can arise in either the left or the right ventricle. In the presence of prior infarction, VTs with a "LBBB"-like pattern virtually always arise on or adjacent to the LV septum. In patients without structural heart disease, QRS complexes tend to be smooth and tall. With scarring of any etiology, the QRS complexes have lower amplitudes and are broader. Notching of the QRS is a sign of scar. QS complexes, other than in aVR, suggest the wavefront is moving away from the recording site, but does not necessarily mean scar/infarct; however, qR or QR complexes in anatomically adjacent sites typically is a sign of infarction. Patients without structural heart disease usually exhibit a single-VT morphology, while in patients with significant structural heart disease multiple VTs are common [54–56].

Multiple monomorphic VT refers to more than one morphologically distinct monomorphic VT, occurring as different episodes or induced at different times. This usually occurs in patients with significant scars (e.g., prior infarct, cardiomyopathy).

Polymorphic VT has a continuously changing QRS configuration from beat to beat, indicating a changing ventricular activation sequence. This may occur as part of the long QT syndrome or other channelopathies, or may be because of reentry in a patient with structural heart disease. The "polymorphic" nature does not define an arrhythmia mechanism.

Pleomorphic VT has more than one morphologically distinct QRS complex occurring during the same episode of VT, but the QRS is not continuously changing. This is most commonly seen in patients with prior infarction and large scars.

Ventricular flutter is a term applied to rapid VT that has a sinusoidal QRS configuration that prevents identification of the QRS morphology. It is preferable to avoid this term, in favor of monomorphic VT with indeterminate QRS morphology.

Ventricular fibrillation (VF) is applied to a ventricular tachyarrhythmia, which has a totally chaotic morphology. The distinction between VF and polymorphic VT may be difficult, but the absence of a QRS that can have a specific morphology applied to it is characteristic of VF. This most often occurs in the setting of structural heart disease, most commonly prior myocardial infarction, but may be seen in otherwise healthy people as a consequence of an ion channelopathy; that is, long QT and short QT syndrome, Brugada syndrome, ryanodine receptor, and calsequestrin mutations, etc. (see subsequent discussions).

Classification according to clinical characteristics of ventricular tachycardia

Clinical VT is a VT that has occurred spontaneously based on the analysis of 12-lead ECG QRS morphology and rate.

Hemodynamically unstable VT is a VT that causes hemodynamic compromise requiring prompt termination.

Incessant VT is continuous sustained VT that recurs immediately despite repeated spontaneous or therapeutic termination.

Repetitive monomorphic VT is defined as continuously repeating episodes of self-terminating nonsustained VT.

VT storm is considered three or more separate episodes of sustained VT within 24 h, each requiring termination by an intervention.

Unmappable VT is a VT that does not allow interrogation of multiple sites to define the activation sequence or perform entrainment mapping and may be because of: hemodynamic intolerance that necessitates immediate VT termination, spontaneous or pacing-induced transition to other morphologies of VT, or repeated termination during mapping.

Conditions associated with ventricular tachycardia/ventricular fibrillation

While PVCs and even runs of nonsustained VT may be frequently seen in people with normal and abnormal hearts, sustained VT and VF usually develop in patients with advanced structural heart disease with the exception of a few patients with various forms of idiopathic VT or VF related to molecular cardiomyopathies, such as congenital short or long QT and Brugada syndrome, covered elsewhere. PVCs in patients without demonstrable structural heart disease are of controversial prognostic significance [9]. Frequent PVCs and

runs of nonsustained VT during exercise may represent a trait implicating an increased mortality risk at least for the population customarily undergoing stress testing. Frequent PVCs in the recovery phase after an exercise test are stronger predictors of mortality than ventricular extrasystoles during exercise [6]. For several decades during the 20th century, frequent and complex VPBs and runs of nonsustained VT in patients with structural heart disease in general, and coronary artery disease in particular, especially if associated with a reduced LVEF, were considered a very ominous sign predicting an increased risk for total mortality and SCD. These data were probably contaminated by the frequent use in those days of class I antiarrhythmic drugs in these patients and the exceptional use of beta-blockers in the presence of an LVEF ≤35%. The CAST study stopped the practice of using class I drugs in patients with coronary artery disease and systolic dysfunction and most cardiologists also refrained from using these agents in patients with a depressed LVEF of other etiologies [57]. There are not good contemporary studies evaluating the meaning of PVCs and runs of nonsustained VT at rest and during or after exercise in patients with systolic heart failure that are receiving an optimal medical treatment including diuretics, ACE inhibitors of angiotensin receptor blocker drugs, beta-blocking agents, and eventually antialdosterone medication. Although one investigation in patients with heart failure and very depressed LVEF has found that ventricular ectopy is of no prognostic significance, other study has shown that postexercise severe ventricular ectopy (triplets, nonsustained VT, sustained VT, or sustained VF) predicts an increased mortality in systolic heart failure patients [58,59].

Coronary heart disease as the most frequent cause of ventricular tachycardia/ventricular fibrillation and sudden cardiac death

Coronary heart disease is the most frequent cause of SCD and clinically documented VT and VF. In the CASCADE study, 82% of the patients resuscitated from an out-of-hospital cardiac arrest in Seattle had coronary heart disease [60]. In the CASH trial, another study in patients resuscitated from an out-of-hospital cardiac arrest conducted in the Hamburg area, 76% of the patients had an underlying coronary heart disease [61]. The AVID and CIDS trials recruiting patients with clinically significant and potentially lethal VT, and to a lesser extent patients resuscitated from a cardiac arrest, showed that a coronary heart disease was the underlying structural heart disease in more than 80% of the patients [61–63].

Natural history of patients with sustained ventricular arrhythmias and ischemic and nonischemic cardiomyopathy

This is not an issue with a simple answer. Conventional teaching and guidelines indicate that patients with systolic LV dysfunction of any etiology resuscitated

from a cardiac arrest or developing hemodynamically unstable VT have a poor prognosis with conventional medical treatment and must receive an Implantable Cardioventer Defibrillator (ICD) [9]. This recommendation is based on the so-called secondary ICD prevention trials AVID, CIDS, and CASH [61–63]. It is beyond the scope of this study to critically examine the soundness of this recommendation. To mention simple items we should keep in mind: (a) that only the AVID trial demonstrated a statistically significant benefit of the ICD in the recruited population [62]; (b) that the group that theoretically should benefit most from this therapy, namely patients resuscitated from an out-of-hospital cardiac arrest, did not show a statistically significant benefit from the ICD [61]; (c) that only patients with an LVEF <35% did better with the ICD as compared to amiodarone [64,65]; and (d) that not all kinds of patients recruited in these three trials benefit from an ICD [65,66].

Even more complex is the definition of the natural history and the most appropriate therapy in patients with systolic ventricular dysfunction and stable, well-tolerated, recurrent, sustained VT. Readers are referred to a very well discussed and profusely referenced controversy recently published in *Circulation* by Callans [67], and Almendral and Josephson [68]. The fact of developing a sustained stable VT does not cancel other risk traits existing in these patients, namely the degree of LV dysfunction, a history of heart failure, and the ischemic nature of the myocardial damage, when these risk factors are present. In other words, should a patient be a candidate to an ICD under primary prevention criteria, there is no reason to neglect the device even if the stable VT has been successfully ablated. However, as stated, this issue is very complex and good-quality evidences are lacking.

Mechanisms of ventricular arrhythmias in ischemic cardiomyopathy

There are three major mechanisms by which an ischemic heart disease can cause SCD because of lethal ventricular arrhythmias: (a) ischemia-induced electrical instability leading to fast VT or VF; (b) macro-reentry in relation to a postinfarction scar in a remodeled left ventricle; and (c) bundle branch reentry usually in patients with intraventricular conduction defects and a dilated (remodeled) left ventricle.

Spaulding *et al.* [69] from Paris, France, demonstrated that there were signs of an acute coronary artery occlusion in 48% of 81 patients resuscitated from an out-of-hospital cardiac arrest undergoing an immediate coronary arteriogram. Clinical and electrocardiographic findings were poor predictors of acute coronary artery occlusion. Therefore, an acute coronary syndrome may result in electrical ventricular instability leading to very fast VT or VF. At the other end of the spectrum, there are patients with chronic coronary heart disease, usually with a postmyocardial infarction scar and remodeled left ventricles that develop sustained VT or VF. While acute ischemia might also produce arrhythmic sudden death in these patients, most of the times

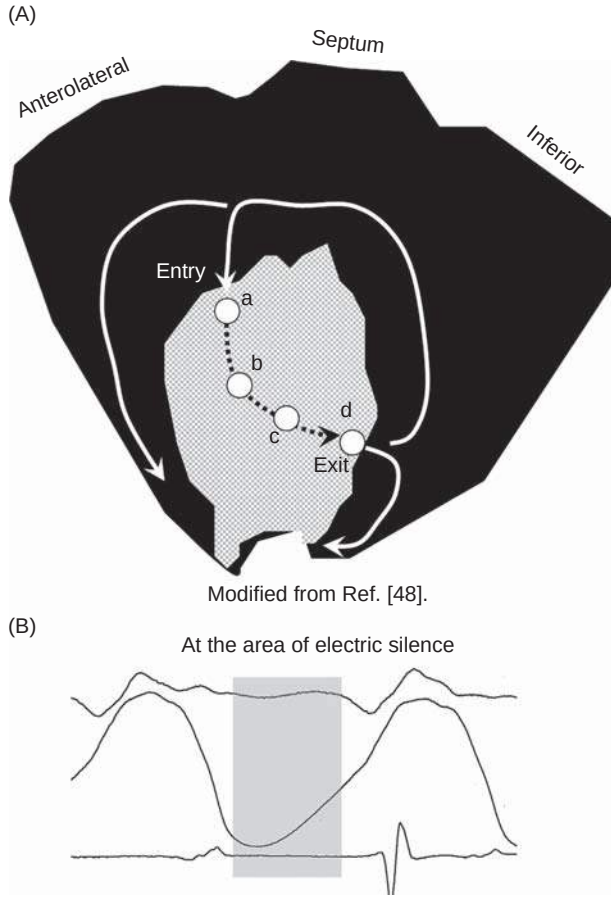


Figure 1.1 Panel A represents the endocardial surface of an opened left ventricle (black) with a postmyocardial infarction scar (gray). Inside the scar there is a bridge of surviving myocardial fibers that connect two sides of the scar so that a reentry pathway can be established. The excitation wavefront exits the scar at "d" from which point it activates the ventricular myocardium entering the scar at "a." The slow conduction arm of the reentry pathway is the bridge of intrascar surviving myocardium (from "a" to "d"). The activation from "a" to "d" takes place during a period of apparent electrical silence in the surface electrocardiogram (ECG) (panel B).

the occurrence of ventricular arrhythmias and particularly the development of sustained monomorphic VT is a result of the existence of an anatomically determined substrate.

de Bakker *et al.* [48,70,71], in The Netherlands, demonstrated in a series of very elegant papers that in postinfarction VT there are bridges of surviving myocardial cells connecting opposite borders of the scar serving as the slow pathway of a figure-of-eight macro-reentrant mechanism (Figure 1.1). Reentry around the scar was found to be rare in these studies. With detailed

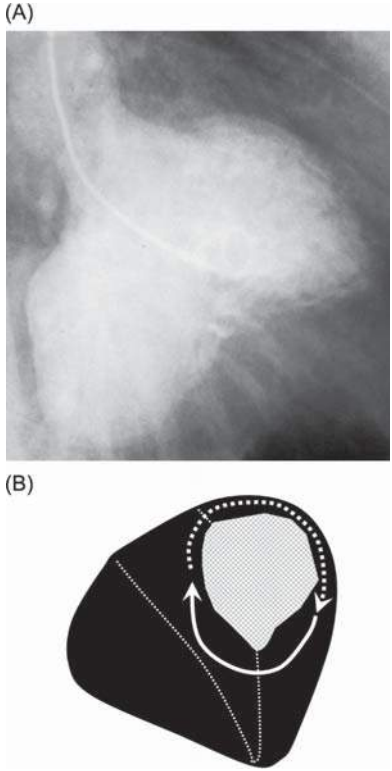


Figure 1.2 Inferior wall basal postmyocardial infarction aneurysm in a patient with recurrent sustained ventricular tachycardia (VT) (panel A). In this patient, the mechanism of VT was a macro-reentry utilizing the isthmus between the submitral border of the aneurysm and the mitral annulus (panel B).

intraoperative endocardial mapping they were able to demonstrate during VT that between the end of a QRS complex and the beginning of the next ventricular activation (a zone of apparent electrical silence) it was possible to follow the pathway of activation within the scar. This group of investigators also performed mapping and histologic studies on Langendorff-perfused human postinfarction hearts from patients undergoing a heart transplant and demonstrated that between the site of latest activation of one VT cycle and the site of earliest activation of the next cycle there were zones of viable myocardial tissue [70]. The group of Josephson while in Philadelphia demonstrated that in patients with VT and a postinfarction inferior wall aneurysm the isthmus between the mitral valve and the scar is a critical component of the reentrant circuit (Figure 1.2) [72]. All these studies proved to be of seminal value in the development of ablation techniques for postinfarction VT.

Not infrequently patients with postinfarction VT may develop, either during an electrophysiological study or in the real life, two or more, morphologically different forms of VT that are usually called pleo- or polymorphic VTs (Figure 1.3). These morphologically distinct VTs can be because of (1) a single reentry circuit used in one or in the opposite direction, or (2) the existence of a common intrascar bridge of surviving myocardium connecting with two

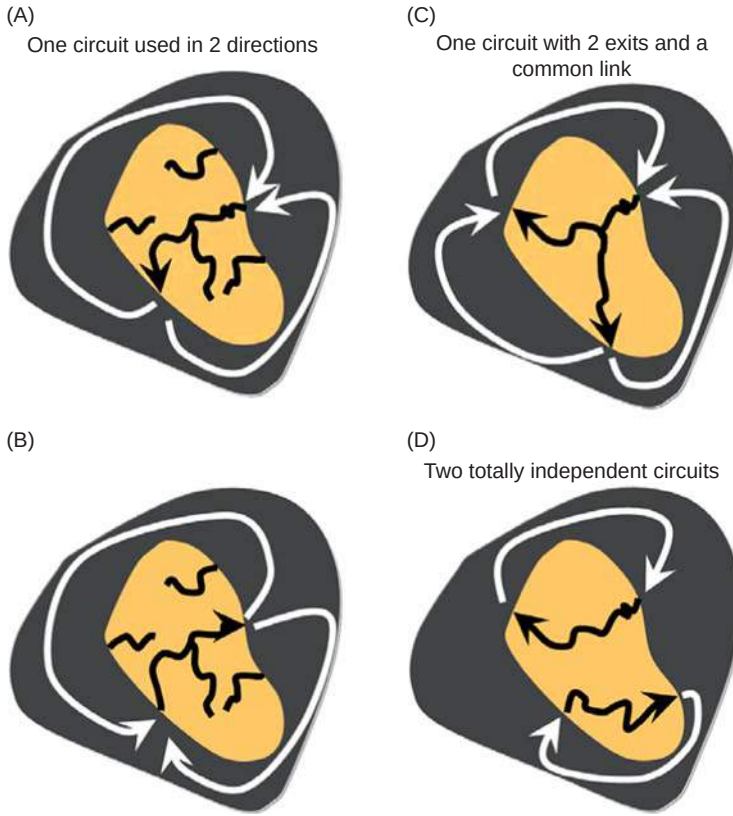


Figure 1.3 Schematic representation of the mechanisms of pleomorphic ventricular tachycardia (VT) in patients with postmyocardial infarction VT. Panels A and B represent the situation in which the same circuit can be used in two opposite directions giving rise to two totally distinct VT morphologies. This situation can be compared to the orthodromic and antidromic Atrioventricular reentry tachycardia (AVRT) in patients with an accessory pathway. Panel C illustrates the situation in which there are two morphologically different VTs because an initial common link is connected with two branches exiting the scar at distant left ventricular myocardial sites. Panel D shows two morphologically different VTs because there are two different bridges of intrascar surviving myocardial bundles well apart in the infarcted area.

different branches that have separate exits at the other side of the scar, or (3) the existence of more than one intrascar bridge. Additionally, some patients with pleomorphic VT may also have bundle branch reentry or a circus movement around the scar as the mechanisms responsible for one of the morphologies in addition to the usual intrascar macro-reentry VT. The intrascar bridges of surviving myocardium can have subendocardial segments that are amenable to endocardial catheter ablation techniques, but they can also be intramyocardial and epicardial. In the latter instances, ablation needs to be performed via a pericardial puncture to access to the epicardial intrascar link of the macro-reentrant pathway [73].

Mechanisms of ventricular arrhythmias in nonischemic dilated cardiomyopathy

The electrophysiological mechanisms of VT in patients with dilated cardiomyopathy (DCM) have created some controversy. Intraoperative mapping studies in patients with idiopathic DCM undergoing cardiac transplantation concluded that these VTs arise from subendocardial or subepicardial sites and were thought to be a result of a focal mechanism on the basis of the absence of intervening electrical activity between the offset and the onset of two consecutive QRS complexes of the VT [74]. In spite of the aforementioned claims of a frequent focal origin of VT associated with nonishemic DCM, most of these arrhythmias are probably because of scar-related intramyocardial reentry [75]. Soejima *et al.* at Stevenson's laboratory in Boston, using endocardial and eventually epicardial electroanatomical mapping in 28 patients with VT and DCM, found that the arrhythmia was the result of myocardial reentry associated with scar tissue in 79% of the instances, had a focal origin in 17% of the patients, and was caused by bundle branch reentry in 2 patients (7%). More than 60% of endocardial scars were adjacent to a valve annulus, deep in the endocardium, and the circuit could be greater in extent on the epicardium than on the endocardium [76]. Midwall fibrosis in MR imaging studies has been found to predict SCD or VT in DCM patients independently of the degree of left ventricular dysfunction and dilation [77]. In patients with nonischemic DCM, an LVEF $\leq$35%, and a history of heart failure, the presence of late gadolinium enhancement increased by a factor of 8 the risk of experiencing a composite outcome of hospitalization for heart failure, appropriate ICD firing, and cardiac death. The presence of late gadolinium enhancement predicts ICD firings or cardiac death alone in this study as well [78].

Bundle branch reentry can also be responsible for sustained recurrent VT in DCM. Although bundle branch reentry is claimed to be responsible for 30–40% of the sustained monomorphic VTs developing in patients with DCM [75], this figure is probably an overestimation of the actual contribution of this mechanism to VT in this patient population. The matter of the fact is that bundle branch reentry is observed in patients with DCM, intraventricular conduction defects, and very dilated ventricular cavities (the left but frequently the right ventricle as well). Some patients with electrocardiographically "normal" intraventricular conduction but with prolonged HV times (because of concordant right and left bundle branch conduction defects) and dilated ventricles can also develop bundle branch reentry VT. Bundle branch reentry VT should be suspected in patients developing a sustained VT whose QRS complexes are identical in configuration to the ventricular depolarizations during sinus rhythm. In spite of the fact that the circuit responsible for bundle branch reentry is present in all hearts, this form of VT rarely develops because in normal circumstances the circuit is so small and the conduction velocities are so fast that the activation head collides with the tail of refractoriness (Figure 1.4). It is only when the ventricles are dilated and there is

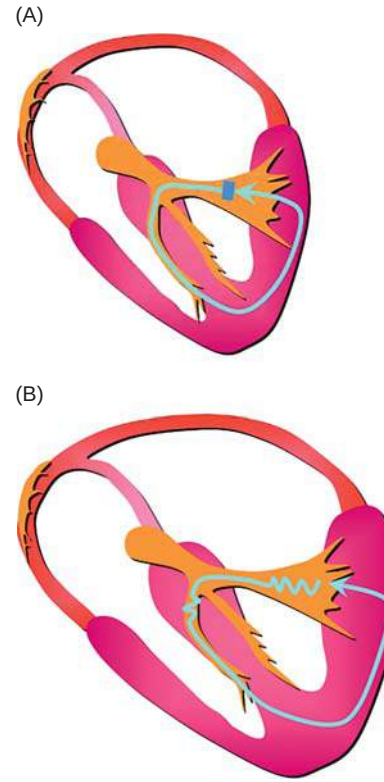


Figure 1.4 Panel A shows that in normal hearts, bundle branch reentry cannot be initiated in spite of the existence of the circuit because the wavelength is shorter than the duration of the refractory period in the reentry loop. In other words, the circuit is too small and the conduction velocities too fast to accommodate the reentry pathway so that the activation head collides with the tail of refractoriness. In panel B, the ventricles are dilated and it is postulated that there is slow conduction at certain sites in the intraventricular bundle branch system. Both circumstances play a role in accommodating the reentry activation front within the circuit so that the excitation head does not find, during its course, tissue that is refractory.

slow conduction within the bundle branches that the reentry loop can be accommodated in this circuit and the excitation head does not find during its course the tissue that is refractory.

Impact of sudden cardiac death in the natural history of ischemic and nonischemic dilated cardiomyopathy with a history of heart failure

In patients with systolic ventricular dysfunction, especially in those with a history of congestive heart failure, SCD competes with end-stage refractory decompensated heart failure to be finally responsible for the patient's death. SCD may not always be arrhythmic [9]. The contribution of sudden death to total mortality in patients with heart failure and systolic left ventricular dysfunction has varied in various trials, most likely in relation with the severity of the heart failure. Thus, in the metoprolol arm of the MERIT-HF trial in which 97% of the patients were in NYHA functional classes II and III, SCD represented 53% of the total mortality [79]. In the bisoprolol arm of the

CIBIS-II trial in which 83% of the patients were in NYHA class III and 17% in class IV, SCD represented 31% of the total mortality [80]. In the carvedilol arm of the COPERNICUS trial recruiting patients in NYHA class IV, SCD was only responsible for 14% of the total mortality [81]. With this information in mind, the expectations of the heart failure secondary prevention ICD trials were very optimistic. The SCD-HeFT study recruited patients with a history of heart failure in NYHA class II or III with an LVEF≤35%, that is to say, a population that was very similar to the one recruited in the MERIT-HF trial whose mean LVEF was 28% [82]. The reduction in mortality observed in the ICD arm of SCD-HeFT was 23%, a figure that is very much lower than the expected 50% mortality reduction looking at the MERIT-HF data. This discrepancy can be because of several possible causes: (a) the 50% SCD mortality rate in MERIT-HF was an error; (b) other non-arrhythmic causes of SCD may be present in these patients; (c) the ICD and/or its therapies may have resulted in a worsening of heart failure with increased mortality.

The different natural history of ischemic and nonischemic dilated cardiomyopathy patients

The SCD-HeFT study has also demonstrated that patients with heart failure and ischemic left ventricular systolic dysfunction have a worse prognosis than nonischemic patients with similar NYHA functional class and LVEF. Thus, the mortality at 3 years in the placebo group in the SCD-HeFT study was 28.5% in the ischemic and 16% in the nonischemic patients [82]. It is to be remembered here that the ICD has had difficulties in statistically establishing the benefit of this device in patients with DCM, very depressed LVEF, and a history of heart failure. For example, the DEFINITE trial conducted after other studies in DCM patients, although showing a trend toward an ICD benefit, failed to demonstrate a statistically significant superiority of a device therapy over a conventional treatment in patients with DCM [83].

Arrhythmogenic right ventricular cardiomyopathy: its role in sudden cardiac death and mechanisms of ventricular arrhythmias related to this entity

Arrhythmogenic right ventricular dysplasia is a term that is being replaced today for arrhythmogenic right ventricular cardiomyopathy (ARVC). There are still doubts as to which are the diagnostic criteria both ante mortem and at pathologic examination. Pathologic studies have suggested that ARVC may be a not too infrequent cause of SCD in young people, at least in certain areas of Europe [84]. Patients with ARVC should avoid competitive sports.

In a recent publication of the European Society of Cardiology on cardiomyopathies [85], ARVC is defined as the progressive replacement of right ventricular myocardium with fibro-adipose tissue, initially at three very characteristic right ventricular sites: the right ventricular inflow, outflow, and

apex (triangle of dysplasia). These pathologic changes can also affect the left ventricle, either alone, in which case they would mimic a DCM phenotype, or as a progression of the initial right ventricular disease. The majority of cases are caused by an autosomal dominantly inherited mutation in genes encoding plakophilin-2 and other proteins of the desmosome of cardiomyocytes. Mutations in TGF-β and ryanodine receptor genes may also result in an ARVC phenotype. There are also autosomal recessive forms of ARVC such as the Naxos and Carvajal syndromes that are caused by mutations in genes encoding plakoglobin and desmoplakin, respectively.

VT can usually be elicited with programmed electrical stimulation in patients with VT and ARVC. It has been assumed that mechanisms similar to those operating in postmyocardial infarction–related VT are the basis of the ventricular arrhythmias in ARVC. There are no detailed mapping studies conducted on a Langendorff-perfused heart setup from specimens obtained in patients undergoing a cardiac transplant [86,87].

Hypertrophic cardiomyopathy and sudden cardiac death with special emphasis on athletes

Sudden cardiac death in athletes has always been of great concern. Some recent sad events watched by a worldwide audience have further increased the social and political sensitivity in relation to this problem. Although the problem is of a greater magnitude than previously estimated, the numbers are fortunately very low. Recent studies conducted in the USA have confirmed that hypertrophic cardiomyopathy (HCM) is the most common underlying structural heart problem in these patients, being present in 36% of the instances. Coronary artery anomalies with an abnormal origin in the sinus of Valsalva are found in 17% of the patients, and myocarditis and ARVC are found in 6% and 4%, respectively [88].

Differentiation of HCM from the so-called athlete's heart is not an easy task [89,90]. This issue is to some extent speculative and it is beyond the scope of this review to further elaborate on this matter. When simple genetic diagnostic tests would be readily available, it would be possible to not only delineate the boundaries of the athlete's heart but also establish which benign varieties of HCM might be allowed for competitive sports practice at no risk of SCD on the pitch.

Also difficult is the estimation of the risk of SCD in the individual patient with an established diagnosis of HCM. A number of risk traits have been suggested to confer a higher risk of SCD to patients with HCM. A previously aborted episode of arrhythmic sudden death is the most powerful predictor of a subsequent fatal arrhythmic event. As discussed elsewhere, a previous syncope or even a family history of SCD may pose a difficult interpretation to attribute them to malignant arrhythmic events [91]. The role of nonsustained VT as a marker of SCD risk seems to be limited to patients with less than 30 years [92]. Another risk factor derived from several studies is the lack of rise of the systolic blood pressure by >20–30 mmHg from baseline during

exercise. This sign lacks of value in patients over 50 years and is of clinical significance in children and young patients [93].

Finally, the extent of left ventricular wall thickness has also been reported to be of prognostic significance. Young patients with extreme hypertrophy (≥30 mm) are at a high risk of SCD, whereas those with walls ≤15 mm are at a very low risk of arrhythmic mortality [94]. More recent studies have further stressed that this factor represents per se a marker of risk when present at a very young age. In patients over the age of 25–30 years, the association between maximum wall thickness and cardiovascular mortality is more questionable [95]. Recently, the variety of HCM with an apical left ventricular aneurysm frequently associated with mid-ventricular hypertrophy has been reported to be linked with substantial cardiovascular morbidity and mortality including malignant ventricular arrhythmias and sudden death [96]. More data on the natural history of the various phenotypic varieties of HCM as defined with MR imaging studies are badly needed. The prognostic role of late gadolinium enhancement in MR imaging studies in HCM has to be determined [97].

Although studies conducted more than one decade ago suggested that certain sarcomeric mutations were associated with a high incidence of SCD, newer investigations further supporting this contention are lacking [98].

Congenital heart disease

Congenital heart disease spans the spectrum from severe cyanotic heart disease to asymptomatic anomalies, some of which may not become clinically manifest until later life. As such, congenital heart diseases range in pathology, anatomic abnormalities, and natural history. In addition, the preoperative and postoperative challenges and risk of ventricular arrhythmias are quite varied as well.

The majority of congenital heart conditions can currently be completely repaired or at a minimum receive some palliative surgery. With advancements in preoperative care, operative technique, and postoperative care, the overall mortality rate has dropped steadily over the past few decades [99]. Recently the number of adults with surgically corrected congenital heart disease exceeded the number of children.

While the majority of early death in individuals with congenital heart disease is usually related to the postoperative period, mortality because of ventricular arrhythmias increases with age. Among patients with surgically corrected congenital heart disease, SCD between ages 1 and 16 years was most commonly seen in patients with tetralogy of Fallot [100]. Other lesions associated with SCD include aortic stenosis, coarctation, D- and L-transposition of the great arteries, Ebstein anomaly, and patients with single ventricle physiology [101–103]. While SCD in this population may be because of AV block and bradycardia, or atrial flutter with rapid conduction as seen in patients who have had atrial switch procedures or Fontan procedures, ventricular arrhythmias remain the most likely and most common cause of SCD. Most

of the data on ventricular arrhythmias and SCD in patients with congenital heart disease are in patients with repaired tetralogy of Fallot; this is not surprising given that tetralogy of Fallot is the most common cyanotic congenital heart disease and has a higher incidence of ventricular arrhythmias than other cyanotic conditions [104]. Several studies have examined the incidence of spontaneous ventricular arrhythmias in patients with repaired tetralogy of Fallot. While sustained VT is not common, spontaneous PCVs can be identified on 24-h monitoring in up to 48% of patients [105]. Patients with documented sustained VT had more frequent PVCs found on 24-h monitoring than those who did not present with sustained VT [105]. In general, ventricular arrhythmias occur more frequently among patients who are older at the time of initial repair, have residual right ventricular obstruction, and have significant pulmonic insufficiency [106–109]. This is understandable when one considers the surgical repair of congenital heart disease. For example, repair of tetralogy of Fallot was initially described in 1954 by Lillehei *et al.* [110]; during the late 1950s and 1960s patients commonly had a palliative placement of a systemic to pulmonary artery shunt and then underwent the surgical repair later in life. During the time while waiting for a complete repair, the left ventricle is exposed to volume overload. In addition, repair of the right ventricular outflow tract requires placement of a patch over the ventricular septum and resection of right ventricular tissue. Cyanosis early in life, as well as the hemodynamic consequences of volume overload, can increase the amount of fibrosis and lead to an ideal substrate for ventricular arrhythmias [111]. In the 1970s, surgical repair during infancy became more commonplace, so palliative surgery and long-term cyanosis became less of an issue. Despite changes in surgical practice, patients with repaired tetralogy of Fallot still present with ventricular arrhythmias at older ages. In addition, many patients who have had surgical repair before the 1970s are still alive and may be at higher risk for development of VT. Another factor is the deterioration of the pulmonic valve with time. Development of pulmonic insufficiency is common among individuals with repaired tetralogy of Fallot and repair of the pulmonic valve seems to potentially have some effect on the width of the QRS as well as possibly ventricular arrhythmias [112–114].

Gatzoulis *et al.* examined the ventricular function as well as the QRS duration in a group of 178 adults who had prior repair of tetralogy of Fallot. QRS duration of >180 ms was associated with chronic right ventricular overload and impaired right ventricular diastolic function. A QRS duration of >180 was the most sensitive predictor of ventricular arrhythmias [108]. In a multicenter study of adults with repaired tetralogy of Fallot, 33 (4.2%) individuals had VT and 16 (2.0%) had SCD [107]. QRS lengthening over time and presence of pulmonic regurgitation were both strongly associated with VT and SCD [107]. Several other studies have confirmed these findings [111,115]. Other ECG parameters have been examined as well, such as the duration of the QRS using signal averaged ECG, QT dispersion, T-wave alternans, and measurements of autonomics determined by 24-h ambulatory ECG recordings [116–124].

Previous studies have also examined the role of invasive electrophysiological studies to determine the risk of ventricular tachyarrhythmias in both symptomatic and asymptomatic patients. Therapy decisions based on electrophysiological testing initially included antiarrhythmic medications, and now the use of ICD. Variations in stimulation protocols have led to differences in the reported inducibility as well as the predictive value of electrophysiological testing [125]. Chandar *et al.* [126] reported a rate of VT inducibility of 17%. Inducibility has been associated with a greater risk on SCD. In a study by Alexander *et al.* [127]—invasive electrophysiology and ventricular stimulation studies of 130 patients with congenital heart disease, 42 patients (33%) with repaired tetralogy of Fallot, and 32 (25%) with D-transposition of the great arteries—mortality was higher among patients with a positive electrophysiological study. In this study, patients were treated with antiarrhythmic medications or ICD [127]. It is also worth noting that 7% of subjects with a negative electrophysiological study died suddenly [127]. More recently, Khairy *et al.* [128] examined a cohort of 252 patients with repaired tetralogy of Fallot who underwent electrophysiology study and ventricular stimulation at six different centers. In this study, sustained monomorphic VT was induced in 30.2% of subjects and polymorphic VT was induced in 4.4%. The induction of either sustained monomorphic VT or polymorphic VT was a strong independent risk factor for SCD (relative risk 4.7) (Figure 1.5) [128]. Placement of an ICD in high-risk patients for primary or secondary prevention of SCD has

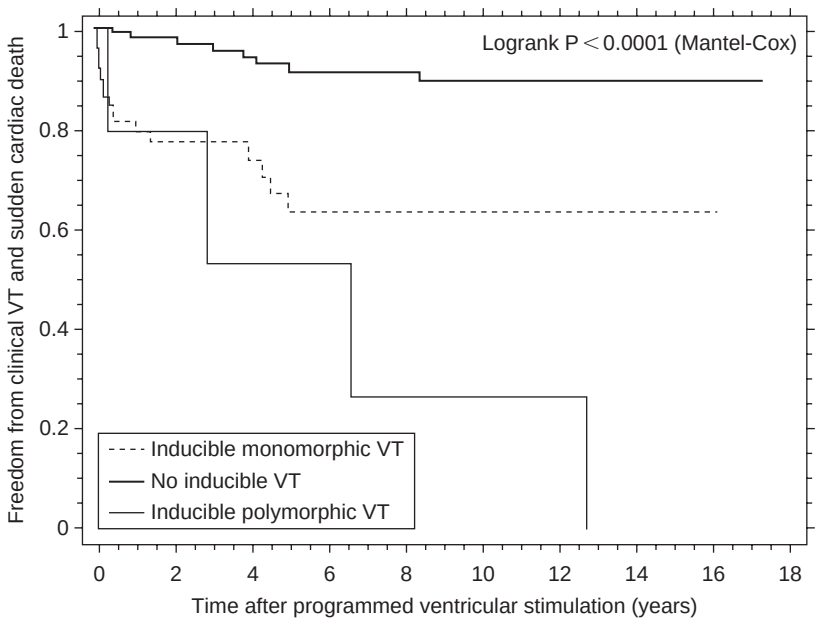


Figure 1.5 Survival from ventricular tachycardia (VT) and sudden cardiac death (SCD) after ventricular stimulation with inducible monomorphic or polymorphic VT [128].

also led to further understanding of risk in these individuals [129,130]. In a study of 121 individuals with repaired tetralogy of Fallot with an ICD, 30.6% of individuals received at least one appropriate therapy [129]. Both a higher left ventricular end diastolic pressure and the presence of nonsustained VT were independent predictors for appropriate shocks [129].

Electrocardiogram, hemodynamic and induced ventricular arrhythmias are understandable risk factors when one contemplates the anatomic and physiologic abnormalities that can lead to electrophysiologic substrate for ventricular arrhythmias. In a small study of three patients who had undergone repair of tetralogy of Fallot and subsequently had VT, careful intraoperative mapping during surgical ablation revealed delayed activation in sinus rhythm as well as clear evidence of macro-reentry around the prior ventriculotomy scar [131]. Resection of tissue specimens revealed diffuse endocardial fibrosis, adiposis invading at least 50% of the myocytes [131]. The myocytes also showed swelling, myofibrillolysis, disarray, hypertrophy, and focal necrosis [131]. Other studies that have reported on catheter ablation of VT circuits in patients with repaired tetralogy of Fallot have characterized the substrate resulting in reentry using contact and noncontact mapping [132–135]. In a recent report by Zeppenfeld *et al.* [132], detailed electroanatomical mapping of the right ventricle during sinus rhythm delineated reentry circuits and defined the isthmuses as being bordered by unexcitable tissue. In individuals with repaired tetralogy of Fallot and VT, four potential isthmus sites were defined: (1) between the tricuspid annulus and the scar/patch; (2) between the pulmonary annulus and the right ventricular free-wall scar/patch; (3) between the pulmonary annulus and the septal scar/patch; and (4) between the septal scar/patch and the tricuspid valve (Figure 1.6) [132]. Examination of postmortem specimens also confirmed the location and distribution of the potential isthmus locations [132]. Location of the isthmus and the direction of rotation (clockwise versus counterclockwise) determines the morphology of the VT [136,137].

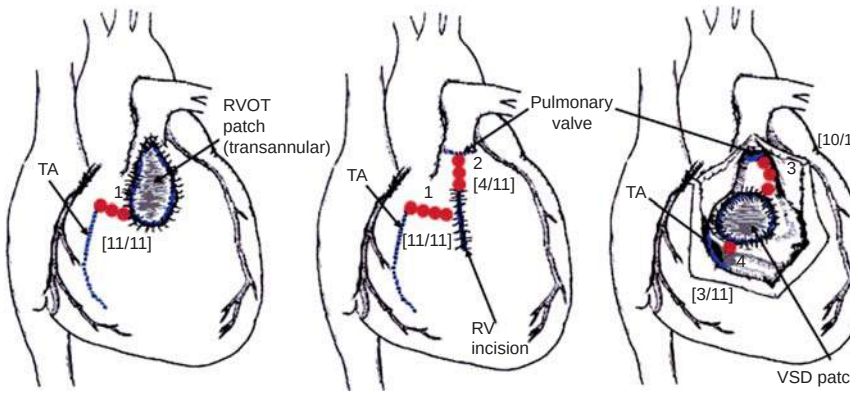


Figure 1.6 Ventricular tachycardia circuits in patients with congenital heart disease after right ventricular surgical repair [132], RVOT, right ventricular outflow tract; RV, right ventricle; TA, temporal artery; VSD, ventricular sceptal defect.

While many types of congenital heart disease are manifest at birth or at an early age, coronary anomalies can remain asymptomatic for years and can contribute to the overall rate of ventricular arrhythmias associated with congenital heart disease. The anomalous origin of the left coronary artery from the right sinus of Valsalva is the most common coronary anomaly that results in SCD [138–140]. From this anomalous origin, the left coronary may become compressed between the aorta and the right ventricular outflow tract. This can result in acute ischemia during exertion and lead to ventricular arrhythmias. Similarly, when the origin of the right coronary is from the left sinus of Valsalva, ischemia and ventricular arrhythmias can occur. While these anomalies can be asymptomatic, presenting with ventricular arrhythmias or SCD, symptoms such as chest pain, lightheadedness, or syncope during exertion can be present in approximately 30% of individuals. Origin of the left coronary artery from the pulmonary artery can also occur, resulting in ischemia and infarction at a young age, and subsequent substrate for ventricular arrhythmias. While this anomaly is usually detected early in life, individuals may present late with ventricular arrhythmias and SCD [141,142].

Catecholaminergic polymorphic ventricular tachycardia

The first description of catecholaminergic polymorphic ventricular tachycardia (CPVT) was made in a case series describing four children with catecholamine-induced syncope and VT by Coumel *et al.* [143]. The features of this disorder described in 1978 are still characteristics of this disease: a normal heart, a normal resting ECG, and ventricular arrhythmias (bidirectional VT) induced with an increase in catecholamines as a result of physical or emotional stress (Figure 1.7) [143]. A more comprehensive study by Leenhardt *et al.* [144] that examined 21 individuals with CPVT further refined our clinical understanding of this disease. In this study, 20 of the 21 subjects had syncope, and all the patients did not have any structural heart disease. The 12-lead ECG in all subjects was normal, with the exception of bradycardia with a mean heart rate of 60.3 bpm. The mean age at which syncope occurred was 7.8 ± 4 years. Ventricular arrhythmias seemed to consistently appear with sinus tachycardia at a heart rate of 120–130 bpm, initially with single PVCs, and then with quadrigeminy, trigeminy, bigeminy, and finally burst of polymorphic or bidirectional VT [144]. Another important finding of this study was the significant family history of SCD, thus suggesting a genetic basis. This was further elucidated in a report by Swan *et al.* [145] who found a pattern of autosomal dominant transmission in two families from Finland. In this study, linkage analysis was used to map the disease to chromosome 1q42-q43 [145]. Further studies identified a mutation in the cardiac ryanodine receptor gene (*RyR2*) in individuals with autosomal dominant transmission of CPVT; this form of CPVT is termed as CPVT1 [146–148]. Another form of this disease has been identified as CPVT2 and is autosomal recessive [149].

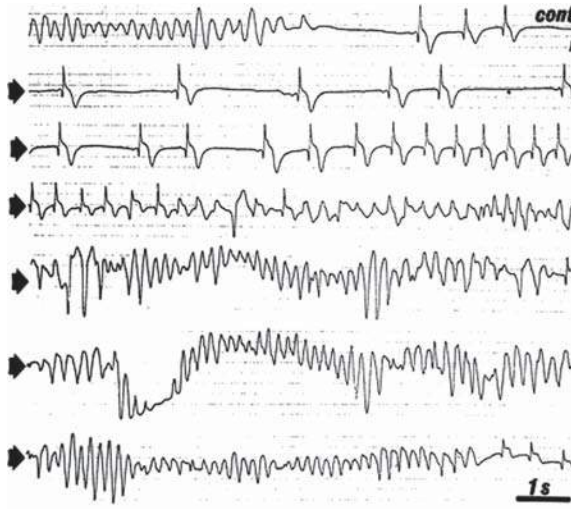


Figure 1.7 Holter recording of a patient with catecholaminergic polymorphic ventricular tachycardia (CPVT) during an episode of syncope [144].

In the autosomal recessive CPVT2, a missense mutation in the calsequestrin gene (*CASQ2*) was identified in a Bedouin tribe with a high rate of consanguineous marriage [149–151]. Both the RyR2 receptor and the *CASQ2* gene are involved in intracellular calcium modulation. Although the exact molecular mechanism is not entirely known, calcium overload and delayed afterdepolarizations play an important role [152–154].

Not all individuals with CPVT have a known mutation. A study by Priori *et al.* [147], examining the clinical phenotype of 30 individuals with exercise or emotional stress–induced VT and of 118 family members, revealed that only 14 of 30 (47%), as well as 9 family members who were screened (including 4 who were asymptomatic), carried a RyR2 mutation. Among individuals with a RyR2 mutation, events occurred at a younger age and syncope was more common among males [147]. Nongenotyped patients were more likely to be female and have syncope at an older age. In this study, polymorphic VT and VF occurred along with bidirectional VT [147].

Treatment with class 1 and class 3 antiarrhythmic drugs is not effective, and there does not appear to be a role of ventricular stimulation in electrophysiologic study for risk stratification [147,153,155]. Treatment with beta-adrenergic receptor blockers may be effective in some patients; however, up to 46% of individuals with CPVT will have episodes while on therapy [147,153]. Therefore, placement of an ICD may be indicated in some patients [147,153,155,156]. Calcium channel blocker therapy in addition to beta-adrenergic receptor blockers may also have a role in the management of these patients [157]. Recently, cardiac sympathetic denervation in three

individuals with CPVT was reported to eliminate symptoms related to ventricular arrhythmias [158].

The Brugada syndrome

The Brugada syndrome, first described as a new clinical entity in 1992, is characterized by a high incidence of syncope or SCD in individuals with a structurally normal heart but characteristic ECG abnormalities [159,160]. The true incidence of the disease is unknown as the first presentation may be SCD; in addition, the ECG characteristics can be dynamic or concealed in some individuals [161,162]. It is estimated that the Brugada syndrome may contribute between 4% and 12% of SCDs in patients with a structurally normal heart and represents a leading cause of SCD in young individuals with a structurally normal heart in areas where the disease has a higher prevalence such as Southeast Asia [161]. The Brugada syndrome has been linked with other forms of sudden death in young individuals in Southeast Asia, such as *Lai Tai* (death during sleep) [163].

The Brugada syndrome is more common in males, and clinical manifestations of syncope or SCD usually occur in the third and fourth decades, although the syndrome has been diagnosed in an infant at age 2 days and an individual at age 84 years [164–166]. VF and SCD commonly occur at night, likely because of an increase in vagal tone; in addition, fever may accentuate the ECG abnormalities and has been reported as a trigger for ventricular arrhythmias in individuals with the Brugada syndrome [161,162,167–170].

The ECG manifestations of the Brugada syndrome include three repolarization patterns seen in the right precordial leads. Type 1 is characterized by a coved ST-segment elevation ($\geq$2 mm), followed by a negative T wave. When this ECG pattern is seen in more than one right precordial lead in association with a clinical event (documented VF, polymorphic VT, syncope, nocturnal agonal respiration, or inducible ventricular arrhythmias with programmed ventricular stimulation), or a strong family history of SCD in an individual younger than 45 years of age, or the presence of the coved-type pattern in family members, the Brugada syndrome can be definitively diagnosed [161]. Type 2 ECG pattern is the presence of a saddleback appearance, ST-segment elevation, and a positive biphasic T wave. Type 3 Brugada pattern is either coved or saddleback with ST-segment elevation of $<$1 mm [161].

As the ECG in patients with the Brugada syndrome can often be normal and the typical ECG manifestations concealed, occasionally the use of sodium channel blockers such as procainamide, flecanide, or ajmaline can expose the ST-segment elevation seen in the Brugada syndrome [171,172]. In general, it is felt that patients with spontaneously occurring ECG manifestations have a worse prognosis than those that require pharmacologic provocation [164,166,171,173]. In addition, placement of the right precordial leads in a more superior space (the second intercostal space) can increase the sensitivity of the ECG, although the effect of this on the specificity is not clear [174,175]. It is important to consider other causes that may account for this

type of ECG abnormality such as atypical right bundle branch block, early repolarization pattern, and myocardial ischemia to name a few [161,162].

The Brugada syndrome is transmitted via an autosomal dominant gene defect. Mutations of the *SCN5A* gene that encodes for the alpha subunit of the cardiac sodium channel have been linked to the Brugada syndrome [176]. There have been a number of mutations of the *SCN5A* gene resulting in loss of function of the sodium channel; however, no mutation has been identified as a marker of higher clinical risk [164].

There is little controversy that symptomatic patients with the Brugada syndrome are at high risk of SCD and warrant protection with an ICD. In a study of 258 individuals receiving an ICD, 52% had received an appropriate shock during 5 years of follow-up. The efficacy of the ICD was 100% in converting ventricular arrhythmias [177–179]. Other therapeutic modalities, for example the use of drug therapy with antiarrhythmic medications such as quinidine, and ablation of triggers of ventricular arrhythmias have also been reported; however, there are no data currently on long-term efficacy of these therapies in the prevention of SCD [176,180–182]. The role of the electrophysiology study in risk assessment is controversial. In a study by Brugada *et al.* [178,183,184], 493 individuals underwent ventricular stimulation during an electrophysiology study. Inducibility of a sustained ventricular arrhythmia was associated with a hazard ratio of 3.85 (after adjustment of other variables) in predicting arrhythmia recurrence. However, Priori *et al.* reported that the electrophysiology testing was not accurate in predicting future arrhythmic events [164,185].

The long QT syndrome

The long QT syndrome has been recognized as a familial condition since the late 1950s, when Jervell and Lange-Nielesen [186] described the familial occurrence of autosomal recessive disorder consisting of sensori-neural deafness and a prolonged QT interval and VT. A few years later, Ward and Romano separately described an autosomal dominant condition of QT prolongation and ventricular arrhythmia but no deafness. Now defects in 12 genes have been identified, which may account for congenital/familial QT prolongation; only the first three of which are common (LQT1, LQT2, and LQT3) [9]. LQT1 and LQT2 are known to be caused by a genetic disorder that results in inhibition of outward repolarizing currents, the slow and rapid components of the delayed potassium regulator current (Ikr and Iks, respectively). LQT3 is because of persistence of the inward depolarizing sodium current (INa). All of these abnormal currents lead to lengthening of the action potential and hence prolongation of the QT interval on the surface ECG. LQT4 is associated with mutations in ankirin-B2, a protein that controls calcium signaling in myocytes, whereas LQT7 has been linked to a defective Kir 2.1 gene resulting in reduction of the Ik1 current.

The long QT syndrome is usually (manifest), but not always (concealed) a result of prolonged ventricular repolarization (a long QT or QTc interval

on the ECG—often above 500 ms). The electrocardiographic disturbance is most often because of abnormalities of cardiac myocyte membrane ion channel function that predisposes to life-threatening ventricular arrhythmias, particularly torsade de pointes [187]. The prolongation of the ventricular action potential leads to afterdepolarizations that give rise to PVCs. The action potential lengthening is not evenly distributed, leading to heterogeneous recovery of excitability of the ventricular myocyte. This is a potential substrate for macro-reentry over continuously varying pathways/circuits. The result may be transient torsade de pointes, which may cause palpitations, lightheadedness, or syncope. Sometimes the arrhythmia may degenerate into VF and the patient may sustain a cardiac arrest or die suddenly.

Different genetic defects give rise to a variety of molecular mechanisms that account for the different phenotype presentations [188]. Patients with LQT1 may suffer from syncope or cardiac arrest during physical exercise, often while swimming. On the other hand, LQT3 patients have bradycardia or pause-dependent QT prolongation and they tend to experience ventricular arrhythmias at rest, often when asleep. LQT2 subjects are particularly vulnerable to emotional stimuli or acoustic alarms, for example, an alarm clock or telephone, which may trigger ventricular arrhythmias and SCD. The genotype/phenotype correlation is not absolute and multiple exceptions exist, probably reflecting the variability of disease expression and/or the influence of other environmental or genetic cofactors.

The management of long QT syndrome is not straightforward, largely because of the unpredictability of cofactors at the genetic and environmental levels. Many of the patients are children for whom medical therapy would be preferable to the implantation of an ICD or pacemaker, but medical therapy may not be fully protective. Beta blockade is generally recommended [189] but may not be helpful for LQT3. More specific therapy also exists, for example mexiletine, flecainide, or ranolazine [190], all of which inhibit the INa current. They have been applied to small numbers of patients with LQT3 and result in shortening of the QT interval but how protective they are against ventricular tachyarrhythmias is unknown. Nicorandil, a potassium channel opener, has been used to shorten the QT interval in several of the LQT syndromes [191]. A variety of other medicinal products that influence the construction or "trafficking" of membrane channels from the endoplasmic reticulum to the myocyte membrane are also being investigated.

In LQT3 (and sometimes in LQT2) bradycardia and pauses precede the emergence of symptomatic ventricular tachyarrhythmias. In LQT3 patients, the implantation of a pacemaker may be valuable [192]. In LQT2 patients, the bradyarrhythmia usually follows, or is aggravated by, the beta-blocker therapy, which is essential, and a pacemaker may then be necessary to support the ventricular rate.

ICD therapy is definitely needed for secondary prevention in all patients who have suffered a cardiac arrest or sustained VT despite beta blockade. Other factors [9] that should be evaluated when ICD therapy is under consideration are

- the duration of the QTc interval (e.g., >500 ms)
- life-threatening arrhythmic event at a young age (e.g., before age 7)
- the presence of LQT2 or LQT3 variants

Issues such as a family history of SCD are also of practical importance.

Drug-induced ventricular arrhythmias

Although ventricular arrhythmias related to cardioactive medication such as quinidine and digoxin had been understood for many years, it was not until the CAST study [57] that the importance and potential prevalence of drug-induced ventricular arrhythmia was fully understood. CAST demonstrated that in patients with ischemic heart disease (postmyocardial infarction and particularly with ongoing episodes of acute ischemia), flecainide and encainide (and, by imputation, any sodium channel blocker with slow offset kinetics) increased rather than reduced death, SCD, and ventricular arrhythmias. It is now well appreciated that powerful cardioactive medications with membrane ion channel blocking properties may disturb the electrophysiological milieu so as to cure (antiarrhythmic effect) or provoke (proarrhythmic effect) ventricular arrhythmias. Sodium channel blocking agents tend to slow or block conduction, which may create reentrant substrates that may support monomorphic VT, which might then degenerate into VF. Similarly, potassium channel blocking agents may increase ventricular refractoriness and its dispersion, induce ventricular afterdepolarizations, and lead to polymorphic VT. These arrhythmias are often transient but may convert into VF and lead to SCD. The SWORD [193] and DIAMOND [194] trials in postinfarct and heart failure patients highlighted this possibility and confirmed the proarrhythmic potential of class III "antiarrhythmic" drugs.

Many other drugs possess cardioactive membrane channel blocking effects, particularly involving the rapid component of the delayed potassium rectifier current (Ikr). Inhibition of this current leads to QT interval prolongation (acquired long QT syndrome), sometimes associated with a polymorphic ventricular tachyarrhythmia known as torsade de pointes. This arrhythmia tends to occur at slow heart rates or following a pause in the ventricular rhythm (often a post ventricular extrasystolic compensatory pause) and is characterized by continuously varying QRS axis appearing to revolve around the ECG baseline.

A large variety of drugs may have this effect, for example, antibiotics such as moxifloxacin [195], antihistamines such as terfenadine [196], antidepressants such as amitriptyline [197], antipsychotics such as thioridazine [198], and antimalarials such as halofantrine [199]. In normal subjects, under normal circumstances, these drugs tend to prolong the QT interval but only by 10 ms or so. But in patients with the long QT syndrome (manifest or concealed), comorbidities such as structural heart disease, for example, heart failure, concomitant hypokalemia, or hypomagnesemia, coadministration of relevant metabolic inhibitors, or when taken in overdose, the QT prolongation

may be more than 100 ms and the rate-corrected or measured QT interval may often exceed 500 ms, at which point torsade de pointes may develop.

Licensed pharmaceuticals that may have this effect are usually labeled with warnings and contraindications in order to minimize the risk of this arrhythmia, although such labeling may go unheeded and acquired long QT syndrome may occur. All new drugs are studied nowadays with cellular/animal models, for example, Ikr current inhibition and transmural dispersion of repolarization in the canine wedge preparation, preclinical pharmacokinetic/ECG studies (a thorough QT study), and clinical testing both pre and post approval, in order to identify this possibility. Not all drugs that prolong the QT interval necessarily lead to the possibility of torsade de pointes; for example, ranolazine (a recently licensed antianginal agent that may prolong the QT interval) may be a case in point [200].

If torsade de pointes VT occurs, the arrhythmia is treated by immediate withdrawal of the offending medication, prompt but careful restoration of serum potassium and magnesium, heart rate support with artificial pacing, and beta blockade. Magnesium infusion may have a salutary effect even if the serum magnesium is normal. The development of torsade de pointes should be a warning that the patient is vulnerable to QT prolongation and may respond similarly to other drugs that have an inhibitory effect on repolarizing currents such as Ikr.

Recreational drugs may also be associated with proarrhythmia. For example, cocaine [201] may provoke VT because of its sodium channel blocking effect, although its action is complicated (acute myocardial infarction, sympathetic activation, QT interval lengthening, and torsade, etc.). It may also induce an electrocardiographic pattern reminiscent of the Brugada pattern (see the preceding text) in patients not otherwise known to have this disorder. Other drugs such as tricyclic antidepressants (amitriptyline), selective serotonin reuptake inhibitors such as fluoxetine [202], class I antiarrhythmic drugs [203], and anesthetic agents such as propofol [204] are also known to cause this ECG pattern and sometimes associated ventricular arrhythmias.

The realization that antiarrhythmic drugs may harm as well as help cardiac arrhythmias and that many drugs, primarily intended to have noncardiac effects, may also have cardiac myocyte membrane channel–inhibitory effects has led to increased awareness of the occurrence of ventricular tachyarrhythmias as a toxic effect. Any patient presenting with monomorphic or polymorphic VT or VF should be carefully screened, usually by taking a good medical history, so that such a possibility is not overlooked.

Ventricular tachycardia/ventricular fibrillation clinical presentation: hemodynamically stable and hemodynamically unstable

Hemodynamically stable ventricular tachycardia

Careful history taking for the electrophysiologist is a necessary undertaking but can be unrewarding as it seldom leads to a precise diagnosis nor does it

Table 1.1 Clinical presentations of patients with ventricular arrhythmias and sudden cardiac death

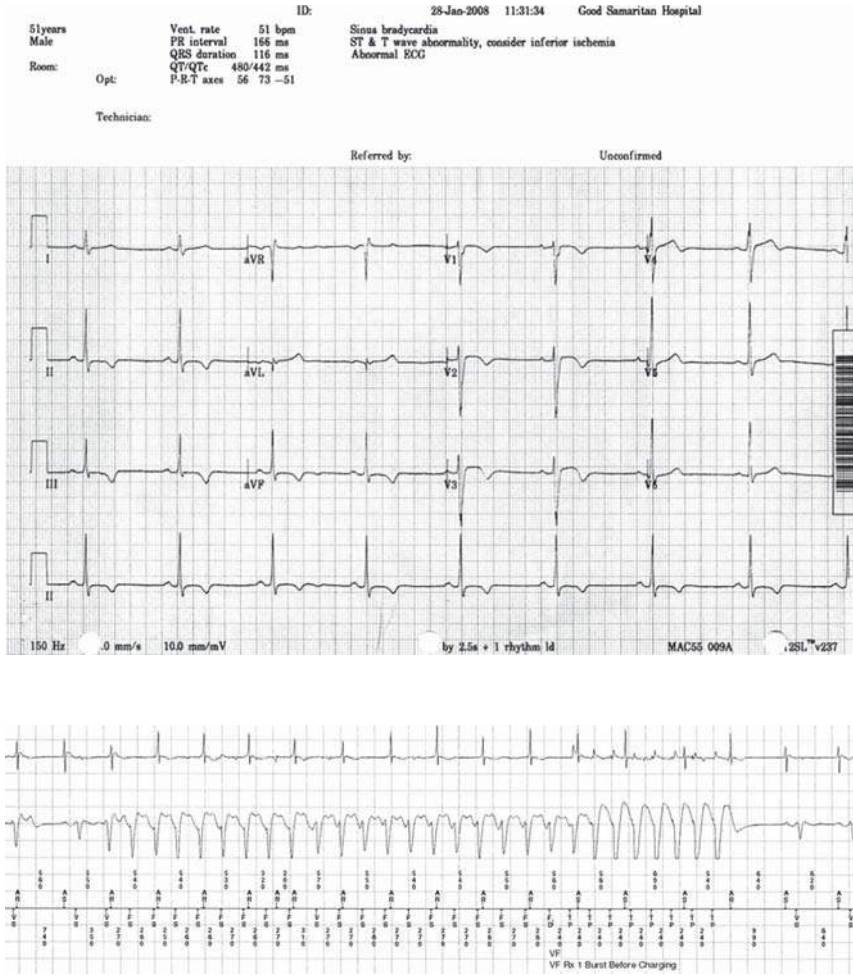
- Asymptomatic individuals with or without electrocardiographic abnormalities
- Persons with symptoms potentially attributable to ventricular arrhythmias
  - Palpitations
  - Dyspnea
  - Chest pain
  - Syncope and presyncope
- Ventricular tachycardia that is hemodynamically stable
- Ventricular tachycardia that is not hemodynamically stable
- Cardiac arrest
  - Asystolic (sinus arrest, atrioventricular block)
  - Ventricular tachycardia
  - Ventricular fibrillation
  - Pulseless electrical activity

convey the clinical seriousness of an underlying arrhythmia. The symptoms of ventricular arrhythmias are very nonspecific and easily confused with supraventricular tachycardias, underlying ischemic disease, heart failure, or neurological disease. Electrophysiologists are trained to conduct elaborate workups rather than spend long hours attempting to make a clinical diagnosis based on symptoms [9] (Table 1.1; Figures 1.8 and 1.9).

Symptoms that occur during VT are highly variable and depend upon the rate of the tachycardia, the duration of the tachycardia, and the extent of any concomitant underlying heart disease. Ventricular rate itself is the most important determinant of how symptomatic a patient becomes during a tachycardia, although if the patient's ejection fraction is under 30% even slower tachycardias can cause syncope. Patients who present with stable VT and a normal heart typically have their VT arising in the left or right ventricular outflow tract or distal coronary sinus and are excellent candidates for catheter ablation. Even if they have a severe syncopal spell in association with their VT, they are not ICD candidates.

There is no clinical symptom that specifically identifies a cardiac rhythm as being a result of VT (Figure 1.10). A patient with VT at a rate of 200 bpm and an ejection fraction of 30% will likely experience syncope and quickly require treatment. In contrast, an elite athlete with an EF of 55% and slow VT (e.g., 150 bpm) might only notice an occasional palpitation (Figure 1.11). However, just the opposite can be true. Patients with a low ejection fraction may not be aware of palpitations nor have syncope even if the VT is incessant. Patients who present in sinus rhythm with a history of recent syncope and known structural heart disease are presumed to have had VT as the cause of their syncope.

The data from a large multicenter secondary prevention trial, the AVID trial, demonstrate both the variability of the presentation of VT as well as the guarded clinical outcome of VT patients in this trial [205]. The AVID trial



Figures 1.8 and 1.9 The patient is a 51-year-old elite swimmer who came to the doctor because of palpitations experienced only when swimming. The electrocardiogram (ECG) is abnormal and consistent with arrhythmogenic right ventricular cardiomyopathy (ARVC). A right ventriculogram was positive for ARVC and the patient received an ICD. He has since had therapy for VT from his ICD. The presenting complaint was extremely benign.

enrolled 4595 eligible patients in a registry; of these patients only 1016 were randomized in the main trial. All the patients in the registry were followed up and their long-term mortality was reported. A wide spectrum of presenting symptoms were represented in the registry including 497 patients who had asymptomatic VT and 390 patients who had unexplained syncope and subsequent inducible VT at electrophysiologic study. These data emphasize the wide variability of presentation of VT. Most importantly, the cumulative

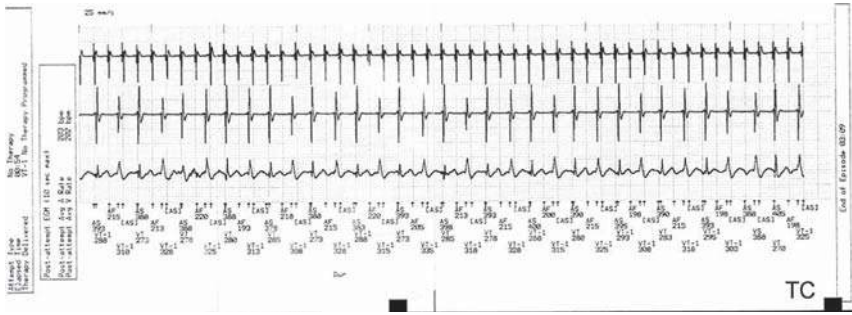


Figure 1.10 This is a 48-year-old male who had hypertrophic cardiomyopathy (HCM) diagnosed at the age of 18. At the age of 30, he had a cardiac arrest leading to ICD implantation. He was placed on sotalol because of palpitations. While running, 10 years later, he had another cardiac arrest and was resuscitated by the paramedics. The intracardiac electrogram showed that this was because of a rapid atrial tachycardia with 2:1 AV block, which was under the device rate cutoff of 220 bpm. Syncope was the symptom and, of course, ventricular tachycardia (VT) was expected; in retrospect, it is unusual that such relatively slow SVT could cause syncope. Perhaps this first cardiac arrest was caused by the same rhythm. The cardiologist involved was very concerned about the rapidity of these beats and implanted an ICD. A normal cardiac catheterization and MRI led to the ICD being removed.

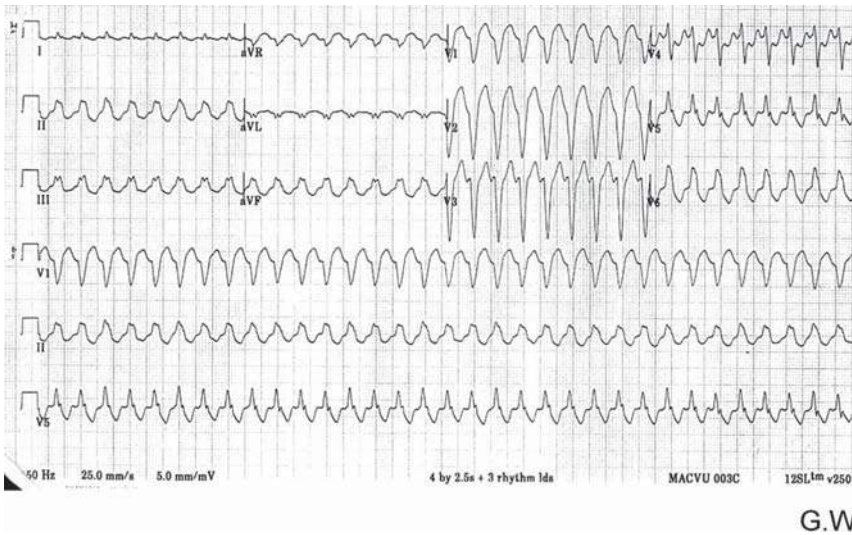


Figure 1.11 A 12-lead electrocardiogram (ECG). This ECG is similar to the one taken after this 35-year-old triathlete completed the Hawaiian Iron Man race. During the last 20 min of the marathon portion of the triathlon, he felt his heart start to race and went from first place to eleventh place. This was the first manifestation of his ventricular tachycardia (VT). He was ultimately treated with radiofrequency ablation. This shows that an elite athlete can perform at high levels even in VT.

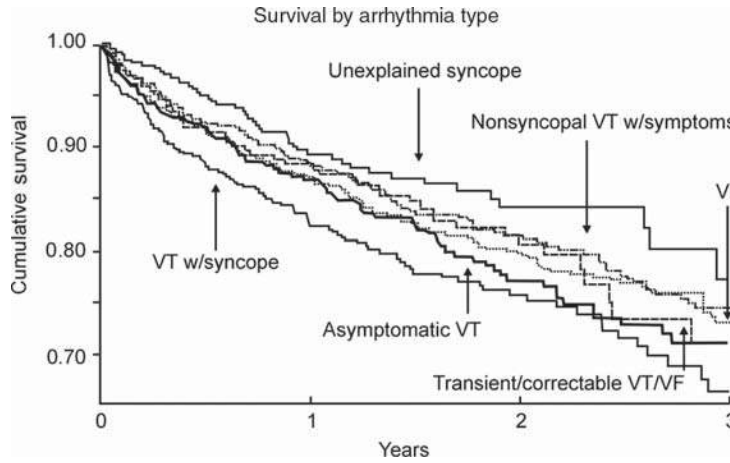


Figure 1.12 Survival curves for AVID registry arrhythmia groups. Despite the wide variability in clinical presentation, the survival of the various groups in the AVID trial was quite similar. This finding underscores the need for a thorough workup of any patient presenting with ventricular tachycardia.

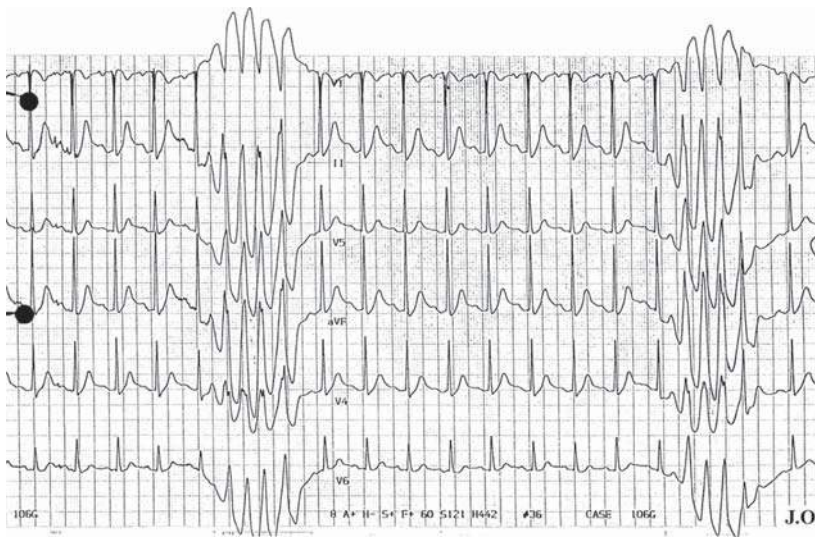


Figure 1.13 This is a 61-year-male who, during a routine treadmill stress test in 1999, had short rapid runs of ventricular tachycardia. He was entirely asymptomatic. The cardiologist involved was very concerned about the rapidity of these beats and implanted an ICD. A normal cardiac catheterization and MRI led to the ICD being removed.

survival of each of these symptomatic subgroups is surprisingly similar (Figure 1.12) and is approximately 70% at 3 years. These data highlight the need to risk stratify all VT patients and assure that ICD therapy is employed based on guidelines data. Ventricular arrhythmias may be detected by monitoring in a patient who is entirely asymptomatic [9,206] (Figure 1.13). This is

Table 1.2 Percentage of patients with palpitations in whom various conditions were diagnosed by continuous event recorders [Adapted from *Massachusetts Medical Society*]

	Study		
	Kinlay et al. (N=100)	*Zimetbaum et al. (N=105)*	*Zimetbaum et al. (N=408)*
Condition	*Percent*		
Sinus rhythm	35	18	39
Ventricular premature depolarizations	12	20	36
Atrial premature depolarizations	0	8	13
Atrtal fibrillation	6	17	2
Ventricular tachycardia (VT)	0	2	1
Sinus tachycardia	29	7	5
Supraventricular tachycardia	18	10	4

In this table from Zemitbaum and Josephson, three large Holter studies evaluating palpitations demonstrate that the majority of rhythms detected are supraventricular with only rare VT documented during the 24-h Holter period. Sustained monitoring of 2–3 weeks gives a higher yield for ventricular arrhythmias.

especially true if the VT is nonsustained. Patients may describe chest pain or dyspnea in association with VT, although in the author's experience this is unusual as the sole symptom. Commonly, less symptomatic patients will use terms such as an episodic "catch" or fluttering sensation in the chest or throat often associated with a cough. Usually, however, such innocent complaints turn out to be supraventricular tachycardias and not VT. Palpitations that have an onset–offset character can be either supraventricular tachycardia or VT but are usually the former. Valsalva maneuvers rarely interrupt VT. Only long-term monitoring and a concerted effort to correlate symptoms with documented rhythms will determine treatment [207] (Table 1.2).

It is important to identify what circumstances trigger a patient's symptoms. Triggers such as food or alcohol are commonly associated with atrial arrhythmias. Exercise especially in a training environment can commonly trigger ventricular arrhythmias in patients with normal hearts and right ventricular outflow tract tachycardia. Exercise can also precipitate the more malignant arrhythmias associated with HCM and/or ARVC and frequently cause abrupt syncope. Syncope induced by swimming should suggest underlying long QT1.

Electrophysiologists commonly associate more serious clinical symptoms, such as loss of consciousness or syncope, as more likely a result of ventricular arrhythmia. However, supraventricular tachycardias can cause syncope. Most electrophysiologists suspect an arrhythmic cause of syncope when there is no prodrome to the syncope, when the patient has underlying left ventricular dysfunction, and when the patient suffers from blunt trauma to

the head or body during syncope. If the patient has a typical vagal prodrome, is young with a normal heart, and has recurrent syncope, the cause is likely autonomic.

Calkins added that patients with syncope as a result of VT or AV block were older, more likely to be males, and less likely to experience fatigue following syncope, and had a shorter duration of recovery symptoms following syncope. Again, exceptions abound and the history is most useful in directing the workup (especially the use of electrophysiologic study) and not in making the final diagnosis [208]. Electrophysiologic testing is a class I recommendation in patients with syncope of unknown cause with impaired LV function [9]. In one study of 67 patients with coronary artery disease and unexplained syncope, the EP study was positive in nearly half of the patients [209]. Bradyarrhythmias also occur in elderly patients. These patients are best identified by extended outpatient monitoring.

As electrophysiologists cannot depend on the history to assess risk, they depend on costly and time-consuming outpatient workups. Two decades of literature emphasizing the importance of thorough risk stratification pressures the clinician to identify every potential SCD candidate in his or her practice. The tools that we use are frustratingly unhelpful, even including invasive studies. Despite our best efforts, we are unsuccessful at predicting subsequent risk and this encourages overtreatment especially with the ICD.

In patients with a chief complaint of palpitations but no other alarming clinical features or positive family history, and no abnormalities on ECG or Holter or echo, the patient can be reassured. Complicating a simple chief complaint like palpitations or presyncope is an associated family history of SCD, or an ECG suggesting ARVC, or an echo suggesting a mild cardiomyopathy. At once, the case can be transformed from a matter of reassurance to a workup that can include heart catheterization, biopsy, genetic testing, and electrophysiologic study, even then the final diagnosis can be equivocal.

Hemodynamically unstable: sudden cardiac death

Sudden cardiac death is a clinical syndrome with a precise diagnosis. It is a natural death "heralded by the abrupt loss of consciousness within 1 h of the onset of acute symptoms" [210] (Figure 1.14). Everyday clinical experience as well as Holter studies has shown that SCD is because of ventricular arrhythmias [211]. As Myerburg carefully points out, there are premonitory signs and symptoms that may exist for days or weeks before the actual event. The difficulty in evaluation of these early symptoms is their nonspecificity even in hindsight. Such prodromes in the coronary patient include chest pain, which typically has an ischemic cause, dyspnea, palpitations, severe fatigue, or diaphoresis. If these symptoms are recognized and a coronary syndrome is successfully treated, then sudden arrhythmic death may be averted.

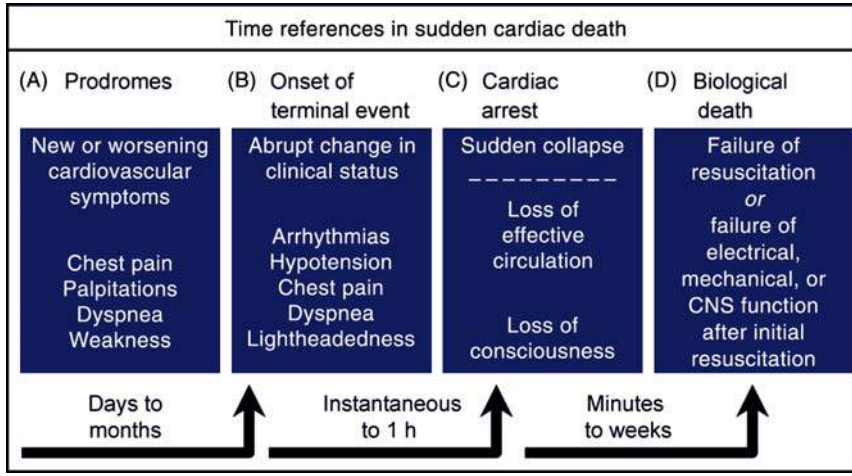


Figure 1.14 Myerburg describes sudden death from four temporal perspectives: (A) prodromes, (B) onset of the terminal event, (C) cardiac arrest, and (D) progression to biological death. The clinical goal is to appreciate the prodromes and, through aggressive intervention, interrupt the cascade of terminal events. Again, the early symptoms can be very nonspecific.

Other less common causes of SCD as a result of unexpected VT or VF are in the patients where prior symptoms such as palpitations or syncope were not recognized or not aggressively worked up and treated. This is especially common in younger patients with genetic heart disease such as long QT syndrome, ARVC, or HCM. Whether to recommend the life-saving properties of a prophylactic ICD in some of the patients who present with palpitations or even syncope, especially when they are part of a population not yet studied in a randomized trial, can be agonizing for the patient, family, and physician. A subsequent SCD in such a patient represents a failure of treatment and a preventable mortality. More and more senior clinicians seem to be following the "better safe than sorry" approach to such young patients—and implanting an ICD—despite the cost and potential complications of the ICD.

The past 30 years in clinical electrophysiology have paid attention to potential patients at risk for SCD and many of them have been randomized to general groups in clinical ICD and CRT trials (e.g., coronary artery disease patient with EF<30%). Little attention has been paid to the symptoms these patients have other than distinguishing their NYHA class. Decisions regarding therapies are not made based on symptoms but rather objective measures of LV function. However, there are large groups of patients who come to the electrophysiologist solely because of symptoms however vague. These symptoms have often been ignored by other physicians. The clinician's impressions of nonspecific symptoms as well as more serious symptoms of presyncope or syncope—including a thorough family history—will initiate the thorough workup that can either reassure a patient that nothing is wrong or, conversely, lead to a device that can be life saving.

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CHAPTER 2

Anatomy of Right/Left Ventricles and Surrounding Structures in Health and Disease

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Introduction

Catheter ablation of ventricular tachycardia (VT) is a highly complex procedure that requires both advanced knowledge in the techniques of electrophysiologic mapping and an in-depth understanding of the anatomy of the left and right ventricles, the aortic root, and surrounding structures. The purpose of this chapter is to review, in detail, the anatomic features of these structures. Special attention is focused on those aspects of the anatomy of the right and left ventricles that are of particular importance to those performing catheter ablation of VT. In this chapter, we will review not only the anatomic structure of the ventricles but also the microscopic and tissue abnormalities seen in a variety of disease states that may result in VT including ischemic heart disease, cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), and hypertrophic cardiomyopathy.

Normal anatomy

Disposition of the ventricular chambers and great arteries

The intricate spatial relationship between right and left ventricles reflects the anatomic fact that right ventricle, being the most anteriorly situated cardiac chamber, overlaps the left ventricle. When the heart is viewed from the front, only a strip that forms the left margin of the cardiac silhouette and the apical portion of the left ventricle is visible. In addition, the shapes of the left and

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right ventricles are dissimilar and the ventricular septum is not straight but curved. The inflow and outflow tracts of the left ventricle overlap each other when viewed from the frontal aspect whereas they are well separated in the right ventricle. Consequently, the conical-shaped left ventricle in cross section appears circular hugged by the crescent-like right ventricle that sweeps from inferiorly to anterosuperiorly. It is particularly relevant to ablations in the outflow tracts to understand the "crossover" relationship between the right and the left ventricular outlets. The right ventricular outlet passes cephalad in a posterior and slightly leftward direction. In some hearts, the tip of the left atrial appendage may overlie the left anterior wall of the pulmonary trunk or musculature of the outflow tract. The left ventricular outlet passes underneath the right ventricular outlet in a rightward and cephalad direction pointing toward the right shoulder (Figure 2.1A).

Furthermore, the pulmonary and aortic valves are not at the same level. The pulmonary valve is the most superiorly situated of the cardiac valves whereas the aortic valve slopes inferiorly at an angle to the pulmonary valve (Figure 2.1B) [1]. The difference in levels between the two sets of arterial valves may be exaggerated by the length of the freestanding cone of muscle supporting the pulmonary valve known as the subpulmonary infundibulum (see the following text). In between the sinuses of the aortic valve and the

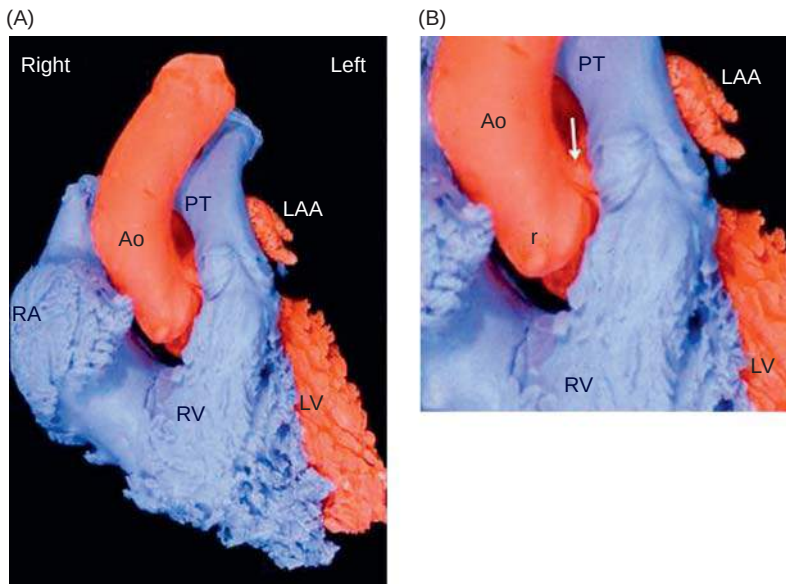


Figure 2.1 (A) Endocast of a normal heart viewed from the front to show the crossover relationship between right and left ventricular outflow tracts and the location of the aortic valve between right atrium (RA) and right ventricle (RV). (B) This magnified view shows the semilunar imprints made by the pulmonary and aortic valves. Note the right (r) and left (arrow) coronary aortic sinuses lying adjacent to the pulmonary valve and subpulmonary infundibulum. Ao, aorta; LAA, left atrial appendage; LV, left ventricle; and PT, pulmonary trunk

infundibulum is an epicardial tissue plane, not a part of the ventricular septum (Figure 2.2A). The posteroinferior wall of the subpulmonary infundibulum overlies the anterior walls of the left and right coronary sinuses to a greater or lesser extent and may give the impression of myocardial sleeves covering the aortic sinuses.

In the sinuses nearest to the infundibulum are the orifices of the right and left coronary arteries. These are located immediately below the level of the sinutubular junction rather than toward the nadirs [2,3]. As the coronary arteries descend toward their respective atrioventricular grooves, they pass within millimeters of the epicardial aspect of the infundibulum [4]. The third aortic sinus, the noncoronary sinus, bulges toward the anterior margin of the atrial septum. Owing to the central location of the aortic root in the heart, the posteroinferior margin of the aortic root is flanked by right and left atrial walls. Another important relationship is the vicinity of the closure line between the right and the noncoronary aortic leaflets with the closure line between the septal and the anterosuperior leaflets of the tricuspid valve. The aortic and tricuspid valves are separated by the membranous septum at the central fibrous body (Figure 2.2). It is well known that the His bundle penetrates through the central fibrous body to emerge as the atrioventricular conduction bundle on the left side of the septum, sandwiched between the membranous component and the muscular ventricular septum.

The right ventricle

A muscular fold known as the ventriculoinfundibular fold separates the tricuspid from pulmonary valves (Figure 2.2A). On its epicardial aspect sits the right coronary sinus of the aortic root. The fold continues superiorly into the muscle of the subpulmonary infundibulum that adjoins the arterial wall of the pulmonary trunk at the ventriculoarterial junction (Figure 2.2A,B). The pulmonary sinuses are not as prominent as the aortic sinuses but they are similarly demarcated by the semilunar-shaped hinge lines of the leaflets that cross the ventriculoarterial junction. Consequently, there is a small segment of infundibular musculature at the nadirs of each sinus. In between adjacent sinuses, the outlet wall comprises of small triangles of fibrous tissue that become incorporated into the ventricular circulation when the valve is in closed position [5]. Extensions of ventricular myocardium into the adventitia reportedly occur in approximately 20% of individuals and have been traced to a maximal distance of 6 mm beyond the junction [6].

Distinctive of the septal surface of the right ventricle is a Y-shaped muscle band, the septomarginal trabeculation. The ventriculoinfundibular fold arises from between the limbs of the Y to form the supraventricular crest. The attachment of the medial papillary muscle to the inferior limb is the landmark for the right bundle branch, which emerges from its transseptal course onto the subendocardium (Figure 2.2A). The moderator band arising from the body of the septomarginal trabeculation carries a fascicle of the right bundle branch to the parietal wall of the right ventricle. The apical

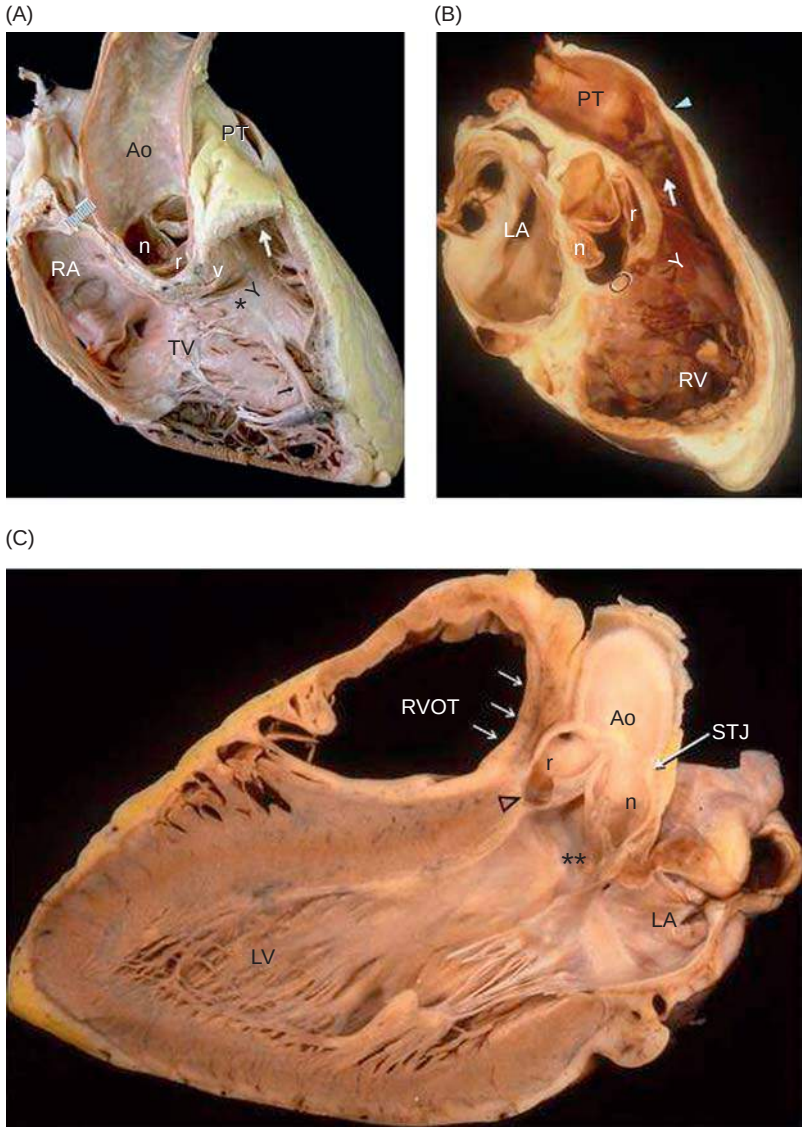


Figure 2.2 (A) and (B) are dissections into the right ventricle and the right ventricular outflow tract (RVOT, white arrow), respectively. (A) The ventriculoinfundibular fold (v) continues into the muscle of the subpulmonary infundibulum that surrounds the outflow tract (arrow). Y marks the septomarginal trabeculation. The moderator band (black arrow) arises from its body while the medial papillarty muscle (asterisk) inserts into its inferior limb. (B) This deeper cut profiles the RVOT to show the muscular infundibulum leading to the pulmonary valve at the ventriculoarterial junction (triangle). The oval marks the area of the central fibrous body. (C) This longitudinal section shows the RVOT passing over the aortic outflow tract. The musculature of the RVOT (small white arrows) overlying the aortic sinuses and the ascending aorta (Ao) can give the impression of there being an extensive muscular sleeve around the aorta. The triangle indicates the presence of muscle at the nadir of the right coronary aortic sinus (r). The location of the atrioventricular conduction bundle is depicted by asterisks. LA, left atrium; LV, left ventricle; n, noncoronary aortic sinus; and STJ, sinutubular junction

portion of the right ventricle is characterized by a meshwork of coarse muscular trabeculations. The ventricular wall in between the trabeculations is about 2 mm thick.

The left ventricle

The central location of the aortic valve in the heart places the outflow tract in between the mitral valve and the ventricular septum. The septal half of the aortic outlet is muscular whereas the other half is an area of fibrous continuity between mitral and aortic valves. Ventricular myocardium rarely exists in between the aortic and the mitral valves. The curvature of the ventricular septum continuing into the free wall forms the anterosuperior wall of the left ventricular outflow tract. The septal extremity of the fibrous continuity is the right trigone which, together with the membranous septum, forms the central fibrous body (see the preceding text). The semilunar hinge lines of the aortic leaflets enclose a segment of ventricular myocardium in the nadir of the right coronary aortic sinus (Figure 2.2C) and the adjacent part of the left coronary aortic sinus.

Each leaflet of the aortic valve is slightly thickened toward the free margin. In the elderly, the leaflets often have small fenestrations above the closure lines. The interleaflet fibrous triangles between adjacent sinuses project like the prongs of a coronet above the ventricular chamber. The triangle between the noncoronary and the left coronary leaflets points toward the left atrium whereas the triangle between the right and the left coronary leaflets leads to the tissue plane behind the subpulmonary infundibulum. The triangle between the right and the noncoronary leaflets potentially leads to epicardial space toward the right atrium. Proximally, this triangle is continuous with the membranous septum, making it a landmark for the atrioventricular conduction bundle, which emerges in the left ventricle positioned between the membranous septum and the muscular ventricular septum (Figure 2.2C). The left bundle branch descends in the subendocardium of the muscular septum and fans into three interconnecting main fascicles that ramify distally into fine strands. Some strands may be carried within so-called false tendons that traverse the cavity to the parietal wall and papillary muscles of the mitral valve. The left ventricle is characterized by fine apical trabeculations and thick muscular walls. However, the wall is thin at the very apex.

Pathologic substrates of ventricular arrhythmias

Ischemic causes

The life-threatening arrhythmias VT and ventricular fibrillation (VF) are usually initiated by mechanisms of reentry in the ventricular myocardium. Reentry depends on the coexistence of an arrhythmogenic substrate, which is a preexistent structural pathological condition in the heart, and a "trigger" such as acute ischemia that initiates the electrical abnormality. In addition,

there are electrophysiological heterogeneities within the normal ventricular myocardium, originating from early heart development as has been proposed recently by Boukens *et al*., that further facilitate onset of VT [7].

Pathologists have studied the arrhythmogenic substrates, mostly in the hearts of victims of sudden cardiac death (SCD) or in the explant hearts of patients with end-stage heart failure, a disease state often associated with malignant arrhythmias. The most common cause of SCD, the leading overall mode of death in Europe and USA, is VF. Autopsy studies of SCD victims have shown that in many, but not all, structural abnormalities of the heart can be found, thus giving insight into the nature of the arrhythmogenic substrates and the cardiac abnormalities that cause them. Causes of arrhythmic SCD vary from congenital heart disease to ischemic heart disease, heart valve disease, primary or metastatic neoplasia, myocarditis, and the spectrum of cardiomyopathies; in other words, any cardiac disease of "sufficient" severity may cause SCD. It has been shown, moreover, that not all diseases found at autopsy bear the same SCD risk, and recently the Association for European Cardiovascular Pathology (AECVP) has established a risk stratification of cardiac diseases with different degrees of certainty to evoke SCD [8].

In the adult population, the incidence of SCD ranges from 36 to 128 per 100.000. The most common substrate for SCD is ischemic heart disease, which in turn in most cases is because of atherosclerotic coronary artery disease.Most of these deaths occur as a result of VF, but mechanical causes such as myocardial rupture are also seen. In the population younger than 30 years, the incidence of SCD is much lower (1/10,000), but relative rate of death because of VF is higher, and the spectrum of underlying diseases is wider (cardiomyopathies, congenital heart disease, and myocarditis) [8]. The common denominator for most diseases is the development of areas of ischemic, inflammatory, or degenerative myocardial cell death/necrosis, recovering by the time in areas of fibrosis, to form a nidus for arrhythmias. Obviously, this will be more dramatic in patients with preexistent familiar cardiomyopathies and adaptive myocardial changes such as hypertrophy and dilatation, which have all an inherent risk of arrhythmias. Most illustrative in this respect is the spectrum of pathology related to ischemic heart disease.

Acute myocardial ischemia and infarction

In myocardial ischemia, the arterial oxygen supply is inadequate to meet the metabolic demands of the myocardial tissue. The commonest disease underlying myocardial ischemia is atherosclerotic coronary artery disease. Ischemia is often initiated by rupture or erosion of a lipid-rich inflamed atherosclerotic plaque, leading to thrombotic occlusion of a coronary artery. But, also lesions causing high-grade stenosis are at risk for onset of ischemia, especially when there are coexistent cardiac abnormalities such as cardiac hypertrophy, dilatation, or both. And, as mentioned in the preceding text, ischemia and infarction may also complicate several other cardiac diseases, such as valvular, myocarditis, and cardiomyopathies [9].

Pivotal to SCD prevention is the notion that the highest risk of ischemia-related arrhythmic death occurs around the time of an acute myocardial infarction. Also at the level of the myocardium functional changes occur already within seconds, in the form of loss of contractility ("atonic death"). The earliest microscopic changes after onset of ischemia (in minutes) are stretching of myofibril and increasing intracellular and extracellular edema, which may disturb intercellular connections. If occlusion persists for more than 20–30 min, irreversible ischemic damage of the myocardium occurs, and in the following hours, depending on the level of energy demand, preexistent myocardial pathology, and presence of collaterals, the infarcted tissue will extend in a wavelike manner from the subendocardial toward the epicardial area of the ventricular wall segment at risk. The morphological hallmark of irreversible cell injury is disruption of the cell membranes, and the central zone of affected myocardium evolves toward a coagulative type of necrosis. Myocardial cells showing another type of necrosis, contraction band necrosis, can be noticed in the surrounding marginal zone. This type of cell injury results from hypercontraction because of massive calcium influx in the cell, and relates to phenomena of ischemia and reperfusion in the border zone of the infarcted area. Ensuing necrosis evokes an acute inflammatory response dominated by neutrophils, followed by macrophage infiltration and a fibrovascular proliferative response. Fibrotic healing of small infarcts is completed within 2 months, but for large infarcts, it may take more than 3 months to form a fully matured fibrotic scar [9]. In addition to collagen, the scar tissue usually contains elastin and some adipose tissue, and rarely may contain areas of calcification and even bone tissue.

Early and late arrhythmic substrates

It is likely, and supported by several experimental designs, that ventricular arrhythmias are often initiated by an interaction between episodes of acute ischemia and an arrhythmogenic substrate already present in the myocardium [10]. For example, temporarily occlusion or even moderate flow reductions in coronary flow increased the incidence of sustained VT in dogs with prior myocardial infarctions, but not in similarly treated dogs without infarction. Such arrhythmias are thought to originate from the rim (border zone) of tissue surrounding the scar [11].

Indeed, infarcts often show marked spatial heterogeneity, with areas of necrosis interspersed with bundles of viable myocytes, particularly at the periphery of the infarct (Figure 2.3). In the reparative phase, this may lead to the formation of fibrocellular, fibrosclerotic, or fibroadipose scars with irregular outlines (Figures 2.4 and 2.5). Heterogeneity in tissue component makeup and also nervous innervations in these regions may create areas of aberrant conduction that generate the substrate for lethal reentrant arrhythmias [10]. Apart from the size and the age of the infarction [12], also the architecture of fibrosis appears to play a role as was observed by Kawara *et al*. after electrical stimulation of Langendorff-perfused explant hearts of 11 patients with

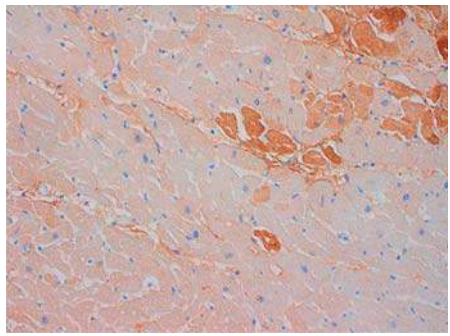


Figure 2.3 Border zone of acute myocardial infarction, 2 days after onset of the event. Necrotic myocytes, which are immunostained in brown with antifibrinogen antibody, are localized amidst vital (not stained) myoctyes. (Antifibrinogen, 200×)

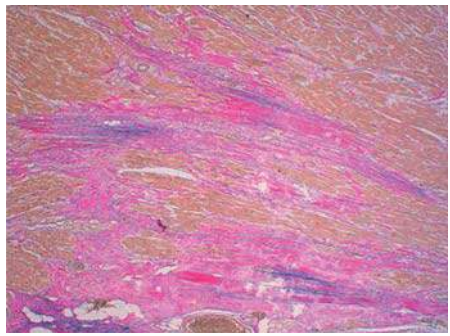


Figure 2.4 Histology of irregular scar. Irregular outlines with long bundles composed of collagen, elastin, and even mature fat, extending into adjacent vital myocardium of left ventricle. (Elastic van Gieson stain, 40×)

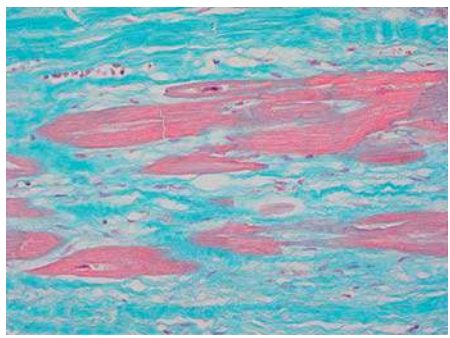


Figure 2.5 Detail of hypertrophic but vital myocytes (red) surrounded by scar tissue (blue). (Masson trichrome stain, 400×)

end-stage heart failure. Detailed histological study of these hearts revealed that conduction abnormalities, which can be linked to arrhythmia, occur in areas with patchy fibrosis showing long compact bundles, as opposed to areas with diffusely distributed fibrosis and only short connective tissue bundles, where such conduction delays are insignificant [13]. Also, extensive remodeling at the subcellular level occurs in these border zones and includes reduced cellular coupling, and reduction and redistribution of the protein connexin 43 (Cx43). Normally, there is a high degree of intercellular connections through gap junctions: ventricular myocytes are connected

to roughly 11 neighboring myocytes, by either side-to-side or end-to-end connections, allowing continuous conduction. However, the average numbers of connections by gap junctions in the border zones of infarctions are reduced by 25% (for end-to-end connections) to nearly 75% (for side-to-side connections) [14].

Adaptive changes in the remote myocardium
In the compensatory hypertrophied and/or dilated parts of the ventricular myocardium remote from infarcted areas, redistribution of connexins, secretion of several subsets of cytokines, apoptotic cell death, and deposition of interstitial fibrosis leading to cellular uncoupling or even cellular sequestration have all been well documented. But also hypertrophied and dilated hearts not related to ischemic insult may show similar changes. There is an increase of interstitial fibrous tissue, and Cx43 can be downregulated and distributed within the cell toward a pattern that is also observed in the fetal heart. Such alterations likely explain the inherent clinically well-documented increased risk of arrhythmic sudden death. Moreover, in severely dilated hearts the situation can be aggravated by a drop in coronary perfusion flow and ischemia, especially in the subendocardial regions of myocardium.

Sympathetic innervation. In the necrotic myocardium, there is destruction of sympathetic nerves, which has been associated with enhanced inducibility of VF, especially in the presence of catecholamines. But also in the reparative phase of myocardial infarction, regional increased nerve densities that result from regenerating sprouting of nerves has been implicated in the onset of ventricular arrhythmias, as was found by means of immunohistochemical investigations in native hearts of 53 transplant patients who had suffered from either ischemic or nonischemic dilating cardiomyopathies [15].

Reperfusion. Timely recovery of coronary patency after thrombotic occlusion of the artery by means of thrombosuction, balloon dilation, and/or stenting results in reperfusion of the area at risk, which halts the advancing wave front of myocardial necrosis. Importantly, incidence of VF in the setting of acute coronary syndromes has decreased as a result of revascularization that limits infarct size. Albeit potentially beneficial for myocardial salvage, reperfusion may elicit further injury, so-called "reperfusion injury," which includes: (1) microvascular reperfusion injury, leading to no-reflow and/or myocardial hemorrhages; (2) myocardial stunning (a postischemic flow—function mismatch apparent by contractile dysfunction); (3) lethal injury of potentially salvageable myocytes; and (4) reperfusion arrhythmias (VT or VF that occurs very early (in seconds)) after onset of reperfusion. Histologic features of reperfusion injury are contraction band necrosis, massive influx of neutrophils, microvascular damage, and myocardial hemorrhages, which form the pathological background for onset of the reperfusion arrhythmia [16].

Coronary microembolization. Coronary artery disease complicated by thrombus may lead to spontaneous microembolization of the distal arterial bed. Postmortem analysis of the myocardium of patients who died of ischemic heart disease has revealed surprisingly high rates (>50% in some studies) of microembolization of the myocardial microvascular bed distal to thrombotic occlusion. The risk of embolization increases during percutaneous coronary interventions, when plaques are crushed mechanically. Important determinants for the occurrence and extent of microembolization are the total atherothrombotic burden in the artery and the invasiveness of the interventional procedure. For example, interventions in aortocoronary saphenous vein grafts cause more emboli than in native arteries, because of larger plaque burden and the friability of (lipid-rich) plaques in grafts. Microscopic small infarctions as a result of microvascular occlusion may also coalesce and create larger lesions, which may serve as a substrate for the onset of ventricular arrhythmias [17].

Cardiomyopathies

There are several heart muscle diseases that can alter the structure of the ventricles, putting the patient at risk of VT/VF. Among inherited cardiomyopathies, arrhythmogenic (ARVC), hypertrophic (HCM), and dilated (DCM) cardiomyopathies need to be addressed [18–21].

ARVC is an inherited cardiomyopathy that presents clinically with ventricular arrhythmias or SCD. The pathologic hallmark of ARVC is myocyte loss with fibrofatty replacement. It is now recognized that ARVC is a disease of the desmosomes, which play a role in cell-to-cell adhesion. The structural abnormalities are more prominent in the right ventricle but the left ventricle can also be involved. The replacement of the ventricular myocardium by fibrofatty tissue is progressive, starting from the epicardium or midmyocardium and then extending to become transmural in the thin-walled right ventricle, whereas it affects the subepicardial and midmural layers in the left ventricle [22,23]. This explains why wall thinning and aneurysms are present only in the thin-walled right ventricle, typically located at the inferior, apical, and infundibular regions ("triangle of dysplasia") (Figure 2.6A). Histological examination reveals islands of surviving myocytes interspersed with fibrous and fatty tissue. Fatty infiltration of the right ventricle should not be considered "*per se*" a sufficient morphologic hallmark of ARVC because a certain amount of intramyocardial fat is present in the RV in the anterolateral and apical region, particularly in the elderly and in obese people. In addition to fat replacement, the presence of replacement-type fibrosis and myocyte degenerative changes are essential for a clear-cut diagnosis of ARVC (Figure 2.6B,C). Clusters of dying myocytes may be seen at histology, providing evidence of the acquired nature of myocardial atrophy. These changes are frequently associated with inflammatory infiltrates that may play a role in triggering life-threatening arrhythmias. Three-dimensional electroanatomic voltage mapping offers the potential to identify low-voltage areas that

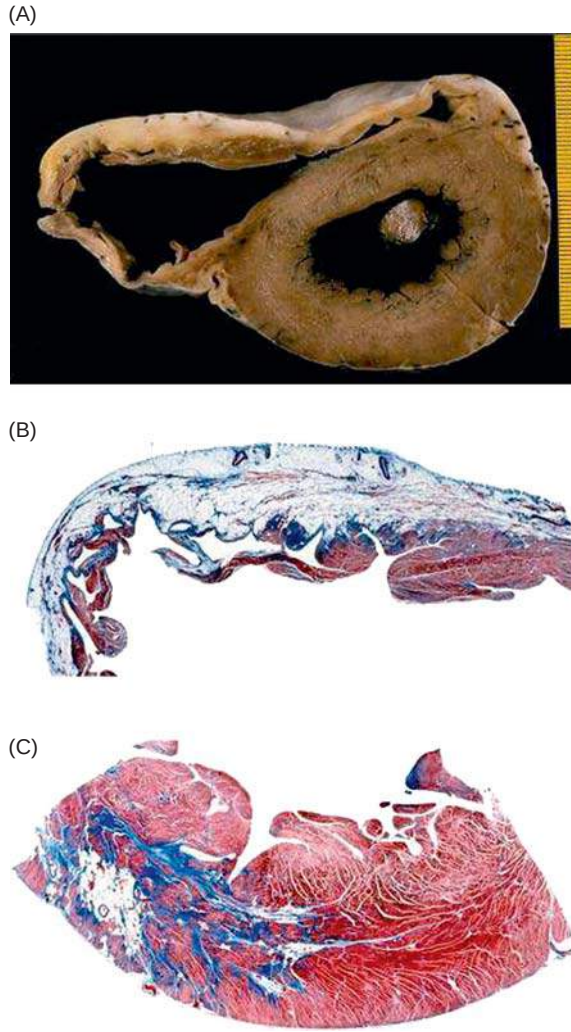


Figure 2.6 ARVC: (A) cross section showing RV anterior and posterior aneurysms, plus spotty involvement of the LV; (B) transmural fibrofatty replacement of the anterior free wall; (C) subepicardial fibrofatty involvement of the posterolateral left ventricular free wall. ARVC, arrhythmogenic right ventricular cardiomyopathy.

correspond to regions of right ventricular myocardial loss and fibrofatty replacement in patients with ARVC. Catheter ablation of VT has acute success rates of 60–90%. However, because of the progressive nature of the disease with the development of new arrhythmogenic focuses over time, relapses are frequent, with a high rate of VT recurrence. It is for this reason that ICD implantation affords the best protection against SCD.

HCM is a disease of the cardiac sarcomere, and the most frequent causes of HCM are mutations in cardiac β-myosin heavy chain, cardiac troponin T,

cardiac troponin I, and myosin binding protein C genes. HCM is characterized macroscopically by concentric left ventricular hypertrophy, which may be either asymmetrical or symmetrical. The asymmetrical variant is the typical form, and involves the basal part of the anterior septum with bulging into the subaortic region, thus accounting for left ventricular outflow tract obstruction (Figure 2.7A). This is often accompanied by "endocardial fibrous plaque" on the septum caused by friction with the mitral valve apparatus. Several morphological variants of HCM, including HCM with mid-ventricular or apical hypertrophy, have been described on imaging with echocardiography and magnetic resonance investigations. HCM may also progress to a dilated phase that mimics DCM. The histopathological hallmarks are myocyte hypertrophy, disarray, and interstitial fibrosis. Myocyte disarray consists of an architectural disorganization of the myocardium, with adjacent myocytes (or bundle of myocytes) aligned perpendicularly or obliquely to each other (Figure 2.7B). The myocytes are hypertrophied and exhibit distinct nuclear changes. Replacement-type fibrosis (Figure 2.7C) is a common finding, particularly within areas of hypertrophy, as well as signs of acute myocardial ischemia, such as myocyte necrosis and neutrophilic infiltrates. Intramural small vessel disease with smooth muscle cell hyperplasia and medial hypertrophy is another pathological feature of HCM [24]. As with ARVC, placement of an ICD provides the best protection against sudden death in the high-risk subset of patients with HCM. Treatment options for the hemodynamic consequences of asymmetric septal hypertrophy include surgical myectomy or transcoronary septal ablation.

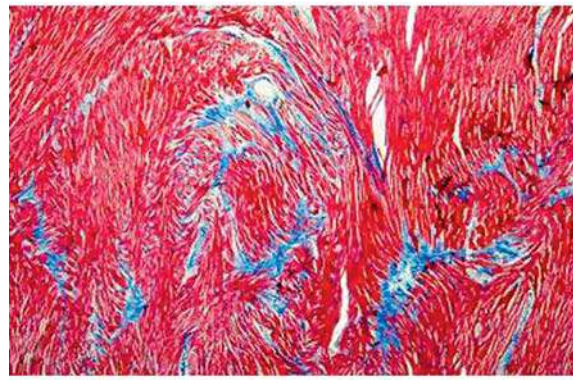
Dilated cardiomyopathy (DCM) and isolated left ventricular noncompaction (LVNC) are cardiomyopathies that are mostly characterized by systolic and diastolic ventricular dysfunction and more rarely by arrhythmic symptoms and signs.

DCM is characterized by a globular shape with eccentric hypertrophy because of a ventricular chamber dilatation and an increase in myocardial mass. Diffuse endocardial thickening as a result of organized mural thrombosis and atrial enlargement with atrial thrombi are frequent findings. The histological changes are mostly nonspecific and include myocyte attenuation, extensive myofibrillary loss with vacuolated appearance and perinuclear halo, dysmorphic and dysmetric nuclei, and interstitial fibrosis. True replacement-type fibrosis is appreciable in only one-third of cases. This is usually patchy and subepicardial fibrosis as contrasted with the subendocardial and regional distribution seen on patients with ischemic heart disease. Interstitial T lymphocytes as well as focal macrophages associated with individual myocyte death are also visible in about one-third of cases. Although the etiology of these cases is largely unknown, up to 35% of individuals with idiopathic DCM have familial disease and gene defects of structural proteins of the myocyte cytoskeleton or sarcolemma have been identified.

Isolated LVNC, which falls into the category of unclassified cardiomyopathies in the recent AHA classification by the WHO, has been grouped among

(A)

(B)



(C)

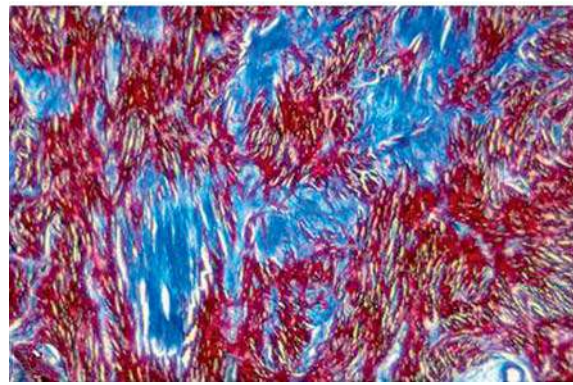


Figure 2.7 (A) Long axis view of the heart showing the typical subaortic stenosis because of asymmetric septal hypertrophy; (B) myocardial disarray and interstitial fibrosis; (C) spot of replacement-type fibrosis

primary, genetically determined cardiomyopathies. This cardiomyopathy is thought to be the consequence of the postnatal persistence of the embryonic pattern of myocyte architecture. The left ventricle is usually affected, with or without right ventricular involvement, and results in systolic and diastolic ventricular dysfunction. More rarely, clinical presentation is with arrhythmic symptoms and signs. Pathologically the noncompacted layer of the myocardium consists of excessively prominent trabeculations with deep intertrabecular recesses extending into the compacted myocardial layer. Typically, the apical and mid-ventricular segments of the free walls of the left ventricle are affected. Histologically, the noncompacted layer is made of numerous "fingerlike" trabeculations. Endocardial thrombus deposition and fibrous organization are frequent features.

Finally, among cardiomyopathies at risk of electrical instability, acquired forms should be mentioned. Inflammatory cardiomyopathies (or myocarditis) have been classified among primary cardiomyopathies, acquired forms in the recent AHA document [18]. Either infective or immune in origin, myocarditis usually presents with signs of pump failure and ventricular dilatation. Nonetheless, ventricular arrhythmias have been described in patients with myocarditis and otherwise structurally normal heart. SCD may occur in active or healed phases as a consequence of ventricular arrhythmias, including VT and VF, that develop mostly in the setting of unstable myocardial substrate, namely inflammatory infiltrate, interstitial edema, myocardial necrosis, and fibrosis [25]. Gross appearance of the heart is not always distinctive because the heart may have hugely dilated cardiac chambers, or be apparently normal. Histology invariably discloses interstitial edema, inflammatory infiltrate, and myocardial necrosis (Figure 2.8). This process can be either focal or multifocal or diffuse; preferentially it involves the myopericardial layers (epimyocarditis). The inflammatory infiltrate is usually polymorphous, less frequently purely lymphocytic. Patchy giant cell myocarditis as well as eosinophilic myocarditis in the setting of allergic conditions has also been reported. A complete "restitutio ad integrum" without structural sequelae can occur. However, replacement-type fibrosis, which represents an additional substrate for reentrant arrhythmias, can develop during the subacute–chronic stages (recurrent or chronic myocarditis) and evolution toward DCM is frequent.

Important structures in the neighborhood of the heart

In some patients, successful catheter ablation of VT requires an epicardial approach. Accessing the epicardial surface via the pericardial space can be advantageous but the operator needs to be mindful of the coronary arteries and veins on the epicardial surface of the heart as well as other important structures around the heart.

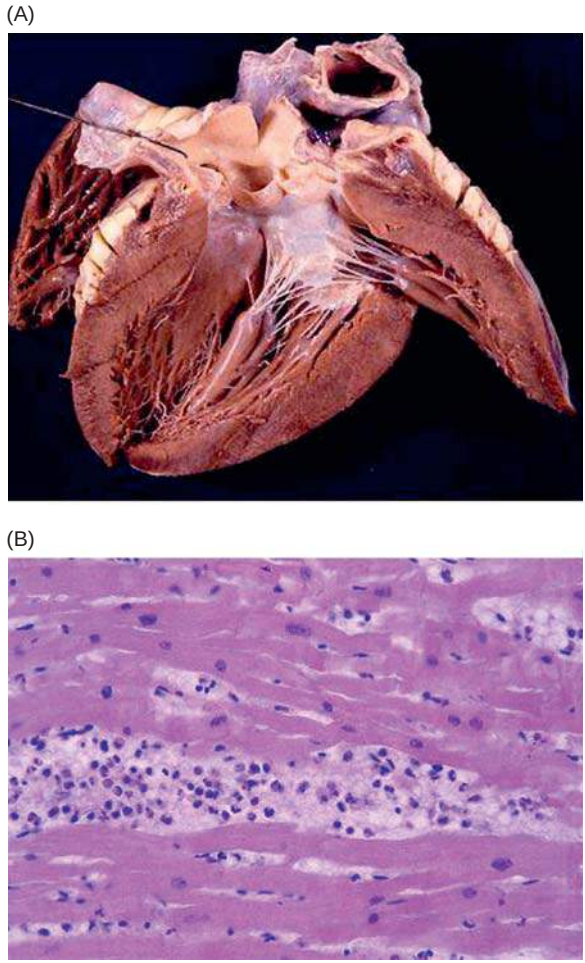


Figure 2.8 Myocarditis: (A) apparently normal heart at gross examination; (B) interstitial edema, polymorphous inflammatory infiltrates, and myocyte necrosis

The pericardial sac

The heart and the adjacent parts of the great arteries and veins are enclosed by pericardium consisting of two components: the fibrous and the serous pericardium. The fibrous pericardium is a sac made of tough connective tissue that completely surrounds the heart and is attached only at its arterial and venous poles (Figure 2.9). The serous pericardium consists of two layers of serous membrane. The inner (visceral) layer forms the epicardium of the heart, whereas the outer (parietal) layer is adherent to the internal surface of the fibrous pericardium [26,27]. The visceral layer is reflected from the heart and the great vessels to continue into the parietal layer, thus enclosing

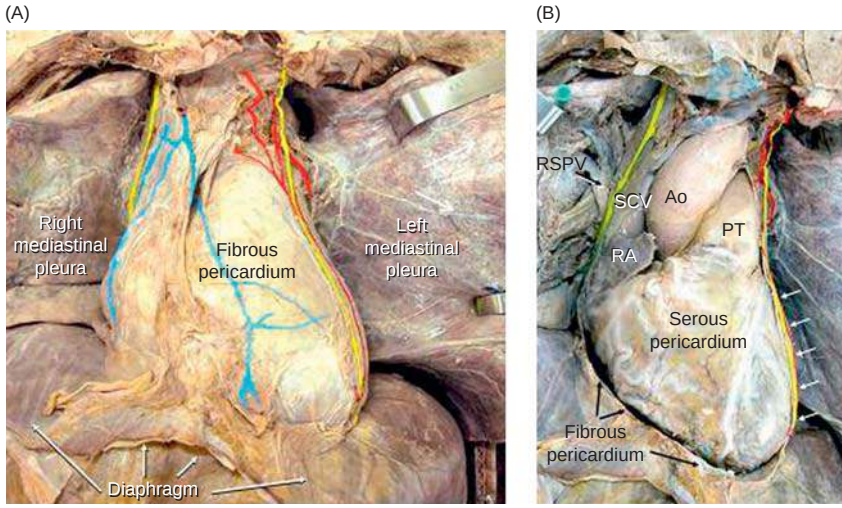


Figure 2.9 (A) and (B) are dissections with the lungs retracted to show the pericardium and diaphragm. (A) The fibrous pericardium is intact with the right and left phrenic nerves traced in yellow, the pericardiophrenic arteries in red, and the veins in blue. (B) The anterior part of the fibrous pericardium has been removed to reveal the relationship between the phrenic nerves and the cardiac structures. In this cadaver, the descending course of the left phrenic nerve (small arrows) is related to the obtuse margin of the heart

between the layers a narrow space, the pericardial cavity, which is filled normally with 20–25 ml of serous fluid.

Fibrous pericardium

Superiorly, the fibrous pericardium is continuous with the adventitia of the great vessels like cuffs attaching to the ascending aorta and pulmonary trunk, and to the superior caval vein several centimeters above the site of the sinus node. Inferiorly, it is attached to the central tendon of the diaphragm and a small muscular area to the left. Posteriorly, it is related to the mediastinal surfaces of both lungs, the esophagus, and descending thoracic aorta. Laterally are the pleural coverings of the mediastinal surface of the lungs. The phrenic nerves, with their accompanying vessels, descend bilaterally between the fibrous pericardium and the mediastinal pleura on each side (Figure 2.9).

Anteriorly, the fibrous pericardium is separated from the thoracic wall by the lungs and the pleural coverings. However, in a small area behind the lower left half of the body of the sternum, and the sternal ends of left fourth and fifth costal cartilages, the pericardium is in direct contact with the thoracic wall. The pericardial space can be accessed via a subxiphoid puncture, and allows relatively free manipulation of catheters around the epicardial surface of the heart, especially the ventricles, except in cases with pericardial adhesions. Inferiorly, the pericardium is separated by the diaphragm from the liver and fundus of the stomach.

Pericardial sinuses and recesses

The pericardial cavity has two sinuses and several recesses (Figure 2.10). These are not complete compartments but represent extensions of the cavity. The first sinus is the transverse sinus, which is delineated anteriorly by the posterior surface of the ascending aorta and pulmonary trunk bifurcation and posteriorly by the anterior surface of the atria and superior caval vein. The second sinus, the oblique sinus, is a cul-de-sac located behind the left atrium and anterior to the esophagus. The transverse sinus lies anterosuperiorly relative to the oblique sinus. The right and left pulmonary venous recesses are at the back of the left atrium between the upper and the lower pulmonary veins on each side, indenting the side walls of the oblique sinus to greater or lesser extents. The pericardial reflections at the veins, particularly the pulmonary veins, are varied and can restrict maneuvers, precluding

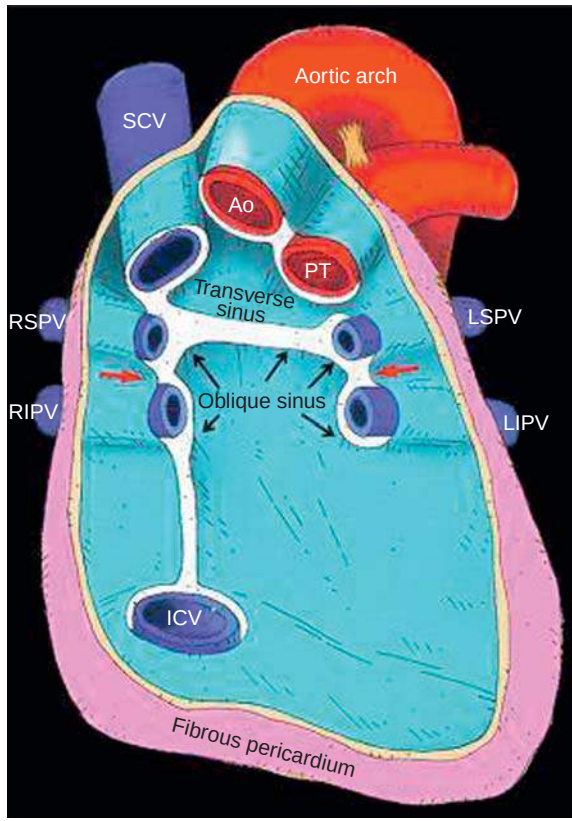


Figure 2.10 Diagram showing the transverse and oblique sinuses revealed after making a window dissection in the fibrous pericardium (colored pink) and removing the heart. The parietal layer of the serous pericardium is colored blue. The white areas depict pericardial reflections. The red arrows indicate pulmonary recesses

complete encirclement for drawing ablation lines around the veins. The inferior and superior aortic recesses are extensions from the transverse sinus. The superior recess lies between the ascending aorta and the right atrium whereas the inferior recess between the aorta and the left atrium extends to the level of the aortic valve.

The diaphragm

The diaphragm is a curved fibromuscular sheet that separates the thoracic from the abdominal cavity. Its upper surface is related to three serous membranes. On each side, the pleura separate the diaphragm from the base of the corresponding lung. Over the middle part, the pericardium interposes between the diaphragm and the ventricles of the heart. The latter area, which is almost flat, is referred to as the cardiac plateau; this extends more to the left than to the right. The profile of the diaphragm rises on either side of the cardiac plateau to a smooth convex dome, which is higher and slightly broader on the right than on the left (Figure 2.9). Most of the inferior surface of the diaphragm is covered by peritoneum. The right side is molded over the convex surface of the right lobe of the liver, the right kidney, and the right suprarenal gland. The left side conforms to the left lobe of the liver, the fundus of the stomach, the spleen, the left kidney, and the left suprarenal gland.

Phrenic nerves

The phrenic nerves accompanied by the pericardiophrenic vessels descend bilaterally onto the pericardium. The right phrenic nerve descends almost vertically, first along the right brachiocephalic vein, then along the right anterolateral surface of the superior caval vein, and continues its descent immediately in front of the right pulmonary veins in the lung hilum before reaching the diaphragm. The right phrenic nerve has a close anatomic relationship with the superior caval vein (minimal distance 0.3 ± 0.5 mm) and the right superior pulmonary vein (minimal distance 2.1 ± 0.4 mm) as it runs through the lateral and posterolateral wall of the right atrium [28,29].

The left phrenic nerve descends behind the left brachiocephalic vein, continues over the aortic arch and pulmonary trunk onto the pericardium overlying the left atrial appendage, and then descends either anteriorly or anterolaterally over the area of the left ventricle to insert into the diaphragm behind the cardiac apex [29]. The course of the left phrenic nerve on the fibrous pericardium has three variants relating to various cardiac surfaces: (a) anteriorly across the anterior surface of the heart related to high part of the right ventricular outflow tract and high anterior left ventricular wall; (b) leftward over the tip of the left atrial appendage and obtuse margin of the left ventricle; (c) posteriorly over the neck of the left atrial appendage and toward the inferior surface of the left ventricle to be related to the epicardial surface of the high inferolateral left ventricular wall and the inferior left ventricular vein.

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CHAPTER 3

Pathophysiology and Mechanisms of Ventricular Tachycardia/Ventricular Fibrillation

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Experimental ventricular fibrillation

While it is possible to induce ventricular fibrillation (VF) in normal human hearts, almost all spontaneous VFs occur in hearts with electrophysiological, structural, and/or neural abnormalities. These abnormalities may be congenital, but mostly are acquired as a result of disease-induced remodeling. Over the past decade, significant progresses have been made to understand how these three factors work together to induce VF.

Electrophysiological abnormalities

Since the discovery that calcium (Ca) sparks are elementary events underlying excitation–contraction (EC) coupling in heart muscle [1], multiple important discoveries have been made related to the importance of Ca dynamics in VF. Under physiological conditions, the sarcoplasmic reticulum (SR) Ca release is triggered primarily by electrical activation. However, it is also possible that SR can release Ca spontaneously, without being triggered by electrical activation. The increased Ca then activates I_{NCX}, which in turn results in arrhythmia. This process is also known as reverse EC coupling [2]. The propensity for spontaneous SR Ca release is increased by abnormal

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functioning of the type 2 ryanodine receptor (RyR2) on the SR [3], which in humans causes catecholaminergic polymorphic ventricular tachycardia (CPVT), VF, and increased incidence of sudden death. Based on the study of mice with RyR2 mutations, CPVT is induced by delayed afterdepolarization and triggered activity from the His-Purkinje system during catecholamine stimulation. RyR2 stabilization may be a novel antiarrhythmic strategy in situations with RyR2 dysfunction [4].

Structural abnormalities

In addition to mice with RyR2 mutation, the His-Purkinje system may also play an important role in the mechanisms of other types of VF. Recent studies [5] showed that abnormal automaticity from His-Purkinje system may contribute to the activations of experimental VF. Ablation of the subendocardium hastens VF spontaneous termination and alters VF activation sequences, suggesting that Purkinje fibers are important in the maintenance of VF [6].

In addition to the His-Purkinje system, there is also renewed interest in the importance of fibrosis in the mechanisms of VF. In Langendorff-perfused human hearts, areas with increased fibrosis may serve as the anchor for reentrant excitation [7]. However, more recent studies showed that pathological conditions, such as ischemic cardiomyopathy and heart failure, may differentiate fibroblasts into myofibroblasts. The presence of myofibroblasts may result in myocyte–fibroblast electrical coupling via gap junctions, leading to increased propensity of reentrant arrhythmia [8].

Neural abnormalities

In addition to electrophysiological and structural remodeling, neural remodeling may also occur after myocardial infarction. The neural remodeling is characterized by heterogeneous cardiac nerve sprouting and sympathetic hyperinnervation in the myocardium [9,10]. The mechanisms of neural remodeling after myocardial infarction may result from immediate local nerve growth factor (NGF) release, followed by upregulation of NGF and growth-associated protein 43 (GAP43) expression at the infarcted site. NGF and GAP43 are transported retrogradely to stellate ganglion, which triggers nerve sprouting at the noninfarcted portion of the left ventricle (LV). Subsequent studies showed that in ambulatory dogs with myocardial infarction, completed atrioventricular block, and increased cardiac innervation, spontaneous sympathetic discharges may cause spontaneous VF and ventricular tachycardia (VT) [11]. The importance of neural remodeling in ventricular arrhythmia is supported by the efficacy of beta-blocker therapy in reducing sudden death after myocardial infarction.

Summary

In summary, the occurrence of spontaneous VF depends on the interaction between sympathetic discharges, electrophysiological abnormalities, and structural abnormalities. Disease conditions that result in abnormalities of one

or more of these three factors may be associated with increased propensity of VF and sudden death. Better understanding of the proarrhythmic interactions among these factors may lead to better prevention and treatment of VF.

Experimental ventricular tachycardia

Much of what we know about electrophysiological mechanisms of VT originates in experimental studies that provide a framework of mechanisms.

Automaticity

The cause of **normal** automaticity in subsidiary pacemakers in the His-Purkinje system is a spontaneous decline in the membrane potential during diastole, the pacemaker potential, that is under autonomic control [12]. Sympathetic stimulation in dogs can generate automatic VT with a maximum rate of around $120\,min^{-1}$ [13]. The flow of current between partially depolarized myocardium and normally polarized latent pacemaker cells enhances automaticity to cause tachycardia arising at borders of ischemic areas after experimental coronary occlusion [14]. Stretch of the ventricles in a dog model causes tachycardia through stretch-activated channels, a model of akinetic areas of chronic myocardial infarction [15].

When resting potentials are reduced, spontaneous diastolic depolarization may occur and cause repetitive impulse initiation by **abnormal automaticity**. Purkinje fibers surviving on the endocardial surface of experimental canine infarcts, 24 h after coronary occlusion, have low membrane potentials and abnormal automaticity, which results in accelerated idioventricular tachycardia [12].

Triggered activity

Triggered activity is dependent on afterdepolarizations. **Delayed afterdepolarizations** are caused by an increase in intracellular Ca^{2+} ("Ca overload") and cause tachycardia in animal models of digitalis toxicity [16]. Ventricular muscle and Purkinje fibers also develop delayed afterdepolarizations with sympathetic stimulation, which cause experimental triggered VT [16]. Mouse models of catecholaminergic polymorphic VT have a genetic defect in the ryanodine receptor causing leakage of Ca from the SR and delayed afterdepolarizations [17].

Early afterdepolarizations are associated with prolongation of action potential (AP) duration and cause triggered torsades de pointes in animal models of antiarrhythmic drug toxicity [18]. Stretch that might occur during heart failure also causes triggered tachycardia [12]. Mutations in Na^+, K^+, and Ca^{2+} channels have also been associated with early afterdepolarization-triggered VT in mouse models and humans [19].

Abnormal impulse conduction and reentry (see Figures 3.1 and 3.2)

Reentry is dependent on unidirectional conduction block and an impulse wavelength (conduction velocity × refractory period) that is shorter than the

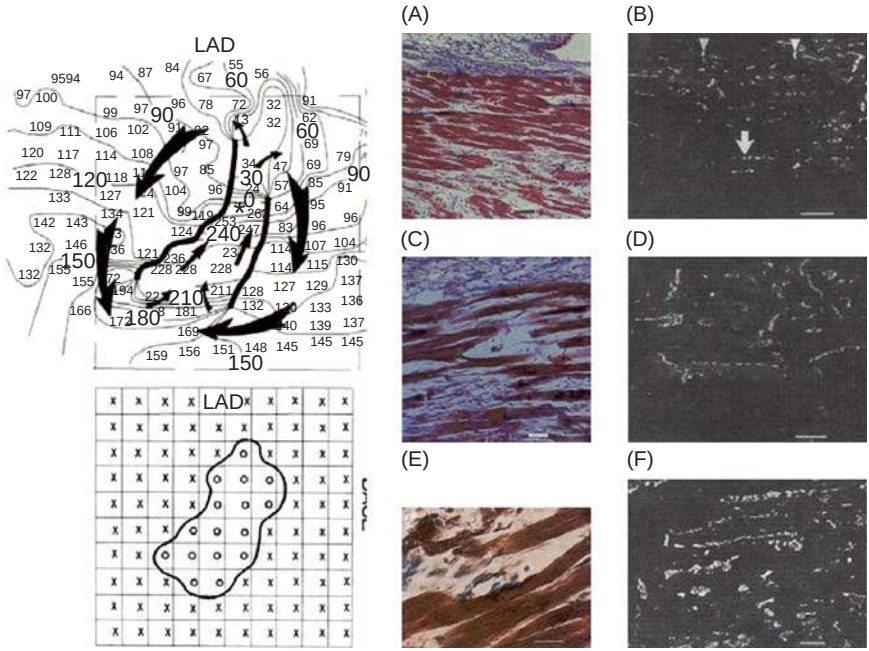

Figure 3.1 Reentry in the epicardial border zone of a canine model of healing myocardial infarction. The left panel at the top is an activation map of a "figure of eight" reentrant circuit during sustained ventricular tachycardia obtained with a multielectrode array. Each number is an activation time, and the arrows point out the direction of wavefront movement around two almost parallel lines of functional conduction block (solid back lines). Below the map is outlined the region of the central common pathway that was subjected to anatomic analysis, which is shown in the right panels. At the right, the left column shows the histology of the surviving myocardial cells that form the infarct epicardial border zone. The right column shows location of connexin43 (Cx43) gap junctions (bright spots) elucidated by immunofluorescence of Cx43-labeled antibodies. Remodeling of Cx43 along lateral myocyte membranes is evident (Reproduced by permission from Peters *et al*. [20])

path length of the reentrant circuit. There are numerous experimental models of reentrant VT; the most thoroughly described are ischemia and myocardial infarction in large animals in which mapping of impulse propagation is feasible. During the first phase (phase 1a) of tachycardia, within minutes after coronary occlusion, reductions in resting membrane potential and inward Na^+ current lead to alterations in conduction, and changes in repolarizing K^+ currents alter refractoriness, all of which contribute to reentrant VT that has been mapped [12,14]. After approximately 15–30 min, uncoupling of myocytes from internalization of connexin43 (Cx43), low intracellular pH, and high intracellular Ca^{2+} contribute to slow activation and block [12,14].

Irreversible myocardial damage after experimental coronary occlusion results in infarction. In a canine infarct model, reentrant circuits with a "figure of eight" pattern have been mapped during VT induced by programmed

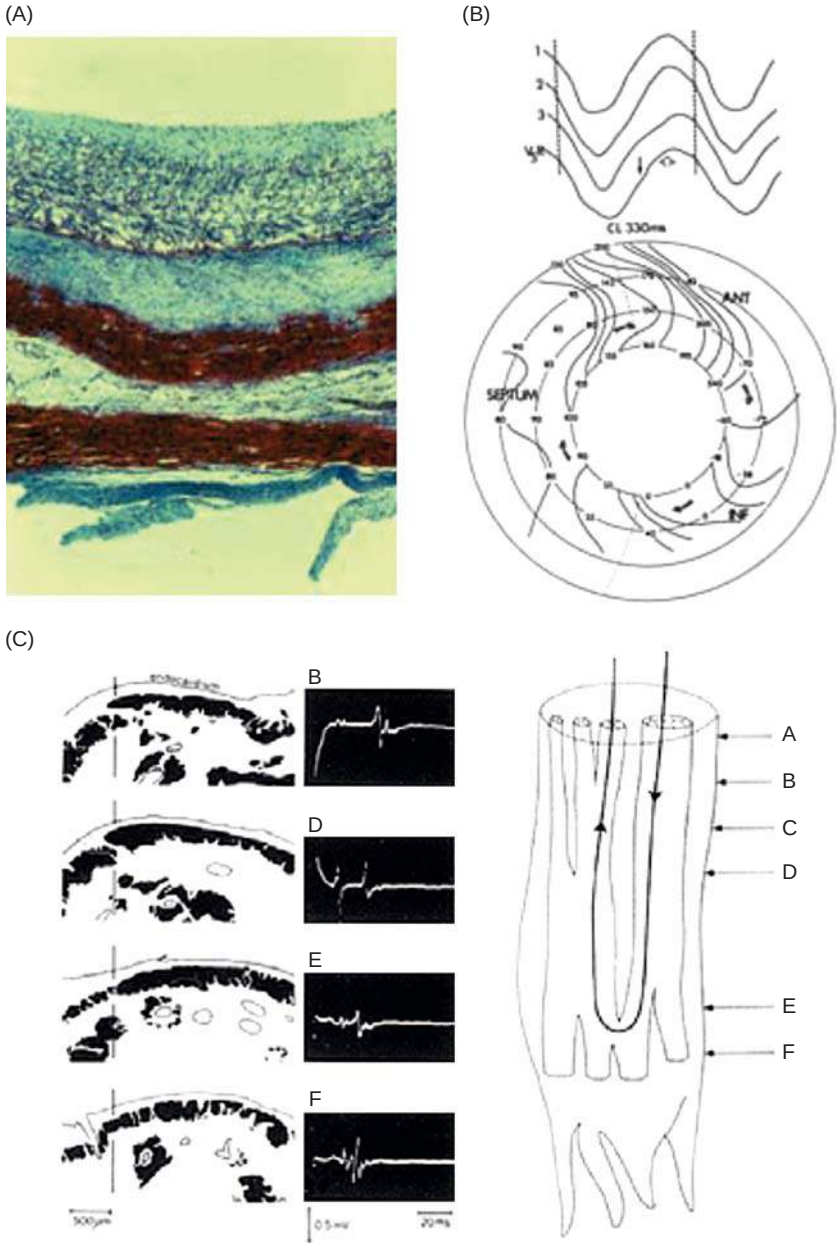

Figure 3.2 Surviving myocytes in healed infarcts from patients with healed myocardial infarction and sustained ventricular tachycardia (VT) form substrates for reentrant circuits. In Panel A is shown the surviving endocardial border zone of viable myocytes (red) embedded in the scar tissue (blue–gray) in a surgical endocardial resection that terminated VT (Reproduced from Fenoglio *et al*. [21]). In Panel B is an activation map of a reentrant circuit (arrows show and isochrones show pattern of activation) in the endocardial border zone obtained during an endocardial resection procedure (Reproduced from Miller *et al*. [22]). In Panel C, surviving intramural myocytes in fibrotic scar are shown by the dark areas throughout sections of the left ventricle from a patient with a healed infarct and VT. Adjacent to each section is shown an electrogram recorded from the adjacent region. At the right is shown the activation pattern in the intramural surviving myocardium that formed a reentrant circuit (Reproduced from de Bakker *et al*. [23])

stimulation [12,14]. The substrate is myocytes surviving as a border zone of the infarct core with changes in ion channels caused by alterations in synthesis of channel proteins and remodeling of Cx43 gap junction connections [20]. In models of chronic infarction reentrant tachycardia, fibrosis forming the infarct scar distorts myocyte size, shape, and interconnections, leading to heterogeneous slow conduction and block and the formation of reentrant circuits [12,14].

Clinical ventricular fibrillation

Ventricular fibrillation is a catastrophic event that occurs in clinical setting and is related to sudden death. Experimental data support the hypothesis that VF is a result of reentry of many spiraliform waves in the ventricular myocardium [24,25]. This chaotic arrhythmia is a result of several pathogenetic expressions, and many interpretations were proposed to explain its onset. Like atrial fibrillation, VF needs an adequate structural substrate as, for example, the one present in the coronary heart disease (CHD) or in cardiomyopathy. Like atrial fibrillation, to start VF, different factors are necessary, such as (1) triggers and (2) the occurrence of complex neuroendocrine interactions, electrolyte changes, hypoxia, inflammation, drugs, and mechanical factors, among many others [26]. The most frequently occurring cause of VF is acute myocardial ischemia, which is because of CHD, coronary spasm (less frequently), or, rarely, anomalous coronary origin. It provokes serious electrical instability, with high automatism, shortening, and different duration of the cell action potential (AP) in the area of ischemic tissue. Very early premature ventricular complex (PVC), when there is an increased adrenergic tone, will induce VF. In ischemic cardiomyopathy, on the contrary, other factors besides myocardial ischemia, are present. The zone bordering the scar area, where there is live tissue with fibrotic tissue, is the structural substrate on which, very frequently, ventricular arrhythmias are triggered [27]. In this area, there exists a wide variability of the AP duration, so that it is the basis of the reentry and electrical instability, particularly where there is a systolic dysfunction and an imbalance of the autonomic nervous system [28,29]. In these patients, often rapid VT with hemodynamic impairment degenerates into VF. Recent studies have shown that, very often, papillary muscles are involved in the electrogenesis of ventricular arrhythmias through a close interface with the His-Purkinje system [30]. His-Purkinje fibers themselves are involved in the genesis of an early onset of PVC, which can trigger VT or VF [31]. The risk of developing malignant ventricular arrhythmias increases especially in patients with heart failure and left ventricular ejection fraction $<40\%$ [32]. This has also been observed in nonischemic cardiomyopathy. The presence of heart failure associated to a higher spatiotemporal dispersion of repolarisation revealed through abnormal T-wave alternance value (TWA) shows a higher risk of cardiac death and life-threatening arrhythmias [33]. In these cases, TWA may reflect cellular Ca abnormalities and provide a

mechanistic link with VT/VF [34]. The substrate of VF in other types of cardiopathy is made of structural alterations, often genetically originated, which are different for each disease, such as arrhythmogenic right ventricular cardiomyopathy [35] (fat degeneration, inflammation), hypertrophic cardiomyopathy (disarray of muscular structure), valvular heart disease (hypertrophy–dilatation, fibrosis), metabolic and inflammatory conditions, and so on. Single PVC, PVC runs, or VT are the triggers on which, in association with several modulating factors, starts a VF. In WPW, VF can be induced by an atrial fibrillation led at high frequency to the ventricles through one anomalous atrioventricular pathway [36]. Idiopathic VF, present in about 5–10% of survivors of out-hospital cardiac arrest, occurred without any heart disease [37]. Recently, attention was focused on the inherited aspects of ion channelopathies without overt structural cardiopathy. Spatial electrical heterogeneity within the ventricular myocardium through different changes of diastolic potential, genetically determined in long QT [38], short QT, and Brugada syndrome [39], as well as in catecholaminergic polymorphic VT, explains high electrical instability in these patients [40]. VF occurs when these alterations in depolarization are stressed by physical–emotional, metabolic, or drug-related factors. Genetic defects can also contribute to drug-induced channelopathies. Polymorphic genetic alterations cause an exaggerated drug action in apparently normal patients. High plasma levels of drugs, which exert a significant proarrhythmic effect, are the result of several changes of pharmacokinetics as for absorption, transport, distribution, and elimination of drugs. The implanting of ICD has proven to be the most effective therapy for prevention of sudden death. However, in some cases arrhythmic storms occurred, hardly controllable through ICD and medical therapy. In ischemic cardiomyopathy, unmappable VT and VF were treated with linear ablation lesion around the scar tissue guided by imaging techniques [41]. Recent studies, though, have shown that ablation can treat VF by eliminating triggers in different heart diseases [42–47]. These triggers start very early in the His-Purkinje fibers close to the area with structural or genetic AP abnormalities. One main feature of early PVC is sharp, low potential before the endocardial ventricular electrogram. These observations suggest that PVCs are a very important physiopathological common event that starts VF. They give new perspectives to the understanding of mechanisms and treatment of VF.

Ventricular tachycardia in structural heart diseases

Sustained monomorphic VT is often the clinical manifestation of underlying structural heart diseases [26,48]. Causes include a prior myocardial infarction, cardiomyopathies, and postoperative congenital heart diseases. VT that occurs in the setting of such structural disorders most frequently appears to be related to reentry arising from a stable substrate. Fibrosis or fibrofatty

replacement of ventricular myocardium creates scar regions that are regarded as the arrhythmogenic disease substrate [49]. Morphologic studies consistently demonstrated that the myocardial lesion responsible for VT is characterized by islands of surviving ventricular myocardium embedded into scar tissue [48,49]. This inhomogeneous histopathologic arrangement accounts for nonuniform intraventricular conduction in the surviving but electrophysiologically abnormal myocardial tissue, with slow regional activation front and areas of functional block that promote a reentrant excitation [23]. Scar-related VT is characteristically "monomorphic" (i.e., it shows a uniform beat-to-beat QRS morphologic pattern), which indicates a repetitive ventricular excitation from the same reentry circuit exit point [49]. The QRS morphology suggests probable site of the VT breakthrough: a right bundle branch block pattern, the LV; a left bundle branch block pattern, the right ventricle (RV) or the interventricular septum.

Old myocardial infarction is the most common source of ventricular scar that gives rise to LV monomorphic VT [50]. The substrate consists of viable myocardium, either on the periphery of the postinfarction scar or around a ventricular aneurysm, which has developed abnormal electrophysiological properties favoring the initiation of a macroreentry circuit. In hypertrophic cardiomyopathy, microreentry circuits related to intraseptal small scar areas produce rapid monomorphic/polymorphic VT, which tends to degenerate into VF and sudden death [51]. Sustained monomorphic VT is rarely observed in dilated cardiomyopathy. The underlying mechanism is usually a scar-related reentry circuit predominantly located close to the valve annulus, although a bundle branch reentry or phase-4 dependent enhanced automaticity may be occasionally involved [26,52].

Scar-related RV tachycardias (with a left bundle branch block morphology) may occur in patients with arrhythmogenic RV cardiomyopathy/dysplasia and cardiac sarcoidosis [53–55]. Scar regions associated with VT can be identified from 3D voltage mapping or contrast-enhanced cardiac magnetic resonance imaging. Reentry circuits often develop around scars or aneurysms in the subtricuspidal, apical, or infundibular regions ("triangle of dysplasia"). Multiple VTs are commonly observed and suggest a widespread fibrofatty myocardial replacement resulting in multifocal arrhythmogenic scar regions; epicardial reentry circuits with an endocardial breakthrough have also been reported. Scar-related VT originating from the RV may occur late after surgical repair of congenital heart disease, such as tetralogy of Fallot [56]. In this condition, postexcisional myocardial fibrosis and/or synthetic patches used to close the septal defect and reconstruct the pulmonary infundibulum act as a substrate for the VT reentry circuit.

Regardless of the specific structural heart disease, the reentry mechanism of sustained monomorphic VT can be initiated and terminated during intracardiac electrophysiologic study. Programmed ventricular stimulation assesses the presence of an arrhythmogenic substrate and its ability to sustain a reentrant circuit [57]. Reproduction of the clinical sustained VT by ventricular

pacing has allowed the development of mapping and ablation techniques for surgical and/or interventional VT therapy [49]. Alternatively, regions of scar and potential reentry circuit channels responsible for hemodynamically unstable VTs can be successfully detected and interrupted during sinus rhythm by a substrate-based approach, using a 3D voltage mapping reconstruction of low-amplitude (scar) regions.

Idiopathic ventricular tachycardia

Idiopathic VT is classified into several categories: (1) verapamil-sensitive left VT or fascicular VT [58,59], (2) outflow VT [60,61], (3) inflow VT of mitral and tricuspid valve annulus origin, (4) left VT of papillary muscle origin, and (5) epicardial VT arising from close proximity to the coronary venous system including the anterior interventricular vein, the distal great cardiac vein, and the anterior interventricular vein–great cardiac vein junction [62].

Verapamil-sensitive left VT is a left posterior fascicular VT predominant in young patients and characterized by right bundle branch block and left-axis deviation electrocardiographic manifestation, and high sensitivity to verapamil. The mechanism of verapamil-sensitive left VT is well demonstrated to be macroreentry involving the Purkinje system at the left posterior fascicular area with the estimated distance of approximately 2 cm between its entrance and exit. The reentry circuit has also been disclosed to be composed of the abnormal Purkinje tissue with decremental conduction properties and verapamil sensitivity as its antegrade limb, and the normal posterior fascicle or Purkinje fiber near the posterior fascicle as its retrograde limb. The exact anatomic counterpart of the slow conduction zone of the antegrade limb of the circuit remains controversial, whether it is the abnormal Purkinje fibers insulated from surrounding myocardium in the septum or false tendon including the Purkinje fibers, or both of them. As rare type of verapamil-sensitive left VT with similar mechanism, there are left anterior fascicle VT with right bundle branch block and right-axis deviation, and left upper septal VT with narrow QRS.

Outflow VT is characterized by the manifestation of repetitive monomorphic VT and exercise-induced sustained monomorphic VT. The basic electrophysiologic mechanism of outflow VT is widely accepted to be triggered automaticity as a result of cyclic AMP-mediated Ca-dependent delayed afterdepolarization or cathecholamine-dependent abnormal automaticity. The actual origin of outflow VT determined by successful ablation distributes at various sites of the right and left ventricular outflow tracts below the pulmonic and aortic valves, above the pulmonic valve, or within aortic sinuses of Valsalva.

Compared with outflow VT, idiopathic VT arising from the mitral and tricuspid valve annulus, the papillary muscles, and the coronary sinus systems is very rare. The underlying electrophysiologic mechanism appears to be the same as outflow VT.

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CHAPTER 4

Electrocardiogram Features of Ventricular Tachycardia/Ventricular Fibrillation as Expression of the Underlying Mechanisms and Site of Origin

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The QRS morphology of ventricular tachycardia (VT) on 12-lead electrocardiogram (ECG) is determined by the site of origin, that is, the site where the activation of the normal myocardium arises in a case of a focal origin or the exit site from a reentrant VT. The ECG pattern during VT can suggest the underlying mechanism (i.e., fascicular reentry, triggered activity from the outflow tract, infarct related reentry, etc.) giving us information about prognosis and helping us to better plan the therapeutic approach. The ability to localize the region of origin on the basis of the ECG morphology also directs mapping to a specific area of the ventricles when VT ablation is planned. However, some factors (presence of fibrosis and scars, effects of ischemia, antiarrhythmic drugs, or metabolic abnormalities, conduction disorders) can affect the ECG morphology and our ability to recognize the site of origin. Thus, the accuracy for ECG localization is higher in the absence of structural heart disease. Despite these limitations, ECG features are useful not only to identify the region of interest but also to help differentiate an epicardial or endocardial VT origin.

Some general rules can be applied to the QRS analysis during VT, regardless of the underlying substrate. First, QRS width is affected by the proximity to the

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Table 4.1 ECG criteria for localizing site of origin of VTs from basal LV sites. ECG, electrocardiogram; VT, ventricular tachycardia; LV, left ventricular; S-P, septal-parahisian; AMC, aortomitral continuity; MA, mitral annulus

	S-P	*AMC*	*Superior MA*	*Superolateral MA*	*Lateral MA*
Lead I	R or Rs	Rs or rs	rs or rS	rS or QS	rS or rs
Lead V1	QS or Qr	qR	R or Rs	R or Rs	R or Rs
Precordial transition*	Early	None	None	None	None or late S wave
QRS ratio in leads II and III	>1	≤1	≤1	≤1	>1

*Reversal of Q to R and vice versa ≤V3 (early) and ≥V5 (late S wave appearance).

septum, been narrower the septal VTs. The appearance of a left bundle branch block-like pattern suggests a right ventricular or left ventricular septal origin, dominant R waves in V1, or dominant negative deflections in lead I indicating a left ventricular (LV) exit. The frontal plane axis indicates whether the exit is on the inferior wall (superior axis) or on the anterior wall (inferior axis). The axis direction, right versus left, may help to further define the region of origin. The mid-precordial leads (V3 and V4) indicate if the exit site is at the base or the apex—basal sites producing dominant R waves and apical sites generating dominant S waves. The presence of QR/QS complexes indicates activation is moving away from the site where the complex is registered. Finally, VTs that originate at the subepicardium generally have slower QRS upstrokes in the precordial leads than those with an endocardial exit (Table 4.1).

Idiopathic ventricular tachycardia

Idiopathic VTs usually arise from the right ventricular outflow tract and less frequently from the left ventricular outflow tract, but can also originate around the mitral or tricuspid annulus, from the papillary muscles (PAPs), or involve the fascicles of the LV. ECG features can help us to distinguish the different regions of origin.

RVOT VTs have an LBBB-like morphology, inferior axis in the frontal plane, and a precordial QRS transition that begins no earlier than V3. Free-wall sites can be differentiated from the septal ones by a later QRS transition and wider QRS duration and notching [1]. LVOT VTs may arise from the LV outflow tract and/or the aortic cusp region. The ECG also has an LBBB-like configuration, inferior axis in the frontal plane, and a precordial QRS transition in lead V2 or V3 in VTs originating from the right coronary cusp and in lead V1 or V2 in VTs originating from the left coronary cusp. It has also been described that a broad R-wave duration in V1 or V2 is present in the cusp region (R-wave duration index ⩾50%) versus the RVOT [2]. Left coronary cusp origin is often associated with an M or W morphology in V1 and rS in lead I. Origin from the right coronary cusp is usually associated with R wave

in lead I. Moving leftward to the aortomitral continuity, a qR complex can be observed in lead V1 [3].

A small proportion of idiopathic VTs can arise from sites around the tricuspid annulus, more frequently at the septal portion. The QRS morphology is usually positive in lead I and aVL as well as in V5 and V6 [4].

Idiopathic VTs can also infrequently originate from the basal LV endocardium. The ECG analysis of the QRS morphology in I and V1, the ratio of the QRS complexes in II/III, and the precordial transition pattern (Table 4.1) may be helpful in differentiating medial from lateral locations around the mitral annulus (MA). Medial sites (septal-parahisian and aortomitral continuity) have narrower QRS, initial negative forces in V1, and predominant positive forces in I. The QRS ratio in II/III is >1 in septal-parahisian and lateral MA and <1 in aortomitral continuity, superior MA, and superolateral MA [3]. Annular VT as with preexcited tachycardia will show dominant R waves in V5 and V6.

Idiopathic LV fascicular VTs also have characteristic ECG features including a RBBB-like pattern left axis deviation (in a small proportion, right inferior axis deviation) with a short QRS duration ($\leqslant$140 ms) and a rapid QRS upstroke as a result of initial activation of the Purkinje system. Recently, VT originating from the papillary muscles (PAPs) in patients with or without prior myocardial infarction has been described. The ECG characteristics for PAPs VTs have been differentiated from those of the fascicular VTs [5,6]. The PAPs VTs had broader QRS complex (150 ± 15 vs. 127 ± 11 ms). All of the fascicular arrhythmias (versus none of the PAPs) had an rsR′ pattern in lead V1. All fascicular arrhythmias had a left anterior or posterior hemiblock pattern including discrete Q waves in leads I and aVL or I, II, III, respectively. The PAPs arrhythmias from the posterolateral or anterolateral PAPs showed the-same axis as the fascicular VTs of the corresponding fascicle but without the discrete Q waves in limb leads.

Arrhythmogenic right ventricular cardiomyopathy

The presence of an LBBB-like superior axis VT in a patient without known structural heart disease suggests a right ventricular dysplasia, especially in the presence of typical ECG features during sinus rhythm [7]. Moreover, a superior left axis with little or no R wave until V6 in the absence of right bundle branch block is very likely to be of right ventricular origin close to the lateral aspect of the tricuspid annulus. The typical VT morphologies are closely related to the area that is predisposed to fibrofatty replacement of myocardium, that is, the triangle of Marcus, which is the lateral and inferior free wall, the apex, and the right ventricular outflow tract. The tachycardia circuits can be either around small islands of affected myocardial tissue or within larger scarred regions, for example, around the base of the right ventricle along the tricuspid annulus. The more extended the disease, the more likely tachycardia circuits become larger and electrogram duration longer. It is quite typi-

cal for VT in ARVC compared to idiopathic VT that the QRS complexes are fragmented and depolarizing forces suppressed, which leads to lesser steepness of the QRS upstroke. In the literature, the most frequently described VT morphologies are intermediate or inferior axis and LBBB or superior axis and LBBB. In the study from Niroomand *et al.*, 48% of the tachycardias displayed an inferior axis, 27% an intermediate, and 20% left superior axis [8]. In contrast, in only 10% of the cases with idiopathic VT the axis was intermediate or superior. The mean QRS duration of the VTs was unfortunately not reported. In a study by O'Donnell *et al.*, patients with idiopathic right VT were compared to patients with ARVC and it was found that, similar to the study by Niroomand, VT was inducible by programmed stimulation almost exclusively in the ARVC group in contrast to the idiopathic VT group where programmed stimulation was not able to induce VT. Further, all patients with idiopathic VT, but only 53% of patients with ARVC, displayed an inferior axis. The remaining 47% of patients with ARVC revealed a normal to superior axis [9]. Kazmierczak *et al.* made the same comparison analyzing the ECG features and mode of initiation of VT in idiopathic VT and ARVC and found a QS-morphology in lead V1 in 3/15 versus 9/11 in idiopathic VT and ARVC, respectively. Finally, an R wave in lead V6 was present in 15/15 idiopathic VT patients and only 6/11 patients with ARVC [10]. VT pleomorphism is another frequent finding in patients with ARVC, numbers ranging from 1 to 12 different morphologies per patient depending on the different ablation series [11]. Satomi *et al.* published a series of 17 patients in whom catheter ablation was performed to control VTs. In their observation, the morphology was in 10/16 patients a left axis deviation, LBBB pattern; in 4 a right axis deviation, LBBB pattern; and in 3 patients a normal axis pattern. They induced 1.5 ± 0.8 VTs per patient. Regarding the corresponding intracardiac findings they revealed in 10/17 patients areas of electrical silence in the base, lateral and inferior right ventricle [11]. The mean area of slow conduction was 16 ± 7 mm. In the 13 mappable VTs, the reentry was a figure of eight in four cases, a single loop in two cases, and a tachycardia of focal origin in four. The mean lesion length was 21 ± 7 mm. Yao *et al.* presented a series of 32 patients with ARVC, in whom they encountered a total of 67 different VTs. Among these 67 VTs, only 7 VTs had a prominent R wave in leads II, III, and aVF. The most common region of origin of the VT was the perivalvular region in 49, the basal mid-lateral wall in 29, and the basal inferior lateral septum in 20 cases [12].

Role of the electrocardiogram to identify the site of origin of postinfarction ventricular tachycardia

The 12-lead ECG can be used to identify the exit site of postinfarction VT. The role of the ECG in localizing the exit site has been described in the literature, [13–15] in reports which, although published long ago, should still be relevant

today as the 12-lead ECG is the standard tool for recording and documenting VT. There are, however, important limitations relevant to prior reports.

1 Endocardial mapping was performed using fluoroscopy to assign the relative location within the heart; 3D mapping systems that allow for precise location of the catheter tip in space were not available yet.

2 The "site of origin" was assessed with catheters with a 0.5 cm interelectrode distance.

3 The site of origin was defined with diverging definitions, which are not in keeping with our current understanding of the VT exit site.

Although appropriate at the time, the results of these data need to be reassessed using current imaging and mapping techniques as well as our current understanding of the mechanism of postinfarction VT. In one of the initial manuscripts assessing the value of the 12-lead ECG for localizing the site of origin of postinfarction VT, the site of origin was defined as the site with the earliest endocardial activation obtained during activation mapping [13]. Although true for focal arrhythmias where the site of origin is located at the site of the earliest local activation, this concept is not true for reentrant arrhythmias. We know that a reentrant mechanism is the basis for most postinfarction VT, and discrete muscle bundles embedded within scar tissue are crucial for the reentry circuit. These muscle bundles can be identified during sinus rhythm and VT by discrete potentials; during VT these potentials can occur anywhere within the electrical diastole or even systole. If located within the reentry circuit, all of these sites might be critical to the VT; yet only the location of the exit site determines the 12-lead morphology of the QRS complex, and not necessarily where the earliest endocardial location of the reentry circuit is located—which might be centimeters away from the VT exit. Hence the concept of "site of origin" of postinfarction VT, by its definition, contributes to inaccuracies of the 12-lead ECG in assigning a particular VT morphology to an anatomic area within the heart. With respect to localizing components of the reentry circuit in postinfarction VT, it is probably preferable to use the terms exit site, entry site, and common pathway. These terms describe the protected zone of the reentry circuit that can be identified during entrainment mapping. Typically, only the exit site can be identified during sinus rhythm when pace mapping is performed.

The localizing value of the 12-lead ECG to identify the exit area of postinfarction VT has been questioned [15]. Only in about 50% of all induced VTs was there a specific ECG pattern that was associated with a distinct anatomic location. These locations were estimated to cover an area of approximately 10–20 cm^2. These numbers are deceptive but might in part be because of the technical limitations and the definitions of "site of origin" used at the time. Furthermore, the value of pace mapping to identify the exit site of postinfarction VT has been called into question also [16,17]. The accuracy for pace mapping to identify an exit area has been estimated to be ~25 cm^2, indicating that often a relatively large area displayed similar pace maps. In contrast, the authors also acknowledge that there might be fundamentally different

pace maps at adjacent or even identical sites, a finding that was later recognized as VT circuits with shared pathways and different exit sites [18]. An important finding was that postinfarction LBBB VTs originated from the left ventricular septum. The common theme of initial reports describing the relevance of pace mapping is that pace mapping has a regionalizing rather than a true localizing value.

Nevertheless, the 12-lead ECG during VT often indicates the area where the exit site of the VT is located. The location and extent of the myocardial infarction affects the 12-lead morphology of the VTs. The larger the myocardial infarction, the less the localizing value of the 12-lead morphology of a given VT. Accordingly, VT morphologies in patients with a prior inferior wall myocardial infarction are more specific compared to VTs in patients with prior anterior wall myocardial infarctions. In postinfarction VT, the presence of an LBBB morphology has more localizing value compared to a RBBB morphology, mainly because only the left ventricular septum can give rise to an LBBB VT morphology. In contradistinction to patients with anterior myocardial infarction, an R wave is often present during VT in patients with prior inferior wall infarction, indicating activation from back to front in these patients. The following criteria are helpful in assigning a specific endocardial exit area within the heart to a particular VT morphology [13,15,16,19]:

- apical location: Often displays Q waves in leads I, V1–V6
- basal location: Often displays R waves in leads I, V1–V6
- septal location: LBBB morphology
- posterior location: Often Q waves in the inferior leads associated with R waves in precordial leads and lead I.

The presence of RBBB versus LBBB morphology additionally influences the location of the VT exit site, in that LBBB morphologies have their exit from the septum whereas RBBB morphologies can originate from the septum or the free wall.

There are specific VT morphologies that can be assigned to a particular endocardial exit location, depending on the location of a prior infarction [15]:

In patients with prior inferior wall infarction:

- LBBB morphology with superior axis and increasing R wave progression from V1 to V6: These VTs most often originate from the inferobasal septum
- RBBB morphology with superior axis and reversed R wave progression from V1 to V6: These VTs often originate from the inferobasal free wall
- RBBB morphology with inferior axis: These VTs often originate from the inferolateral free wall.

In patients with prior anterior wall infarction:

- LBBB morphology with superior axis and negative precordial concordance: These VTs originate from the inferoapical septum
- LBBB morphology with inferior axis: These VTs originate from the anteroapical septum
- RBBB morphology with inferior axis and abrupt loss of R waves: These VTs often originate from the anteroapical septum.

Table 4.2 Morphologic and metric criteria described useful to recognize the epicardial origin of the ventricular tachycardias

ECG criteria	*Main particular limitations*
Berruezo criteria: – Pseudodelta wave ≥34 ms – Intrinsicoid deflection V2 ≥85 ms – Shortest RS complex ≥121 ms	LBBB-like VTs excluded
Q wave in leads that reflect local activation	Not useful if prior myocardial infarction or baseline Q waves
Precordial maximum deflection index	Described for LVOT VTs (paraseptal)

The VT morphology with the least predictive pattern is the RBBB morphology with a superior axis, especially in patients with prior anterior wall myocardial infarction. This VT morphology accounted for the majority of the VT patterns in patients with prior anterior wall infarction [15].

Epicardial origin of ventricular tachycardias

The discrimination between endocardial versus epicardial VTs is of great interest because the VT ablation approach will be completely different, requiring a pericardial access and epicardial mapping and ablation in a case of an epicardial VT. Berruezo *et al.* demonstrated that the epicardial origin of the ventricular activation can be recognized on the ECG by slurring of the initial part of the QRS complex (pseudodelta) [20]. The duration intervals and cutoff values obtained for the "pseudodelta wave" and "intrinsicoid deflection in V2" obtained a high sensitivity and specificity in identifying an epicardial origin of the VTs (Table 4.2).

Daniels *et al.* [21] quantified the slowed initial precordial QRS activation of the epicardial LVOT VTs by a novel measurement, the maximum deflection index (MDI). The MDI is the result to divide the time to maximum deflection in precordial leads by the QRS duration. A delayed shortest precordial MDI ≥0.55 identified epicardial VT remote from aortic sinus of Valsalva with a high sensitivity and specificity. Later, Bazan *et al.* [22] showed that the presence of a Q wave in leads that reflect local ventricular activation may be useful to distinguish epicardial LV VTs in patients without ischemic heart disease.

Polymorphous ventricular tachycardia

Polymorphous ventricular tachycardia (PVT) is recognized by beat-to-beat changes in the QRS complexes and may precede development of VF. When PVT is accompanied by a prolonged QT interval, a diagnosis of torsades de

points is made. The latter points to a genetic mutation causing the congenital long QT syndrome or the acquired syndrome, which is usually because of drug and/or electrolyte abnormalities.

Polymorphous ventricular tachycardia with normal QT interval

This situation may occur in patients with severe ischemia or structural cardiac disease. In ischemic disease, the PVT is often preceded by ST elevation in the appropriate leads. PVT may also occur in those with Brugada syndrome or ARVC. In addition, PVT may occur in those without structural disease; for example, it may occur in patients with catecholaminergic PVT where it is often exercise induced. Furthermore, patients with idiopathic VF associated with short-coupled PVCs frequently have PVT triggered by Purkinje extrasystoles. Hence proper recognition of the cause of PVT allows for appropriate drug, device, or catheter ablative therapy.

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CHAPTER 5

Pre- and Intraprocedural Management

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Preprocedural evaluation of the patient undergoing catheter ablation for the treatment of ventricular tachycardia

Routine preprocedural assessment in patients referred for catheter ablation of cardiac arrhythmias comprises a careful physical examination, electrocardiogram analysis, and laboratory evaluation. In patients scheduled to undergo catheter ablation for the treatment of ventricular tachycardia, additional steps in the evaluation process are necessary.

Identification of presence and extent of obstructive coronary artery disease

In patients with reversible myocardial ischemia, surgical or percutaneous revascularization may be pursued to improve patient outcome.

Although myocardial infarction is a common cause of myocardial fibrosis and scar-related ventricular tachycardia, myocardial ischemia rarely results in recurrent sustained monomorphic ventricular tachycardia. In patients with known coronary artery disease, further testing is warranted only if the severity of coronary artery disease has not been previously established or prior episodes of ventricular tachycardia caused hemodynamic compromise. This would suggest poor tolerance to extended periods of ventricular tachycardia during entrainment or activation mapping. In contrast, in patients with frequent or incessant ventricular tachycardia, catheter ablation may have to precede assessment for coronary artery disease in order to gain prompt control of the ventricular arrhythmia.

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Identification of etiology and extent of myocardial disease

The etiology and extent of myocardial disease need to be defined prior to catheter ablation of ventricular tachycardia. To date, no consensus exists that tests modality is best employed, because of lack of evidence from clinical trials demonstrating improved outcome utilizing any of the available diagnostic modalities. At minimum, a transthoracic echocardiogram and assessment for coronary artery disease are recommended. In patients with nonischemic cardiomyopathy, further evaluation may include cardiac computed tomography or magnetic resonance imaging, in addition to endomyocardial biopsy.

Identification of type and burden of ventricular tachycardia

The type and burden of ventricular tachycardia needs to be identified. In patients with scar-related ventricular tachycardia, multiple distinct morphologies may occur. Ideally, a 12-lead electrocardiogram should be obtained to identify the origin or exit site of the clinical ventricular tachycardia. In patients with ICD, early termination of ventricular tachycardia may preclude recording of an electrocardiogram, hence stored device data such as electrogram morphology and cycle length may be used to identify the clinical ventricular tachycardia.

In patients with suspected peripheral vascular disease further evaluation may be reasonable. Anticipating a difficult arterial access, the operator may select the transseptal route for left ventricular access. In addition, a transseptal route should be the preferred approach in the elderly people. Lastly, the presence of a left ventricular thrombus should be excluded in all patients undergoing ventricular mapping, especially in those with a history of ventricular aneurysm or ventricular noncompaction.

Imaging

Cardiac imaging facilitates identification of anatomic variations serving as substrate for ventricular tachycardia initiation or impediment to successful catheter ablation. Although evidence is lacking that sophisticated cardiac imaging results in improved ablation outcome, pre- and postprocedural imaging is widely used in clinical practice [1–22].

Preprocedural imaging

Cardiac imaging should not be limited to patients undergoing catheter ablation for the treatment of ventricular tachycardia, but is warranted in all patients with ventricular arrhythmias in order to assess for the presence and severity of cardiac disease. Preprocedural imaging should be limited to magnetic resonance imaging for the identification of myocardial scar, arrhythmogenic right ventricular dysplasia, noncompaction of left ventricle, and left ventricular aneurysm. Echocardiography is used to identify left ventricular thrombus [23–25].

In patients with impaired ventricular function undergoing left ventricular mapping, the presence of a left ventricular thrombus needs to be excluded.

Transthoracic echocardiography may be used for this purpose, although apical thrombus because of anterior myocardial infarction may be difficult to visualize [17]. Alternately, intracardiac echocardiography may be employed intraoperatively if the operator is experienced in its use. In patients with a history of atrial fibrillation, transesophageal echocardiography should be utilized to exclude the presence of a left atrial thrombus, which may preclude left ventricular access via the transseptal route and intraoperative electrical cardioversion or defibrillation for ventricular arrhythmias.

Intraoperative imaging

Coronary angiography is commonly used to delineate the course of the coronary arteries in relation to site of ablation. Intraoperative intracardiac echocardiography provides an alternate means to directly visualize proximity of catheter tip to adjacent coronary artery if ablation is performed within the left ventricular outflow tract or the aortic cusps. Furthermore, intracardiac echocardiography allows proper identification and ablation of ventricular tachycardia originating from the papillary muscles [28,29]. Its use, however, requires additional technical skills and expertise in interpretation [18,27]. Integrating electroanatomic mapping with intracardiac echocardiography provides the operator with a three-dimensional anatomical reconstruction of the ventricular chambers [26]. In the future, intracardiac echocardiography may facilitate differentiation of normal myocardium from scarred one and denote the presence of epicardial scar necessitating pericardial mapping and ablation.

Newer strategies to guide intraoperative mapping have integrated cardiac computed tomography, magnetic resonance imaging, or positron emission tomography–computed tomography with electroanatomic mapping systems to allow for a three-dimensional anatomical reconstruction of ventricular chambers. Although, these innovative concepts are able to visualize the arrhythmogenic substrate or delineate potential obstacles to successful ablation, evidence is lacking that intracardiac echocardiography or pre-acquired volumetric imaging integrated into electroanatomic mapping systems improves efficacy or safety of catheter ablation procedures [30].

Anticoagulation

Perioperative thromboembolism in patients undergoing catheter ablation of ventricular tachycardia may occur during insertion and manipulation of catheters or during lesion formation because of activation of the coagulation cascade [31,32]. The thromboembolic risk may differ according to individual patient factors and ablation site. Structural heart disease is an independent risk factor for complications during catheter ablation procedures [33]. In addition, complications are more prevalent in patients undergoing catheter ablation for ventricular rather than supraventricular tachycardia, because the latter often demonstrates structurally normal hearts [34]. Accordingly,

patients with structural heart disease undergoing catheter ablation within the left ventricle are at particular risk for thromboembolism.

Although no data exist comparing different perioperative anticoagulation schemes, it is recommended that left ventricular ablation procedures be performed using systemic anticoagulation for the prevention of systemic arterial emboli.

Table 5.1 summarizes different heparin regimens, thromboembolic events, and hemorrhagic complications during radio frequency catheter ablation in 1079 patients as published in 13 series including patients with a history of myocardial infarction [35–47]. Heparin regimens, particularly in series published after the year 2000, usually were controlled by measuring the activated clotting time (ACT), with a common target value of ⩾250 s. The most serious complications were cerebrovascular accidents (CVA) and transient ischemic attacks (TIA) with an incidence of 1.3%. Other embolic complications were less frequent. Pericardial tamponade, likely because of pericardial hemorrhage, occurred in 1% of cases. Local hemorrhagic complications (large hematomas or arterial pseudoaneurysms) occurred in more than 2% of patients. Thus, these procedures involve a significant risk of thromboembolic and hemorrhagic complications despite the protective effects of heparin.

The following sections describe recommended anticoagulation schemes according to site of ablation and presence or absence of structural heart disease.

Right ventricular mapping and ablation

Unless other risk factors are present, catheter ablation within the right ventricle does not require use of systemic heparin. Some centers may use heparin for the prevention of deep venous thrombosis and pulmonary embolism, especially if a prolonged procedure is anticipated. Placement of multiple venous catheters or extensive catheter ablation may warrant the use of systemic anticoagulation. Similarly, patients with a prior history of deep venous thrombosis or pulmonary embolism, presence of a hypercoagulable state (e.g., factor V Leiden), or right to left cardiac shunt with increased risk for paradoxical embolism should undergo systemic anticoagulation.

Anticoagulation is not needed following the procedure; however, some centers advocate the use of aspirin at a dose from 75 mg to 325 mg for 3–12 weeks.

Left ventricular mapping and ablation in the absence of structural heart disease

Systemic anticoagulation with intravenous heparin is recommended intraoperatively for all patients undergoing left ventricular catheter ablation procedures. In case of extensive ablation, aspirin may be given postoperatively at a dose from 75 mg to 325 mg for 4–8 weeks. Some centers advocate postprocedural warfarin use in patients with additional risk factors for thromboembolism or if extensive ablation was performed.

Table 5.1 Studies on post-myocardial infarction ventricular tachycardia (post-MI VT)

					Thromboembolic complications		*Local hemorrhage/tamponade*	
Authors	*Number of patients*	*Number of patients with post-MI VT*	*Number of procedures in CAD*	*TE prophylaxis*	*CVA/TIA*	*Other*	*Hemorrhage/ pseudoaneurism*	*Tamponade*
Morady *et al*. [35]	15	15	15	5000 IU, 1000/h	0	0	0	0
Kim *et al*. [36]	21	21	30	4000 IU, 1000/h	0	0	0	0
Rothman *et al*. [37]	35	35	44	NA	0	1	1	0
Stevenson *et al*. [38]	52	52	69	5000 IU, 1000/h	1	0	1	0
Callans *et al*. [39]	66	66	95	5000 IU ACT 250–300	3	0	0	2
Ortiz *et al*. [40]	34	34	42	5000 IU, 1000/h	0	0	0	0
Calkins *et al*. [41]	146	119	171	ACT > 250	4	1	1	3
O'Callaghan *et al*. [42]	55	55	55	ACT > 300	0	1	1	0
Borger *et al*.* [43]	151	89	89	ACT >2.5–3 x baseline	2	0	0	1
Della Bella *et al*. [44]	124	124	139	5000–10,000 IU ACT 200–250	1	2	0	0
O'Donnell *et al*. [45]	109	109	109?	ACT > 250	1	0	8	3
Segal *et al*. [46]	40	40	44	ACT > 250	2	0	2	3
Stevenson *et al*. [47]	231	231	252	Heparin dose not specified	0	0	11	1
Total	1079	990	1154		14 (1.3%)	5 (0.5%)	25 (2.3%)	13 (1.0)

*Data from this series refer to the 89 patients with post-MI VT.
IU, international units; ACT, activated clotting time; CVA, cerebrovascular accident; TIA, transient ischemic attack.

Left ventricular mapping and ablation in the presence of structural heart disease

Patients with a history of structural heart disease referred for left ventricular catheter ablation may already receive systemic anticoagulation for other reasons. In these patients warfarin therapy may be stopped 3–5 days prior to the procedure. Subsequent bridging with unfractionated or low-molecular-weight heparin is indicated in patients at high risk for thromboembolism.

Preoperative screening for left ventricular thrombus is required in all patients. Mobile left ventricular thrombus is an absolute contraindication to catheter ablation. In contrast, left ventricular catheter ablation may be performed despite the presence of laminated thrombus, if the patient has been therapeutically anticoagulated with warfarin for at least 4 weeks prior to ablation.

Intraoperative anticoagulation schemes differ between centers. Unfractionated heparin is administered as an initial bolus (5000–10,000 IU or 50–100 IU/kg) followed by intermittent boluses or continuous infusion to maintain a target ACT ⩾250 s. Certain electrode arrays with high thrombogenicity may require an ACT ⩾300 s. Some centers give the initial heparin bolus after catheter placement within the left ventricle is confirmed in order to preserve the option of transseptal access if difficulties with retrograde arterial access are encountered. Pericardial access should be obtained prior to ventricular instrumentation and the subsequent need for intraprocedural anticoagulation.

Sedation and analgesia

In order to provide safe sedation and analgesia during catheter ablation for ventricular tachycardia, a careful preprocedural assessment of the patient is indicated. Consultation with an anesthesiologist should be considered in high-risk patients. Trained personnel familiar with monitoring of blood pressure, pulse, and oxygen saturation need to be present throughout the procedure as dictated by state and institutional policy [48]. Training requirements for the safe administration of intravenous sedation and analgesia should follow the recommendations of the American Society of Anesthesiologists [49].

Conscious sedation or general anesthesia is commonly used during catheter ablation of ventricular tachycardia. The optimal strategy depends on the patient's characteristics such as age, additional comorbidities, and arrhythmia targeted for ablation. Short-acting benzodiazepines and opiod analgesics are often sufficient in the adult population. Conscious sedation is the preferred strategy in patients with catecholamine-sensitive ventricular tachycardia or if ventricular tachycardia was not inducible during a prior electrophysiology study. During conscious sedation, propofol may be added to acquire deeper levels of sedation in critical situations, for example, to prevent patient movement during epicardial puncture. The level of sedation may subsequently be titrated to allow induction of ventricular tachycardia.

General anesthesia is favored in children and in patients with high-risk features such as potential risk for airway obstruction. The advantages of general anesthesia include enhancing patient comfort and minimizing patient movement, thereby facilitating vascular and epicardial access as well as catheter manipulation and ablation. In addition, ventilator cycle length settings may be adjusted to minimize catheter movement during ablation.

Lastly, the use of paralytic agents during epicardial mapping and ablation may preclude accurate identification of the phrenic nerve using high-output pacing.

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CHAPTER 6

Mapping Methods for Ventricular Tachycardia Ablation

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Introduction

The mapping techniques employed to guide ventricular tachycardia (VT) ablation depend on the likely mechanism of VT and the nature of its substrate. Focal origin VTs may be caused by automaticity, triggered activity, or small reentry circuits (microreentry). Wavefronts propagating away from the focus depolarize the ventricles producing the QRS complex. These foci can be localized by activation mapping and/or pace mapping. VTs that are a result of scar-related reentry often arise from large reentry circuits. Activation mapping and pace mapping alone can be misleading. Entrainment mapping can be useful, but is limited when VT is unstable. Substrate mapping is useful in these cases. Mapping procedures commonly combine these different mapping techniques to facilitate identification of desirable ablation sites.

Activation mapping of ventricular tachycardia

Activation mapping is the method of choice for identifying a hemodynamically stable, focal VT. This method can be useful for defining macroreentrant VTs when the entire activation sequence can be defined, or may be applied in a more limited manner combined with entrainment mapping to guide ablation of macroreentrant VTs.

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Activation sequence mapping may be performed by point-by-point mapping with a roving mapping catheter, with the use of multiple catheters or multielectrode arrays. Electrograms may be recorded with unipolar, bipolar, and/or combinations of both recording methods as each have different advantages and weaknesses.

Unipolar recordings are typically obtained with minimal filtering (e.g., high-pass filter corner frequency set to 0.5 Hz or lower), in which case the morphology of the recordings provides potentially useful information [1–3]. A QS configuration is typically seen at the origin of focal arrhythmias. An rS or RS configuration indicates a wavefront moving toward the recording electrode; hence the recording site is not at the origin of a focal VT. These morphologic characteristics are not sufficient, however, to be the sole guide to a VT origin, as a qS complex may be recorded over a region adjacent to the focus. In uniform tissue, the onset of activation in a unipolar recording coincides with the point of maximal negative slope of the electrogram. Unipolar recordings contain a substantial contribution from far-field signals as a result of depolarization of myocardium remote from the recording site. In the areas of scar, the far-field signal can obscure low-amplitude signals of interest that arise from slow-conduction regions and reentry circuit isthmuses. Therefore, bipolar recording is favored for catheter mapping of scar-related VT.

In bipolar recordings much of the far-field signal is subtracted out, facilitating recognition of low-amplitude signals [1,3,4]. Local activation is usually taken as the first peak of the bipolar signal. In bipolar recordings, spatial resolution is reduced by the fact that a discrete potential of interest may be because of depolarization of the tissue beneath either or both of the recording electrodes. When the signal of interest arises from the tissue beneath the proximal electrode, ablation at the distal electrode may fail. This situation can be potentially recognized by simultaneous recording of unipolar and bipolar electrograms and high-pass filtering the unipolar electrogram to reduce the far-field contribution to the signal.

For most activation sequence mappings, a clear point on the QRS complex provides a useful fiducial point for measurement. The relation of this point to the onset of the QRS is determined. Depolarization that precedes the QRS onset, typically by less than 30% of the VT cycle length, is referred to as presystolic. Electrograms that are depolarized between the QRS complexes, in "electrical diastole" are often referred to as diastolic electrical activity. For focal VTs, such as idiopathic outflow tract VT, activation at the focus precedes the onset of the QRS and is the earliest point of activation in the ventricle.

Most scar-related VTs are caused by macroreentry. There is no earliest or latest point of activation. Presystolic activity is recorded from reentry circuit exit regions. Depolarization of isthmuses (channels) proximal to the exit is expected to occur during electrical diastole, often indicated by isolated potentials. Definition of the entire reentry circuit by activation mapping traces a continuous path of activation covering the entire tachycardia cycle length (TCL). In scar-related macroreentry VT, there are several factors that

limit creation of complete activation maps. Identification of true local activation time can be difficult in areas with fractionated and split potentials, some of which can be far-field activation. Portions of the reentry circuit can be intramural or epicardial, and not sampled. Diastolic activity occurs in some bystander regions in scars that are not part of the reentry circuit. For macroreentrant VTs a complete activation map can be achieved for some stable VTs, but is not commonly achieved or necessary. When used in isolation, activation mapping is not a reliable method for guiding ablation of scar-related VTs. Activation mapping data are often combined with entrainment mapping to distinguish bystander sites from reentry circuit sites and with substrate mapping data.

Activation mapping is the basic mapping technique in targeting idiopathic VT or PVCs originating from the RVOT or papillary muscles, albeit pace mapping can provide additional assistance [5,6]. This technique is also the primary mapping tool in the ablation of His-Purkinje-related VTs, which include intrafascicular verapamil-sensitive left ventricular (LV) VT [7–9]. Activation mapping is also the primary method for targeting foci that are triggering recurrent episodes of VF or polymorphic VT with or without structural heart diseases [10–13]. Successful target sites often have a sharp potential, consistent with a Purkinje potential, preceding the QRS onset of VT or PVCs by 20–160 ms. In some patients, PVCs that arise from the infarct scar originate from the exit site of a reentrant VT, such that activation mapping of the PVCs can be used to target ablation of a macroreentrant VT [14].

Although activation mapping is generally performed during VT, it can also be performed during sinus rhythm to identify areas of delayed activation that are the potential substrate for VT [15–17]. Mapping during sinus rhythm, referred to as substrate mapping (see the following text) focuses on other electrogram characteristics discussed below.

The spatial and temporal resolution of point-by-point activation mapping is limited by the number of contact electrodes and the time required. Systems that provide greater spatial sampling are available. Basket catheters that have splines with multiple electrodes can be deployed in the ventricle [18]. These catheters have been used successfully to guide ablation of idiopathic RVOT VT/PVCs, and are of particular interest in patients with infrequent arrhythmia that limits mapping [18]. Spatial sampling is limited by the interspline and interelectrode distances, and endocardial contact is often limited because of the complex geometry of the ventricles. These catheters are not commonly used.

The noncontact multielectrode array mapping system records signals from a 64-electrode array and calculates 3000 virtual unipolar electrograms over the endocardial surface that is defined by roving mapping catheter [19]. The sequence of depolarization is displayed visually from single beats, making it potentially useful to define activation sequence during nonsustained and poorly tolerated arrhythmias. This sequence is not accurate for points that are more than 4 cm from the multielectrode array, and must be used with caution in dilated ventricles [20,21]. Filter settings have a significant effect on

the activation maps, and unipolar virtual electrograms with a QS onset, consistent with a VT origin, must be confirmed by inspection to ensure that they are not a result of artifact. Studies using the system to define areas of scar for substrate mapping and intramural foci support feasibility [20,22,23].

The activation sequence identifies focal origins and exits for VTs. The system has been successfully used for mapping to guide ablation of focal origin left or right ventricular VTs and intrafascicular VTs [24–28]. In scar-related arrhythmias a presystolic region of activation commonly defines the endocardial exit, but low-amplitude electrograms from within scars may escape detection. Identification of the endocardial exit region has been used successfully to target scar-related VTs in ischemic cardiomyopathy and ARVC [27,29–32].

Pace mapping

Pace mapping is pacing in the absence of tachycardia to assess the possible relation of the pacing site to a tachycardia focus or reentry circuit [33,34]. Unipolar pacing from the distal ablation electrode may be performed, but it causes a large stimulus artifact in the surface ECG [35]. Bipolar pacing from the closely spaced distal electrodes of the mapping catheter is more commonly used. Although the possibility for capture at either the distal or the proximal bipolar electrodes can reduce spatial accuracy, this does not appear to be a major limitation [36,37]. Use of current strengths near threshold should improve accuracy by limiting the size of the virtual electrode in the tissue and preventing capture of myocardium distant from the pacing site. Pacing thresholds $\geqslant$5–10 mA typically indicate insufficient electrode–tissue contact or inexcitable scar areas.

Comparison of the paced QRS morphology with that of VT provides information as to the location of the pacing site relative to a focal VT origin, or the exit of a VT reentry circuit [31,38]. The morphology comparison should be based on the 12-lead ECG. At the VT origin or exit, the paced QRS resembles the VT QRS. For idiopathic VTs, an exact match with all amplitudes and notches in 12-lead ECGs is sought.

Studies comparing detailed analysis of QRS morphologies during pace mapping for outflow tract VT have shown that the resemblance to VT progressively decreases at sites further from the VT focus, but good pace map matches can be seen over areas more than 1 cm and more than 2 cm from the successful ablation site in some patients [34,39]. Thus, pace mapping is likely to be less accurate than activation mapping. In contrast to activation mapping, however, pace mapping can be utilized during sinus rhythm, in the absence of VT. Therefore it is particularly useful for identifying an initial region of interest when VT is rapid or difficult to induce.

The quality of the information obtained from pace mapping is critically dependent on the spatial resolution of the mapping procedure within the 3-D chamber/area of interest. Therefore, the combination of pace mapping

with 3-D mapping systems may be helpful to achieve better spatial resolution than fluoroscopy alone.

Specific clinical applications

Focal ventricular tachycardias

Pace mapping can be useful for locating the origin of focal VTs and has been used extensively in patients with idiopathic RV outflow tract arrhythmias, especially if the arrhythmia is infrequent or difficult to induce [39]. In patients with paroxysmal outflow tract tachycardia, pacing is performed during sinus rhythm at cycle lengths that are comparable to the TCL. In patients with PVCs that are targeted for ablation, pacing for several beats at cycle lengths of 500–600 ms may be used. The QRS complex in the 12-lead ECG obtained during the pacing should exactly replicate the QRS complex morphology of the arrhythmia, including small notches ("12/12-lead match"). Catheter ablation at sites with a "perfect" pace map are typically successful [39,40].

Pace mapping can also be useful for LV focal VTs, but is less reliable for arrhythmias originating from the aortic sinus cusps [41]. The potential for varying routes for conduction from the focus to the ventricles appears to render pace mapping and ECG algorithms less reliable, such that activation mapping is needed.

Scar-related ventricular tachycardia

Pace mapping may also be used to define likely exit regions and reentry circuit isthmuses for scar-related VTs [31,38,42,43]. The QRS morphology of the VT in the 12-lead ECG is an indication of the location of the reentrant circuit exit site. Pace mapping at the presumed exit site region from the "central common pathway" or "isthmus," replicates the QRS morphology of the VT with a relatively short (<40 ms) stimulus-QRS (S-QRS) interval. However, an exact exit site pace map match typically can be achieved over a relatively large area. It is important to recognize that pace mapping at reentry circuit sites that are not near the exit may produce a QRS that is different from the VT, even though ablation may be effective at that site [43].

Pace mapping can also provide additional information relevant to the arrhythmia substrate. A long S-QRS, exceeding 40 ms, indicates slow conduction, away from the pacing site, that can be the substrate for reentrant VT [43]. Areas of electrically unexcitable scar have been defined as regions with a pacing threshold >10 mA [35]. These areas may indicate dense fibrosis that may form the border of a reentry circuit path.

Entrainment mapping

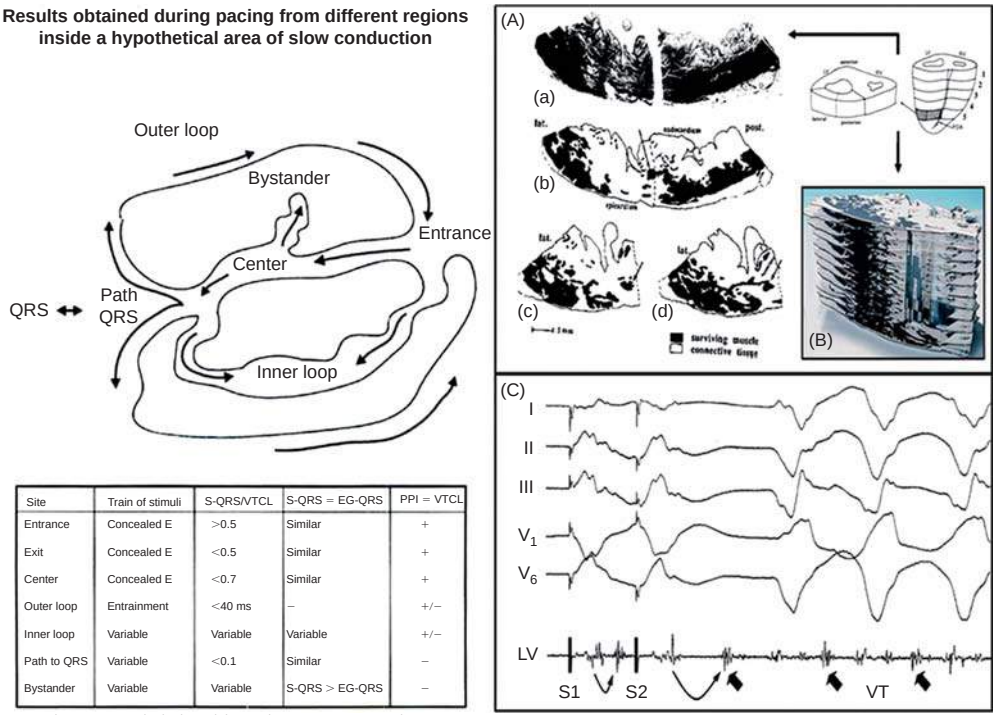
Entrainment mapping is useful in patients with reentrant VT, particularly VT that is related to areas of scar in which is possible to identify reentry circuit sites and distinguish them from bystander sites [44]. During entrainment,

pacing stimuli at a rate slightly faster than the tachycardia continuously reset the reentry circuit. Analysis of the surface electrocardiogram and electrograms recorded during entrainment can be used to assess the proximity of the pacing site to the reentrant circuit.

In patients with scar-related VTs the anatomic complexities of reentry circuits and regions of slow conduction (Figure 6.1A and B) make it difficult to adequately define reentry paths with activation mapping alone. A schematic drawing of a hypothetical reentry circuit with isthmus, loops, and bystander is shown in Figure 6.1. The reentry wavefront travels from the entrance of the isthmus to the center and then exit of the isthmus. This wavefront then propagates around the scar as an outer loop, or through the scar as an inner loop, to reach the entrance. Entrainment findings consistent with different sites in and remote from reentry circuits are summarized in Figure 6.1.

Four observations during entrainment are analyzed to identify the relation of the pacing site to the reentry circuit. The postpacing interval (PPI), measured from the last stimulus that entrains or resets tachycardia to the next depolarization at the pacing site, represents the conduction time from the pacing site to the reentry circuit, through the circuit, then back to the pacing site. Thus the PPI-TCL difference indicates the conduction time between the pacing site and the circuit. The PPI-TCL difference is not influenced by QRS fusion during entrainment and can help identify loops in the reentry circuit as well as isthmuses where pacing entrains tachycardia with concealed fusion [44]. The PPI-TCL difference is based on the assumption that the recorded ECG represents depolarization of the pacing site. Inability to distinguish far-field potentials, which are caused by depolarization of tissue remote from the pacing site, from the local electrogram is a source of error [46]. Recordings from the pacing site are not always obtainable or interpretable because of electrical noise after the stimulus. However, because the beat following the last entrained QRS (QRS_{n+1}) is not influenced by QRS fusion during entrainment, the QRS_{n+1} can be used as a timing reference to assess the PPI-TCL difference [47]. The S-QRS_{n+1} to local electrogram difference indicates the PPI-TCL difference allowing assessment when the PPI cannot be measured directly from the pacing site electrograms.

When pacing is performed from the protected isthmus, the QRS is the same as the VT QRS and there is no evidence of QRS fusion (concealed entrainment). Clear fusion will be observed when pacing is performed from an outer loop region. If the pacing rate is substantially faster than the VT, fusion will also been seen when pacing at the entrance of the protected isthmus. At sites with concealed entrainment, bystanders can be identified by comparing the stimulus to QRS and electrogram to QRS intervals. Bystander areas have an S-QRS interval longer the ECG-QRS interval. In this situation, the interpretation of the PPI-TCL difference is not necessary. The S-QRS indicates the conduction time from the pacing site to the reentry circuit exit. Longer S-QRS intervals indicate likely inner loop sites. At outer loop sites entrainment occurs with QRS fusion, but the PPI indicates that the site is in



Site	Train of stimuli	S-QRS/VTCL	S-QRS = EG-QRS	PPI = VTCL
Entrance	Concealed E	>0.5	Similar	+
Exit	Concealed E	<0.5	Similar	+
Center	Concealed E	<0.7	Similar	+
Outer loop	Entrainment	<40 ms	–	+/–
Inner loop	Variable	Variable	Variable	+/–
Path to QRS	Variable	<0.1	Similar	–
Bystander	Variable	Variable	S-QRS > EG-QRS	–

E-entrainment; S-QRS-stimul to interval; (Q-Qrs-electrogram to QRS Interval; PPI-post-peasing Interval; VTCL-ventricular techycardia cycle length

Figure 6.1 Panel A shows histologic view of the infarcted tissue in the inferoapical wall of the left ventricle (LV), as indicated by the schematic representation of the heart on the right upper corner. Bundles of surviving myocardium are seen (in black) connecting the two borders of scar (in white) at different levels. Panel B shows a 3D model of the infarct. Several connections among the bundles of surviving myocardium are seen at different levels, which may serve as possible substrates for a reentrant ventricular tachycardia (VT). By definition, a reentrant VT continuously depolarizes some quantity of myocardial tissue. As the mass of the myocardium in the protected channels inside the scar is small, it contributes only negligibly to the surface QRS complex. Therefore, the QRS complex during VT initiates when the activation wavefront emanates from the border of the scar (from an exit). Panel C shows induction of VT during ventricular-programmed stimulation (S1 and S2 represent pacing stimulus artifacts). Following S2, a long interval is seen on surface EKG followed by initiation of VT. However, intracardiac recordings from inside the scar (LV) reveal presence of mid-diastolic potentials (thick arrows). Although essential for initiation and maintenance of a reentrant VT, the electrical activation of these small bundles is not seen on surface EKG. Rather, they are only seen during electrical recordings from inside the scar. Panel A was obtained and modified from reference 4 [45]. Panel B was kindly provided by JMT de Bakker. In order to confirm that the area where the mid-diastolic potential is being recorded is part of the VT circuit, entrainment maneuvers should be performed. The panel on the left summarizes entrainment findings that allow differentiation among possible regions inside the scar area [45]

the reentry circuit. Successful interruption of VT by ablation is low [48]. Sites where ablation is most likely to interrupt reentry are those with features of an isthmus site with an S-QRS less than 70% of the VT cycle length and an isolated potential [48–50].

Pacing for entrainment mapping occasionally produces VT termination without global capture [51]. This finding is likely to indicate that the pacing site is in a reentry circuit isthmus that is a desirable target for ablation. Capture of the stimulus may occur with block of the orthodromic wavefront between the stimulus site and the exit, and collision of the stimulation wavefront traveling in the antidromic direction in the circuit. Similarly, mechanical termination of VT can also be an indication that the catheter is at a reentry circuit site [52].

There are many limitations of entrainment mapping. A stable tachycardia is required. Pacing that terminates or alters tachycardia complicates mapping and renders the entrainment mapping findings uninterpretable. This pacing is difficult to apply to unstable VTs, although limited substrate mapping combined with limited entrainment mapping at selected sites followed by prompt tachycardia termination can be used to help locate a region for ablation during sinus or paced rhythm [53].

Substrate mapping

A majority of patients with sustained VT in the setting of structural heart disease have one or more VT morphologies that are not sufficiently well tolerated to allow detailed mapping during VT [54]. In a recent multicenter ablation study, 31% of patients had only unmappable VT and 38% had both mappable and unmappable VT morphologies targeted [55]. Substrate mapping is the approach of utilizing techniques that allow the majority of the mapping and ablation to be performed in sinus rhythm, and is required in many patients with VT in the setting of structural heart disease. This mapping is often combined with limited activation and entrainment mapping.

The concept of substrate mapping evolved from the success of surgical subendocardial resection for postmyocardial infarction VT, which established the physical link between the VT circuit and the infarct scar [56]. Nonetheless, there were two important obstacles to overcome for application with catheter methods. First, large volumes of infarct were eliminated with surgical subendocardial resection. In contrast to the idea of limited ablation at a VT circuit isthmus, substrate ablation often involves the creation of extensive lesion sets. Second, unlike the surgeon, who could visually identify the infarct, electrophysiologists needed a method to localize the substrate in space (Figure 6.2). Several studies in animal models have demonstrated that voltage mapping using 3D electroanatomic mapping systems provides a reasonably accurate assessment of the location and extent of the infarct substrate [57,58]. The initial clinical study of voltage map-guided substrate ablation not only demonstrated the usefulness of this strategy, but also provided the initial

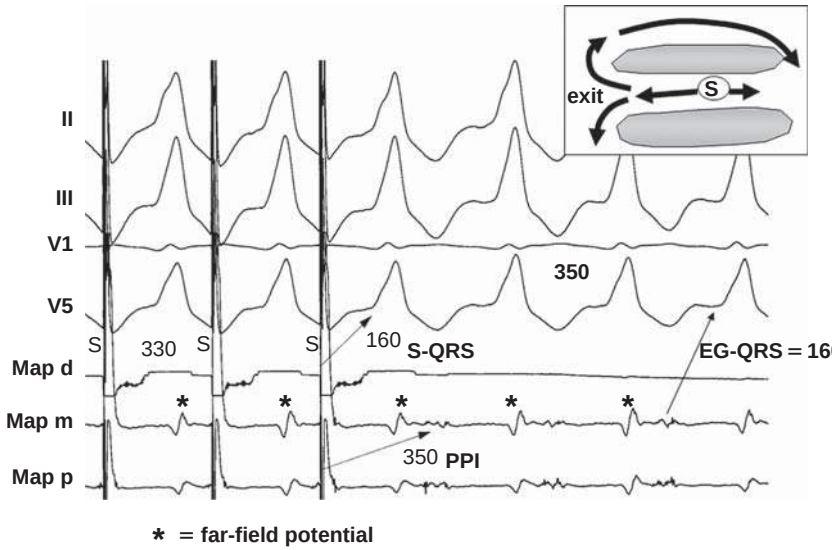


Figure 6.2 Entrainment of VT from an isthmus site. The VT cycle length is 350 ms. Pacing entrains tachycardia without producing QRS fusion (concealed entrainment; entrainment with concealed fusion). A far-field potential is evident in the mapping catheter. The postpacing interval (PPI) measured from the last stimulus to the local potential matches the VT cycle length of 350 ms. The S-QRS interval matches the electrogram to QRS interval (EG-QRS) measured to the local potential of 160 ms. The inset shows the mechanism (see text for discussion). Maps d, m, and p: bipolar recordings from the distal, mid, and proximal electrode pairs of the mapping catheter; S: stimulus

insights to extend voltage mapping to patients with VT in nonischemic forms of structural heart disease [38]. Infarct regions are identified from areas where electrograms have an amplitude of <1.5 mV (bipolar electrograms recorded from catheters with a 4-mm-tip electrode, 1-mm interelectrode spacing, and filtered at 10–400 Hz) [38,59]. This voltage threshold has also been applied to identify areas of scar in nonischemic cardiomyopathies and arrhythmogenic right ventricular dysplasia [60–63].

In patients with scar-related VTs, the low-voltage area is often large, such that complete ablation of the area or complete encircling ablation is often not feasible, nor necessarily desirable. There are several concepts that guide selection of ablation targets, all determined by different philosophies regarding the relationship of the VT circuit to the substrate. The first concept was pace mapping to identify exit regions in the border zone of the scar [38]. Linear ablation lesions were placed through each exit region, extending away from the border region into the denser scar as a result of the recognition that the critical isthmus may be deeper within the scar. Other lesion sets have been employed and these different strategies have not been directly compared. A line of lesions may be placed parallel to the scar border within the

low-voltage area encompassing the exit region [64]. These strategies, although successful, are limited by their focus on individual VTs, requiring induction of VT to assess QRS morphologies for guidance during pace mapping, making it difficult to conceive of substrate ablation of undetected morphologies. Several investigators have advanced strategies directed at other substrate characteristics. Ablation has targeted all isolated late potentials present during sinus rhythm or ventricular pacing, which are often present at reentry circuit isthmus sites identified for mappable VTs [65]. In some patients, areas of unexcitable scar that may be border-forming for reentry circuits have been defined to attempt to identify isthmuses for ablation [35]. Alternatively, a "channel" may be identified as a region of larger voltage bordered by low voltage within the scar [66,67]. In an animal model, these channels have been have been identified functionally (rather than anatomically with voltage mapping), and may be fairly limited in number [22].

These different substrate ablation strategies have not been directly compared and differences in outcomes are not apparent in the literature. The use of large areas of ablation, which is dictated largely by current technology, with all of these strategies may reduce and contribute to obscure potential differences among mapping approaches. Variations in anatomy may also influence the effectiveness of the different methods. Although ablation guided by substrate mapping avoids the hemodynamic consequences of prolonged mapping during VT, the lack of a precise reentry circuit target is compensated by extensive ablation lesion sets, which increases the potential for complications. In a recent multicenter study, major complications including worsening heart failure were observed in 7.3% of patients, and 3.0% died within 7 days of ablation [55]. A substrate-guided approach to VT ablation did not produce detectable deterioration in ventricular function in another study [68].

In general, substrate-guided ablation achieves a marked reduction in VT episodes (usually measured by a reduction of ICD shocks) in patients with scar-related VT [38,42,53,55,65,66]. It is a reasonable approach for patients with unmappable VT and may be combined with other mapping approaches in patients with mappable VTs.

Transthoracic epicardial mapping and ablation

Recently introduced in 1995, transthoracic epicardial mapping and ablation has recently become an important adjunctive or even a preferable strategy to eliminate a diverse range of cardiac arrhythmias [69–71]. Briefly, a regular Tuohy-17G needle designed for epidural anesthesia is introduced at the subxiphoid region at a 45° angle and gently advanced under fluoroscopy until close to the cardiac silhouette. The precise site of the needle tip is determined by injection of 1 ml of contrast media. When the needle enters the pericardial space, contrast medium can be seen surrounding the cardiac silhouette (Figure 6.3). A wire and introducer sheath is inserted, allowing a mapping

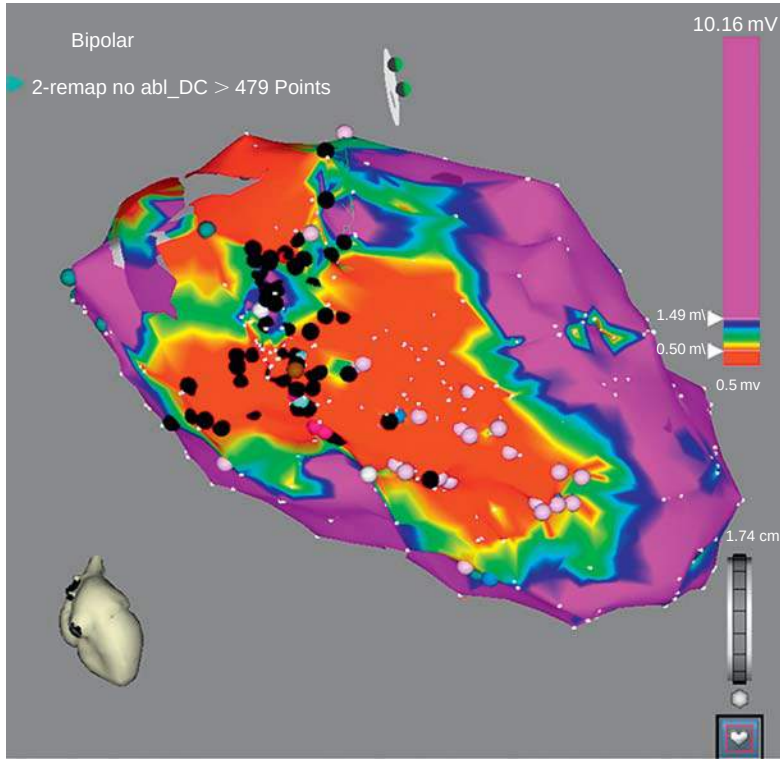


Figure 6.3 Electroanatomic mapping for substrate ablation. A 3D left ventricular endocardial voltage map is shown in a patient with healed inferior myocardial infarction and VT. A voltage map constructed during sinus rhythm is designated by the color display: sites with bipolar voltage <0.5 mV are coded in red, sites with voltages >1.5 mV in purple, and the border zone of intervening voltages with the intervening colors. In this example, the location of late (black dots) and fractionated (pink dots) electrograms are also displayed

catheter to be inserted into the pericardial space, where it can be manipulated to explore the entire surface of the right and left ventricles. Electrogram recording and interpretation of epicardial mapping are essentially the same as for endocardial mapping, including the use of activation mapping, pace mapping, and entrainment mapping (Figure 6.4). Epicardial mapping is facilitated by smooth epicardial surface, without the limitation of papillary muscles, trabeculae, and chordae, as well as absence of catheter induced ventricular extrasystoles that are encountered during endocardial mapping.

Is there an electrogram pattern predictive of successful application during transthoracic radiofrequency epicardial catheter ablation to treat ventricular tachycardia?

Mapping in patients with VT as a result of chronic Chagasic cardiomyopathy is difficult because of heterogeneous ventricular involvement and a

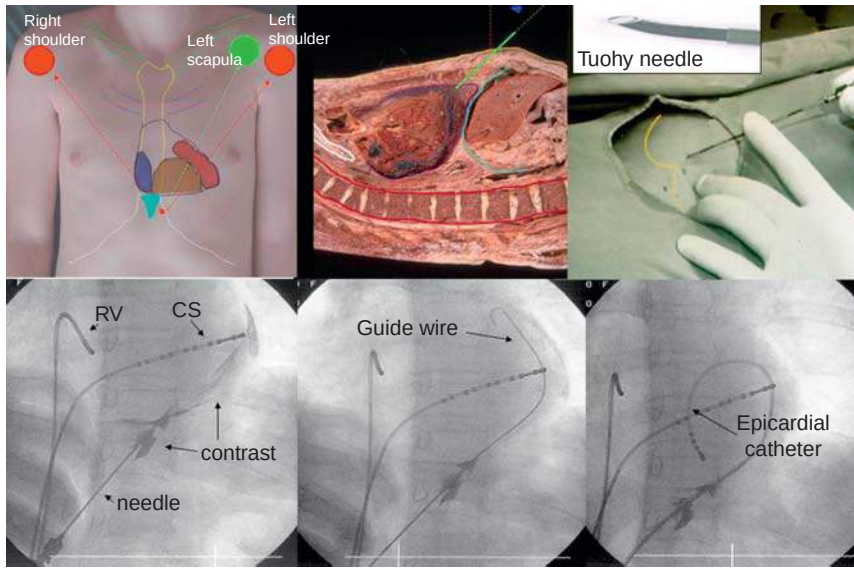


Figure 6.4 A Touhy needle (right superior corner) and anatomy relevant to epicardial access is shown. The saggital anatomic image indicates the path of the needle for pericardial access (green line). Fluoroscopic images show contrast, a guide wire, and catheter in the pericardial space

frequently high epicardial stimulation threshold in areas of slow conduction that limits or prevents entrainment maneuvers. Sosa and colleagues recently performed an evaluation of epicardial electrogram patterns and limited RF current applications to predictive ablation success to assess whether thermal RF mapping could be safely and effectively used to guide RF epicardial ablation in this disease (E Sosa, pers. comm., 2009).

During epicardial mapping at 21 procedures in 19 consecutive patients with Chagasic VT, 239 sites were analyzed. The electrograms were defined as mid-diastolic potentials, continuous activity, or an early signal. A 60ºC RF pulse was delivered for 10 s at each site. Electrogram duration and prematurity were determined for each application, and a 12-lead ECG for ST segment analysis was obtained after VT interruption. VT was interrupted at 47 of 239 sites (19%). At 57 sites (24%) with mid-diastolic signals, VT was interrupted at 5 sites (9%), whereas 52 applications did not interrupt VT. Duration and prematurity did not differ between termination and no termination sites. At 27 sites (11%) with continuous electrical activity, interruption occurred at 8 (30%); RF had no effect at 19 sites. At 155 sites (65%) with an early electrogram, RF interrupted VT at 34 sites (22%); but electrogram duration (181 ± 72 ms vs 177 ± 68 ms) and prematurity (107 ± 47 ms vs 94 ± 44 ms) did not differ among sites with or without VT interruption. No early or late complications occurred during follow-up.

Electrogram pattern was therefore not helpful in defining a site for a successful epicardial RF application. Although safe, epicardial catheter ablation based on empirical thermal mapping is not ideal. VT interruption based on this technique was achieved at only 20% of the sites selected based on electrograms, making a large number of applications necessary to successfully treat these patients.

Epicardial radiofrequency ablation

Standard RF ablation can be used during epicardial catheter ablation (Figure 6.5), but the lack of circulating blood for convective cooling of the ablation electrode limits power delivery in the pericardial space, potentially limiting lesion creation and efficacy of standard RF ablation [72]. Irrigated RF ablation allows greater power delivery and an increased lesion size that can be effective even when the epicardial target is covered by fat [72,73]. External irrigation requires intermittent drainage of the pericardial space to prevent tamponade. While the operator can choose between intermittent and continuous drainage, continuous drainage is not mandated as small amounts of irrigation fluid do not cause tamponade, and the pericardial cavity can be drained intermittently through the epicardial sheath or a pigtail catheter. A second sheath may be placed for this purpose, avoiding a second epicardial puncture by double wiring the initial puncture site.

Alternatively, use of an introducer that is larger than the mapping catheter allows aspiration around the ablation catheter. The amount of fluid infused can also be limited. One strategy uses no irrigation flow during mapping, and the other uses temperature-guided RF with temperature set to 60°C, initiating ablation at 25 W, and a flow rate of 1 ml/min. The irrigation flow rate is then increased as needed, typically up to 10 ml/min to allow delivery of up to 40–50 W (E Sosa, pers. comm., 2009).

Risks of epicardial mapping and ablation

The potential for coronary artery injury is a major concern. There are three potential means by which damage could occur to the coronary arteries during transthoracic epicardial mapping and/or ablation. The needle can perforate a coronary artery during access; however, this risk is exceedingly unlikely because there are no major epicardial vessels close to the right apical ventricular wall (the area where the needle tip is inserted). It has been suggested that once in the pericardial space, the ablation catheter or sheath could lacerate an epicardial vessel; this is also unlikely because the coronary vessels are covered by the visceral pericardium and often lay in a groove of adipose tissue in the epicardial ventricular muscle. The major concern is the risk of RF ablation on a coronary artery. Experimental data suggest that coronary artery occlusion depends on the vessel caliber [72,74]. Sosa *et al*. found that the minimal distance between catheter tip and the artery for coronary occlusion was 12 mm (three times the catheter tip) [72]. It is recommended

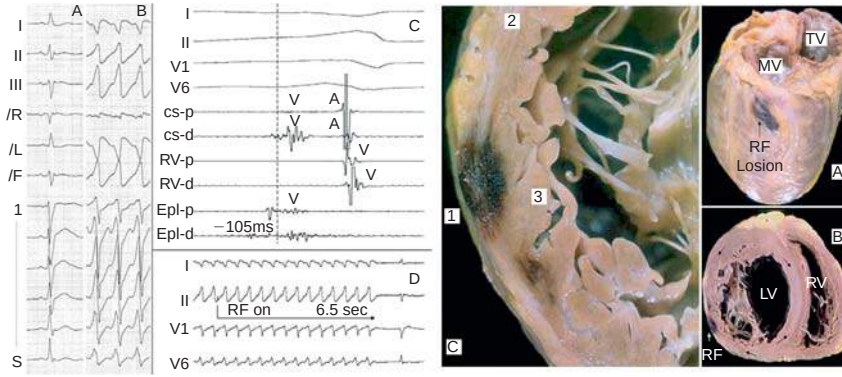


Figure 6.5 Data from a 63-year-old patient with idiopathic dilated cardiomyopathy and recurrent VT while awaiting heart transplant. ECG of VT (Panel B) showed a pseudodelta wave of 45 ms, an intrinsicoid deflection time of 100 ms in V2, and an RS complex duration of 155 ms, suggesting that VT exit site was located in the epicardial basal–lateral wall of the left ventricle. A 4-mm-tip ablation catheter was used for ablation. Epicardial mapping of well-tolerated incessant VT identified fractionated ventricular electrograms −105 ms (Panel C) before the onset of the QRS complex at a site where coronary angiography showed no adjacent coronary artery. The first RF ablation interrupted VT within 6.5 s (Panel D). A second 60-s RF pulse was delivered at the same site in sinus rhythm. Patient remained free of VT for the following 10 days when elective cardiac transplantation was carried out. Endocardial mapping/ablation was not performed. The heart examined after transplant shows the epicardial RF lesion. The upper right panel shows a posterior view of the left ventricle. The mitral (MV) is apparent. RF lesions are black/purple spots located basally (close to the mitral annulus) and lateral to a marginal branch of the circumflex coronary artery. The visceral pericardium is intact without evidence of pericarditis. The left and lower right panels show a cross-sectional view of the left and right ventricles at the level of RF epicardial lesion (white arrow and RF towards the black spot). The left ventricle was dilated and a circumferential intramural layer of scar tissue can be noted (black arrows) mainly in the interventricular septum and at the inferolateral wall of the left ventricle. The RF lesion extends from the epicardial surface of the heart to about 1 mm beyond the intramural layer of scar with underlying preserved myocardium [3]

that proximity to the coronary arteries be defined by a coronary angiogram if the ablation site is suspected of being within 12 mm of a coronary vessel.

On the other hand, there are groups that do not perform routine angiograms without any occurrence of acute and chronic coronary events [75,76].

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CHAPTER 7

Imaging Tools, Energy Sources, and Catheters for Ventricular Tachycardia/ Ventricular Fibrillation Ablation

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Imaging tools

In recent years, cardiac imaging techniques have been successfully applied in interventional electrophysiology, especially in the setting of atrial fibrillation ablation. In many institutions, techniques like intracardiac echocardiography (ICE) or the integration of left atrial models, taken from computed tomography (CT) or MRI studies and imported into EP workstations, are routinely used to plan and guide the ablation procedures. Compared to these procedures, imaging techniques at the present time play only a minor role in the field of catheter ablation of ventricular tachycardia (VT). However, imaging techniques play an important role both in preprocedural planning and in postprocedural follow-up. In addition, identification of the underlying heart disease and visualization of a potential arrhythmogenic substrate may facilitate selection of appropriate mapping and ablation strategies during catheter ablation of VT [1], and will likely increase the role of preprocedural and periprocedural imaging techniques.

Echocardiography

Transthoracic echocardiography is a widely available, rapid method to detect structural and functional disorders. This method serves as a reliable tool to rule out ventricular thrombi before left ventricular procedures. Additionally, it helps to identify relatively infrequent cardiomyopathies associated with VTs, for example, arrhythmogenic right ventricular dysplasia and hypertrophic

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cardiomyopathy, and is used for postprocedural detection of pericardial effusions and cardiac tamponade, respectively.

Transesophageal echocardiography may be used in patients with atrial fibrillation or flutter to detect thrombi within the left atrium and the left atrial appendage, respectively, to prevent thromboembolic events when a transseptal access to the left ventricle or cardioversion is required. Severe atheroma in the aorta detected on transesophageal echo may encourage the operator to avoid the retrograde approach to the left ventricle.

Intracardiac echocardiography applied from the right atrium and the right ventricle has been used for real-time imaging during VT ablation procedures [2]. This echocardiography allows for visualization of scarred tissue and thus may help to identify the target area of ablation. ICE may guide ablation of right or left ventricular outflow tract VT by visualizing the relationship between semilunar valves and coronary artery ostia, respectively, and the sites of VT origin [3]. In a small cohort of patients with VT originating from papillary muscles, ICE helped to establish the site of origin and to successfully guide radiofrequency (RF) ablation [4]. Feasibility of standard ablation for atrial fibrillation based on 3D ICE-acquired imaging was shown in a prospective study including 15 patients [5].

Computed tomography and cardiac magnetic resonance imaging

Both CT and cardiac magnetic resonance imaging (CMR) are valuable tools for assessing cardiac anatomy and function, and for identifying structural abnormalities serving as arrhythmia substrate. CT is a validated noninvasive method to assess the presence and degree of coronary artery disease [6–8]. Visualization of the cardiac venous system (coronary sinus, great cardiac veins) is feasible and may facilitate catheter navigation for left ventricular mapping and ablation [9,10]. CT and CMR allow for highly reproducible measurements of volumes, ejection fraction, wall thickness, and regional wall motion. Delayed contrast-enhanced CMR delineates regions of scar tissue potentially forming part of the arrhythmia substrate in patients with ischemic and nonischemic cardiomyopathies [11,12]. Additionally, this imaging technique allows to determine a specific etiology of nonischemic cardiomyopathies predisposing for a higher susceptibility for VT such as myocarditis, sarcoid, and arrhythmogenic right ventricular dysplasia.

Cardiac magnetic resonance imaging may emerge as a useful tool for risk stratification in patients with ischemic or nonischemic cardiomyopathies. The presence of midwall fibrosis as detected by late gadolinium enhancement CMR is a predictor of adverse cardiac events in patients with dilated cardiomyopathy [13,14]. In a prospective study including 48 patients with coronary artery disease, infarct size and mass as assessed by CMR were found to be highly predictive for VT inducibility [15]. In another study including 47 patients with prior myocardial infarction, it was shown that the amount of tissue heterogeneity within the periphery of the infarct zone correlated strongly with VT inducibility [16]. In both studies, left ventricular ejection

fraction (LV EF) did not influence the incidence of inducible VT. In patients with nonischemic cardiomyopathy, predominance of scar distribution involving 26–75% of wall thickness was a predictor of VT inducibility independent of ejection fraction [17].

In an animal model of myocardial infarction, registration of epicardial activation mapping to very high resolution 3D delayed enhancement CMR demonstrated a clear correlation of both the isthmus of the reentry circuits and the epicardial exit sites with the complex 3D structures of the viable and scar myocardium within the border of the infarct area [18]. Feasibility of LV catheter navigation and ablation guided by registration of pre-acquired CRM with real-time electroanatomic mapping was demonstrated in a porcine infarct model [19]. Lardo *et al.* reported the first-time use of real-time CMR in an *in vivo* animal model [20]. Ablation catheters were successfully positioned to intracardiac target sites under direct visualization by CMR fluoroscopy. The spatial and temporal extent of ablation lesion development could be visualized and lesion size corresponded well with findings from postmortem studies. Transseptal puncture tracked by real-time CMR was feasible in an *in vivo* swine model [21]. These findings suggest that imaging of the complex scar morphology may evolve as a supplementary imaging technique for intraprocedural guidance, particularly in the case of unmappable or epicardial VT. Visualization of ventricular anatomy and obstacles of procedural success, for example, epicardial fat in the case of epicardial mapping approaches, and integration of pre-acquired images into conventional mapping may have the potential to facilitate catheter navigation and thus reduce procedure time, decrease the rate of complications, and increase success rate [22,23]. Taking into account the potential advantages of CMR-guided VT ablation, including detailed visualization of the arrhythmia substrate, reliable device placement under real-time tracking, and assessment of ablation success in terms of lesion size without concern for radiation exposure, CMR technique may possibly play a major role in the ablative treatment of complex arrhythmias when applied to human subjects. One potential disadvantage remains concern regarding the safety of MRI in patients with implanted devices. Increasing data suggest that MRI at 1.5 T is possible when appropriate precautions are taken [24], and reports of MRI at 3 T have been published for patients with implantable defibrillators [25]. Industry is also working to improve the MRI compatibility of devices.

Other imaging tools

Left ventricular angiography performed in addition to coronary angiography provides valuable information about LV EF, global and regional wall motion, and valvular function. This procedure allows detection of aneurysmal dilatation, representing potential sites of VT origin; and ventricular thrombi, representing a relative contraindication to catheter manipulation. Angiographic evidence of akinetic or dyskinetic bulgings within the right ventricle is highly specific to arrhythmogenic right ventricular cardiomyopathy/dysplasia [26].

In patients with scar-related VT, positron emission tomography/CT may be beneficial as it provides additional tissue characterization by displaying metabolic and morphologic information [23,27]. Registration of the acquired 3D image into electroanatomic mapping systems may facilitate ablation procedures.

Energy sources and catheter technologies for ventricular tachycardia ablation

Introduction

The principle problem facing catheter technology when applied to ventricular ablation is to deliver a controlled lesion with both sufficient size to abolish the arrhythmia substrate and sufficient accuracy in order to prevent damage of nonarrhythmogenic tissue. While most supraventricular or atrioventricular arrhythmias have a discrete and well-circumscribed substrate, for example, ectopic atrial tachycardia, AV-nodal tachycardias, or accessory pathways, many patients with VT have an extensive arrhythmia substrate involving endocardial, intramural, as well as epicardial structures. In addition, areas of highly diseased tissue (fibrosis, scars) may be involved in the arrhythmia substrate and thus be part of the target area of catheter ablation. On the other hand, induction of very limited tissue damage may be desired during catheter ablation of certain forms of VT, for example, focal idiopathic VTs. Thus, from a biophysical perspective, catheter ablation of VTs is a true challenge. This chapter summarizes the catheter technologies and energy sources currently used for ablation of VTs.

Energy sources

High-voltage direct-current ablation ("fulguration")

The first energy form used for catheter-based VT ablation was high-voltage direct current [28,29]. This approach was based on intracardiac delivery of direct-current defibrillator pulses to the ventricular myocardium via an electrode catheter. Tissue damage is caused through a combination of thermal, electrical, and mechanical (barotrauma) factors. However, its uncontrollable nature and the association with serious complications such as death, induction of VTs and fibrillation, prolonged hypotension, cardiac tamponade, pericarditis, and systemic embolization [29,30] prevented the widespread use of the technique and encouraged the search for alternate energy sources for catheter ablation of VTs.

Radiofrequency ablation

Since its first description in 1978 [31], RF evolved from an experimental approach to the most commonly, if not exclusively, used energy source for catheter ablation of all VT entities. RF alternating current is usually administered with a continuous sinusoidal unmodulated waveform of 300–1000 kHz. In contrast to direct-current RF ablation allows a more controlled energy

application with generation of well-circumscribed myocardial lesions. RF current is predominantly delivered in a unipolar mode between the tip electrode of the ablation catheter and a large skin electrode serving as indifferent electrode. The most important mechanism of myocardial necrosis induction is based on the conversion of electrical energy into heat within the myocardial tissue, which leads to distinct metabolic, electrophysiological, and structural alterations of the cells [32]. Hyperthermia results from both rapid resistive heating and delayed heat conduction (convection) to the surrounding tissue [33]. Resistive heating refers to the process whereby alternating electrical current that traverses through the intervening tissue with a distinct electrical resistance dissipates power to that tissue. Thus, electromagnetic energy is converted into mechanical energy of charged carriers and tissue heating. As resistive heating decreases with the distance from the ablation electrode to the fourth power, these effects are concentrated within a narrow rim of tissue (1 mm) in close proximity to the ablation electrode [32]. The extent of passive heat propagation from this small volume to deeper tissue layers, which proceeds after discontinuation of energy delivery ("thermal latency"), depends on the duration of RF-energy application [34–36] and the temperature in the resistive heating zone with higher RF power delivery invigorating an increase in lesion size [37]. However, at a certain energy level electrode overheating may occur leading to coagulum formation and charring on the tip electrode accompanied by a rapid increase in electrical impedance which in turn leads to a loss in effective myocardial heating [33]. To prevent overheating at the electrode–tissue interface, temperature-controlled energy application systems have been developed. A thermistor or thermocouple embedded in the tip of the ablation catheter allows temperature monitoring at the electrode–tissue interface during energy application. Maximal RF energy (usually 50 W) is delivered until the preselected target temperature has been reached and thereafter automatically titrated down to maintain the target temperature. Temperature-controlled RF ablation is the standard technique for ablation of VTs whenever conventional nonirrigated ablation electrodes are used. The extent of lesion formation depends not only on RF power and duration, but also on nonmeasurable variables like electrode–tissue contact and orientation (perpendicular vs parallel to the tissue) and external cooling by the circulating blood flow.

Irrigated radiofrequency ablation

Despite a lack of randomized trials comparing different approaches for VT ablation, there is general agreement that irrigated electrodes provide advantages over standard RF ablation in the setting of scar-related VT. Active cooling of the ablation electrode, either by circulating fluid within the electrode (closed loop) or by flushing saline through pores in the electrode (open irrigation) [33] allows greater energy delivery before a critical temperature rise at the electrode–tissue interface occurs. Cooled RF using both external and internal irrigation abolished scar-related VT more effectively than standard RF ablation in a nonrandomized retrospective study, which is consistent with

larger lesion formation observed in prior *in vitro* preparations, animal models, and anecdotal reports [34,38–41].

Although currently no clinical studies are available directly comparing closed loop irrigation with external irrigation, it seems that the latter technique may have distinct advantages. External saline irrigation resulted in a lower interface temperature and decreased the risk of thrombus formation and severe tissue damage as compared to closed loop irrigation at similar levels of impedance, lesion depth, and tissue temperature in an experimental preparation [42]. However, administration of relatively large amounts of saline using external irrigation (which may exceed 2000 ml) may cause hemodynamic or respiratory compromise, especially in patients with severely impaired left ventricular function, which necessitates continuous monitoring of fluid balance.

Saline irrigation cools the electrode itself and thus impedes electrode temperature feedback resulting in an increased risk of unnoticeable tissue overheating. If the intramyocardial temperature exceeds approximately 100ºC, gas bubble formation may occur leading to an explosion of steam, which may in turn cause myocardial perforation and cardiac tamponade. These "steam pops" are audible in the electrophysiological laboratory, but usually without consequences when energy is applied to the left ventricle. However, perforation of the right ventricle after "popping" has been reported. Modifying configuration of the tip electrode by adding thermal insulation between the electrode and the saline irrigation channels reduced internal cooling and facilitated temperature feedback during RF ablation without affecting lesion and thrombus formation [43].

The first large-scale prospective multicenter evaluation of an internal irrigation system included 146 patients with a history of scar-related VT [44]. Energy delivery was initially set at 25 W and gradually increased until a target electrode temperature between 40 and 50ºC was reached. Before and during energy application, saline was infused through the catheter at 0.6 ml/s. Duration of RF delivery was measured between 60 and 180 s. RF power output was automatically titrated down if the electrode temperature exceeded 65ºC. Acute success defined as elimination of all mappable VTs was observed in 106 patients (75%). Twelve patients (8%) experienced a procedure-related major complication including cardiac tamponade in four patients (2.7%), stroke or transient ischemic attack in four patients (2.7%), and complete atrioventricular block in two patients (1.4%). Only one cardiac tamponade was considered to be temporally related to RF-energy application. Additionally, there were four procedure-related deaths. After a follow-up of 243 ± 153 days, 66 patients (46%) had at least one VT recurrence.

External irrigation was prospectively evaluated in a multicenter study including 231 patients with prior myocardial infarction and recurrent episodes of monomorphic VTs [45]. During mapping, saline was infused at 2 ml/min. Irrigation flow was increased to 30 ml/min during RF application. RF power was delivered at a maximum of 50 W as long as temperature recorded from the electrode remained below 50ºC. RF application was stopped immediately

once temperature exceeded 50ºC or an impedance rise of 10 Ohm or greater was observed. After a follow-up of 6 months, 49% of patients were free from recurrent or intermittent VT (primary endpoint). A median volume of approximately 1350 ml (median) was administered. Twenty-four patients experienced nonfatal procedure-related complications, for the most part related to heart failure and vascular access. No thromboembolic complications or stroke occurred. There were seven procedure-related deaths.

Pulsed radiofrequency ablation versus continuous radiofrequency ablation

In addition to the abovementioned techniques, energy delivery to the myocardium can be influenced by the mode of RF application. RF energy can be applied either continuously over a certain period of time or repetitively with the single periods (duty cycle) lasting a few milliseconds. The latter approach, referred to as "pulsed RF ablation", allows the application of higher energy levels to the myocardium at comparable electrode temperatures [46]. As compared to continuous RF current delivery, the pulsed mode is associated with higher intramyocardial temperatures and larger lesion depths *in vitro* and *in vivo* [46,47].

Alternate energy sources

Experience with alternate energy sources for catheter ablation of VT is very limited. Most data concerning this matter were derived from highly experimental studies of animal models.

Alcohol ablation

Chemical ablation for VT is based on cytotoxic and irreversible tissue damaging effects of ethanol and other agents leading to myocardial necrosis and coronary vessel occlusion with resultant ischemic injury. Before ethanol application is performed, it is crucial to identify the target coronary artery that supplies blood to the arrhythmogenic area.

One means of target vessel identification is by selective injection of cooled saline, radiographic contrast medium, or antiarrhythmic drugs into different coronary branches [48–50]. VT termination identifies the branch supplying the arrhythmogenic substrate. Alternatively, mapping of diastolic potentials as well as entrainment and pace mapping may be performed from inside the coronary artery to locate the critical reentry circuit isthmus as for standard VT approaches [51]. The artery branch should be sufficiently distal to avoid extensive myocardial damage. After an appropriate target branch has been identified, ethanol is applied in a manner similar to the approach used for septal alcohol ablation in patients with hypertrophic obstructive cardiomyopathie.

The feasibility of transcoronary VT ablation by means of chemical agents was first described in an animal model in 1987 [52]. In this study, most of the VTs could be successfully ablated after injection of phenol or highly concentrated ethanol into the target coronary artery.

In 1989, Brugada *et al.* reported successful target vessel identification by saline mapping and VT ablation using highly concentrated ethanol in three patients presenting with VT after prior myocardial infarction.

Most of the clinical studies using alcohol ablation have been performed in the 1990s. Twenty-three patients with sustained drug-refractory monomorphic VTs after myocardial infarction were prospectively studied to assess efficacy and safety of transcoronary ethanol ablation [50]. The target vessel could be reliably identified in 11 patients. Immediately after ethanol administration VT was inducible in only one patient, but during a follow-up of 5–7 days VT became inducible in two more patients. In a retrospective single-center analysis including nine patients who previously failed RF ablation for scar-related VTs, immediate success, defined as noninducibility of any monomorphic VTs, was achieved in five patients [53]. The clinical targeted VT was successfully ablated in eight patients. During a mean follow-up of 29 ± 23 months, three patients died and four patients remained free of VT recurrences.

Ethanol ablation bears potential of serious complications including permanent complete atrioventricular block, pericarditis [48,50], reflux of ethanol into adjacent vessels leading to infarction of unintended myocardium, and a worsening of heart failure as a result of a significant loss of myocardium.

In conclusion, transcoronary ethanol ablation may be considered in selected patients suffering from highly symptomatic drug-refractory VT who failed previous endocardial and/or epicardial RF ablation, especially in a subset of patients with suspected deep intramural or epicardial reentry circuits. Additionally, ethanol ablation may be a treatment option in patients with epicardial VT and insufficient pericardial access because of previous cardiac surgery. However, success rate remains moderate and there is a considerable risk of serious complications. The procedure should be performed in centers with highly experienced interventional cardiologists, electrophysiologists, and on-site surgical standby.

Cryoablation

For more than two decades, cryoenergy has been successfully used for ablation of ventricular myocardium during surgical ablations of VTs. Transcatheter ablation systems using cryoenergy are also available and have been successfully used for ablation of supraventricular and atrioventricular tachycardias, and idiopathic outflow tract VTs [49,54,55]. Cryoablation produces more circumscribed and generally smaller lesions as compared to RF current. This technique possibly involves lower damage to adjacent coronary arteries in the setting of epicardial ablation as compared to RF ablation [56,57]. Currently, no data from controlled clinical studies exist concerning the use of cryoenergy for catheter ablation of VTs.

Other energy sources that have been investigated for catheter ablation of VTs include high intensity focused ultrasound, laser energy, as well as radiation energy applied transcutaneously. No clinical studies exploring these energy sources have been performed so far.

Ablation catheters and electrode design

Electrode catheters used for ablation of VTs usually have a size of 7.5 French and unidirectional or bidirectional steering capabilities. RF energy is usually delivered via the distal tip of the electrode catheter. Currently, platinum–iridium is the most commonly used catheter tip material. In *ex vivo* animal studies, RF delivery to gold-tip electrode induced deeper lesions as compared to platinum-tip electrodes [58,59]. This effect was attributed to the higher thermal conductivity of gold compared to platinum resulting in greater heat dissipation from the electrode–tissue interface to the circulating blood and the tissue, and thus allowing for higher power transmission to the tissue. However, in two prospective randomized trials comparing platinum-tip and gold-tip electrodes for ablation of AV-nodal reentry tachycardia and isthmus-dependent atrial flutter, respectively, no statistically significant difference could be found in terms of power delivery, procedural endpoints, and safety endpoints except for a considerable reduction of char formation with the gold-tip electrode [60,61].

One advantage of RF ablation is the simple design of the energy delivery system, that is, a wire connects a generator to the tip electrode. In principle, larger electrodes allow the application of higher energy levels to the tissue because of greater exposure to the circulating blood resulting in more effective electrode cooling [62]. With the voltage of the delivered RF current kept at a constant level, smaller electrode sizes are accompanied by higher tissue temperatures, larger lesions, and lower dependence of lesion size on the electrode orientation [63]. For conventional nonirrigated ablation procedures, the length of the ablation electrode measures 4, 5, 8, and 10 mm. There are certain disadvantages of large ablation electrodes: the spatial resolution of catheter mapping and the electrogram signal quality is reduced compared to 4-mm electrodes. Additionally, larger electrodes provide less accurate temperature control [33]. Furthermore, using larger electrodes involves greater disparity of temperatures across the electrode surface with a considerable risk of overheating of certain electrode areas resulting in thrombus formation. Because of unequal distribution of RF power fields across the ablation electrode, especially when large electrodes are used, overheating is most likely to occur where the proximal edge of the ablation electrode meets the catheter insulation material.

Ablation electrodes used for external irrigation ablation have a 3.5-mm tip. The tip has six to nine irrigation holes that are used to homogeneously distribute the saline over the ablation electrode during energy application.

Mode of energy application, selection of ablation catheters, and energy settings

The selection of the mode of RF-energy application, that is, nonirrigated versus irrigated ablation, the ablation catheter, and the energy application setting depends on the type of VT targeted by ablation.

Idiopathic (outflow tract) ventricular tachycardias
These arrhythmias are focal in nature and the target tissue consists of structurally nondiseased myocardium. Thus, extensive tissue injury is usually not necessary for successful ablation. Steerable catheters with 4-mm or 5-mm-tip electrodes and conventional nonirrigated energy application are generally used. Because of the thin ventricular myocardium, especially in the right ventricular outflow tract, and the considerable risk of perforation and cardiac tamponade, target temperature and output power should be limited to a maximum of 60ºC and 30–40 W, respectively. Duration of energy application should not exceed 30–60 s. Because of the close anatomic relationship between energy application sites and the ostia of the coronary arteries, special caution is necessary for ablation of outflow tract tachycardias arising from the coronary cusps. Lower energy and temperature levels may be adequate in this situation. Some investigators recommend the use of lower target temperatures and irrigated electrodes for left-sided idiopathic focal VTs assuming a higher risk of coagulum formation and thromboembolic complications "*compared to ablation in the right ventricle*".

Idiopathic left ventricular ("fascicular") tachycardia and bundle branch reentrant ventricular tachycardia
Because of the discrete nature of the arrhythmia substrate, the same settings as for idiopathic outflow tract VTs are recommended. However, as there is no relevant risk of perforation and tamponade in this setting, higher power output may be applied. Some investigators recommend irrigated ablation in the left ventricle assuming a lower risk of thromboembolic events.

Ventricular tachycardias originating from structurally diseased myocardium, scar-related ventricular tachycardias
Catheter ablation of scar-related VTs usually requires induction of more extensive tissue injury to abolish the arrhythmia substrate. Therefore, larger or irrigated electrodes are preferred. Currently, there are no randomized studies available comparing the efficacy and complications of these two approaches. Using 8-mm electrodes, a maximum output power of up to 70 W with a target temperature of 70ºC or an impedance fall of 10 Ohm is reasonable in the left ventricular myocardium [64]. When irrigated ablation is used, output power is usually limited to 50 W delivered during a saline irrigation rate of 20–30 ml/min whereas maximum catheter tip temperature should not exceed 50ºC. Application duration of up to 90–120 s may be chosen.

For catheter ablation of VT in right ventricular cardiomyopathy, lower energy settings and shorter application times may be adequate to reduce the risk of perforation and cardiac tamponade.

Epicardial ablation
Ablation of epicardial idiopathic focal VTs may be performed with standard 4-mm electrode catheters at power settings between 25 and 40 W. Although

the coronary arteries are usually protected from severe injury induced by RF energy by the high flow rate in the vessel (leading to significant convection of heat), caution is recommended. Coronary angiography may be performed before energy delivery and energy setting may be adjusted to the individual situation. For patients with structural heart disease undergoing epicardial ablation, use of irrigated catheters may have significant advantages compared to conventional ablation: usually larger lesion are desired that can be more reliably induced with irrigated ablation. In addition, energy delivery during conventional RF application may be limited by the fact that application of relatively low power results in rapid heating of the ablation electrode, thereby preventing the generation of large lesion because of the absence of cooling of the electrode by the circulating blood. External irrigation leads to saline accumulation in the pericardium during epicardial mapping and ablation. Thus, periodic aspiration is necessary to prevent hemodynamic compromise.

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CHAPTER 8

Ablation of Ventricular Tachycardia/ Ventricular Fibrillation in Patients with Structural Heart Disease: Techniques and Results

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Overview of ablation techniques

In patients with structural heart disease, ventricular tachycardia (VT) frequently arises from reentry circuits involving areas of ventricular scar. The scar occurs most commonly because of prior myocardial infarction (MI), right and left ventricle cardiomyopathy, hypertrophic cardiomyopathy (HCM), congential heart diseases, Chagas disease, sarcoidosis, other nonischemic cardiomyopathies, and surgical ventricular incisions. In these patients, dense fibrotic scars and the valve annuli create areas of anatomic conduction block that often define reentry circuit borders. Various patterns of reentrant excitation, including single-loop and figure-eight configurations, have been delineated (Figure 8.1) [1–4]. Such reentrant excitation undoubtedly is facilitated by areas of slow conduction, because of damaged myocardium, by alterations of passive properties such as anisotropy, and by islands and streaks of fibrosis that provide anatomic obstacles. These reentry circuits may be subendocardial, intramural, or epicardial, and contain isthmuses of surviving myocardial bundles with abnormal conduction that are critical components of the circuit and desirable target of the ablation [5–9]. Catheter mapping of sustained VT

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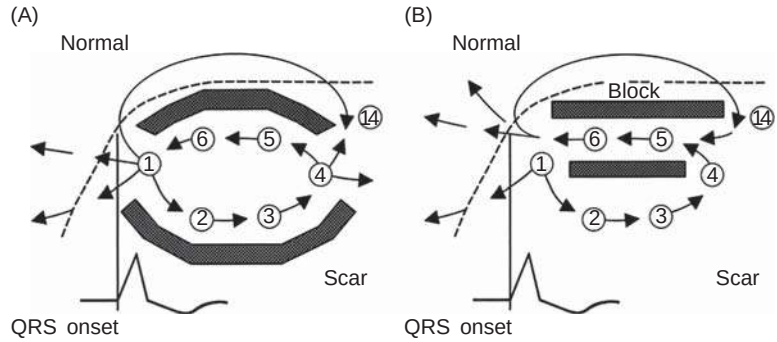

Figure 8.1 Schematic diagrams depicting reentrant circuits associated with myocardial fibrosis. An area of scar is present inferior and to the right of the dashed line. Areas of fixed conduction block are indicated by the hatched rectangles. Solid arrows indicate direction of excitation wave fronts through the circuits. Sites 1–6 depict propagation of wave front within the reentry circuit; site 14 is adjacent to the entrance of an area of slow conduction. Panel A: The protected, simple reentry circuit. Reentry occurs around a central area of conduction block (hatched ellipse). Arcs of block (hatched rectangles) allow wave fronts to enter and exit the circuit only at site 1 and site 4. The onset of the QRS complex (vertical line) occurs when the excitations wave exits the circuit at site 1 and propagates to the myocardium outside the scar. Depending on the circuit characteristics, collision of waveforms from within the circuit with the wave front propagation from site 1 to site 14 occurs either within (near site 4) or outside the circuit (near site 14). Panel B: The figure-eight reentry circuit. Two excitation wave fronts propagate from site 1 to site 4 around two lines of block. Propagation from site 1 to site 14 in the edge of the scar is associated with activation of myocardium outside the scar. Propagation from site 1 to site 4 is confined within the scar (Reproduced from Ref. [1], with permission from the American Heart Association)

is dependent on many factors, including (1) hemodynamic tolerance of the VT, (2) overall left ventricular function, (3) extent of coronary artery disease, and (4) detailed catheter manipulation focusing on scar regions most likely to contain the VT circuit.

Endocardial ablation targeting critical isthmuses for stable ventricular tachycardias

For catheter mapping and ablation, the critical zone of slow conduction involves the isthmus, which is typically surrounded by myocardial scar that may act as a fixed anatomic barrier. The limits of the isthmus may also be functionally determined. Conduction through the isthmus typically cannot be detected on a surface ECG. The QRS complex on the surface ECG is inscribed when the excitation wave emerges from the isthmus at the exit site to activate the bulk of the myocardium. After exiting and activating ventricular myocardium, the reentrant wave front returns to the proximal end of the isthmus (Figure 8.1). This may occur before the entire myocardium has been depolarized.

Identification of a critical isthmus allows ablation to eliminate VT with a smaller set of radiofrequency (RF) lesions. However, to map and identify the critical isthmus of VT this arrhythmia need to be monomorphic and hemodynamically tolerated. In this case, the critical isthmus can be selected using

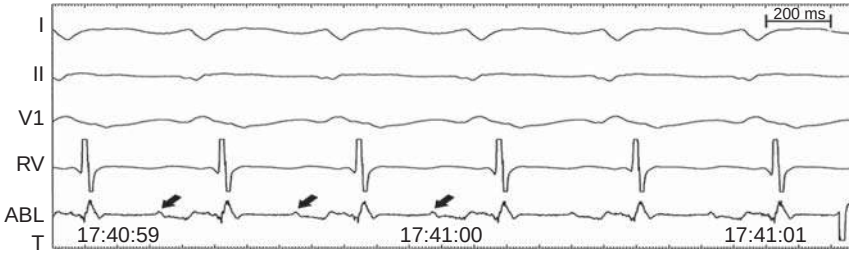

Figure 8.2 Isolated mid-diastolic potential (arrow) during ventricular tachycardia (VT). Ablation at this site successfully terminated the VT

the following criteria during VT as previously described (see Chapter 6): (1) Endocardial activation mapping that identifies the earliest diastolic local endocardial activation time relatively to the QRS complex [10–15]; (2) low-amplitude isolated diastolic potentials (Figure 8.2) [16]; and (3) entrainment mapping [17–24]. In particular, during entrainment mapping, several criteria, including: (a) entrainment with concealed fusion or "concealed" entrainment, in which QRS morphology with pacing mimics VT-QRS morphology on all 12 ECG leads; (b) following termination of pacing, a return cycle length at the site of pacing for the VT within 30 ms of the baseline VT cycle length; and (c) presystolic potentials with an activation time to QRS during VT within 30 ms of the stimulus to QRS have been used to identify areas that may be amenable to a more limited or targeted ablation (Figures 8.3 and 8.4).

De Chillou *et al.* observed in tolerated post-MI VTs that the critical isthmuses have an average length of 31 ± 7 mm (range 18–41 mm) and a width of 16 ± 8 mm [9] and may be ablated with a small number of RF lesions targeting the entire width of the isthmus. However, bystander pathways and inner loops, which may not participate in the reentrant process but may pose difficulty in identifying the critical isthmus, or broader isthmuses, may be present as well. Attending to the details of the appropriate entrainment response (long return cycle and stimulus to QRS interval) can identify protected bystander pathways. Multiple RF lesions may be required to interrupt broad reentrant pathways analogous to interrupting right atrial cavotricuspid isthmus-dependent flutter. When RF energy or a pacing stimulus is applied in the critical isthmus, termination of VT, without producing propagated depolarizations distal to the site of RF energy application or pacing stimulus, can be a sign that conduction has been interrupted in the reentry circuit. At isthmus sites identified by entrainment, RF ablation typically terminates VT within 20 s [18]. The interruption of tachycardia by ablation with single RF energy application suggests that the ablation site is located in a relatively narrow portion of the reentry circuit. Similarly, mechanical trauma from the mapping catheter that terminates VT without eliciting ventricular premature beats and renders the VT noninducible is another indication that the mapping catheter is at a reentry circuit isthmus and the ablation at this site can be successful [26]. As indicated when the critical isthmus is a broad

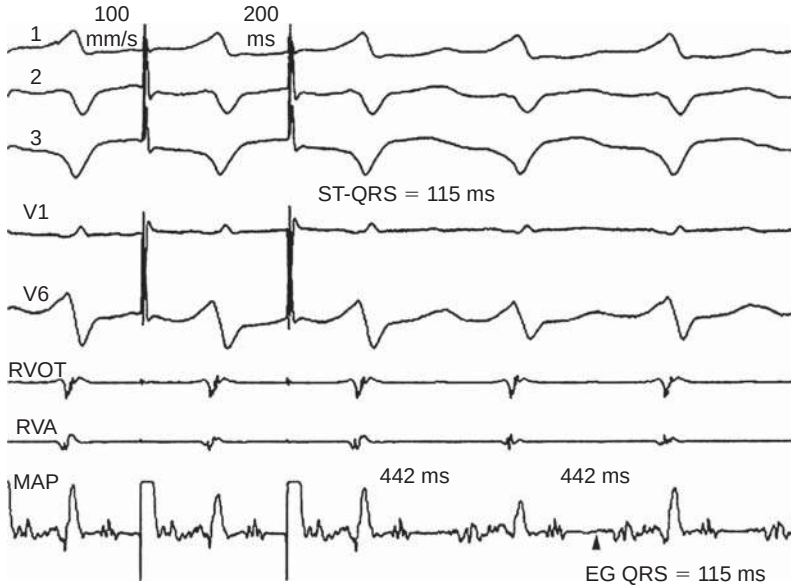

Figure 8.3 Characteristics of the "perfect map" for ablation of VT. The optimal single ablation site for VT has the following characteristics: (1) entrainment from the site will produce an exact match of the spontaneous VT-QRS in all 12 leads; (2) the return cycle (the duration from the pacing stimulus to the first nonpaced beat, measured at the pacing site) will equal the VT cycle length; and (3) the stimulus (ST) to QRS will equal the electrogram (EG) to QRS (Reproduced from Ref. [24], with permission from the American Heart Association). VT, ventricular tachycardia

path, the diameter of a single lesion may not be sufficiently large to impair the isthmus function and interrupt the tachycardia, and more RF applied in a linear fashion aided by entrainment mapping is required to achieve the isthmus block. Ablation targeting critical isthmuses for stable VTs is successful, abolishing the inducible "targeted" or "clinical" VT in 71–86% of selected patients [22,23,27–31]. However, during follow-up 13–46% of patients with acutely successful ablation experience VT recurrences and this percentage is higher in patients with persistence of other inducible VT after the ablation compared with patients without VT inducible of any morphology (60–64% and 14–20%, respectively) [27,32]. Some of these arrhythmic recurrences are because of VTs different from those initially targeted for the ablation. The identification of only one predominant morphology of VT as target for ablation is rare in patients with scar-related VT representing less than 10–30% of population with post-MI VTs [30]. Most patients have multiple morphologies of inducible VT, and even if one VT is identified as predominant, other VTs that are inducible may subsequently occur spontaneously. Stevenson *et al.* proposed, in patients with post-MI VTs, to attempt ablation of all sustained VTs that were sufficiently tolerated hemodynamically to allow mapping. With this approach 67% of their patients remained free of VT during follow-up [23].

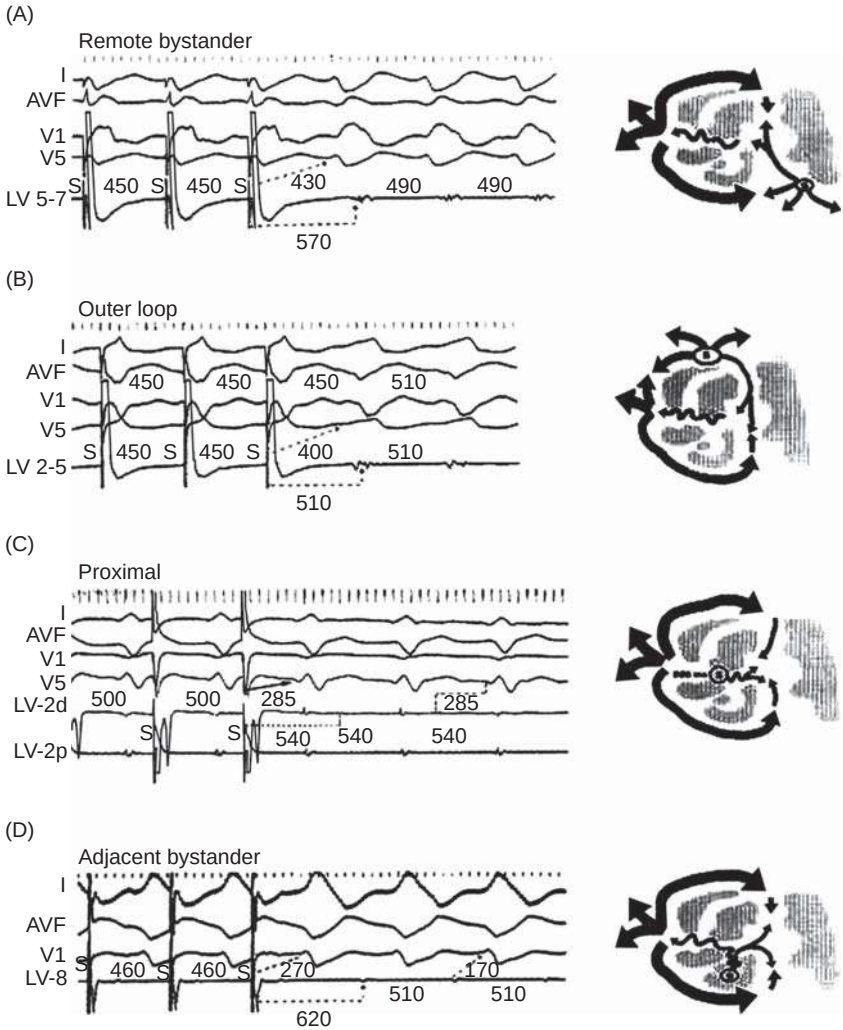

Figure 8.4 Computer model of VT within unexcitable infarct scar (gray stipple areas, right panels), demonstrating the response to entrainment with pacing at different sites within the circuit. The circuit is depicted as a "figure of eight" activation utilizing a central common pathway with slow conduction. Pacing from remote bystander areas (A) will show some degree of fusion, and the return cycle is longer than the VT cycle length (by twice the conduction time from the site to the VT circuit). Pacing from outer loop sites (B) will show manifest entrainment, as the pacing site has access to recruit areas away from the circuit because it is not bounded by the infarct. The return cycle length equals the tachycardia cycle length. Pacing from sites within the central pathway (C) demonstrate concealed entrainment with a stimulus to ECG equal to the electrogram to QRS during VT; the return cycle measured at this electrogram is equal to the VT cycle length. Pacing from adjacent bystander sites (D) results in concealed entrainment, but the return cycle is longer than the VT cycle length (by twice the conduction time from the site to the VT circuit) (Reproduced with permission from Ref. [25]). VT, ventricular tachycardia; ECG, electrocardiogram

Substrate-based endocardial ablation

In the majority of patients with structural heart disease referred for VT ablation, the arrhythmia is not tolerated hemodynamically, frequently changes QRS morphology with entrainment mapping attempts, or cannot be reproducibly inducible to allow identification of the appropriate isthmus target sites with extensive mapping. It is estimated that only 10–30% of patients with structural heart disease have VTs suitable for ablation guided only by activation and entrainment mapping during the arrhythmia [12,33–35]. Unstable scar-related VTs can be approached by identifying and characterizing in detail the substrate responsible for the VT. Sinus rhythm surrogates for the VT circuit can then be targeted eliminating the requirement for detailed activation and entrainment mapping of all ventricular arrhythmias. This approach allows one to extend the ablation therapy to patients with unmappable/unstable VTs. Using electroanatomic mapping systems, it is possible to measure the peak-to-peak amplitude of bipolar electrograms and create an anatomic display of the voltage map information. Marchlinski *et al.* observed that the normal myocardium had bipolar electrograms of voltage >1.5 mV [12]. Dense scar consistent with the aneurysm removed at the time of VT surgery was characterized by low-voltage potential with a signal amplitude <0.5 mV. The area with electrograms ranging between 0.5 and 1.5 mV was defined as a "border zone" consistent anatomically with the subendocardial border zone removed with surgical subendocardial resection. The areas with different voltages can be shown graphically in the three-dimensional (3D) electroanatomic maps by color coding the bipolar electrogram amplitude. Conventionally, purple, red, and colors ranging between purple and red represent normal myocardium, dense scar, and border zone, respectively. The identification of dense scar, border zone, and normal endocardium is crucial for the substrate-based ablation technique and allows the application of findings learned from cardiac surgery. Indeed, in patients with VTs, the subendocardial resection of the arrhythmogenic substrate in the border zone achieved 70–80% arrhythmia cure rate [36,37]. On the basis of surgical experience, Marchlinski *et al.* proposed to create linear lesions that connected the dense scar area to the normal endocardium or to anatomic boundaries across the border zone [12]. The purely anatomic approach with circumferential ablation of the scar along the border zone was considered not practical considering the large extension of the scar (ranging in size from 30 to 110 cm^2) [12,38,39] and the unknown size and 3D characteristics of VT circuit. Therefore, the ablation was guided by pace mapping and linear lesions were created in the region that crossed the border zone and showed the best pace-map site. Linear lesions were typically placed both perpendicular and parallel to the best pace-map site to optimize the interruption of the VT circuit. Pace mapping is not sufficiently specific or sensitive to be the sole guide for focal ablation (see Chapter 6) [40]. However, it is useful to approximate the reentry circuit exit to limit the size of linear lesions. To enhance the specificity of the QRS morphology during pacing to identify a site consistent with

a VT isthmus, the time from the stimulus to the QRS can also be assessed. Sites where pace mapping matched the spontaneous VT morphology and where the delay between the stimulus and the onset of the QRS complex was at least 40 ms are classified as potential target sites within a protected isthmus. Linear lesions can be then delivered through these sites to interrupt the isthmus. Typically, these lines are delivered approximately parallel to the border zone of the scar (Figure 8.5) or to connect anatomic boundaries or unexcitable areas within the dense scar. Areas of unexcitable myocardium have been defined by failure of capture with pacing at 10 mA and 2 ms pulse width. Occasionally, a second pacing site with a similar or longer stimulus to QRS will help guide further the location and direction of the route of conduction of the VT circuit and the location and direction of the line. If VT is still induced after a line has been made, lesions are extended further, and the process of induction and ablation is repeated. Importantly, a QRS morphology, similar to VT and long S-QRS, could also be obtained from bystander areas where ablation is less likely to be successful unless the line extends by chance through the adjacent isthmus. More recently, it has been demonstrated that the scar tissue is not homogeneous and that there are areas of larger voltage acting like a corridor for preferential signal transmission within the scar [11,41]. These channels may also be targeted for linear ablation to eliminate unmappable VT. Up to 86% of these preferential conducting channels as indexed by regions of increased voltage were related to a component of the mapped induced VT circuit identified based on entrainment criteria. Arenal *et al.* also observed that the voltage limit of 0.5 mV precluded the identification of electrograms with lower amplitude that characterize these conducting channels within the more dense scar. The majority of conducting channels

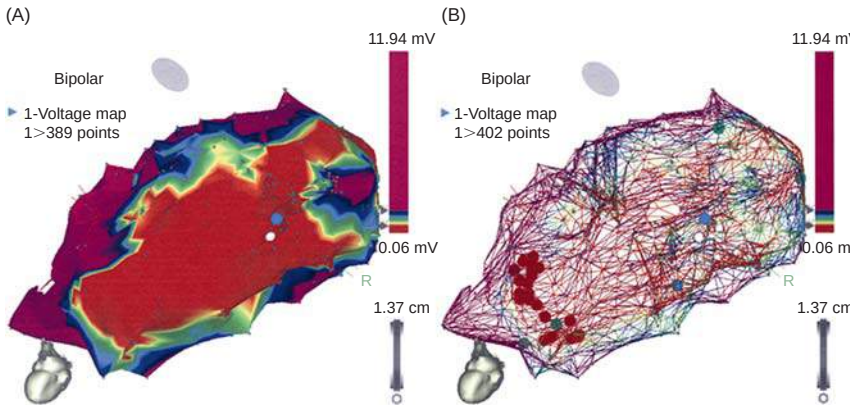

Figure 8.5 Substrate mapping data from a patient with VT because of prior infarction. A voltage map of the LV is present in panel A. Purple indicates normal bipolar electrogram amplitude >1.50 mV. Amplitude diminishes from blue, to green, to yellow, to red; with red indicating voltage ≤0.5 mV. A large low-voltage infarct area is present. Ablation sites more clearly defined as brown spots in the mesh areas in panel B have been delivered along the scar border zone. VT, ventricular tachycardia; LV, left ventricular

were identified within dense scar when the voltage scar definition was set at ⩽0.2 mV. The ablation lesions targeting these channels of higher voltage suppressed the inducibility in 88% of VTs and these arrhythmias recurred in only 23% of patients during follow-up [11]. Conducting channels targeted for ablation have also been identified as excitable areas between areas of inexcitabilty defined by pacing techniques [10]. Another surrogate for the VT circuit defined in sinus rhythm that has been targeted for substrate-based ablation has been the presence of discrete late potentials [42]. Late potentials during sinus rhythm are frequently recorded from isthmus sites during VT. These sites can also be recorded from so-called dead-end pathways or may represent the late activation of disease myocardium in an area that normally activates late, such as the base of the left ventricle in inferior infarction or basal scars in nonischemic cardiomyopathy. Thus, the specificity of these sites as an appropriate target is more limited. Nevertheless, these sites had been targeted using typically a much more extensive ablation strategy to successfully eliminate VT [42] (Table 8.1).

With substrate-based ablation techniques 75% of patients remained free of any recurrence of VT during follow-up [12,4]. Volkmer *et al.* compared the outcome of patients treated with VT ablation based on substrate mapping or complete tachycardia mapping and did not found significant differences [43]. Substrate mapping can also be combined with limited mapping during VT, allowing regions of interest to be defined during stable sinus rhythm. Soeijima *et al.* used sinus rhythm voltage mapping, pace mapping, and limited entrainment mapping during VT to define a potential isthmus in 40 patients with stable and unstable VTs. Ablation at sites identified with this approach was able to abolish inducible VTs in 75% of cases [38].

Another approach used to assess the propagation of the impulse in patients with rapid and poorly tolerated VT is represented by the noncontact mapping system. This system uses a multielectrode array of 64 unipolar electrodes on an inflatable balloon. The electrode array measures the unipolar potential generated from the endocardial surface. From the sampled far-field potentials and the measured distance from the recording array to the endocardium an "inverse solution" is calculated for the potentials to create virtual unipolar

Table 8.1 Sinus rhythm targets for ablation of unmappable/unstable VT

- 12-lead ECG pace-map match of QRS
- Pace map match of QRS with stimulus to QRS >40 ms
- Preferential channels of conduction
- High voltage surrounded by lower voltage when low-voltage region is scanned with decremental color range
- Excitable myocardium surrounded by unexcitable myocardium (lack of capture at 10 mA and 2 ms pulse width)
- Late potentials (discrete and separated from QRS by 40 ms)

electrograms. This allows simultaneous acquisition of electrical activation from the endocardial surface with the advantage of defining the propagation during even a single VT beat. In the case of macro-reentrant VT, activation can be traced within the ventricles throughout the whole tachycardia cycle, and the color-coded isopotential maps are used to identify an exit for most and a protected zone of the reentrant circuit or diastolic pathway in many VTs. Usually, the noninducibility of VT is achieved by creating a transecting line of ablation perpendicular to the documented spread of activation. Once the ventricular anatomy during sinus rhythm has been reconstructed, a dynamic substrate map (DSM) can also be created. This new feature for the mapping system defines an area of consistently low-peak negative voltage exhibiting <25–35% of the largest unipolar deflection recorded on the endocardium during the duration of the surface QRS complex. The areas of low voltage are considered to be areas of potential conduction block and therefore substrate for the development of macro-reentrant circuits and potential targets for ablation. The isopotential color-coded maps can be studied during sinus rhythm or pacing to identify propagation of ventricular activation along the anatomic landmarks and suspected low-voltage areas to define appropriate substrate-based targets for VT ablation.

Ablation catheters for ventricular tachycardia/ventricular fibrillation ablation

A standard 4-mm electrode catheter and, at times, an 8-mm electrode have been used for mapping and ablation. A 4-mm electrode provides higher resolution for mapping. Although ablation in regions of scar is quite safe, a sudden increase in temperature at the catheter tip–tissue interface can cause coagulum and char formation, causing limited delivery of RF energy and lesion formation. In view of this, most centers now prefer to use irrigated RF ablation where cooling the ablation electrode with saline causes greater energy application without coagulum formation [44–48]. Open irrigated catheters may be associated with significant volume administration during a lengthy ablation procedure and appropriate management of fluid load is indicated both during and after the procedure.

Epicardial ablation

Scar-related reentry circuits commonly extend deep into the endocardium, although a portion is usually located on the endocardium particularly in the setting of prior MI. Epicardial reentry circuits seem to be more common with inferior rather than anterior wall infarctions and in patients with nonischemic cardiomyopathy [5,49,50]. The presence of epicardial circuits has been considered one of the reasons for the failure of endocardial ablation. In 1996, Sosa *et al.* first described the usefulness of a subxiphoid percutaneous approach to the epicardial space for unrestricted mapping and ablation of the epicardial surface of both ventricles in patients with Chagas disease [51]. After this initial report, several authors have used this technique for the ablation of

substrate-related VT with epicardial circuits. This procedure is typically performed with the patient under general anesthesia because RF pulses applied in the epicardial surface are painful [52]. The subxiphoid approach to the pericardial space is typically performed using a commercially available epidural spinal needle. Needles with a shaped tip are preferable to reduce the risk of damage to epicardial vessels and cardiac perforation. The puncture is performed at an angle between the left border of the subxiphoid process and the lower left rib (Figure 8.6A). The spatial orientation of the needle is important and will determine what portion of the ventricles will be reached. The needles points to the left shoulder and it must be introduced more horizontally if the target is the anterior portion of the ventricles and more vertically if the diaphragmatic portion of the heart is the area of interest. When the needle reaches the pericardial sac, injected contrast will spread around the heart, restricted to its silhouette. Thereafter, the guidewire can be introduced. The fluoroscopic position of the guidewire needs to be verified to demonstrate that it is adequately inserted in the pericardial sac. This is best done in the left anterior oblique projection. After reaching the pericardial space with the guidewire, the needle is withdrawn and a standard sheath introduced [52].

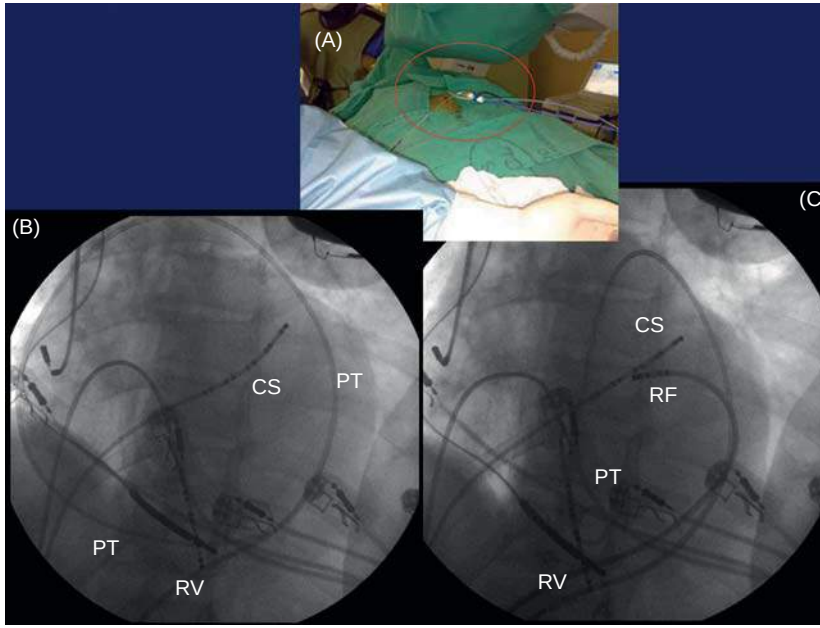

Figure 8.6 Percutaneous epicardial ablation using open irrigation ablation catheter. Two introducers are placed in the subxyphoid area—one for the ablation catheter and the other for a pigtail catheter placed around the pericardial space to allow continuous removal of the pericardial fluid added by the irrigated catheter (panel A inset). Fluoroscopic views of catheters in the RV apex (RV), coronary sinus (CS), and epicardial space (RF, irrigated ablation catheter; PT, pigtail catheter) are shown in panels B and C

The use of longer sheaths should be considered, especially in patients with a larger thorax. Catheters for conventional mapping and ablation can be introduced and easily moved inside the pericardial sac, allowing the exploration of the entire epicardial surface (Figures 8.6B,C). In patients with history of myocarditis or cardiac surgery the pericardial adhesions can make the epicardial approach difficult and restrict the movement of the ablation catheter into the pericardiac sac. In postsurgical patients, the adhesions are mostly concentrated in the anterior portion of the heart; therefore, the puncture must be directed toward the diaphragmatic area. In patients with epicardial VT, the target for ablation of mappable VT is selected exactly like the endocardial target is selected (Figures 8.7–8.9). However, entrainment maneuvers are usually difficult to perform using bipolar pacing because of a very high epicardial stimulation threshold (more than 15 mA) in around 70% of the cases [52]. The reason for this high stimulation threshold is not clear, but may be related to epicardium catheter contact or to the presence of fat tissue. Substrate-based ablation needs to be approached with caution. Epicardial fat and coronary vessels will attenuate the bipolar voltage signal. Care to target regions where electrograms are not only low in amplitude but also wide (>80 ms), split, or late is essential. The following complications of the epicardial approach have been reported: hemopericardium, pericarditis, intraabdominal bleeding as a result of inadverted puncture of subdiaphragmatic vessels, and injury of epicardial structures like coronary vessels and phrenic nerve (see Chapter 10) [51–54]. In patients undergoing epicardial ablation, coronary angiography should be also obtained to identify the location of the coronary vessels, to avoid delivering ablation in close proximity to these vessels [52,55]. When performing epicardial ablation, care also needs to be employed to avoid damage to the left phrenic nerve, which commonly courses over the basal lateral left ventricle

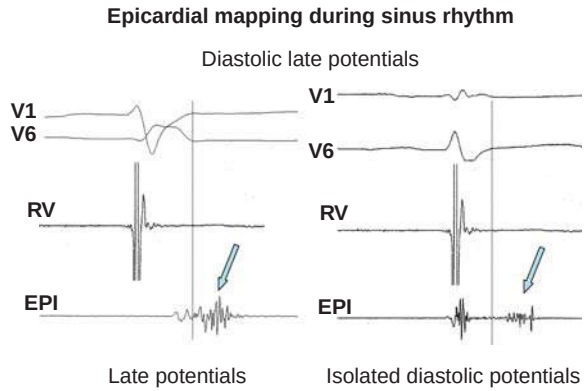

Figure 8.7 Electrogram recording during epicardial mapping (Epi) with examples of late potentials recorded in sinus rhythm. Left panel: Late potentials adjacent to the systolic recording. Right panel: An isolated potential in the middle of the diastole. RV, right ventricular apex recording

[52,56] through the VT substrate. Balloon technology may be used to push the phrenic nerve from the epicardial surface [56,57]. Air insufflation may also work but can produce dramatic increases in defibrillation requirements and the air may need to be withdrawn emergently if unstable ventricular arrhythmias are initiated that require emergent cardioversion [58,59].

Ventricular tachycardia ablation in the setting of ischemic heart disease and prior myocardial infarction

Sustained VT, in association with chronic coronary artery disease, constitutes the most commonly encountered form of VT in the adult population [1–3,60,61]. The typical substrate is the healed MI [1–4]. It has been demonstrated from clinical studies, as well as in animal models of VT, that the underlying mechanism for VT in this setting is scar-related reentry as evidenced by (1) induction and termination of VT with programmed ventricular stimulation, (2) inverse relationship between the last extrastimulus and the first beat of the tachycardia, (3) entrainment and resetting of VT with progressive fusion at shorter cycle lengths or coupling intervals, and (4) direct myocardial activation mapping techniques [1–3,61]. Because of the nature of the arrhythmia and the underlying substrate, these types of VT are amenable

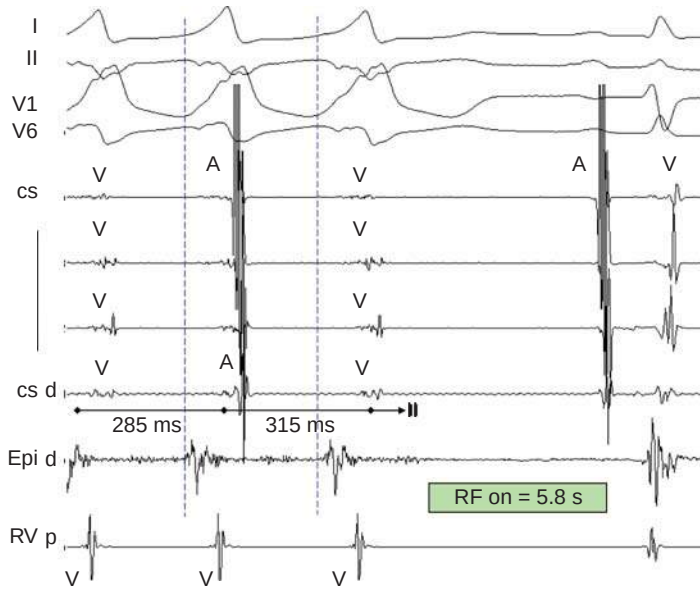

Figure 8.8 Epicardial electrogram recording (Epi) during VT showing mid-diastolic potential. During RF application, slowing of the VT cycle length is observed (from 285–315 ms) followed by termination after 5.8 s. CS, recordings from an octapolar catheter placed the coronary sinus; RV, right ventricular apex recording; VT, ventricular tachycardia; RF, radiofrequency

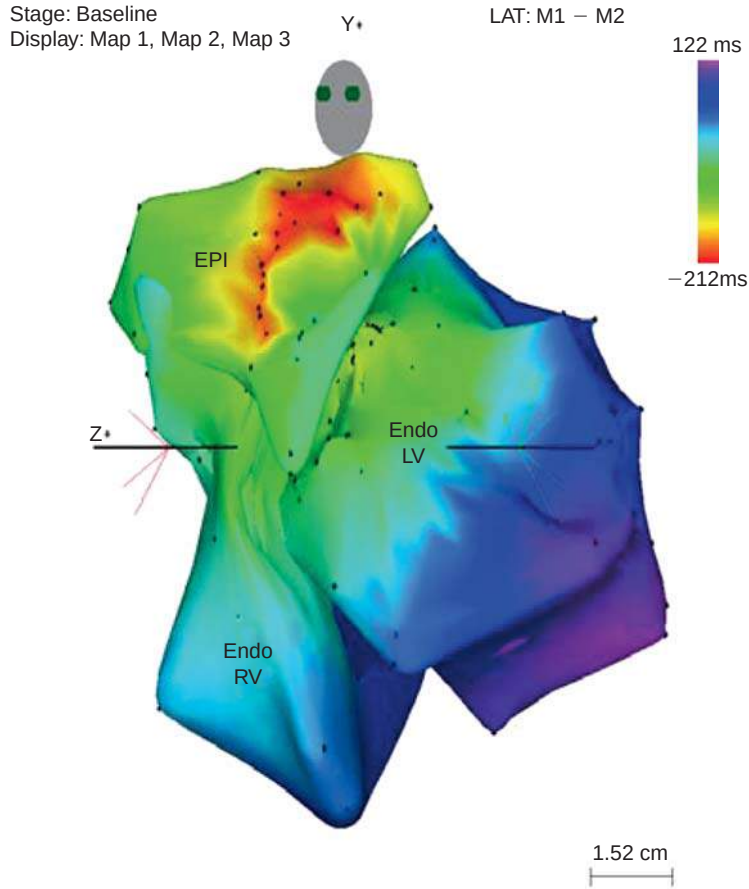

Figure 8.9 Electroanatomic activation mapping of both ventricular endocardial surfaces and the LV epicardial surface during VT. Earliest activity (red) is clearly recorded in the epicardium. LV, left ventricular; VT, ventricular tachycardia

to catheter ablation. Although an epicardial approach to catheter ablation may be needed in some refractory patients, most of these VT are amenable to endocardial ablation.

VT ablation, in most patients with prior MI, is performed in patients receiving multiple ICD shocks [53,62–64]. Although attempts have been made recently to use VT ablation as a first line of therapy in place of antiarrhythmics drugs in patients receiving ICD shocks [35], many of these patients have failed multiple antiarrhythmics drugs before undergoing ablation.

Approach to catheter ablation of ventricular tachycardia in the setting of prior myocardial infarction

Prior to ablation an assessment of the status of coronary disease, including an effort to identify the presence of ongoing ischemia and location of the prior

infarction, should be routine. The severity of LV dysfunction should be determined. Some patients will require hemodynamic support in the form of an intraaortic balloon pump. Vascular access concerns and the possible need for a transseptal puncture should be addressed. It is important to obtain ECG recordings of all clinical VTs when available. Similarly, electrogram analysis from the device interrogation can be helpful in determining the cycle length of the VT, whether the triggering event was reproducible and multiple VT morphologies have occurred clinically. Antiarrhythmic drug therapy at the time of VT events should be noted. All of these factors may play a role is designing the best ablation strategy and optimally protecting the patient during the procedure.

With the electrophysiologic procedure and ablation attempts, an effort should be made to induce all potential morphologically distinct VTs. Bundle branch VT, although less commonly identified in prior MI, should be excluded. Three or more different VT morphologies are typically induced during mapping and ablation. However, all of these may not correlate with the clinical VT based on 12-lead ECG analysis and comparison of ICD recordings of induced and spontaneous VT. In patients with stable VT, detailed activation mapping and electrogram analysis for mid-diastolic potentials, and entrainment mapping strategies, including evidence of concealed entrainment, S-QRS timing that matches the electrogram to QRS timing, and postentrainment pacing interval (PPI) that matches the VT cycle length are all helpful in identifying critical components of the reentrant circuits as previously described in this review.

In patients without inducible sustained VT and those with unstable VT a substrate-based ablation, as previously described, is used. Initial attempts are made to induce VT and define all the QRS morphologies that may guide pace mapping. The details of the scar are then carefully defined with bipolar voltage mapping with care to identify sites with isolated late potentials. Preferential channels of conduction in the scar can also be identified by titrating the color range of the bipolar voltage map from the typical setting of 1.5–0.5 mV to values down to 0.2–0.1 mV. Pace mapping can be performed along the dense scar border (0.5 mV) based on an assessment of the 12-lead ECG morphology of all spontaneous and induced VTs. During pace mapping not only the similarity of the QRS morphology to the pace map but also the time to the QRS is assessed with intervals greater than 40 ms, suggesting areas of slow conduction that may approximate VT isthmus sites. Sites of inexcitability defined by failure to capture at 10 mA and 2 ms pulse width are also identified; these sites may also serve as anatomic boundaries for VT circuits and help further define channels of preferential conduction. Once bipolar scar voltage mapping has been performed and pace mapping identifies areas of interest, ablation lines are created. Lines are drawn to cross through sites of good pace maps and defined channels. Lines have been effectively deployed extending parallel to the scar edge in the border zone of the scar. When lines are deployed parallel to the scar, they should be

within the zone defined by a color range of 0.5–1.0 mV to avoid damaging normal myocardium under subendocardial scar. Lines perpendicular to the scar border and connecting the scar to anatomic boundaries have also been successful in eliminating VT. Many operators will draw lines in both directions. The success of the linear ablation technique crossing through exit sites and channels bespeaks of the sizable macro-reentrant nature of the VT circuits in this setting. In one study, critical isthmus was identified in 25 (63%) of the 40 patients and linear lesions, averaging 4.3 cm, abolished all inducible VTs. [38,65]. If the VT is still inducible, the lines are extended further or a line perpendicular through the first is targeted. When targeting late potentials, lesions are frequently applied in clusters to eliminate the potentials.

The endpoint for VT ablation tends to be hierarchal in nature and is currently based primarily on VT inducibility. The highest priority goes to trying to eliminate VT that has been documented to occur clinically, easily inducible VT with a slow rate, and then finally all inducible VTs. Because noninducibility is currently used as the gold standard for the ablation procedure, it is recommended that a standardized protocol of single, double, and triple extrastimuli be used from at least two sites to define success. Baseline stimulation results and the use of antiarrhythmic drug therapy can influence decision-making regarding both ablation strategies and acceptable endpoints. Poorly tolerated VTs and the ongoing use of antiarrhythmic agents warrant a more aggressive substrate base ablation approach if reproducible VT triggers have not been identified.

Outcome with ventricular tachycardia ablation in the setting of prior infarction

Successful acute termination of the targeted VT, when it is stable and can be localized using activation and entrainment mapping, can be achieved in 70–95% of patients with limited RF application [24]. However, following ablation, VT can recur in up to 35% of patients [24,32,66]. Outcome appears to be improved with irrigated ablation techniques [44].

Substrate-based ablation results have produced comparable outcome results in single-center reports. Recurrence rates during intermediate-term follow-up have varied from 17 to 36% but patients with recurrences have demonstrated a reduced frequency of VT episode if they have VT recurrences and elimination of incessant VT [11,12,38,39,64,67–69]. No studies have compared or identified the optimum substrate-based ablation strategy.

Several multicenter prospective trials have assessed the efficacy of VT ablation in the post-MI patients [35,47,48]. In the first reported multicenter trial of 146 patients with mappable VT and ablation performed with an internally irrigated catheter, 82% of the patients had coronary artery disease. During an average follow-up of 8 months, 54% were free of VT [47]. Eighty-one percent of patients followed for more than 2 months had a greater than 75% reduction in VT episodes. Procedure-related mortality was 2.7%. Other complications included tamponade and stroke each in 2.7% and MI in 0.7%.

The Multicenter Thermocool Ventricular Tachycardia Ablation Trial also enrolled 231 patients with recurrent VT in the setting of prior MI [48]. VT ablation used an open irrigation RF catheter guided by an electroanatomic mapping using both entrainment mapping and/or substrate mapping to guide ablation [48]. Unmappable VT was present in 69% of patients. During the 6-month follow-up period, 51% had recurrent VT. The frequency of VT was reduced with a >75% reduction in VT recurrence in 67% of patients. Procedure mortality was 3% with 6 of 7 deaths related to uncontrollable VT, and one because of tamponade with MI. There were no strokes or thromboembolic events. Nonfatal complications occurred in 7% of patients, including heart failure and vascular access complications.

Finally, the Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia (SMASH-VT) multicenter study enrolled 128 patients with prior MI [35]. All patients received an initial ICD for ventricular fibrillation (VF), unstable VT, or syncope with inducible VT [35]. Patients were randomized to substrate-based ablation versus a control group handled in a routine fashion. There was no procedure mortality. During an average follow-up of 23 months, 33% of the control group and only 12% of the ablation group received appropriate ICD therapy for VT or VF.

Ventricular tachycardia ablation in the setting of nonischemic cardiomyopathy

Sustained monomorphic VT in the setting of nonischemic dilated cardiomyopathy is most common because of reentry associated with a scar-related substrate [70,71]. Less commonly bundle branch reentry or a focal automatic or triggered rhythm is the VT mechanism. In patients with bundle branch reentrant VT, baseline conduction abnormalities may be present but significant substrate abnormalities absent. Some patients can have both bundle branch reentrant VT and scar-related VT. In most patients, the cardiomyopathy is idiopathic but sarcoidosis, giant cell myocarditis, Chagas disease, and prior cardiac valve surgery can produce similar arrhythmogenic substrates [72–74]. Many patients with VT in the setting of nonischemic cardiomyopathy will be refractory to antiarrhythmic drugs and ablative therapy plays an increasing role in arrhythmia management. It is important to identify reversible arrhythmic causes of cardiomyopathy such as frequent ventricular ectopy or atrial arrhythmias. Idiopathic VT in this setting is frequently assumed to be secondary to the cardiomyopathy and is less likely to be treated appropriately with early ablative therapy and ICDs all too frequently implanted. A single morphology outflow tract tachycardia in the setting of depressed LV function should result in a search for frequent arrhythmias with the appropriate monitoring and efforts to identify an arrhythmia substrate with gadolinium-enhanced MRI or detailed sinus rhythm voltage mapping [75–77].

Substrate for ventricular tachycardia

The substrate for VT in the setting of nonischemic cardiomyopathy is characterized by an area of low voltage and variable size that typically surrounds the aortic and mitral valve region and then extends apically [76]. Frequently, the substrate for VT identified by sinus rhythm voltage mapping or gadolinium-enhanced MRI may be solely or predominantly intramural or epicardial [71,77–79]. ECG criteria recorded during VT suggesting an epicardial origin [80–82] and intracardiac echo or magnetic resonance imaging (MRI) to identify a predominantly epicardial substrate play an important role in identifying/suggesting the need for epicardial mapping and ablation [77,83]. Because of the frequent presence of an epicardial substrate, some experienced operators using a simultaneous endocardial and epicardial mapping approach regardless of preprocedure findings. Epicardial mapping to define the VT substrate is confounded by the effects of coronary anatomy and fat on the voltage criteria for defining an abnormal substrate [84,85]. The presence of a wide (>80 ms) split and late electrograms are required to identify an arrhythmogenic substrate and care is needed to define the coronary anatomy [79].

Ventricular tachycardia/substrate ablation

Typically, hemodynamically tolerated VT in nonischemic cardiomyopathy can be mapped/localized using standard activation/entrainment criteria [17,70,71]. Activation mapping frequently identifies a critical component of the VT circuit on the epicardium when an endocardial substrate and early site is not present (Figure 8.10) [51,54,71,76,86,87]. Substrate-based ablation has been used with some degree of success targeting endocardial voltage abnormalities. Linear ablation crossing through the endocardial substrate and extending to the valve annulus, guided by pace mapping or clusters of late potential, has been used with modest long-term success [12,70,68]. There have been only preliminary reports on epicardial substrate-based VT ablation in the setting of nonischemic cardiomyopathy. In most cases, the substrate abnormality is located over the basal superolateral LV [78,79]. Electrogram abnormalities that are multicomponent, late, and wide need to be targeted [79], and caution needs to be employed when delivering ablation lesion within 0.5–1.0 cm of an epicardial coronary vessel.

Outcome with ventricular tachycardia ablation

There are only a few single-center reports on acute outcome of VT ablation with short- to intermediate-term follow-up in a relatively small number of patients in the setting of nonischemic cardiomyopathy [70,71,88]. Acute success in eliminating inducible VT has varied from 56 to 74% with VT recurrence of 42–75% with endocardial ablation. Outcome appears to be somewhat improved with epicardial ablation, but long-term follow-up in a large cohort of patients has been lacking [71,79]. Furthermore, efficacy of endocardial and epicardial ablation may be limited when mid-myocardial substrate is present. Intraoperative cryoablation may be effective when percutaneous access is

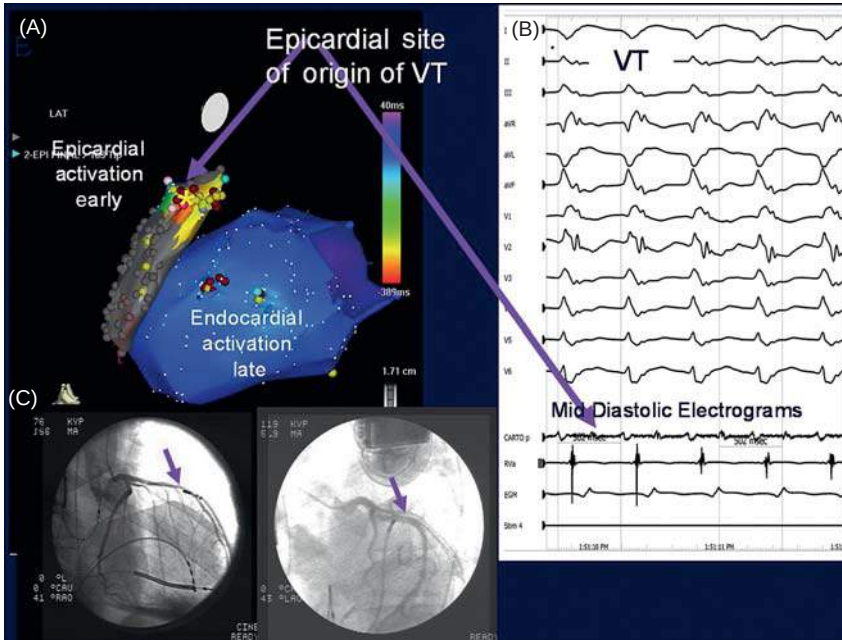

Figure 8.10 Epicardial VT in the setting of nonischemic cardiomyopathy. Panel A shows electroanatomic endocardial and epicardial activation map with earliest activation recorded from the epicardium consistent with mid-electrograms recorded during VT as shown in panel B. Panel C shows catheter tip location away from epicardial coronary vessels. RF energy at site immediately terminated VT. VT, ventricular tachycardia; RF, radiofrequency

limited by adhesions and/or epicardial catheter-based ablation is ineffective, but clinical experience has been limited.

Ventricular tachycardia ablation in the setting of right ventricular cardiomyopathy

VT is a relatively uncommon manifestation of right ventricular cardiomyopathy. It is most frequently observed in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC/D) and occasionally with RV involvement with sarcoidosis [12,41,72,89]. Indeed, unimorphic VT is rare in other settings of pressure or volume overloaded failing RV. The important exception to this rule is in the setting of prior surgical repair for tetralogy of Fallot, which is discussed in a separate section of this report. ARVC/D appears to be a genetically determined degenerative disease process that leads to fibrofatty replacement of myocytes [90]. There is considerable variability related to its rate of progression and debate regarding triggering events for its progression. Many patients demonstrate a stable endocardial substrate

based on repeated voltage mapping separated by more than a year [91]. The triggering mechanism for progression of the disease process has not been determined, and it has been speculated that perhaps bouts of myocarditis in the setting of a well-defined genetic abnormality in desmosomol function leads to persistent areas of low-voltage scarring that characterize the disease substrate. The stability of the substrate would support an important role of ablative therapy in establishing relatively long-term VT control. Sarcoidosis is characterized by noncaseating granulomas with progression to cardiac fibrosis that can be frequently quite extensive and as a result may mimic the substrate defined by voltage mapping in ARVC/D [89]. Associated evidence of noncardiac sarcoidosis and if necessary myocardial biopsy guided by electroanatomic mapping may be helpful in establishing a diagnosis [42,92].

Substrate mapping for diagnosis and to identify ventricular tachycardia targets

It is critical to distinguish benign "idiopathic" focal VT originating from the outflow tract or peritricuspid valve regions of the RV from VT associated with ARVD/C. Most patients with ARVD/C will have multiple morphologies of spontaneous and/or induced VT with a characteristic LBBB-type QRS pattern with poor wave progression in the anterior precordial leads. The diagnosis of ARVD/C is dependent on meeting Task Force criteria [42,93]. However, in the presence of VT in the setting of RV dilation and precordial T wave changes, voltage mapping should also be used to help establish the presence of a significant substrate abnormality consistent with the disease process [94,95]. The distribution of the bipolar voltage substrate abnormality has been documented to originate near and extend from the pulmonic and/or tricuspid valve regions [94]. Substrate changes involve primarily the free wall but can extend to include RV septum. Rarely, the voltage abnormality extends to the RV apex. RV apical aneurysms may be observed but are not typically the source of VT, which originates from the more basilar areas of more extensive fibrosis. Mapping of the RV free wall, especially in the perivalvular region, may be technically challenging depending on the level of mapping experience. Conformation of contact by demonstrating capture at low pacing output and identification of signals that are not only small in amplitude but also frequently split or late can allow one to eliminate small signals as a result of poor contact or intracavitary points and help identify important targets for subsequent mapping and ablation [94]. The use of magnetic guided catheter navigation systems may improve the ability to acquire detailed sampling of the RV free wall [96,97].

Of note, LV involvement is probably more frequent than previously recognized at the time of clinical presentation with VT in patients with ARVD/C [98]. The induction of VT with RBBB QRS morphology should make one suspicious of LV involvement. A perivalvular mitral origin results typically in a positive precordial QRS pattern for the VT. Data from both pathological studies and recent reports on detailed substrate mapping suggest that

epicardial involvement is more common than endocardial involvement with the disease process [99–101].

Ventricular tachycardia mechanism and ablation

The profound perivalvular scarring results in reentrant VT. The recognition of scar-related reentry as the mechanism is an important feature of ARVD/C that can also help distinguish these VTs from idiopathic RVOT VT, which has a focal origin most consistent with triggered activity [102]. In some cases of ARVD/C, a focal mechanism has been suggested based on endocardial mapping and the behavior of the VT with respect to gradual rate acceleration [103]. Given the epicardial to endocardial pathophysiologic process, it is also possible that some of these cases represent an epicardial and intramuscular reentry with a focal endocardial breakthrough and more investigation is required to determine the mechanism of some of these VT.

Because most VTs occur in the setting of a significant substrate abnormality and are reentrant in mechanism, standard activation and entrainment mapping techniques used for localizing scar-based VT in coronary disease can be applied to identify a critical isthmus to target for ablation for hemodynamically tolerated VT [17–19,23,40]. Activation mapping aided by noncontact isopotential mapping has also been reported to have value in this setting [104]. Substrate-based ablation techniques have been applied to patients with ARVC/D, in particular patients with poorly tolerated, unmappable VT, and were originally described in 2000 for nine patients with ischemic cardiomyopathy and six patients with ARVC [12]. The substrate-based ablation strategies include linear ablation transecting scar and extending to and anchoring at the valve orifice [12,94,105], identification and targeting channels of higher voltage surrounded by low voltage in the region of abnormal voltage [41] or targeting clusters of late potentials surrounding best pace maps [106]. Irrigated ablation targeting sites of interest in the abnormal substrate has been used with reported success without an anticipated increase in risk despite the reported transmural myocardial thinning of the RV free wall frequently reported (Table 8.2). Power titrated to achieve an impedance drop of 10–15 ohms with a maximum temperature of 42–45°C appears to allow for safe lesion formation without steam pops.

The endpoint for ablation remains the noninducibility of unimorphic VT with programmed stimulation through triple extrastimuli. Some investigators have suggested the elimination or alteration of endocardial late potentials may be used to identify a substrate-based endpoint that may also be associated with long-term success [107].

The decision to go to the epicardium must be weighed with the risk and level of complexity of the epicardial ablation procedure and the skill set of the operator. Patients with limited endocardial substrate, those with late VT termination with RF delivery, and certainly those with persistent VT despite aggressive endocardial ablation should be considered for an epicardial approach. Surface ECG criteria suggesting an epicardial origin by identifying a QS complex in lead V2 or leads III and aVF during VT may also prove to

Table 8.2 Outcome with endocardial catheter ablation of ARVC/D

Study	*No. of patients*	*Acute success (% without inducible VT)*	*Mean follow-up (months)*	*VT recurrence (%)*	*Irrigated tip used*	*3D mapping used*
Nogami *et al.,* 2008 [102]	18	50	61	33	No	Rarely**
Dalal *et al.,* 2007 [107]	24	46	32	83	No	Rarely**
Yao *et al.,* 2007 [103]	32	75	29	20	Commonly*	Yes
Satomi *et al.,* 2006 [106]	17	88	26	24	No	Yes
Verma *et al.,* 2005 [105]	22	82	37	36	Commonly*	Yes
Miljoen *et al.,* 2005 [108]	11	73	36	50	No	Yes
Marchlinski *et al.,* 2004 [104]	19	74	27	11	Commonly*	Yes
O'Donnell *et al.,* 2003 [94]	17	71	58	47	No	No

Commonly*, irrigated ablation used in the majority of patients reported; rarely**, 3D mapping was used in the minority of patients reported.

be helpful in selecting patients who should be considered for an epicardial approach with the initial ablation procedure [109]. Epicardial mapping and ablation should follow the same localizing principles followed for the endocardium. Because many patients will not tolerate induced VTs during general anesthesia, a substrate-based approach targeting and transecting the site of the best pace map and ablating surrounding late potentials has been used with resultant good VT control [101,110].

Outcome with ventricular tachycardia ablation

No large prospective multicenter studies have been performed to assess the value of endocardial ablative therapy in reducing VT recurrences in this patient population (Table 8.2). Single-center studies reporting on the outcome of 15–32 patients have in general been fairly consistent in their acute and follow-up outcome results with endocardial catheter ablation. The ability to eliminate all inducible VT appears to range from 72 to 88%. Most patients have remained arrhythmia-free during long-term outcome with recurrence rates of 11–50% in part related to duration of follow-up. To date only one study has reported a very poor acute (46% noninducible) and then long-term outcome (83% recurrence rate). This study included a series of patients who did not undergo irrigated catheter ablation and/or substrate-based ablation [108]. The use of 3D mapping systems was also limited in this report. Nevertheless, recurrence of VT after endocardial ablation does occur and the requirement of antiarrhythmic drug therapy has been commonly reported by some investigators [105]. Because the disease substrate is predominantly epicardial there is some optimism based on preliminary reports [101,110] that outcome will be improved by earlier mapping and ablation of epicardial targets. Surgical epicardial cryoablation has also been reported with a successful outcome.

Ventricular tachycardia ablation in the setting of hypertrophic cardiomyopathy

The relationship between ventricular arrhythmias and HCM has been known for years; the mechanisms of sudden death and syncope in this clinical setting are not fully clarified but may be related to lethal ventricular arrhythmias, myocardial ischemia, or the severity of left ventricular outflow tract obstruction. The most common ventricular arrhythmias observed with programmed electrical stimulation in these patients include polymorphic VT and VF, while monomorphic VT is less frequent [111]. In contrast, clinical sustained monomorphic VT in patients with HCM seems uncommon but may be underestimated because of early degeneration into VF [112]. Patients with HCM and left ventricular apical aneurysm represent an underrecognized but important subgroup within this heterogeneous disease spectrum. Previous reports have described that the presence of an apical aneurysm in the setting of HCM identifies patients with an increased risk for adverse clinical

events including stable and unstable monomorphic VT and sudden cardiac death. Under these circumstances, an implantable defibrillator is frequently used for primary prevention [113]. Catheter ablation has recently become an additional treatment strategy in those subgroups of patients who develop sustained or nonsustained monomorphic VT.

In HCM, two main factors may predispose to ventricular arrhythmias: (1) the myocardial disarray and (2) the increase in left ventricular mass. Myofibrillar disarray, myofilaments disorganization, and interstitial fibrosis can cause dispersion of activation throughout the ventricular myocardium and can result in fibers with differences in conduction velocities and refractory periods, thus promoting the occurrence of reentry [114]. Perivalvular scarring may also occur similar to nonischemic dilated cardiomyopathy that can serve as a VT substrate. In patients with mid-ventricular obstruction, the presence of an apical aneurysm may lead to a different arrhythmic substrate, related to local ischemic phenomena and aneurysm formation. In a case report described by Rodriguez *et al.* [115], the induced VT seemed to be because of a reentry mechanism, based on: (1) the presence of mid-diastolic potential preceding the QRS complex during VT; (2) the interval from the mid-diastolic potential to the beginning of the QRS complex during VT being equal to the interval from the pacing spike to the QRS; (3) the occurrence of entrainment without fusion; and (4) postpacing interval equal to the cycle length of the VT. Ablation at this site was effective in terminating the arrhythmia (Figure 8.11). In this case as in other ones, application of RF energy suggests the presence of scar/fibrous tissue of the endocardial layers with surviving muscle. This is a potential explanation when epicardial coronary vessels are normal and the endocardial ischemia may be as a result of high intramural pressures in the distal vessel or spasm of the coronary arteries leading to myocardial damage. In other cases, during VT mapping, early diastolic fractionated electrograms are recorded, suggesting an area of slow conduction within the circuit, which can be targeted successfully for ablation [116].

Catheter ablation strategy

The ablation strategy applied to a monomorphic VT in patients with HCM is the same as in the setting of an old MI, including the use of activation, entrainment, and substrate-based ablation. More recently, clinical unstable VTs were successfully eliminated guided by pace mapping during sinus rhythm to identify and ablate the exit sites [117]. A detailed electroanatomic voltage map of the left ventricle during sinus rhythm is required and can reconstruct the left ventricular aneurysm (Figure 8.12). Usually, low-amplitude signals are recorded within the aneurysm and frequently noncapture at high pacing outputs is demonstrated, suggesting the presence of inexcitable scar tissue. In case of unstable VTs, it is reasonable to perform pace mapping around the neck of the aneurysm and deliver RF current in a linear fashion through the site where the best pace mapping has been achieved [117].

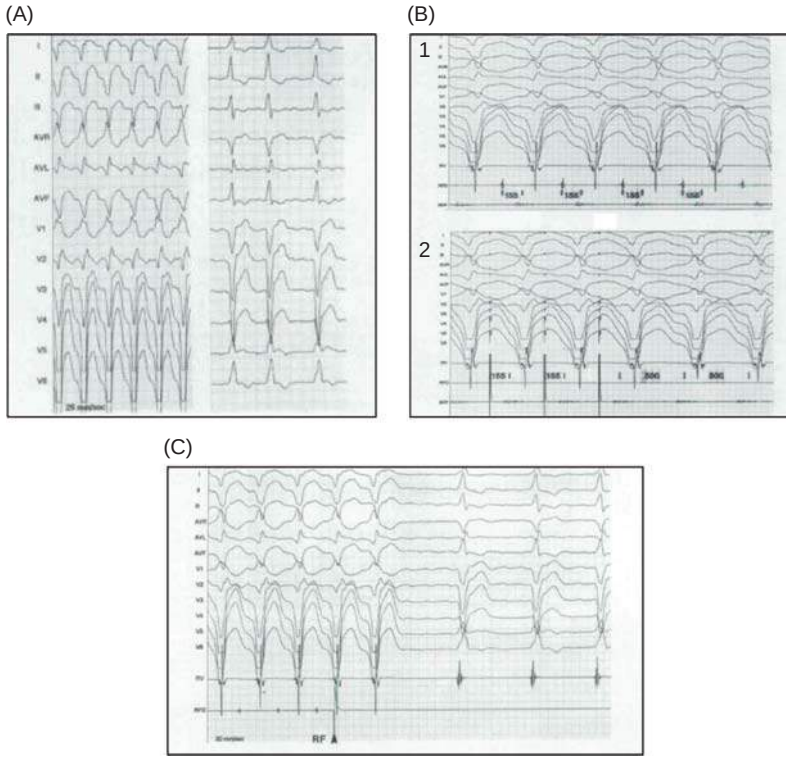

Figure 8.11 VT ablation guided by conventional electrophysiological mapping in patient with hypertrophic cardiomyopathy. Panel A: Clinical induced VT with a cycle length of 500 ms. Panel B1: Endocardial recordings from the right ventricular apex (RV) and from the distal (RFD) and proximal (RFP) electrodes of the ablation catheter. Low-amplitude diastolic activity is recorded from the septoapical portion of the aneurysm (RFD and RFP). The interval from the mid-diastolic potential (EG) to the beginning of the QRS is 155 ms. Panel B2: Pacing from the distal electrodes of the ablation catheter during VT (first three beats) shows an interval of 155 ms from the pacing stimulus to the QRS onset that is equal to the EG-QRS interval observed in the panel B1. The postpacing interval is equal to the tachycardia cycle length. Panel C: RF delivering at this site terminates the tachycardia within 2 s (Adapted from Ref. [115]). HCM, hypertrophic cardiomyopathy; VT, ventricular tachycardia

Although noncontact mapping system may be useful in localizing most hemodynamically unstable VTs, the size of the multielectrode array is too large and the aneurysm neck frequently too small to map effectively in this setting. It is also important to mention that placement of ablation catheter into the narrow neck of the aneurysm can be technically challenging because the narrow neck frequently obliterates during systole. Before maneuvering the ablation catheter, it is advisable to perform an angiography or other detailed echocardiographic or computed tomography (CT) imaging of the aneurysm and its neck (Figures 8.12 and 8.13). Such imaging could facilitate the entrance into the aneurysm and may identify the presence of a left ventricular thrombus that may cause the procedure to be aborted.

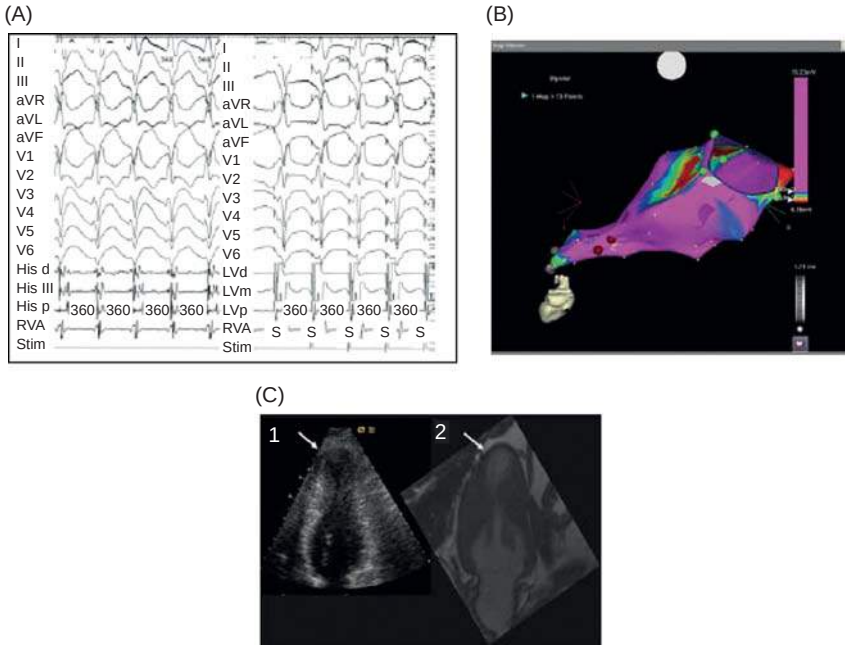

Figure 8.12 VT mapping and left ventricular (LV) echocardiography/MRI in patient with HCM. Panel A: Spontaneous VT (on the left) and the best pace mapping during sinus rhythm (on the right). Standard ECG and endocardial electrograms are recorded. The pace mapping is performed on the neck of the LV apical aneurysm. Panel B: Electroanatomic voltage map during sinus rhythm. The gray dots indicate the sites at the LV apex without capture, whereas the red dots depict the sites at the neck of the LV aneurysm where the best pace map was achieved and ablation performed. Panel C: Two-chamber echocardiographic apical view (panel C1) and cardiac MRI (panel C2) showing systolic mid-ventricular hypertrophy with apical aneurysm (arrows) (Adapted from Ref. [117]). VT, ventricular tachycardia; HCM, hypertrophic cardiomyopathy; ECG, electrocardiogram; LV, left ventricular; MRI, magnetic resonance imaging

Ventricular tachycardia ablation in the setting of congenital heart diseases

The occurrence of arrhythmia disturbances and, in particular, VT in the setting of congenital heart disease (CHD) varies according to the underlying anatomic defect and method of surgical repair. Usually, the congenital malformations are severe in 30–50% of cases, requiring surgical procedures during early childhood. Therefore, arrhythmia mechanisms involve a complex interplay between gross cardiac anatomy, chamber enlargement, cellular injury from hypoxia and cardiopulmonary bypass, and fibrosis at sites of suture lines and patches. Although operative innovations have led to surgical solutions for nearly all anatomic heart defects, the improved hemodynamic longevity may be responsible for morbidity and mortality for this population, central among which are cardiac arrhythmias. In the majority of cases,

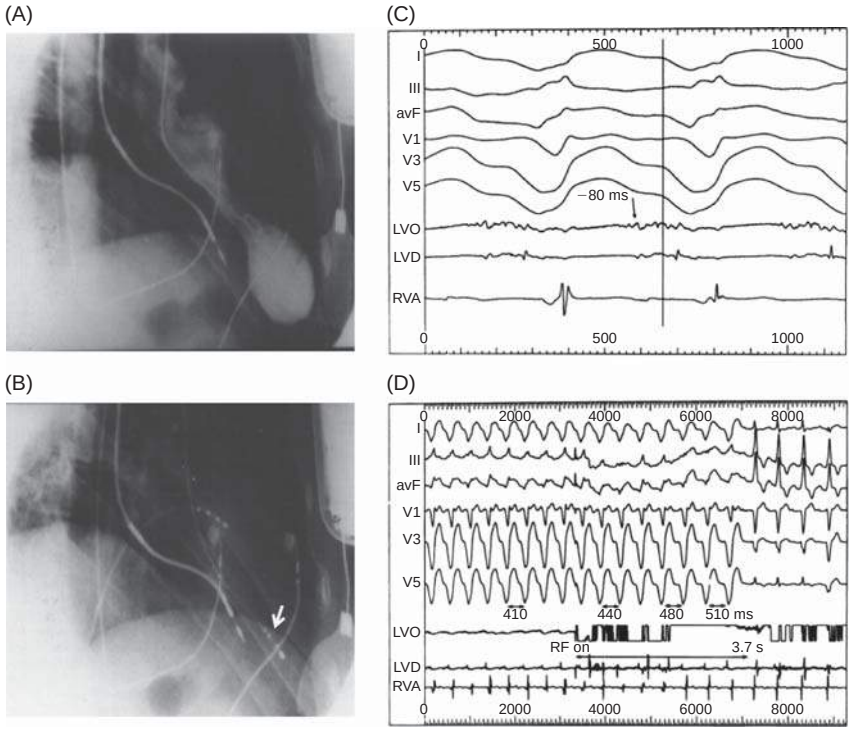

Figure 8.13 LV angiography (panel A) showing the LV apical aneurysm and fluoroscopic view (panel B) of the ablation catheter (arrow) advanced through the narrow neck of the apical aneurysm. Panel C shows low-amplitude, fractionated electrogram recorded during VT, close to the neck of the aneurysm, that precedes the QRS onset of 80 ms. RF delivering at this site terminates the arrhythmia after 3.7 s (panel D) (Adapted from Ref. [116]). LV, left ventricular; VT, ventricular tachycardia

VT is a consequence of prior corrective surgery, which can create the ideal substrate for reentrant tachycardias as a result of the action of patches and sutures in conjunction with hypertrophy and fibrosis that create the necessary block and slow conduction to promote reentry. Approximately, 45% of adults with CHD are considered to have mild forms of CHD (atrial septal defects, valvular pulmonary stenosis), 40% are classified as having moderate disease (tetralogy of Fallot, Ebstein's anomaly), and 15% are considered to have complex disease (single ventricle, transposition of great arteries). Arrhythmias can arise in each group, but they are more frequent in patients in the moderate and severe categories. In this regards, it is important to recall that repaired tetralogy of Fallot is an instructive example of moderate CHD with a large arrhythmia burden. In fact, serious ventricular arrhythmias develop in a consistent segment of the population of repaired tetralogy, contributing to a sudden death risk that is currently measured at 2% per decade of follow-up [118], and an increasing number of patients are now receiving implantable defibrillator for treatment of VT. Ventricular arrhythmias are

not very frequent in CHD patients during the first or second decade of life, but they can become serious and life-threatening arrhythmic disorders once adulthood is reached. In fact, VT and sudden death become a real concern in select cases. In this regards, patients at greatest risk for developing VT appear to be those who have undergone a ventriculotomy and/or patching for certain types of ventricular defects. It seems that late-onset arrhythmias in adulthood is the price to pay for decades of effective hemodynamic palliation and for creating scars around which a reentrant circuit can develop.

In terms of VT prediction and treatment in CHD patients, there is lack of recognized guidelines and therefore, in most cases, therapy continues to be individualized for asymptomatic patients largely depending on physician and/or single-center experience. This could also be explained by the fact that VT occurrence and sudden death in CHD is quite low compared with clinical conditions such as ischemic heart disease. In contrast, now that the population of adults with CHD at potential risk to develop VT has reached a substantial size, the need to identify patients at risk becomes apparent.

Catheter ablation has become an indispensable treatment option for this group of patients who demonstrate VT. The majority of data regarding the relationship between CHD and VT are centered on tetralogy of Fallot. Therefore, as far as the goal of this section is concerned, almost all the clinical considerations and the treatment options will be referred to patients with repaired tetralolgy of Fallot, which has a prevalence of VT between 3 and 14% [118–122].

Ventricular tachycardia mechanism in patients with congenital heart disease

In this clinical scenario, the pathophysiologic mechanism of VT is a macro-reentrant circuit in most cases, often involving narrow conduction corridors defined of regions of surgical scars with natural conduction barriers such as the edge of a valve annulus [123,124]. In other circumstances, ventricular arrhythmias can arise independently of surgical scarring whenever a long-standing volume overload can produce ventricle dysfunction or hypertrophy. Examples of CHD that can produce this myopathic variety of VT encompass: (1) aortic stenosis; (2) transposition of the great arteries; (3) severe forms of Ebstein's anomaly; (4) certain forms of single ventricle;(5) Eisenmerger's syndrome; and (6) unrepaired tetralogy of Fallot.

In patients with operated tetralogy of Fallot and VT, the most common mechanism is a macro-reentry involving the RVOT, either at the site of right anterior ventriculotomy or at the site of ventricular septal defect patch. The VT circuit rotates around an RVOT patch and this is possible only if the patch does not extend to the pulmonic valve, as a transannular patch would. With conventional pacing maneuvers, it is possible to demonstrate in some patients the importance of the right ventricular isthmus between the tricuspidal annulus and\or pulmonary valve and the RVOT patch [125]. In those patients with transannular patches, the isthmus between RVOT patch and the pulmonic

valve is not available; therefore, a critical isthmus is probably located between the patch and the tricuspid valve.

Ventricular tachycardia ablation strategies in patients with congenital heart disease

In the last decades, RF catheter ablation has been used successfully for several forms of tachycardias in CHD. For sure, the most challenging aspect is the distorted cardiac and vascular anatomy that precludes the use of conventional fluoroscopic landmarks and complicates catheter manipulation. To better plan the ablation strategy, details of the underlying structural disease and surgery need to be understood in advance of the intervention. During a baseline electrophysiological evaluation, it is important to recognize the atypical conduction patterns in certain forms of CHD and locate a His-potential, to minimize the likelihood of damage to the normal conduction system. To overcome potential difficulty in the interpretation of altered cardiac anatomy, 3D mapping systems are employed and the preacquired CT image scan can be imported and integrated in the process of mapping.

The majority of experience reported with catheter ablation is for the treatment of inducible monomorphic VT, based on macro-reentrant circuits that can be mapped accurately and treated with RF applications [125–134]. As in ischemic VTs, a variety of mapping strategies have been described, including entrainment maneuvers (if VT is hemodynamically tolerated), pace mapping, activation sequence analysis, and, more recently, 3D electroanatomic mapping and noncontact mapping (especially for those forms of nontolerated VT). Low-amplitude and fractionated electrograms have been described. Areas of inexcitability as a result of patch material or sutures are common.

In the occurrence of sustained, hemodynamically tolerated VT, the principal electrophysiologic diagnostic maneuver is the entrainment mapping to prove the macro-reentrant feature of the arrhythmia. In patients with very fast, poorly tolerated VT, mapping study and ablation strategy can be performed using nonconventional mapping approaches. In particular, the use of electronatomic mapping systems with voltage maps can be quite useful for detecting areas of scars in the RV. In the past, intraoperative mapping of the RVOT in the beating heart, employing an endocardial electrode balloon, and a simultaneous epicardial electrode array, has been used as a guide to create successful cryolesions [124]. Currently, electronatomic mapping of the arrhythmia circuit represents probably the most useful tool for mapping VT in the setting of tetralogy of Fallot and therefore in other forms of CHD. A combination of entrainment mapping and voltage maps constructed in sinus rhythm is an alternate approach that is able to define areas of scar and create a line of block between the RVOT and the tricuspidal annulus (Figure 8.14). The importance of creating bidirectional block of conduction between the tricuspidal annulus and the RVOT patch is also linked to the fact that in some patients two or more different QRS morphologies of tachycardia may exist because of conduction in both clockwise and counterclockwise directions through the isthmus.

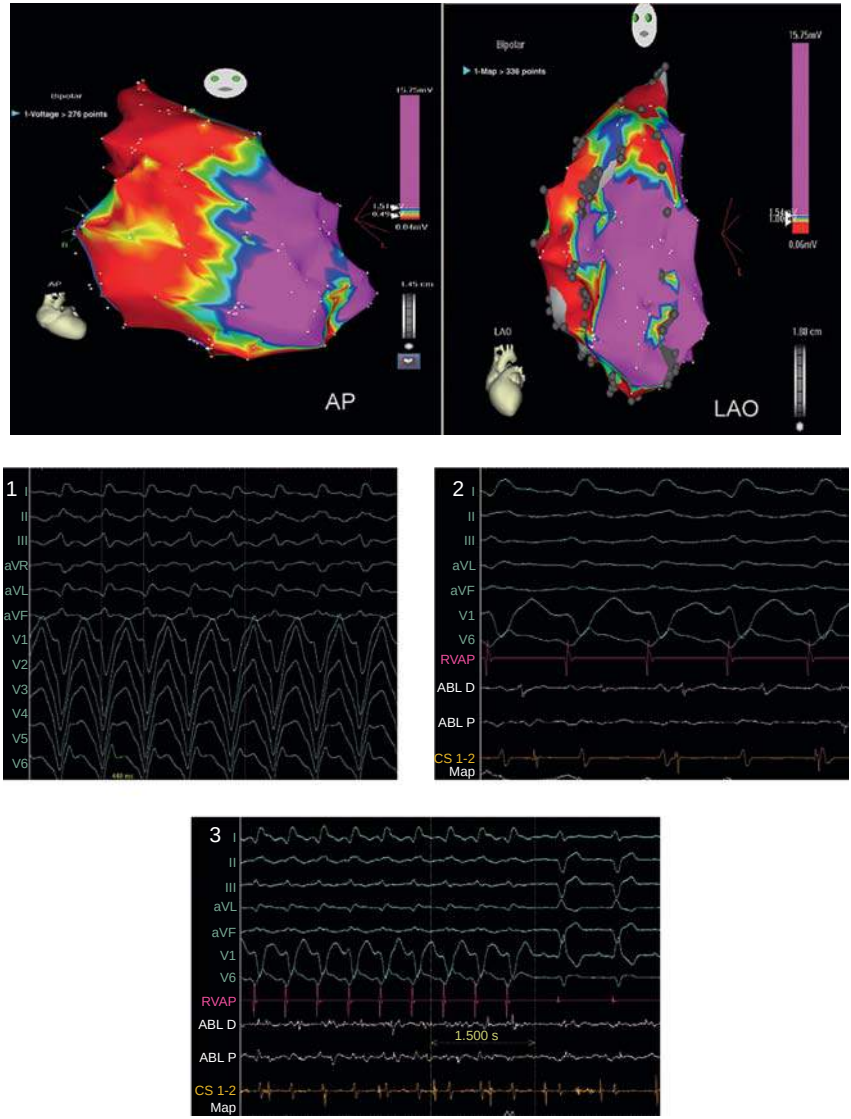

Figure 8.14 VT substrate mapping in patient with repaired tetralogy of Fallot. Panel A shows the voltage map of the right ventricle. The red color indicates the extensive scar as a result of surgical repair and fibrosis following volume overload. The gray dots in the LAO view indicate sites where entrainment maneuvers were performed. AP, anteroposterior view; LAO, left anterior oblique view. Panel B shows the 12-lead ECG during VT (1) and the site mid-diastolic potential (2), recorded on the anterolateral wall of RVOT, where the ablation was effective (3).
ECG, electrocardiogram

Creating a bidirectional block may allow to perform ablation in sinus rhythm without the need to map or ablate during VT [125]. The isthmus between the anterior wall of RVOT scar/patch and tricuspidal annulus is involved in approximately 75% of VT cases in patients with repaired tetralogy of Fallot [135]. Slow-conduction area can be part of the circuit and their presence is suggested by a prolonged S-QRS interval during pace mapping or entrainment mapping [17–19,23,40]. RV remodeling induced by pressure or volume overload may promote hypertrophy and fibrosis with slow conduction, thus providing the link between impaired hemodynamics and VT. Alternatively, surviving myocytes embedded in fibrous tissue may resemble areas with slow conduction usually found in the border zone of infarcted myocardium.

The use of noncontact mapping has been already described for fast, ischemic, and idiopathic VTs, while its use in patients with CHD, namely after repair of tetralogy of Fallot, and fast, hemodynamically unstable VT is quite new (Figure 8.15). In the literature, it is reported a success rate of 60% using electroanatomic mapping and/or conventional techniques [136] and of 50% using the noncontact mapping in patients with VT after surgical repair of CHD [137]. When using noncontact mapping, pacing and entrainment techniques are often useless, because of high ventricular rates and therefore efficacy is usually demonstrated by noninducibility of VT and pacing from adjacent sites along the lines of ablation to confirm block of activation.

The most recent technological advances in substrate mapping may further elucidate the distorted anatomy in patients with CHD and VTs. In fact, the location and morphology of scar/fibrous tissue can be elucidated by preprocedural CT or MRI. In detail, delayed-enhancement contrast MRI is noninvasive, imaging modality that can allow distinction of normal from chronically scar cardiac tissue. Therefore, by knowing in advance the location and extension of scar tissue could be useful and serve as a guide for substrate-based catheter ablation. Also CT imaging can provide anatomic information with high spatial resolution, although with more limited ability to discriminate scar from normal tissue. With current technology, CT imaging can directly image scar tissue probably only in those patients with partially calcified tissue. However, one of the most promising applications of this current technology also in repaired CHD is the 3D cardiac MRI/CT images integration with electroanatomic information to guide catheter navigation to the target areas. This is currently accomplished for atrial fibrillation ablation, but one could imagine to apply the same approach also for the RV. This could improve our understanding about the anatomy of the RV after surgical repair and, more importantly, guide to the target sites for ablation more precisely.

The other recent major advance is remote navigation technology to facilitate and enhance ventricular mapping. In fact, one of the limitations of substrate mapping and the ablation is that the accuracy and detail of ventricular map is almost completely dependent on operator's ability and skill. With remote navigation, there is potential advantage to reach difficult locations and, when used in concert with electroanatomic mapping system, it is possible to achieve

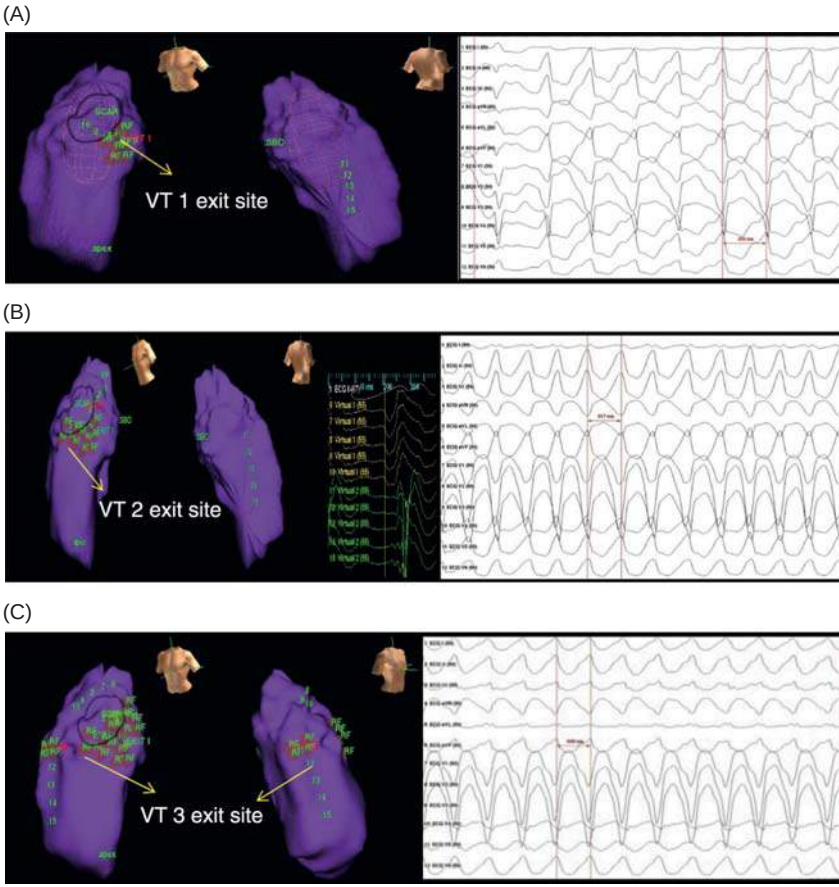

Figure 8.15 Noncontact mapping (NCM) of three different sustained VTs in patient with repaired tetralogy of Fallot. Panel A shows the VT1 (cycle length 433 ms) mapped with NCM system (left) and the corresponding 12-lead ECG morphology (right). After ablation of this tachycardia other two VTs were inducible with cycle length of 317 and 310 ms, respectively. Panels B and C show the noncontact maps and the ECGs of VT2 and VT3, respectively. The arrows indicate the sites of effective ablation of each tachycardia. RF delivery at these sites prevents inducibility of any VTs. NCM, noncontact mapping; VT, ventricular tachycardia; ECG, electrocardiogram; RF, radiofrequency

a high-density ventricular substrate map, as already shown during atrial fibrillation ablation procedures.

Outcome with ventricular tachycardia ablation

Several case reports have been described in the last few years, but unfortunately the follow-up is not uniform. In two small series [137,138], a total of 30 patients have been assembled, including tetralogy of Fallot (17 cases), ventricular septal defect (8 cases), and miscellaneous CHD (5 cases). Based on these results, catheter ablation was acutely successful in 25 out 28 procedures

(89%) and later VT recurrence was documented in 5 cases (20%). Some of the recurrences could have been related to the difficulty with RF current to create a sufficient lesion in the often thick-walled chamber, like the right ventricle in the tetralogy of Fallot. The recent advance in the mapping studies, the use of irrigated-tip ablation catheters, has portrayed catheter ablation as an exclusive therapy for select patients with CHD, especially those with well defined and single circuits of tolerated VT and otherwise good hemodynamics. Still, because of the lack of a very long follow-up, catheter ablation is often relegated to a secondary treatment option, to reduce the shock burden in patients with frequent VT episodes who already have an ICD implanted.

As final statement, successful ablation of VT circuit in patients with surgically corrected CHD does not necessarily mean reduction or elimination of the risk of sudden death; therefore, many patients will be appropriate candidates for implantation of implantable cardioverter defibrillator, particularly those with a strong risk profile for sudden death such as pulmonic insufficiency, severe RV dilatation and dysfunction.

Ventricular tachycardia ablation in other clinical settings

Chagas disease

Chagas disease is caused by the protozoan *Trypanosoma cruzei*, transmitted to humans mainly through bloodsucking insects in areas where the disease is endemic and occasionally by blood transfusions. It is a major health problem in Latin America, where approximately 18 million are chronically infected and 200,000 new cases occur each year [139]. Involvement of the heart is one of the main causes of morbidity and mortality [140], especially when accompanied by conduction system disturbances and ventricular arrhythmias. Right bundle branch block and left anterior hemiblock frequently precedes more severe heart manifestations such as cardiac dilatation and biventricular failure.

VTs in Chagas disease can have heterogeneous presentations but occurs predominantly as a result of a reentrant mechanism [141,142], sometimes clustered in electrical storms [143,144] The clinical course of the disease is variable, making identification of patients at risk particularly challenging [145–147]. Recently, a risk score has been created and validated to establish the prognosis in those with chagasic cardiomyopathy [148].

Myocardial damage can occur in various areas of both ventricles, but the inferolateral segment of the LV is the most commonly involved site, with frequently observed wall motion abnormalities; apical aneurysmal formation and mitral isthmus circuits are also common [76,149–152]. In this area, endocardial mapping frequently depicts fragmented late potentials in sinus rhythm (Figure 8.7) as well as continuous or diastolic activity during VT (Figure 8.8). Histological analysis of those segments has shown focal and diffuse fibrosis that is predominantly subepicardial with nonuniform anisotropy of the surviving fibers.

Initial attempts to control VT episodes by endocardial RF catheter ablation in a small series of 24 patients were hampered by low success rates (~17%) over 2 years of follow-up [149]. This group hypothesized that epicardial circuits (Figure 8.9) could justify the poor results of standard endocardial ablation, and pioneered the performance of percutaneous nonsurgical transthoracic access for mapping and ablation of the epicardial surface [51,150,153].

Using the epicardial approach in 10 such patients [52,153] VTs were targeted; 78% [76] of those had an epicardial circuit. Four VTs (22%) were interrupted by endocardial applications after a mean of 20 s but all were reinduced. The other 10 VTs were interrupted by epicardial RF after 4.8 s, none being reinduced. Earliest epicardial activation was recorded 107 msec earlier than the QRS complex; mid-diastolic potentials or continuous electrical activity were seen in 7 patients. In this series complications were infrequent. Hemopericardium requiring drainage occurred in one patient; three others developed brief pericardial discomfort controlled with the use of antiinflammatory drugs.

However, with further experience in 112 patients [149], 95 of 231 VTs (41%) could not be mapped while 56 other VTs could not be ablated. Only 60% of all mappable VTs were ablated (50% endocardial and 50% epicardial VTs).

In their latest report on 138 patients [52], successful ablation (defined as termination and noninducibility) was possible in 52% of patients. Importantly, only two major complications were described (one abdominal cavity bleeding because of an injured diaphragmatic vessel that required laparotomy and another with coronary artery occlusion of a marginal branch that caused non-Q wave MI). Minor complications were represented by precordial distress, present in 29% and always controlled by standard antiinflamatory medications, as well as avoidable puncture events such as dry RV puncture and drainable hemopericardium, present in 4.5% of cases.

It is clear that although the endo/epicardial mapping technique allows for better mapping of the circuit, improved technology is greatly needed to allow transmural lesions to be performed. One of the problems related to adequate power delivery is the presence of epicardial fat and the lack of cooling flow in the epicardial space [52,154]. It is hoped that irrigated-tip catheters, cryoablation, and near infrared laser catheters could circumvent some of these issues (Figure 8.6).

Sarcoidosis

Sarcoidosis is a multisystem, granulomatous disease of unknown etiology associated with an exacerbated immunological response to an antigenic stimulus. Twenty-five percent of patients with sarcoidosis have cardiac lesions, but only 5% of all patients have clinical manifestations [155,156]. Cardiac sarcoidosis may present as congestive heart failure [157], conduction system disease (bundle branch block, atrioventricular block, and sinus node arrest), supraventricular and ventricular arrhythmias [158], and sudden cardiac death [159].

Ventricular arrhythmias are commonly caused by directed granulomatous involvement of the myocardium [160]. Corticosteroid therapy may suppress

inflammation and granuloma formation and reduce the number of arrhythmias, but the resolution process produces fibrosis and consequently the substrate for arrhythmogenesis [161,162].

VTs in cardiac sarcoidosis are usually multiple reentrant monomorphic VTs (scar-related), with either left or right bundle branch morphology; low-amplitude and fragmented potentials are recorded in both the endocardial and epicardial regions of both ventricles [73,163]. Two patterns of regional wall motion abnormalities are frequently observed, involving the basal free wall and the anteroapical septum [76].

Catheter ablation for VT is indicated in patients with frequent episodes refractory to medical treatment. The reported success rates ranges from 25 [72] to 70% [163] in a recently reported registry and depends on the location of the reentrant circuit. In the aforementioned registry, nine patients underwent RF ablation for uncontrolled VTs (eight endocardial and one epicardial ablation). Out of 44 induced VTs, 32 (70%) were successfully eliminated. The most frequent circuit was found in the peritricuspid area, suggesting a preferential involvement of the basal RV by the disease process. Other reports have also suggested that the success rates appear better for VTs originating in the right ventricle, during inactive disease activity and in patients with higher ejection fractions.

There are also reports of multiple VTs originating in the posterolateral LV (similar to what is observed in Chagas patients), with corresponding electrogram abnormalities and nuclear perfusion defects unrelated to coronary disease [76].

Idiopathic left ventricular aneurysms

Idiopathic left ventricular aneurysms are defined as aneurysms of unknown etiology in the presence of normal coronary arteries and absence of angina or history of MI; it is a rare condition (only few cases reported in the literature) frequently associated with reentrant VTs [164,165]. Life-threatening arrhythmias may be the first manifestation of an idiopathic LV aneurysm [166], as well as syncope and palpitations [167–169]. Specific causes of myocardial damage such as sarcoidosis, tuberculosis, Chagas disease, syphilis, rheumatic fever, mycosis, and a flu-like syndrome should be ruled out.

The LV aneurysms are smaller in size and more often located at the posterior and/or inferior wall, as opposed to postinfarction aneurysms that are often located at the anterior wall [168,169].

Management strategies in these patients include antiarrhythmic drug therapy, surgical aneurysmectomy [62], defibrillator implantation [62,167], and catheter ablation for refractory cases [168–170].

The inducibility of VT on EP study is high, and the majority has right bundle branch morphology. Abnormal endocardial and epicardial electrograms were recorded in most of the patients, usually closely related to the dyskinetic area that provides the anatomic substrate for reentry [168,169].

One of the largest reported series of cases [169] described an approach using irrigated endocardial and epicardial catheter ablation of VT from a left

ventricular aneurysm in four patients. In that report, 75% were VT-free during 31 months of follow-up using an aggressive ablation approach.

Other reports have shown that RF catheter ablation could be performed around the neck as well as inside the aneurysms based on recording diastolic potentials during sinus rhythm with excellent success rate [169–171].

Ventricular tachycardia after cardiac surgery

Coronary artery bypass surgery usually has an antiarrhythmic function in patients with VT or VF and an ischemic substrate; there is, however, a selected group of patients to either develops or experiences aggravation of ventricular arrhythmias after surgery; these may present as increased ventricular ectopy, nonsustained VTs, or *de novo* VTs occurring as a consequence of surgery, as reported in small case series.

One of the largest published series reported on 3820 patients undergoing CABG in a single center [172]; 12 patients (3%) developed *de novo* sustained VT a mean of 4.1 days after surgery. In most cases (92%), no postoperative complication could explain the development of VT. Mortality rate was high (25%). Patients with VT were more likely to have prior MI, severe CHF, and EF <40%. In fact, when all these three factors were present, the VT risk increased 14-fold (30%). Importantly, placement of a bypass graft across a noncollateralized total occlusion in a vessel supplying an infarct zone was the only predictor of VT occurrence, suggesting reperfusion injury as the trigger for the VTs.

More recently a report by Echardt *et al.* demonstrated that most VTs that occur after corrective valve surgery appear to be scar based and to have a reentrant mechanism although bundle branch reentry must be excluded [73]. The scar appears to be predominantly located around the periaortic and mitral valve regions. Mapping strategies as described for VT in the setting of prior infarction can be used successfully to eliminate VT.

Ablation of ventricular fibrillation

Background

Ventricular fibrillation is a deadly heart rhythm, usually initiated by a premature ventricular complex during the vulnerable period of cardiac repolarization. VF is most frequently seen in patients with alterations of cardiac repolarization such as inherited or acquired long QT syndrome or conditions that promote premature depolarizations in the vulnerable period such as ischemic or infiltrative cardiac disease. It is also seen in the postcardiac surgery period; however, some patients present without any known cardiac pathology [173–175].

Ablation therapy for VF has been described and increasingly reported. Most cases of VF appear to originate from the His-Purkinje system, although some cases report initiating events that are distinct from the cardiac conduction system. Ablation has targeted these initiating premature contractions

as well as the substrate of possible reentry within the cardiac conduction system [176–181].

In general, these ablations appear to have a high success rate and are relatively easy to perform, although precise mapping is required.

Vulnerable populations

Ischemic heart disease

Ventricular fibrillation can present in patients with coronary artery disease in the setting of acute MI or well after infarction with well-healed myocardial scars. During acute MI, it is believed that an ischemic His-Purkinje system is the source of depolarizations that induce VF. In addition, the ischemia frequently prolongs the global repolarization and vulnerable periods, as seen in lengthening of the QT interval on EKG, that make the heart more susceptible to these depolarizations. Frequent episodes of VF may be controlled with medication including beta-blockers or antiarrhythmic agents, such as lidocaine, but resolution of the ischemia is the ultimate therapy. Ablation is only rarely required in cases that are refractory to medical and interventional or surgical therapy.

In patients with healed MIs, VF may present without an acute ischemic syndrome. These patients may not have a surgical or interventional treatment option, and medical therapy may not be effective in some cases. Also, these patients do not appear to have QT prolongation as often. When required, ablation targets the initiating premature ventricular contractions (PVCs), which may originate from the His-Purkinje system or the border of the scar from the healed MI. In addition, the scar border may appear to have Purkinje-like potentials that are not usually found in these locations. It has been suggested that arborization of the microconduction system may be seen in these patients [182–185].

Long QT syndrome

Ventricular fibrillation may present in patients with acquired or inherited long QT syndrome. Either a chanelopathy or medication may prolong the time of repolarization in these patients. This prolongation of repolarization appears to increase the vulnerable period and allow for premature depolarizations to occur during this period. Typically, these patients present with a prolonged QT interval on EKG and frequent monomorphic PVCs. Patients may respond to medical therapy with beta-blockers or medications that shorten the QT interval, such as lidocaine. Medications or therapies that increase the heart rate and reduce the refractory period such as pacing or isoproterenol may be effective. In patients with acquired long QT syndrome, withdrawal of the offending agents may be effective.

In patients with VF, which is refractory to these therapies, ablation may be performed. The initiating PVCs are typically from the His-Purkinje system, although their origin from the right ventricular outflow tract has been described [186,187].

Brugada syndrome

Like other ion channel disorders, Brugada syndrome may present with recurrent VF initiated by monomorphic PVCs; however, unlike other chanelopathies, these are most frequently from the right ventricular outflow tract. Only the minority of reported cases are successfully ablated from the HPS system [187–189].

Infiltrative cardiac amyloidosis

In two cases of presumed normal heart VF, endomyocardial biopsy was performed revealing infiltration with amyloid proteins. These patients had drug refractory VF and underwent successful ablation of triggers associated with the HPS. Because of the relatively rare diagnosis of infiltrative amyloidosis, this may be an underrecognized cause of VF [190].

Postcardiac surgery

Rarely, patients who are in the recovery period after cardiac surgery may develop drug refractory VF. Coronary artery bypass grafting seems to be the most frequent surgery that is associated with this phenomenon. However, this may occur in patients without significant coronary artery disease and has been described after valve repair or replacement surgery. In general, the most common location of the initiating PVC is the HPS [191,192].

Normal heart ventricular fibrillation

Patients with normal systolic function and no evidence of coronary artery disease or other cardiac abnormality are referred to as having idiopathic VF. The initiating events tend to be from the HPS [176–178].

Ablation techniques

As described in the preceding text, the HPS is the most frequent site of initiation of VF. This adds some complexity to the mapping process. Recording of the 12-lead ECG of the triggering event can prove invaluable in regionalizing the origin of VT for more detailed mapping, and an effort to record such a trigger should be routine. During activation mapping of the PVC, special attention must be paid to preceding sharp Purkinje-like signals. These may precede the local ventricular activation during the PVC by tens of milliseconds. Mapping should be focused on the earliest activation of this potential. One may see earliest Purkinje-like potential activation in one spot and later activation of the potential proximal and distal to that spot. With multipolar catheters placed in the His position and down the left ventricular septum, one can see the progression of the signal through the conduction system with the His-potential activating last. Sometimes, the potential may be seen with block to the myocardium and not producing the PVC (Figure 8.16). Determining the earliest potential is the key to successful ablation. Local ventricular activation is usually significantly delayed. During sinus rhythm, the potential will usually appear to be closely related to the local ventricular activation, in fact just preceding it; however during the PVC, it is usually much earlier (Figure 8.17). Pace mapping

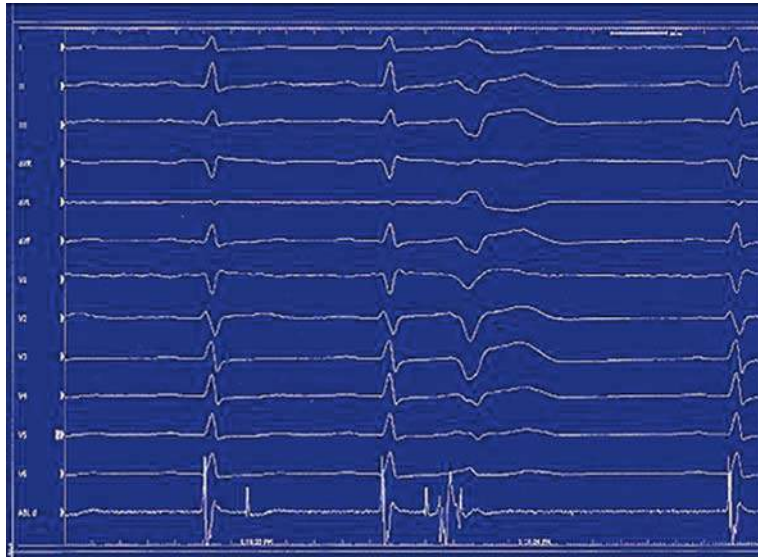

Figure 8.16 Premature ventricular contraction with a delayed sharp potential that precedes the clinical PVC. This was the successful ablation site. PVC, premature ventricular contraction

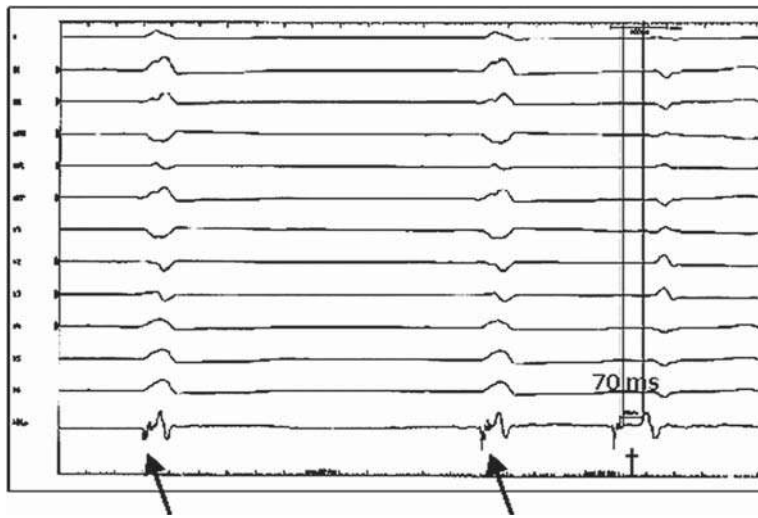

Figure 8.17 Location with a sharp prepotential that is markedly early during the clinical PVC. PVC, premature ventricular contraction

of the area of interest also requires special care. The pacing amplitude output should be adjusted to attempt to capture the HPS alone; otherwise, the pace mapping will appear dissimilar.

The Purkinje network is present on the superficial endocardium and tends to respond to ablation quickly and without the need for prolonged ablation

times or high power. After ablation, dissociated firing may be seen. In cases when the PVC is not spontaneous or inducible, ablation may be performed along the distal LV septum with Purkinje-like potentials in sinus rhythm, assuming the PVC has this morphologic type.

In patients with myocardial scar from previous MI, a high-density scar map should be performed, with careful attention to the border of the scar and normal tissue, because the PVCs may originate from this border. Along the border, one may see Purkinje-like potentials. Once again, mapping and ablation of the earliest potential during the PVC is the goal of this process. Further ablation may be performed in the area of arborized Purkinje-like potentials and around the scar border. Just as with VT ablations, the power and time of ablation within the scar border tend to be higher.

In patients with normal hearts and PVCs that appear to be from areas other than the HPS, standard ablation techniques of activation mapping of the earliest local electrogram and pace mapping are typically employed.

Results

No randomized, controlled trials exist on the ablation of VF, and at this point, such a trial should not be performed. Most people who experience VF in the community die, unless CPR and defibrillation are immediately available. In general, patients who undergo ablation of VF are critically ill with storms of lethal arrhythmias, not responding to medical therapy, and very likely to die without further intervention. Patients with ICDs or in ICU settings have received over 50 shocks in a 24-h time period [184]. Discussions on ending life-sustaining measures are frequently initiated before ablation is offered, and many physicians do not realize that ablation is a potential therapy. Understanding this, ablation is frequently associated with success rates greater than 90%. Of course, this is a very select population who survive to make it to the electrophysiology laboratory. Complications have not been well reported, but one may expect complication rates similar to those for ablations of patients with storms of VT. Perforation, stroke, and death may be expected as anticipated risk with any VT ablation.

The study of ablation for VF should be performed but as an earlier intervention, perhaps before the initiation of medical therapy or after much fewer events. It has been suggested that ablation could be prophylactic in populations that are at risk [193]. Animal studies have shown that a selected set of ablations may make the heart less vulnerable to VF [194].

Ventricular fibrillation is a lethal arrhythmia that may be present in a diverse population of individuals with and without other cardiac abnormalities. In most cases, VF is induced from PVCs, originating in the HPS. Ablation aimed at the initiating PVC is associated with high success rates in people that survive to undergo ablation. Further study is needed to define the role of ablation in cases that are not medically refractory.

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CHAPTER 9

Ablation of Ventricular Tachycardia/ Ventricular Fibrillation in Patients without Structural Heart Disease: Techniques and Results

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Definition

The term "idiopathic" ventricular tachycardia (VT) refers to a rapid (more than 100 beats/min) arrhythmia originating in the right or the left ventricle in patients with a structurally normal heart. To sustain the clinical arrhythmia, no other segments of the heart (i.e., atrial tissue or AV node) are required.

The term idiopathic illustrates our lack of knowledge about the cause of arrhythmias in a patient with a normal heart. As new mechanisms are discovered, segments are removed from the body of idiopathic arrhythmias and a more detailed classification is developed. A good example is represented by idiopathic ventricular fibrillation (VF). Recent studies have shown that a large number of VFs are a result of inheritable genetic mutations causing channelopathies such as Brugada syndrome, short QT syndrome, long QT syndrome, catecholamine-induced polymorphic VT, or newly recognized structural abnormalities, for example left ventricular noncompaction.

Idiopathic ventricular arrhythmias can be broadly classified as monomorphic and polymorphic VTs (Table 9.1). Idiopathic monomorphic VTs occurring in structurally normal hearts commonly arise from foci occurring in perivalvular areas. These include VTs with site-of-origin at the mitral or tricuspid

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Table 9.1 Idiopathic ventricular tachycardias

Monomorphic ventricular tachycardia	*Polymorphic ventricular tachycardia*
Outflow tract VTs	Idiopathic VT/VF
RVOT VT	Catecholaminergic polymorphic VT
LVOT VT	Long QT syndrome
Aortic cusp VT	Brugada syndrome
Pulmonary artery VT	Early repolarization
Annular VTs	
Mitral annular	
Tricuspid annular	
Para-Hisian	
Epicardial VTs	
Fascicular VTs	
LPF VT	
LAF VT	

VT, ventricular tachycardia; VF, ventricular fibrillation; RVOT, right ventricular outflow tract; LVOT, left ventricular outflow tract; LPF, left posterior fascicular; LAF, left anterior fascicular.

annuli, right ventricular outflow tract (RVOT), pulmonary artery, left ventricular outflow tract (LVOT), or the aortic cusp. In addition, idiopathic left ventricular epicardial VTs occurring near the perivascular regions have been recently described.

The use of specific antiarrhythmic drugs targeting particular arrhythmias is predicated on the understanding of the electrophysiology. In addition, detailed appreciation of the anatomy and recent technologic advances in mapping technologies have also led to the development of effective catheter ablative inventions with a high success rate.

Idiopathic ventricular tachycardia

Ventricular outflow tract tachycardia

In patients without detectable structural heart disease, VT usually has a focal origin, and most often has its origin in the outflow tract. Nearly 80% of idiopathic VT originates from the right ventricle, most commonly from the RVOT [1]. Three main clinical forms have been described: (1) nonsustained, repetitive monomorphic VT; (2) paroxysmal sustained VT; and (3) frequent premature ventricular contractions (PVCs) [2,3]. Often, more than one form is present in the same patient, and VT can be induced by exercise or emotional stress. Most forms of RVOT VT are adenosine sensitive and may be terminated using adenosine, vagal maneuvers, or calcium channel blockers [4]. VT can sometimes be suppressed by treatment with calcium channel blockers and beta-blockers. The RVOT VTs are likely caused by catecholamine-mediated delayed afterdepolarizations or triggered activity resulting from increased cAMP and intracellular calcium overload [3–6]. Less commonly,

idiopathic VT may be a result of abnormal automaticity that is provoked by adrenergic stimulation. Although some imaging studies have found structural abnormalities in the outflow tract in relation with RVOT VT, it is usually believed that the arrhythmia is an electrical disorder without relation to structural abnormalities [7]. Outflow tract tachycardias are not easily inducible at baseline EP testing and may require rapid burst pacing and/or stimulation by isoproterenol. VT may become incessant under stress or with isoproterenol, and cannot be terminated by programmed electrical stimulation. VT can be abolished with discrete radiofrequency (RF) lesions, demonstrating that the cells responsible for the arrhythmias are contained in a very small area [8]. The origin of idiopathic VT in the RVOT has a distinctive QRS morphology characterized by left bundle branch block (LBBB) morphology with inferior axis. However, many other less common sites of origin have been described, including the endocardium of the LVOT below the semilunar valves, the area above the pulmonic valve, or the area within the aortic sinuses of Valsalva, as well as the mitral and tricuspid annuli [9–15]. Furthermore, epicardial foci close to the coronary venous system at the base of the LV or at the crux of the heart have been described [13,16]. In addition, foci located in the Purkinje fibers of the left and right ventricles can be encountered [17], to be distinguished from verapamil-sensitive reentrant fascicular tachycardia. Localization of the area from which the VT arises can be predicted using the surface ECG. Although LVOT VT and RVOT VT have many similar characteristics because of the common embryonic origin [18], salient features on 12-lead ECG that distinguish RVOT from LVOT arrhythmias, as well as septal from lateral LVOT locations, can be identified. In general, the LVOT arrhythmia is associated with an early precordial R-wave transition (before V_2) because of the more posterior location compared to the RVOT. The presence of an S wave in lead I is also helpful in identifying a left ventricular origin [19,20]. Based on QRS morphology in lead I, and V_1, precordial transition patterns, and the R/S ratio in leads II and III, successful localization of clinical LVOT VT/PVC by blinded reviewer can be achieved in a majority (83%) of patients [20]. The presence of an S wave in leads V_5–V_6 may help to distinguish coronary cusp from infra-aortic LVOT locations [19,21].

Repetitive forms of RVOT or LVOT/PVCs may cause a tachycardia-mediated cardiomyopathy, which can be reversed after suppression of ectopy with antiarrhythmic drug therapy or catheter ablation [22]. Sudden cardiac death is usually not associated with this tachycardia, but there have been a few reports of VF triggered by outflow tract arrhythmias. In rare occasions, RVOT tachycardia is associated with structural abnormalities of the heart muscle (minor form of RV dysplasia), which is important to recognize because of the prognostic implications.

The treatment of outflow tract arrhythmias depends on the etiology of the VT, the underlying cardiac status, the patient's symptoms, and the arrhythmia burden. In the electrophysiology laboratory, acute termination of inducible outflow tract VTs can be achieved with adenosine administration or

blockade of slow inward calcium current [23]. Beta-blocker and calcium channel blockers may be considered as the first-line therapy, and are effective in 25–50% of the patients [24,25]. Using Holter monitoring, treadmill exercise testing, and programmed ventricular stimulation, class IA (procainamide), class IC (flecainide), and class III (sotalol, amiodarone) antiarrhythmic drugs have also been shown to be effective in suppressing idiopathic outflow tract VTs in symptomatic patients, either as monotherapy or in combination with beta-blocker and calcium channel blocker [24,26].

Catheter ablation represents a viable alternate to medical therapy, especially in those patients who do not respond or are intolerant to pharmacologic treatment. In the absence of inducible tachycardia, pace mapping is used to localize the discrete site-of-origin of focal idiopathic VT/PVCs. Comparable efficacy between pace mapping and activation mapping has been demonstrated [27]. Subtle variations in QRS morphology of ventricular arrhythmia can be observed, which may represent a wider endocardial "breakthrough" with the arrhythmia focus located deeper in the myocardium or in the epicardial layer [28,29]. RF energy delivery, however, is associated with a high long-term success rate [30–33].

In cases where the target VT or PVCs are infrequently induced, the use of multielectrode or basket catheters can be of value [32,34]. In patients who had previously failed ablations, the use of electroanatomic mapping systems, either nonfluoroscopic or noncontact systems, may provide potential benefits in facilitating the procedure and attaining a high acute success rate [23,29,34,35].

The utility of 12-lead ECG in localizing the site-of-origin of RVOT VT has been evaluated [27,36]. These algorithms are based on the pace-mapping technique and a detailed understanding of the anatomy of the outflow tract region. The RVOT is oriented diagonally from right to left, from posterior to anterior, across the LVOT and the aorta. It is superior and more leftward relative to the ventricular septum. Both the limb-lead morphology (aVL and I) and the precordial R-wave transition can be useful in differentiating anterior from posterior sites on the RVOT (Figure 9.1). The anterior RVOT sites showed a dominant Q wave or a qR complex in lead I and QS complex in aVL, whereas the posterior sites produced a dominant R wave in lead I and an early precordial transition ($R/S \geqslant 1$ by V_3) [27]. Site-specific ECG patterns are also observed for distinguishing septal from the free wall RVOT sites [36]. Free wall RVOT sites are associated with wider and "notched" QRS in the inferior leads and a late precordial R-wave transition ($R/S \geqslant 1$ by V_4). Such ECG algorithm allows accurate identification of outflow tract VTs, and is associated with a good sensitivity (88%) and specificity (95%) [21].

Other variants of outflow tract VTs include ventricular arrhythmias arising from the aortic cusps, pulmonary artery, and epicardial foci remote from the sinus of Valsalva. Limited electropharmacologic data are available for these arrhythmias. The anatomic considerations of the ventricular outflow tracts and the aortic sinuses are highly relevant for understanding of origin

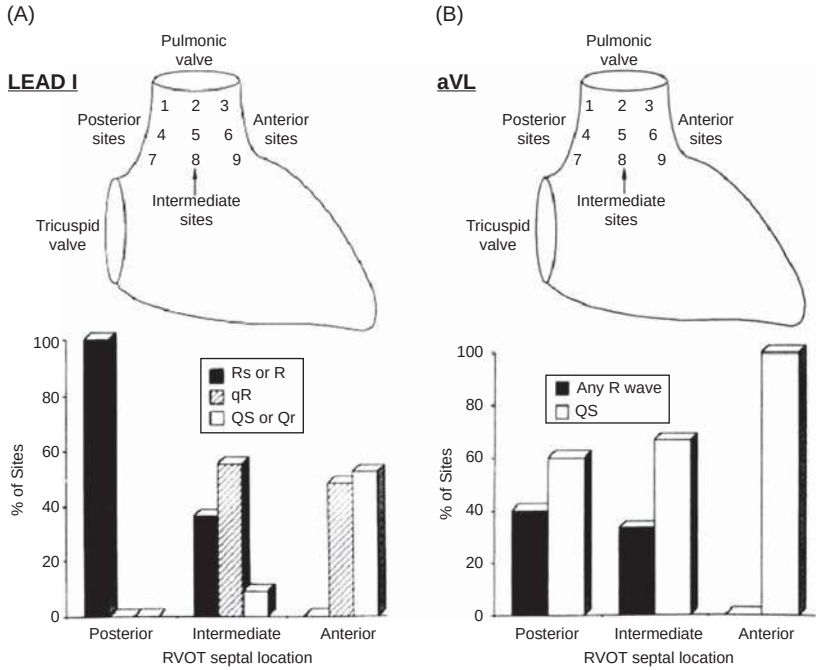

Figure 9.1 (A) Characteristic QRS morphologies observed in lead I while pacing the septal right ventricular outflow tact (RVOT) endocardial regions. The RVOT is divided into anterior, intermediate, and posterior sites. Posterior RVOT septal sites are associated with an R wave in lead I, while anterior septal RVOT sites result in qR or QS in lead I. (B) QRS morphologies in lead aVL with RVOT pacing. The anterior septal RVOT sites are associated with QS, whereas the posterior locations are associated with R waves in aVL (Reproduced with permission from Jadonath *et al.* [27])

of these arrhythmias. The RVOT consists of a complete muscular infundibulum to which the pulmonic valve is attached [37]. Ventricular arrhythmia may thus arise from the entire circumference of the RVOT. In contrast, the LVOT has part muscular and part fibrous walls. The noncoronary cusp and the posterior part of the left coronary cusp usually overlay the fibrous continuity between the aortic and the mitral valves; whereas a large part of right coronary and a portion of the left coronary aortic leaflets are related to the ventricular musculature [15,38,39]. Myocardial sleeves extending above the line of attachment of the semilunar valves are relatively common (22%) and are located near the adventitial–epicardial surface [40,41].

Case reports of idiopathic VT that failed ablation from RVOT and LVOT but were successfully ablated from the coronary cusp were first described in 1999 [42,43]. The electrocardiographic patterns associated with such arrhythmias that originate from the aortic sinus of Valsalva include LBBB, inferior axis morphology with tall monophasic R waves (lack of S wave), and an early precordial R-wave transition ($R/S > 1$) by V_2 or V_3 [19,21]. VT from the left aortic cusp had an rS pattern in lead I, and VT arising from the posteriorly

situated noncoronary cusp had a notched R wave in lead I [44]. Compared to RVOT arrhythmias with similar LBBB-inferior QRS pattern, the relative R-wave duration (R-wave duration index $>55\%$) and the R/S amplitude ratio in leads V_1 and V_2 were significantly greater for VT originating from the aortic sinus cusp [15]. Ventricular arrhythmias originating from the junction between the right and the left aortic cusps have also been identified recently. Arrhythmias arising from this location have unique ECG characteristics, namely a qrS pattern in the right precordial leads (V_1–V_3) and a narrow QRS duration, which is highly specific in distinguishing this site from other locations in the right or left outflow tracts and the aortic cusps [39].

The potential for acute coronary artery occlusion is a major risk consideration with catheter manipulation within the aortic cusps. Coronary angiography or intracardiac ultrasound imaging have been used to define the anatomy and the proximity of the coronary ostia to the ablation site (Figure 9.2). RF energy can be safely delivered in the aortic cusp and is associated with a long-term efficacy (~90%) in eliminating aortic cusp VTs [15,44,45]. The presence of double, delayed potentials during sinus rhythm may be predictive of the site of successful ablation [15].

Epicardial left ventricular VT originating remote from the sinus of Valsalva may occur in ~9% of patients referred for catheter ablation and represents a clinically under-recognized variant of idiopathic VTs. These arrhythmias often originate from the epicardial surface of the left ventricle, along the distribution of major epicardial vasculature [16,46]. The arrhythmia typically demonstrates catecholamine enhancement and adenosine sensitivity, most compatible with triggered activity as the underlying mechanism. However, the anatomic substrate with the predilection for perivascular regions along the epicardial veins is unclear.

The idiopathic epicardial VTs commonly have an LBBB pattern because the arrhythmia foci are located along the interventricular veins near the septum,

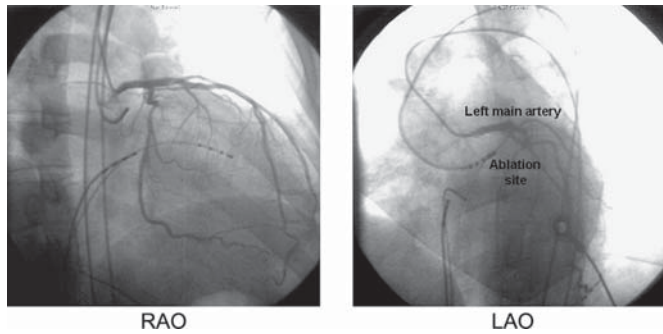

Figure 9.2 Mapping and ablation of idiopathic ventricular tachycardia originating from the left aortic cusp. Fluoroscopic images of the ablation catheter located at the aortic cusp in right anterior oblique (RAO) and left anterior oblique (LAO) views. Simultaneous coronary angiography is performed to visualize the left main artery to assess its distance from the ablation site

although right bundle branch block (RBBB) QRS morphology can be observed [16,46]. The ventricular activation is usually slow with a slurred QRS onset that resembles a delta wave. The interval from the onset of the QRS to the earliest maximal deflection in the precordial leads is also prolonged, consistent with a delayed access of the activation wave front to the endocardial Purkinje system [16,47]. Epicardial mapping and ablation via the epicardial vein with coronary sinus cannulation, or direct access with percutaneous pericardial catheterization can be successfully performed [48]. Surgical approach may also be considered in rare patients with unusual anatomic constraints.

Idiopathic VTs originating from tissues above the pulmonic valve have also been described (PAVT) [49,50]. Although the PAVTs have features similar to those of the RVOT arrhythmias (LBBB-inferior axis), certain electrocardiographic and electrophysiologic characteristics are notable. Compared to arrhythmias originating from the RVOT, R-wave amplitudes on inferior leads, aVL/aVR ratio of Q-wave amplitude, and R/S ratio on lead V_2 are significantly greater with PAVTs. These findings can be explained by the fact that the site-of-origin within the pulmonary artery is higher than that in the RVOT, and the anatomic location is more leftward and more anterior. The pulmonary artery VTs appear to arise from remnants of muscular sleeves that extend into the pulmonary arterial trunk [47,48]. This is supported by the presence of a sharp local potential that precedes the onset of ventricular activation during VT at the site of successful ablation [37,49,50]. During sinus rhythm, an atrial potential is frequently recorded (>58%) along with a diminished, low-amplitude local ventricular potential at the successful ablation site (Figure 9.3).

Despite careful mapping and use of sophisticated techniques, identifying the precise location of arrhythmias may be difficult because of the complex anatomic relationship and the proximity of various structures from the venous and arterial circulations. Significant overlaps in electrocardiographic features in predicting the area of origin can be observed [13]. Precise localization relies on the combined use of pace mapping and activation mapping, as well as a detailed appreciation of the anatomy. In addition to electroanatomic mapping, the use of intracardiac or transesophageal ultrasound to identify anatomic landmarks and catheter contact may facilitate ablation of idiopathic outflow tract or aortic cusp VTs (Figure 9.4) [51]. A stepwise systematic approach, from endocardial mapping and then epicardial mapping up to six anatomic accesses (RVOT, LVOT, coronary sinus, aortic cusp, pulmonary artery, and LV epicardium), can lead to successful RF catheter ablation [13].

Annular ventricular tachycardias

Idiopathic ventricular arrhythmias can also arise in proximity to the valvular annuli. Focal VTs from the mitral annulus (MAVT) accounted for 5% of the idiopathic VTs in one series [12]. The arrhythmia typically has an RBBB morphology and may originate from different portions of the mitral annulus (anterolateral, posterior, and posteroseptal), resulting in different QRS axis.

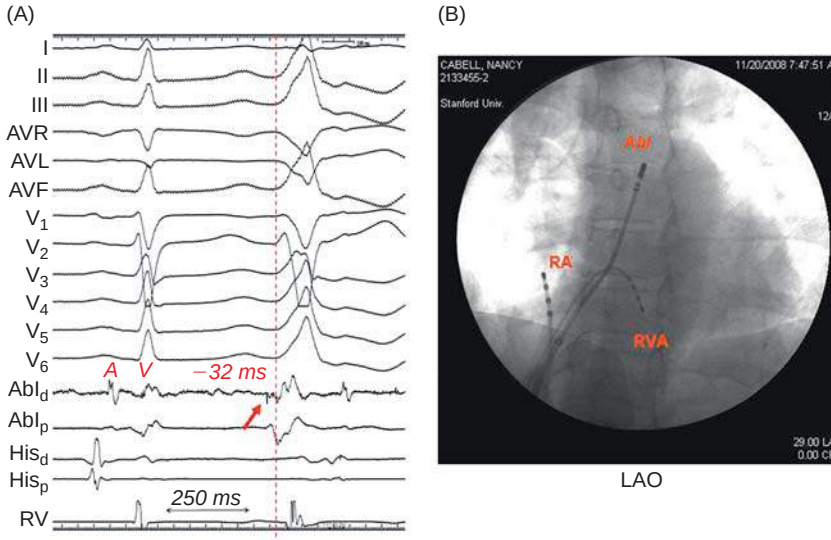

Figure 9.3 (A) Successful catheter ablation site of ventricular tachycardia originating from the pulmonary artery. Characteristic ECG patterns were noted with intracardiac recordings demonstrating a sharp presystolic potential associated with the premature ventricular contraction. During sinus rhythm, the successful site has a large atrial electrogram signal with relatively small local ventricular electrogram amplitude. (B) Fluoroscopic images of the ablation catheter located at the main pulmonary artery in the left anterior oblique (LAO) view

Polarity of the QRS complex in the inferior leads, leads I and aVL, is useful for differentiating various origins of mitral annular VTs [20]. A delta wave-like QRS onset, a late intrinsicoid deflection, early precordial transition, and an S wave in lead V_6 are often observed [11,12]. Most MAVTs could be successfully eliminated by RF energy applications to the endocardial mitral annulus, with the successful target site recordings of nearly equal amplitudes of atrial and ventricular signals [11,52].

Idiopathic ventricular arrhythmias originating from tricuspid annulus (TAVT) have also been described recently [14]. The predominant (74%) site-of-origin is located at the septal portion of the tricuspid annulus with the remaining arrhythmias arising from the annular free wall. The detailed origin can be determined by ECG analysis based on QRS duration, precordial Q-wave amplitude, "notching" of the QRS complex, and the R-wave transition. RF catheter ablation appears to be less effective for VT/PVCs from the septal tricuspid annulus compared to that originating from the tricuspid free wall. The most likely reason for the failure is the inadequate RF energy delivery near the annular septum for fear of creating AV block. However, arrhythmia site-of-origin located deep in the septum or at left endocardial surface of the septum may also play a role.

Repetitive monomorphic right VT originating near the His-bundle may be recognized as a specific entity with distinctive ECG characteristics [53].

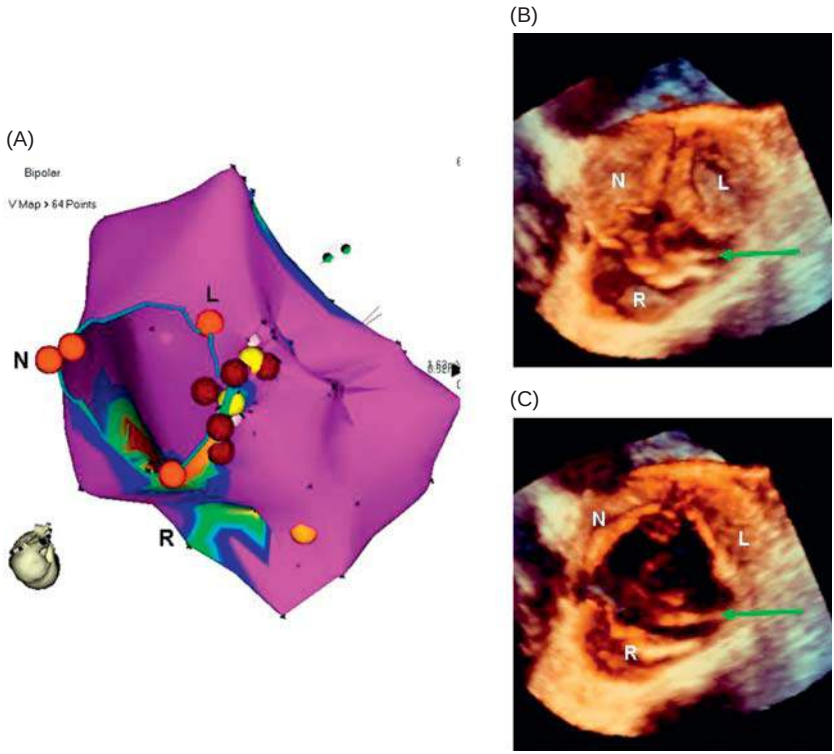

Figure 9.4 (A) A coronal view of an electroanatomic voltage map. The right and left cusps (orange tags) as well as the noncoronary cusp (N) are displayed. Normal voltage (color purple: >1.5 mV) was noted without scar. Successful ablations were performed at the commissure between the right and the left cusps. (B) Images from the 3D transesophageal echocardiogram with a coronal view of the aortic valve during diastole when the valves are closed. The aortic cusps are designated as right (R), left (L), and noncoronary cusp (N). The arrow depicts the ablation catheter beneath the valve plane with the cusps coapted. The catheter tip is located at the commissure between the right and the left aortic cusps. (C) The same view of the aortic valve plane during systole when the cusps are opened

Recognition of this arrhythmia is important because of its unique location and the potential risk associated with catheter ablation. His-bundle is located inferior and leftward of the RVOT. Compared to the RVOT arrhythmias, the para-Hisian VTs have: (1) a relatively low R-wave amplitude in the inferior leads, especially a smaller R wave in lead III than in lead II; (2) a narrower QRS duration; (3) a monomorphic tall R wave in lead I; (4) an R wave in aVL; and (5) a QS pattern in lead V_1. Knowledge of the characteristic QRS morphology will facilitate catheter mapping and successful ablation (Figure 9.5). The use of a supporting sheath to assure catheter stability, careful RF energy power/temperature titration, and cryoablation may improve the outcome and minimize complication [53,54].

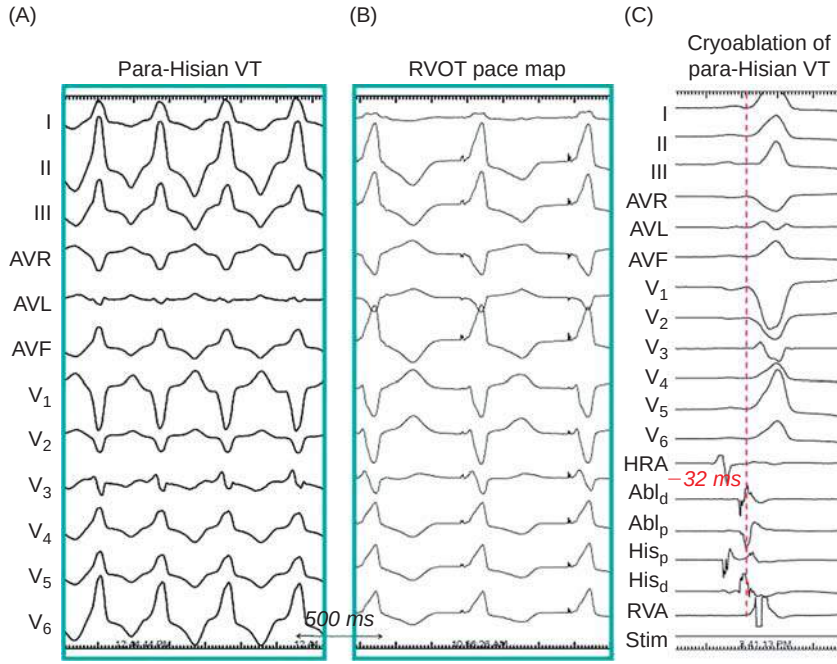

Figure 9.5 (A) Characteristic ECG patterns associated with idiopathic ventricular tachycardia (VT) originating near the His-bundle. Compared to the QRS morphology created from pacing in the right ventricular outflow tract (RVOT) sites (B), the para-Hisian VTs have (1) a monophasic tall R wave present in lead I; (2) a smaller R wave in lead III than in lead II; (3) an R wave present in lead aVL; and (4) a QS pattern in lead V_1. (C) Cryoablation of VT originating from the para-Hisian region. A sharp presystolic potential (−32 ms) was present at the successful ablation site

Verapamil-sensitive intrafascicular tachycardia

Intrafascicular left ventricular verapamil-sensitive VT (ILVT) occurs in patients without structural heart disease. This form of VT was first recognized in 1979 by Zipes *et al.*, who identified the characteristic diagnostic triad: (1) induction with atrial pacing; (2) RBBB with left axis deviation; and (3) manifestation in patients without structural heart disease [55]. In 1981, Belhassen *et al.* demonstrated verapamil sensitivity as a fourth diagnostic feature of this tachycardia [56]. The mechanism of ILVT is reentry within the Purkinje fibers of the left ventricular septum, most often arising from the left posterior fascicle with a characteristic RBBB superior axis deviation (Figure 9.6) [5,57–59]. Less often, the reentry circuit is located in fibers distal to the anterior fascicle or may arise from fascicular locations high in the septum, and has a relatively narrow RBBB pattern and right inferior axis deviation (Figure 9.7) [60]. Fascicular tachycardia usually presents in patients between 15 and 40 years of age, in the absence of structural heart disease. ILVT can be incessant and, because of this, it may cause a reversible tachycardia-mediated cardiomyopathy. Sudden cardiac death is rarely associated with this arrhythmia. Although

ILVT can occur at rest, it is sensitive to catecholamines and often occurs during exercise, post exercise, or emotional distress.

Verapamil is effective in both the short-term and the long-term treatments of this arrhythmia. RF catheter ablation can be performed successfully (>80%) from the VT exit site (at the site of earliest ventricular activation), or the zone of slow conduction where a Purkinje potential was recorded in diastole during VT [61]. Critical sites of the reentrant circuit can also be identified by the earliest retrograde Purkinje network activation during sinus rhythm [59]. For patients with noninducible or nonsustained ILVTs, a linear ablation strategy (mean 1.7 cm) perpendicular to the long axis of the ventricle, targeting the mid-inferior septum marked by the presence of Purkinje potentials in sinus rhythm and the best pace map match of the VT, has been shown to be safe and effective for VT control [62].

Idiopathic ventricular fibrillation

Idiopathic VF in the absence of structural heart disease or surface ECG abnormalities accounts for 5–10% of survivors of out-of-hospital cardiac arrest. The diagnosis is made by consensus criteria by the exclusion of other potential causes of VF. Following diagnostic workup, the widely accepted management of idiopathic VF is the insertion of an ICD to prevent sudden cardiac death. Use of class 1a antiarrhythmic drugs has also been proposed as they have been shown by Belhassen *et al.* to prevent re-induction of tachycardia during acute testing. These patients may suffer from drug refractory storms of arrhythmia resulting in multiple shocks from implanted devices and requiring frequent generator changes. Particularly in this setting, a curative ablative strategy is an attractive alternate.

Recent work has demonstrated that the Purkinje network is critical in the triggering and maintenance of VF in animal experiments and patients [63–65]. Catheter ablation targeting the ventricular ectopic(s) or Purkinje potentials responsible for triggering VF, or both has been shown to be both possible and efficacious in a number of conditions, ranging from the Brugada syndrome, to ischemic VF, to idiopathic VF. Although there are relatively few reports of catheter ablation of VF in the literature, the method appears robust as it is being repeated by a number of different groups around the world.

To map and then ablate VF using the methods that are described in the following text, it is essential that there is accurate documentation of the triggering VPB, with a 12-lead ECG (Figures 9.9 and 9.10). Because of the unpredictable nature of triggering beats, the optimal time for ablation is often at the time of an electrical storm when the VPBs tend to be frequent. The source of triggers is localized by the earliest electrogram relative to the onset of the ectopic QRS complex. An initial sharp potential (<10 ms in duration) preceding the ventricular electrogram during sinus rhythm as well as during premature beats indicates that the latter originates from the Purkinje system, whereas its absence at the site of earliest activation indicates an origin from

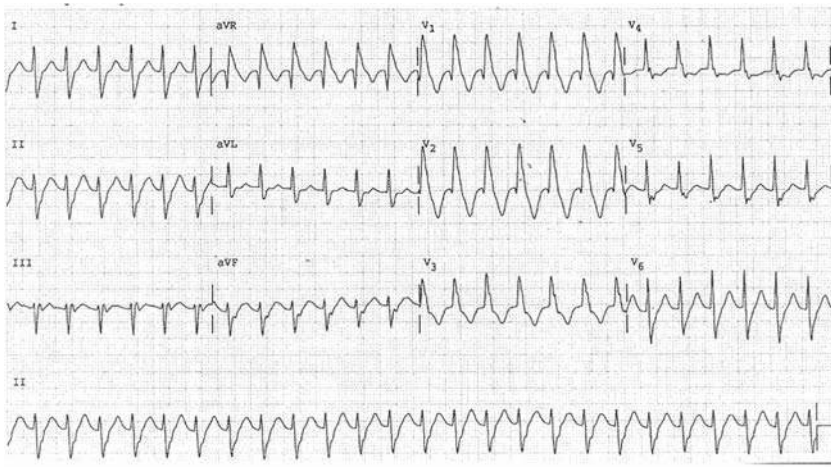

Figure 9.6 A 12-lead electrocardiogram of idiopathic left ventricular tachycardia often involves the left posterior fascicle at the mid-inferior left ventricular septum. A right bundle branch block QRS morphology and a superior-left axis are characteristic for such "verapamil-sensitive" ventricular tachycardia

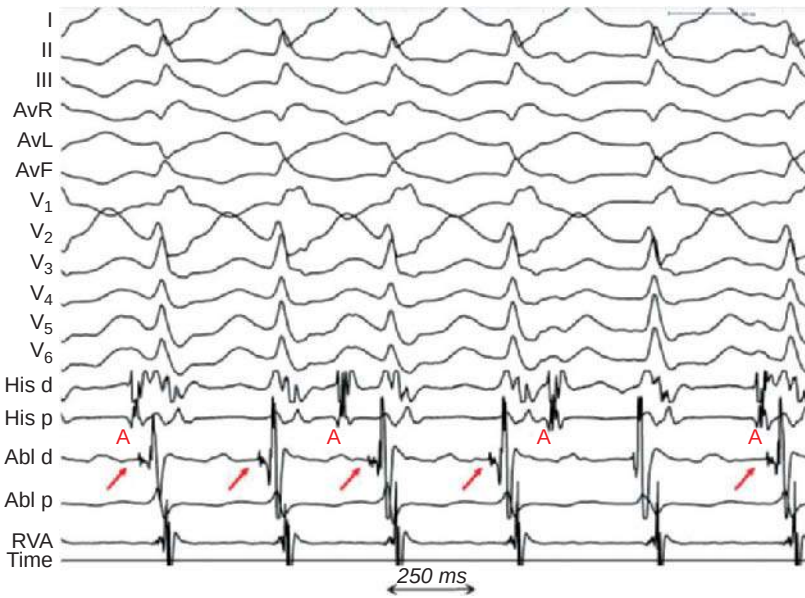

Figure 9.7 An example of an idiopathic left ventricular tachycardia involving the left anterior fascicle. The electrocardiographic pattern showed a right bundle branch block, right-inferior axis. A presystolic Purkinje potential (arrows) was recorded with cycle length oscillation. Ablation at this site was successful in eliminating the ventricular tachycardia

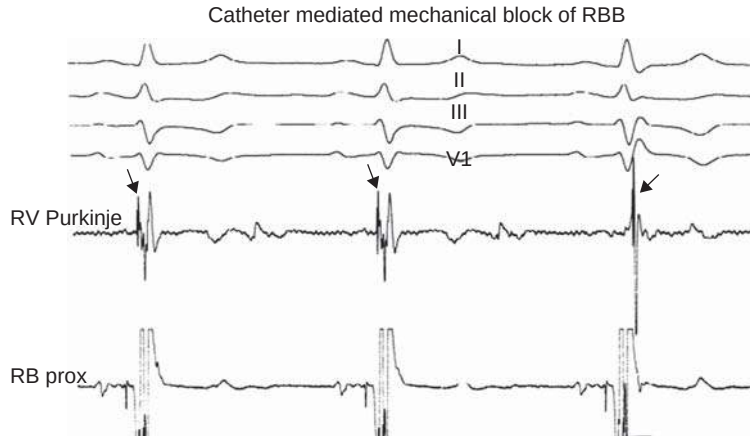

Figure 9.8 Catheter manipulation produced right bundle branch block (RBBB) (distal to the recording site of proximal bundle). As a result, peripheral Purkinje potential (arrows) no longer preceded the local ventricular activation in sinus rhythm because it is now buried within the ventricular electrogram

ventricular muscle. Great care should be taken to avoid mechanical bumping of the right bundle branch while mapping as this would mask ipsilateral Purkinje activation during sinus rhythm (Figure 9.8).

Myocardial ectopics triggering ventricular fibrillation

As mentioned in the preceding text, the RVOT is the most common site-of-origin of VT in structurally normal hearts and this is true for ectopics triggering malignant monomorphic or polymorphic VT, which rapidly degenerates into VF. A study by Noda *et al.* [66] investigated 16 patients with episodes of idiopathic VF or polymorphic VT triggered by premature ventricular ectopics that arose from the RVOT. All patients had documentary evidence of a ventricular ectopic beat triggering VF or polymorphic VT, and prior to the procedure, frequent ventricular ectopic beats with a morphology identical to that of the triggering beat were present. The coupling interval of the triggering ventricular ectopic beats was relatively late, 409 ± 62 ms. The culprit ventricular ectopic beat was mapped in a conventional manner, and ablation was targeted to the site of earliest activation and pace mapping. With the exception of one patient, an area was ablated around the most successful site, as determined by cessation of ventricular ectopics with ablation. During the follow-up period of 54 ± 39 months, no patient experienced VF, syncope, or cardiac arrest, with 11 patients free from all antiarrhythmic drugs.

This type of ablation is essentially no different to ablation of idiopathic RVOT ectopy or VT with a discrete and usually solitary focus located in a well-defined anatomic region. The coupling interval is significantly longer

for ectopics of an RVOT origin compared with short-coupled Purkinje origin (mean coupling interval of 300 ms). Furthermore, the number of ectopics to guide mapping is usually very high in contrast to the capricious occurrence of ectopics in other patients with idiopathic VF.

Purkinje-triggered idiopathic ventricular fibrillation

Anatomically, the Purkinje system is a small fraction of the myocardial mass, consisting of specialized fibers insulated from the underlying ventricular myocardium till their peripheral arborization into the muscle. It ramifies from a single branch in the anterior wall of the right ventricle, whereas in the left ventricle at least two fascicles are profusely interconnected over a wide area in the septum. Accordingly, there were relatively uniform electrocardiographic morphologies for right Purkinje sources, whereas left sources displayed more strikingly different morphologies, however with a short QRS duration. While narrow ventricular beats are certainly strong ECG markers that can be used to noninvasively identify Purkinje origin, the specificity of close-coupled premature beats in indicating Purkinje triggering needs to be assessed. What is still undetermined is how much of the complex Purkinje network is involved in each patient, and the issue of multiple foci versus differing activation routes from limited foci requires further studies with appropriate mapping tools.

In the earlier report [64], 23 consecutive patients from five centers underwent attempted ablation of primary (i.e., not secondary to monomorphic VT) idiopathic VF. Six patients had a family history of sudden death. In 19 patients, VF as well as premature beats was temporally clustered within a few days (electrical storm) while the remaining four patients had persistent ventricular arrhythmias over long periods of time. A mean of 4 ± 2 (median 4) oral antiarrhythmic drugs were unsuccessfully tried, including Vaughan–Williams class I drugs in 19 patients, beta-blockers in 16, amiodarone in 11, and verapamil in 13 (despite the efficacy of intravenous verapamil in suppressing all ectopics or polymorphic VT in 7 patients). Facilitating factors were found in some patients, similar to those described for VF occurring in the Brugada and long QT syndromes, fever or infectious disease, electrolyte disturbances (hypercalcemia or hypokalemia), and drug exposure.

Electrocardiogram morphology of Purkinje beats

The 12-lead ECG showed different characteristic morphologies of premature beats (Figure 9.9). Their coupling interval was usually variable with runs of repetitive beats or VF initiated at the shortest coupling intervals (297 ± 41 ms) in all but three patients: coinciding with the peak of preceding T wave (R on T phenomenon) or its descending slope. Interpolated beats were frequently noted. During hospitalization immediately prior to ablation, 20 patients had frequent premature beats; 3 patients had no ventricular premature beats at

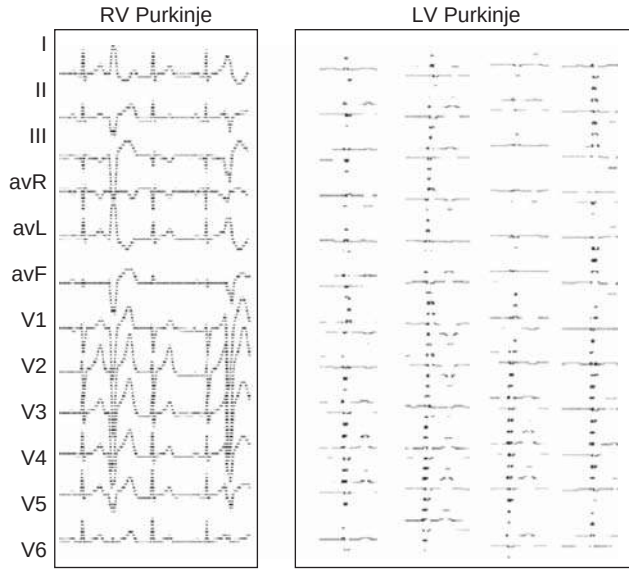

Figure 9.9 The 12-lead morphologies of Purkinje beats. Those from left ventricular origin are polymorphic with significant morphologic variations predominantly in limb leads with, however, a characteristically short QRS duration. Those from right ventricular origin have a superior axis and display subtle morphologic differences

the time of mapping, but there was prior 12-lead documentation of spontaneous initiating beats. Premature beats with a positive morphology in V_1 (left ventricular origin) were polymorphic in all patients but two, exhibiting significant morphologic variations predominantly in limb leads with, however, a characteristically short QRS duration (115 ± 11 ms) similar to that seen during left fascicular VT. Premature beats negative in V_1 (right ventricular origin) had a superior axis and displayed a significantly longer QRS duration (143 ± 10 ms). Subtle morphologic differences were observed in 10 patients, and a strictly monomorphic pattern was observed in 3; an initial rapid ventricular depolarization (R wave <40 ms in V_1, V_2) was noted in 10.

Endocardial mapping and ablation

The use of polygraph system at high sampling rate (>2 kHz) and high gain amplification (commonly 1 mm = 0.1 mV) was optimal to clearly identify Purkinje potentials. In 20 patients with frequent ventricular ectopy, the site-of-origin was as follows: right ventricle in seven patients, left ventricle in nine, and both ventricles in four (three with a family history of sudden death). The three patients without ectopy were considered to have Purkinje beats based on identical morphologic characteristics of spontaneous beats previously documented on 12-lead ECG. The Purkinje sources were localized to a limited part of the anterior right ventricle or in a wider region of the

lower half of the septum in the left ventricle: from the ramifications of anterior or posterior fascicles resulting in superior and inferior axis, respectively, and from the intervening region resulting in intermediate morphologies. Recording of stable Purkinje activity was more difficult in the right ventricle. During premature beats, the earliest Purkinje potential preceded the local muscle activation by a conduction interval of 38 ± 28 ms, with a greater precocity in the left than in the right ventricle (46 ± 29 ms vs 19 ± 10 ms). At the same site, differing conduction times were associated with varying morphologies suggesting either changes in ventricular activation route or origin from another part of Purkinje system. During sinus rhythm however, the Purkinje potential closely preceded the ventricular muscle activity by 11 ± 5 ms, indicating distal arborization. Importantly in 10 patients, multiple repetitive beats were recorded, with each complex being preceded by a Purkinje potential strongly suggesting their active role in perpetuation of VF (Figure 9.10).

Ablation of Purkinje beats frequently produced temporary exacerbation of arrhythmia (including VF) followed by a disappearance of premature beats. Different morphologies were progressively eliminated by ablation at multiple sites with early Purkinje potential using a mean of 9 ± 5 (range 2–19) RF applications. Local electrograms showed the abolition of the local Purkinje potential and a slight delay in the occurrence of the local ventricular

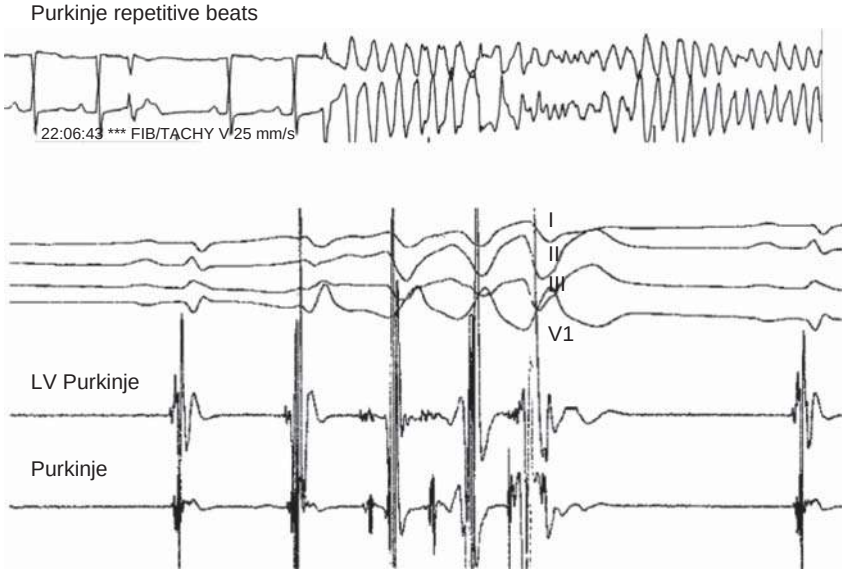

Figure 9.10 The top tracing shows initiation of ventricular fibrillation on Holter recording with the initiating beat shown later to originate from the Purkinje tissue. On the bottom tracing, repetitive Purkinje ectopic beats are recorded with each complex being preceded by a Purkinje potential with a variable delay ranging from 15 to 120 ms, and variable relationship between proximal and distal recording bipoles

electrogram. In three patients, transient abrupt QRS widening suggestive of left anterior or posterior hemiblock was observed during inadvertent catheter movement toward the proximal Purkinje system, associated with a Purkinje-muscle interval >15 ms.

In the three patients without ectopy, the putative source of premature beats was ablated in sinus rhythm based on pace mapping followed by RF delivery at local sites exhibiting Purkinje potentials.

Follow-up

During a follow-up of 24 ± 28 months, there was no sudden death, syncope, or recurrence of VF in 21 of 23 patients (91%) including all 3 without ectopy during mapping.

There have also been a number of case reports of successful VF ablation for patients with idiopathic VF. Using the EnSite array with virtual unipolar electrodes, successful ablation of a ventricular ectopic that initiated VF was successfully performed, with the source of ectopy being the right free wall [67]. Following the procedure, the patient was free of ventricular arrhythmia in a follow-up period of 11 months. Several other groups have reported successful ablation of ventricular ectopics triggering VF, again with a Purkinje potential seen prior to the triggering ectopic, and also located in the anterior right ventricular wall or the left ventricular septum [68–71]. The patients in these reports were free of ventricular arrhythmia in the follow-up period of up to 6 years, despite having multiple episodes of syncope or VF prior to the procedure.

Summary

In summary, there have been significant advances in our understanding of the multiple forms of VTs occurring in patients without structural heart disease. Recognition of these idiopathic VTs has important clinical value because specific electropharmacologic profiles exist for selection of appropriate antiarrhythmic drug therapy. In addition, curative intervention with catheter ablation can be performed.

Idiopathic VTs are commonly associated with characteristic QRS morphologies, and the 12-lead electrocardiography can provide important clues to the probable location of the arrhythmia. However, precise localization of the site-of-origin may be difficult because of the complex relationship and the proximity of various anatomic structures. Successful catheter ablation depends on a detailed appreciation of the anatomy, as well as a systematic mapping approach. Multielectrode recordings, electroanatomic mapping, or noncontact mapping systems may facilitate the procedure and attain a high success rate.

Catheter ablation of polymorphic VT and VF still in its infancy is indicated in patients with frequent ICD discharges and having triggering premature beats. The above-mentioned reports demonstrate that it is possible to

eliminate the recurrence of idiopathic VF by catheter ablation of the source(s) in the specialized conduction system as proved by implanted devices in a relatively large cohort of patients from multiple centers. Further attempts at mapping and ablation in these patients may require specific mapping tools to facilitate these techniques.

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CHAPTER 10

Acute and Periprocedural Complications

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Overview

Radio frequency catheter ablation has become a major therapeutic option for ventricular tachycardia (VT), particularly when drugs are ineffective in preventing recurrences. Despite significant advances in mapping and ablation technique, there are still some complications associated with ablation of VT.

Idiopathic VT mostly originating from the right (RVOT) or left (LVOT) ventricular outflow tract can be successfully treated by ablation in the majority of cases [1]. Serious complications are generally rare, ranging from 0% to 4% and include pericardial effusion/tamponade, heart block, coronary artery injury, and damage to the aortic valve [2–8]. Death was reported in one case as following right ventricular perforation [9]. Data regarding idiopathic VT originating from the pulmonary artery, aortic cusp, or mitral annulus are limited. Therefore, ablation risks are not well defined in this setting [10–15]. However, injury to the left main or right coronary artery is a potential complication of aortic cusp VT ablation. Careful energy titration, and intraprocedural imaging including coronary angiography or intracardiac ultrasound, may help minimize this complication [12].

In patients with VT associated with structural heart disease, catheter ablation appears associated with a greater risk of complications. This is likely related to the more extensive mapping and ablation associated with these procedures, and greater prevalence of concomitant comorbidities in this population. In two large multicenter studies, major procedural complications

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ranged from 3.8% to 8% [16,17]. Death was reported in 2.7% of cases [17]. In more recent investigations, cardiac tamponade, stroke, transient ischemic attack, hemodynamic deterioration, valve damage, vascular injury, and heart block have been reported (Table 10.1).

Only few reports have been published on catheter ablation of VT in arrhythmogenic right ventricular cardiomyopathy. The incidence of severe complications appears low; right ventricular perforation in the presence of extensive fibrofatty replacement of the free wall, remains a risk [26–29]. Bundle branch reentry tachycardia is an uncommon clinical entity, which can be treated by catheter ablation [30,31]. These patients often have extensive preexisting infranodal conduction disease, and advanced heart block requiring pacing may occur in 10–15% of patients. Ventricular fibrillation (VF) can be triggered by ventricular premature beats originating from the Purkinje system of both ventricles [32]. Catheter ablation of the arrhythmogenic source has been demonstrated to prevent recurrences of idiopathic VF [33]. Even after myocardial infarction, electrical storm could be treated by the ablation of triggering premature beats [34–36]. However, experience is limited and procedural risks have been not exactly established. It can be speculated that complications in part depend on the patient conditions at the time of ablation. In addition, the same complications observed for VT ablation, with particular regard to the damage of the conduction system, may potentially occur in VF ablation procedures.

Thromboembolic complications

Incidence and high risk

The thromboembolic complication rate of general electrophysiologic study is reported to be 0.7–0.8%. The rate of thromboembolic events increases to 2.8% in the ablation of ventricular arrhythmias [16,37,38]. Ablation of ischemic VT is likely to have a greater risk than is observed for ablation of idiopathic VT or supraventricular tachycardia. Higher incidence of thromboembolic events in the VT patients might be related to the site of ablation (frequently the left ventricle), longer procedure time, multiple RF current applications, preexisting atherosclerotic aortic disease, and the possibility of preexisting thrombus, which was not detected by transthoracic echocardiography. The coronary artery can be damaged by inadvertent insertion of the ablation catheter, which can traumatize an atherosclerotic plaque.

Strategies to minimize thromboembolic complications

Several attempts to avoid the occurrence of thromboembolic complications during catheter ablation have been tried. Aspirin is prescribed (81–325 mg) just before the procedure and an optimal dose of heparin is infused for systemic anticoagulation. During the procedure, an intravenous bolus of unfractionated heparin 80–100 units/kg is injected and then ACT is monitored every 30 min to maintain its level between 300 and 400 s. When using transseptal

Table 10.1 Incidence of acute and periprocedural complications of ablation of VT/VF

Authors	*Year*	*Number of patients*	*Heart disease*	*Major complications*	*Death*	*Tamponade*	*Stroke/TIA*	*Shock*	*Heart block*	*Vascular injury*	*Aortic valve damage*	*Others*
Calkins *et al*. [17]	2000	146	I, NI	12 (8%)	4 (2.7)	4 (2.7)	4 (2.7)		2 (1.4%)	1 (0.7%)	1 (0.7%)	
Soejima *et al*. [18]	2001	40	I	4 (10%)						4 (10%)		
Marchlinski *et al*. [19]	2000	16	I, NI	1 (6%)			1 (6%)					
O'Donnel *et al*. [20]	2002	112	I	7 (6%)		3 (2.6%)	1 (0.9%)		2 (1.8%)	1 (0.9%)		
Kottkamp *et al*. [21]	2003	28	I	1 (3.5%)			1 (3.5%)					
Arenal *et al*. [22]	2004	26	I	0								
Ventura *et al*. [23]	2008	30	I	1 (3%)					1 (3%)			
Klemm *et al*. [24]	2007	12	I	2 (17%)				1 (8%)	1 (8%)			
Stevenson *et al*. [25]	2008	231	I	34 (15%)	7 (3%)	1 (0.4%)		12 (5%)		12 (5%)		9 (4%)

TIA, transient ischemic attack; I, ischemic cardiomyopathy; NI, nonischemic cardiomyopathy.

approach, an intravenous heparin bolus (5000–8000 units) is infused at least 5 min before the transseptal puncture. For the patients who show VT of epicardial origin, heparin is started after pericardial puncture if endocardial LV mapping is performed concomitantly. After ablation, prolonged anticoagulation may be required in some patients as thromboembolic complications can occur even 3 months after ablation [39,40]. Therefore, patients with severe LV dysfunction, LV aneurysm, or other risk factors (diabetes, history of prior embolic events), should receive warfarin for 3 months. Aspirin could be substituted for warfarin in patients who are at minimal to moderate risk.

Second, it is important to monitor the change in the impedance of the ablation catheter during delivery of radio frequency (RF) energy. As RF energy is delivered to the tissue through the ablation catheter, the measured impedance decreases by about 10% from baseline, but a sudden increase in the impedance of more than 20 ohms is associated with coagulum formation. Although a thrombus can form without impedance rise in an animal model [41], careful monitoring of impedance during RF is helpful to prevent thrombus formation or "steam-pop" during ablation.

Transthoracic echocardiography and transesophageal echocardiography should be used for routine screening of mural thrombus in the cardiac chamber, especially for ischemic VT with LV dysfunction. For patients with severe atherosclerotic aortic disease, catheter access via transseptal approach should be considered to avoid thromboembolic complications.

To make large transmural lesions without unfavorable heating injury and thromboembolic complications, a cooled RF ablation catheter is preferable. Although thromboembolic complications are rare during open-irrigated catheter ablation [25], one animal study showed no significant difference in the rate of thrombus formation among open-loop irrigation, closed-loop irrigation, and conventional ablation catheters [42]. For ischemic VT ablation, open-irrigated catheter ablation demonstrated greater success rates compared to conventional catheter ablation [17,43].

Perforation and tamponade

Incidence of cardiac tamponade or hemopericardium requiring immediate drainage is 1–3% in catheter ablation performed for VT. This number is comparable to the incidence in catheter ablation for atrial fibrillation (0.8–2.4%) [44–46]. Ventricular perforation usually results in more serious hemodynamic deterioration because of higher chamber pressure of the LV. This can develop during transseptal puncture, catheter manipulation, or ablation. Perforation of the LV by the ablation catheter is uncommon because the LV is thicker, however, the thin-walled RV (particularly near the apex) may be more vulnerable to perforation by an ablation or pacing catheter, particularly during vigorous contractions associated with catecholamine infusion. For prevention of RV perforation, a power setting not exceeding 40 W and careful monitoring of the impedance are required. While percutaneous drainage of the hemorrhagic

effusion is usually sufficient, spontaneous closure of the perforation may not occur, and subsequent surgical intervention may be required [47]. RF ablation in the cardiac vein tributaries carries the risk of perforation because of low blood flow. The impedance frequently rises immediately after RF is turned on. Although there are no reported cases of perforation by low RF energy delivery inside the cardiac vein, cryoablation is a feasible alternate [48].

During urgent pericardiocentesis, retransfusion of aspirated blood has the risk of systemic inflammatory response [49]. Venkatachalam *et al*. [50] reported that the autologous blood recovery system (cell salvage system) is useful for reducing systemic inflammatory response, allogenous blood transfusion, and additional surgery.

Valvular complications

The incidence of valvular injury is reported to be 1.9% and is often minor [51]. Damage to the mitral valve can result from inadvertent manipulation across the valve, or from an injury to the papillary muscles or chorda tendineae during or after ablation of VT, particularly in patients with idiopathic VT or mitral annulus-dependent VT. In patients with VT originated from aortic cusp, damage to the aortic valve could occur, however, it rarely has been reported. To avoid these valvular complications, it is important to make sure there is no entrapment of the ablation catheter in these structures and to watch the change in impedance during RF delivery. Aortic valve damage requiring surgical correction developed in patients who had prior aortic valve disease and post-MI VT. For patients who have aortic valve regurgitation, a transseptal approach should be considered to ablate inside the LV. During RF energy delivery at the aortic cusps, temperature-directed ablation not exceeding 55 C could minimize aortic valve damage [12].

Mitral regurgitation associated with catheter ablation is thought to be caused by entrapment of the catheter tip by leaflet or chordate rather than direct injury of RF energy. RF ablation targeting the base of the papillary muscle can cause the mitral regurgitation [52].

Conduction system complications (AV block and new bundle branch block)

The rate of AV block or newly developed bundle branch block after VT ablation is known to be less than 1–2%. The incidence of these complications depends on underlying conduction disorder, the mechanisms of VT, and how close critical isthmus or VT foci are to the conduction systems. In patients with bundle branch reentrant tachycardia, the reported incidence of conduction system impairment requiring implantation of permanent pacemaker was 0–30% [30,53–55]. For patients with preexisting left bundle branch block and bundle branch reentry tachycardia, ablation of right bundle may cause complete AV block; however, a compensating conduction may occur through the

left bundle, suggesting that right bundle ablation may be safe in the majority of patients with baseline left bundle branch block. Ablation of the left bundle has been proposed as ideal, but this technique is difficult to perform and usually requires application of multiple lesions. A recent report showed persistent slow conduction over the left bundle in patients with bundle branch reentry and ablation of left bundle using electroanatomical mapping showed successful bundle branch reentry ablation without producing AV block [56].

For ablation of left posterior fascicular VT, ablation at the apical third of the inferior septum is preferred to avoid producing a left bundle branch block or AV block.

Worsened heart failure or left ventricular function

Sustained VT is an important cause of morbidity and sudden death in patients with heart disease. In patients with significant heart disease, VTs are frequently unmappable, because of the hemodynamic intolerance [57]. In addition, VTs can change from one form to another. For these reasons, substrate mapping or multielectrode mapping approaches have been developed to guide ablation of these VTs. These approaches can involve multiple applications and long lines of RF lesions in already deteriorated LV function. Unfortunately, few data are available on the real impact of catheter ablation on LV function.

In a short series, Marchlinski *et al*. [19] reported that none of their six patients in whom LV ejection fraction was measured before (mean 24 ± 6%) and after (mean 23 ± 9%) ablation suffered deterioration greater than 5%. In another series of 62 patients, Khan *et al*. [58] reported that multiple RF ablation lesions confined to infarct regions did not measurably affect LV function. Sites of successful post-MI ablation of monomorphic VTs are often located in the scar border zone, as defined by substrate voltage mapping [59]; for this reason, it is prudent to try to confine ablation lesions to the low-voltage scar in patients with LV dysfunction.

Coronary artery injury and complications

Thermal injury to the coronary arteries has been described during the ablation of various arrhythmias, including atrioventricular reentrant tachycardia, atrial flutter, and VT [60,61]. Septal regions of the RVOT, especially in the region of the pulmonary valve, are in close proximity to the left main coronary artery, and in most cases within the penumbra of potential ablation sites of VT. Quantitative CT, invasive angiography, and echocardiographic studies also show that the left main coronary artery, left anterior descending, and right coronary artery are in close proximity to the RVOT. Coronary artery stenosis has been found to be a late consequence (12–24 months) of vessel trauma or vasospasm. In a canine model, D'Avila *et al*. reported that the

effects of RF ablation performed in proximity to the left anterior descending were limited to the media, but when RF was delivered directly to the artery, severe intimal hyperplasia and intravascular thrombosis developed 14 days postablation. Moreover, susceptibility to damage is inversely proportional to the vessel size [62].

As the use of catheter ablation is increasing, especially in children and young adults, a detailed understanding of coronary artery anatomy is critical for safe ablation. Coronary arteriography or ICE may be considered when ablation sites are in the high-septal aspect of the RVOT [63]. When the distance between the coronary arteries and the ablation sites is found to be less than 5 mm, cryoablation or 4 mm tip catheters may be considered, in order to avoid short- and long-term damage to the coronary arteries.

Transthoracic epicardial ablation of VT has recently been shown to be feasible, primarily in patients with Chagas heart disease, ischemic heart disease, and dilated cardiomyopathy. However, the safety and efficacy of epicardial RF ablation, especially in the vicinity of the coronary artery, remain unclear. Kawamura *et al*. showed that epicardial RF ablation lesions close to the coronary artery were shallower and smaller than those further from the coronary artery, and that no damage to major epicardial arteries occurred when the catheter tip was positioned 5 mm away from these arteries and an irrigated-tip ablation catheter was used [64].

In order to avoid coronary artery injury, coronary angiography is usually performed to visualize the relationship between RF target sites. This approach, however, requires frequent coronary contrast injections in different projections. Recently, some authors have suggested a different approach based on the fusion of CT and endocardial and epicardial electroanatomical mapping data to improve visualization of the catheter tip in relation to the epicardial coronary arteries [65].

Vascular access complications

Aortic atheroembolism

The formation of multiple cholesterol emboli is a rare but serious complication. It is caused by cholesterol crystals that embolize and block small arteries. No specific treatment is available, and morbidity and mortality are high. It tends to be associated with difficulty in manipulation of catheters within a severely diseased aorta. A common feature is leg pain with livido reticularis despite palpable pulses. Confusion, renal failure, and death ultimately ensue [66]. In patients with severe aorta disease, it might be reasonable to use a long vascular sheath to advance the ablation catheter directly into the left ventricle. Alternately, a transseptal approach could be considered.

Pseudoaneurysm, local hematoma, and arterovenous fistula

All interventional procedures carry a risk of local vascular complications, such as pseudoaneurysm, hematoma, and arteriovenous fistula (AVF).

The incidence of these complications is particularly related to the type of procedure performed (right- or left-side catheterization).

In 1993, Hindricks *et al*. published the Multicentre European Radiofrequency Survey (MERFS) on the complications of RF catheter ablation. In this series of 4398 patients who underwent RF ablation, the incidence of major bleeding at the puncture site ranged between 0.23% and 0.63% [37]. Moreover, several groups have described the impact of this complication in single-center experiences. Van Hare *et al*. [67] reported a 4% incidence of hematoma without pulse loss and 1% of femoral AVF requiring repair in about 100 children. In a large series of patients undergoing cardiac catheterization, Kelm *et al*. found that almost 1% suffered femoral AVF. One-third of iatrogenic AVF closes spontaneously within 1 year. Cardiac volume overload and limb damage are highly unlikely with AVF persistence. Thus, conservative management for at least 1 year seems to be justified [68]. In another large series of 18,165 patients who underwent cardiac catheterization, 2% suffered femoral AVF or pseudoaneurysm for which patient- or procedure-related risk factors could be identified [69]. In this series, most AVF and pseudoaneurysm were also managed conservatively or underwent no treatment, and overall mortality was low.

Femoral pseudoaneurysm is a common complication, and occurs in up to 6% of diagnostic or therapeutic catheterization procedures. Spontaneous closure is the rule for small pseudoaneurysms. Large and complex pseudoaneurysms need treatment to prevent complications such as embolization [70]. Manual compression repair, with or without ultrasound guidance, remains first-line treatment. A surgical approach is indicated in selected cases; this requires anesthesia, longer hospital stay, and higher costs. New therapies have recently emerged that are non-invasive and suitable for most patients, even those who are critically ill. Nonsurgical treatment options in addition to compression therapy include endoprosthesis placement, coil embolization, and percutaneous collagen and thrombin injection.

The prophylactic use of anticoagulation therapy after the ablation procedure could increase the risk of developing vascular complications. Another important risk factor for this complication is the size of the sheaths used to introduce the catheters into the vessel.

Complications associated with epicardial mapping/ablation

Access

During the epicardial access, multiple fluoroscopic projections are helpful to confirm the intrapericardial location of the guidewire prior to sheath insertion.

Compared to endocardial approach, epicardial ablation has some additional risks. Some degree of pericardial bleeding is recognized in approximately 30% of cases [71], mostly because of the unintentional right ventricular puncture or lesion of pericardial vessels. Bleeding usually resolves with

repeated aspiration of the pericardial space [72], and rarely requires surgical intervention [73]. To prevent the laceration, the sheath should never be left without a catheter inside. Puncture of a subdiaphragmatic vessel causing intraabdominal bleeding has been reported and can potentially require surgery [71,74]. Anterior access may have less risk of intraabdominal bleeding, including liver puncture, compared to the inferior access.

Mapping/ablation

RF injury to coronary arteries can cause acute thrombosis [74]. In addition, severe coronary artery spasm has been reported during epicardial mapping [62]. Prior to the ablation, coronary angiography should be performed to visualize the distance to the coronary artery. While distances less than 5–15 mm have been reported to be associated with increased injury, the absolute risk associated with specific distances from the coronary artery are poorly defined, and likely vary depending on the applied power, coronary artery diameter, and the epicardial fat [62,75]. In particular, the long-term consequences (beyond 1–3 months) of ablation near the coronary arteries are unknown.

Injury of the left phrenic nerve has been reported [76]. Proximity to the nerve can be detected by pacing with high stimulus strength [77]. To prevent the phrenic nerve damage, moving the nerve away from the myocardium by injection of air into the pericardium, or placement of a balloon catheter between the ablation site and nerve has been reported [78,79]. Air in the pericardial space can increase the defibrillation threshold, requiring emergent evacuation if defibrillation is required [80].

Postprocedure

Symptoms of pericarditis can be observed in about 30% of cases [74] after the procedure. Pericardial instillation of a glucocorticoid following the procedure has been shown to reduce inflammation in a porcine model [81], and is performed routinely in some centers.

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CHAPTER 11

Post-Ventricular Tachycardia Ablation Follow-Up Management

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Introduction

Follow-up and postablation management of patients after catheter ablation for ventricular tachycardia (VT) is largely determined by the type of VT being ablated. For patients with structurally normal hearts and idiopathic VT, follow-up can be straightforward and similar to the follow-up after an ablation procedure for a supraventricular tachycardia. However, in patients with structural heart disease, follow-up management can be complex and depends on the nature of the underlying disease. In addition to proper surveillance for procedural complications and outcome, management also includes the possibility of ongoing antiarrhythmic drug therapy and optimization of medical therapy to control the underlying heart disease. At present, there are no guidelines or widely accepted consensus statements for the postablation management of VT patients. Follow-up management should focus on (1) understanding and improving long-term prognosis and (2) medical therapy and ongoing monitoring.

Prognosis post-ventricular tachycardia ablation

Knowledge of the prognosis post-VT ablation is important to understand the postablation management priorities for these patients, including medical management. In case of idiopathic VT without detectable structural heart disease, such as VTs arising from the right ventricular outflow tract, aortic

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cusp, or left ventricular fascicles, the long-term prognosis is, in general, excellent with or without arrhythmia elimination [1]. Catheter ablation is primarily performed to limit symptoms and to improve quality of life, with low long-term morbidity or mortality risk. In the rare situation of premature ventricular contraction (PVC) or VT-induced cardiomyopathy, failure of left ventricular function to resolve post ablation likely represents a worse long-term prognosis. However, improvement in LV function is common after a successful ablation procedure, even without total elimination of the PVCs.

In patients with structural heart disease, long-term prognosis is often worse compared to the patients without detectable structural heart disease. Because of the progressive nature of most cardiomyopathies, recurrence of (non) ablated VT and/or death from nonarrhythmic cardiac causes (such as pump failure) become more prevalent over time. After VT ablation in patients with structural heart disease, the arrhythmic outcome over 1–5 years follow-up seems to be directly correlated to the degree of acute procedural success [2–10]. Acute success may be defined as "total," "partial," or "failure":

Total success	Inability to induce any monomorphic VT at the end of the procedure
Partial success	Clinical VT has been eliminated, but one or more nonclinical monomorphic VTs remain, usually with a stimulation protocol more aggressive than used at the start
Failure	the clinical VT or other monomorphic VTs remain inducible using the same protocol

Unfortunately, the literature has used varying definitions of "clinical VT" (especially when 12-lead documentation was not available) and varying stimulation protocols (3–5 extra-stimuli), stressing the necessity to standardize definitions of success [11]. However, regardless the definitions used, studies have reported the best results in "total" success patients with VT recurrence rates as low as 4–16% over 1–2 years' follow-up. "Partial" success patients have an intermediate recurrence rate of 40–65%, while "failures" have recurrence rates in excess of 90–99% [2,4,10].

The mortality rate in VT patients with structural heart disease is also substantial with reported 1-year mortality rates to be 16–18% with 70–75% of those deaths attributable to a cardiac cause [4,10]. Importantly, 53–65% of these cardiac deaths are because of a nonarrhythmic cause, indicating the importance of optimizing management of the underlying heart disease. Interestingly, the rate of death from nonarrhythmic cause is also directly related to acute procedural success, with the highest mortality rates in patients where VT could not be successfully or totally eliminated [4]. Finally, the occurrence of an electrical storm (one of the most common reasons for VT ablation) is a strong predictor of increased long-term mortality (about 25–30% over 2 years) [12].

Medical therapy post-ventricular tachycardia ablation

For patients with idiopathic VT and no detectable structural heart disease, medical management is similar to that for reentrant supraventricular tachycardia. Because elimination of all medication is often the goal of ablative therapy in this population, immediate discontinuation of drugs post ablation is the best strategy to allow for monitoring of recurrence. In patients with a VT recurrence, the decision to pursue repeat ablation, or restart medication will be an individualized decision. Antiplatelet therapy with ASA 80–325 mg/day for 4–6 weeks post ablation can be considered for idiopathic VT patients who have had left-sided ablations or extensive ablation lesions to minimize the risk of thrombus, although there is little evidence that is a clinically relevant problem or that such therapy would prevent it.

In VT ablation patients with structural heart disease, medical therapy can be subdivided into four major headings: antiarrhythmics, anticoagulation, beta-blockade, and heart failure (HF) management.

Antiarrhythmics

Antiarrhythmic drug therapy is often continued in most patients post-VT ablation. In two recent reports, 70–90% of patients were maintained on their pre-ablation antiarrhythmic drug therapy, with only about 25–30% of these patients having their doses reduced [2,4,9,10]. In contrast to the atrial fibrillation (AF) population, freedom from antiarrhythmic drugs may not be a reasonable goal given the complexity and progressive nature of the VT substrate. Even after apparently successful procedures, recurrence rates within 2 years are as high as 10–15% [4,8,10]. Furthermore, many of these patients are on antiarrhythmics for concomitant reasons (such as AF), and thus, total elimination may not be feasible. Dose reduction may be an important goal, particularly for amiodarone for which the incidence of side effects is closely related to daily dose [13]. In various trials, dose reduction of amiodarone is reported and doses may be reduced in a progressive manner starting within the first 3–6 months post ablation [4]. There are, of course, some patients where ablation is pursued as an alternate to antiarrhythmics, particularly where drugs may be causing unacceptable side effects. In these patients, drugs may be discontinued post ablation, probably after a minimum of 3 months follow-up to assess clinical outcome.

Anticoagulation

Within the first 3 months post ablation, particularly on the left side, there may be a risk of systemic thromboembolism, particularly if extensive ablation lesions were applied. However, there is no absolute proof of this, because only 2 TIAs were reported out of 390 patients (0.5%) accumulated from three recent, large-scale reports [4,10,14] using antiplatelet or no anticoagulant therapy only. Furthermore, most VT patients with structural heart

disease are already on some form of antithrombotic or anticoagulant therapy, such as antiplatelet therapy in the coronary disease patients, or warfarin for patients with dilated cardiomyopathy and/or AF. On the basis of consensus opinion, and on postablation procedures from published data, it is recommended that a minimum of ASA 80–325 mg/day be used for 3 months post ablation in patients who have had left-sided or extensive ablations. Warfarin may be used for higher risk patients (documented thrombus, previous stroke/TIA, AF, severe LV dysfunction, etc.). Surveillance with echocardiography for thrombus is discussed later.

Beta-blockade

Beta-blockers should be maximized in most patients post-VT ablation with structural heart disease. Effective beta-blockade has been shown to reduce both arrhythmic and nonarrhythmic death in patients with left ventricular dysfunction [15]. Furthermore, concomitant use of beta-blockers with other antiarrhythmic agents is superior to the use of either agent in isolation, as shown by the OPTIC trial [16]. Even in patients receiving low-dose sotalol, there is not much beta-blocker effect in doses of 80 mg BID or less. Thus, addition of a traditional beta-blocker in combination with low-dose sotalol may be warranted.

Other heart failure therapy

Many VT ablation patients have coexisting cardiomyopathy and given the high rate of death from HF over the first 1–5 years post ablation (see the preceding text), appropriate long-term heart function management must be optimized. Keep in mind that therapy shown to reduce mortality in HF patients (such as angiotensin-converting enzyme inhibitors) affects both arrhythmic and nonarrhythmic death [15].

Acutely, attention must be paid to volume status, particularly because patients are lying flat for prolonged periods and often, an open-irrigated tip ablation catheter is used that can add 1–2 l of volume acutely to the patient. Significant volume overload requiring prolonged admission can occur in as many as 1–2% of patients post-VT ablation. Thus, diuretic doses may need to be increased in the days post ablation to achieve a baseline fluid status. Electrolytes should also be closely monitored and corrected in the first few days because disturbances may have triggered the original VT episode, and changes in fluid status post ablation may further upset the balance.

Of course, optimization of an ACE-inhibitor and/or angiotensin receptor blocker should be performed given the preponderance of clinical evidence in favor of this for HF patients [15]. Spironolactone may also be added for patients with advanced NYHA status (three or more), or chronic hypokalemia. Use of digoxin should be carefully managed, because many of these patients are on concomitant amiodarone (which raises digoxin levels) and digoxin toxicity is not an uncommon cause trigger for ventricular arrhythmias.

While there is some preliminary evidence in favor of using both statin therapy [17] and fish oils [18] to reduce the incidence of ventricular arrhythmias in cardiomyopathy patients, there is no definitive study to date to support their routine use for this indication alone [19,20]. Fish oils may be useful for HF management in general based on the recent GISSI-HF trial [21]. Finally, referral to a formal heart function program/clinic may be beneficial for most of these patients.

In patients with ischemic heart disease, care must also be taken to optimize management of the ischemic substrate, whether it is with medical management or revascularization (surgical or percutaneous) as per standard guidelines. Medical therapy would include optimal beta-blockade, ACE-inhibition, and statin therapy, all of which have been discussed in the preceding text.

Monitoring post-ventricular tachycardia ablation

For patients with idiopathic VT and no structural heart disease, ablation is usually undertaken for symptomatic arrhythmias. Following a successful ablation procedure, patients should be seen at the outpatient clinic at regular intervals up to 1 year following the initial procedure. Follow-up should include 24–48 h Holter monitoring at regular intervals. For patients with little or no symptoms or patients with infrequent arrhythmia episodes prior to ablation, prolonged monitoring with loop recorders or transtelephonic monitoring should be considered. Exercise stress testing may be useful for patients with a history of exercise-induced VTs. Echo monitoring at regular intervals to assess LV/RV function should be considered in postablation patients with a history of suspected PVC-induced cardiomyopathy. After an unsuccessful ablation procedure, it is advised to wait at least 3 months before scheduling a repeat ablation procedure to assess the burden of recurrent arrhythmias.

In VT ablation patients with structural heart disease, monitoring recommendations may be grouped as described in the following sections.

Implantable defibrillator (ICD)

Most patients with structural heart disease and VT undergoing ablation either already have an ICD or will get an ICD implanted after the procedure. If an ICD is present, ICD functions should be checked immediately and 3 months after ablation to detect any device-lead malfunctions such as lead dislodgement/damage, change in sensing or pacing thresholds, or device infection. Thereafter, ICDs should be checked every 3–6 months. Given the monitoring capabilities of ICDs, they are ideal to monitor arrhythmia recurrences. However, documentation of every PVC or nonsustained VT episode may not be clinically useful or relevant. The suggestion from the United States Food and Drug Administration (FDA) in 1999 was to document only those VTs requiring therapy (antitachycardia pacing or shock) or nonsustained VT episodes lasting >20 s as clinically relevant [22]. The FDA

guidelines suggested a minimum of 6 months follow-up post-VT ablation for clinical trials, but a minimum of 1 year seems reasonable [22].

Postablation programming should be performed as per emerging guidelines to minimize ICD shock delivery, such as using higher cutoff rates for VT and VF zones, extending detection limits, and aggressive use of antitachycardia pacing even for faster VTs. Monitor zones at lower rates may be programmed to look for slower VTs that may have been targeted during ablation, but do not necessarily warrant shock therapy.

Other rhythm monitoring

For ICD patients, other forms of rhythm monitoring are probably not warranted beyond standard ECGs acquired at each clinical visit. For patients without ICDs, intermittent ECG and 24–48 h Holter monitoring should supplement symptom monitoring with each clinical visit at 3 and 6 months and every 6 months thereafter. Loop recorders and/or transtelephonic monitoring may increase the yield of asymptomatic VT detection, as suggested by the AF literature, but whether such VT would be clinically relevant or not in this population is not well known.

Echocardiography

Echocardiography is performed routinely in most VT ablation studies both pre and post ablation out of concern of ventricular thrombus formation and the consequent risk of a thromboembolic event. At a minimum, echo should be performed within 24–48 h pre-ablation and within 1-week post ablation to look for thrombus or deterioration in ventricular function. Repeat echo should be considered at 3 months post ablation for those patients who have documented thrombus and have been started on warfarin to study if the thrombus has resolved. The 3-month echo is also useful to document changes in ventricular function post ablation. For some patients, such as those with PVC-induced cardiomyopathy, it may take at least 3 months to detect improvement in LV function. Conversely, in severe cardiomyopathy patients, LV function may deteriorate if extensive ablation is performed in viable tissue.

Repeat ablation

The decision and timing of performing a repeat VT ablation will be dependent on the context and urgency of the clinical situation. If possible, in-line with the FDA guidelines one should wait for at least a 1 week following ablation to assess possible procedure related complications and to study the recurrence rate [22]. However, in case of frequent recurrences or even an electrical storm, the repeat procedure should be scheduled as soon as possible. Other indications for repeat ablation would include failure of the first procedure, ongoing delivery of ICD therapy, ongoing high burden of ventricular arrhythmias, or inability to stop antiarrhythmic medication that is causing side effects.

Other monitoring

The FDA guideline recommends a neurologic examination by a neurologist both pre- and post-VT ablation for surveillance of thromboembolic complications [22]. While this has been a recommendation, only a small number of published trials included a neurological screening. From a practical point of view, clinical surveillance for thromboembolic events should be undertaken at routine follow-ups but does not necessitate an examination by a neurologist.

It should be mentioned here that use of the percutaneous, epicardial approach has become increasingly used for VT ablation. This is typically performed by accessing the pericardium from the subxyphoid location. Periodic drainage of the pericardium must be performed during the procedure to avoid tamponade, especially if the patient had traumatic access and is anticoagulated or when using irrigated-tip catheters. Patients should also be monitored for tamponade post procedure, perhaps with retention of pericardial access for 12–24 h post ablation to allow for drainage if necessary. Finally, pericarditis is common post ablation, and a short 5–7 day course of nonsteroidal anti-inflammatory medication will help alleviate this problem.

Conclusions

Postablation management of VT patients requires an appreciation for the long-term prognosis of this population, particularly those with structural heart disease. Thus, management not only consists of rhythm monitoring and antiarrhythmic drug management, but also management of the underlying disease process.

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CHAPTER 12

Surgical Ablation

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"The severity of LV dysfunction is parallel to the severity of arrhythmia and surgical risk." GMG

Introduction

Since the first human EP-guided surgical intervention in 1973 (Figure 12.1), surgery for ventricular tachycardia has never been considered a first-line alternate to antiarrhythmic drug therapy, ICDs, or other catheter-based interventions.

Early attempts to EP-guided surgery for ventricular tachycardia [1–11] were based on the translation of the experience gained with intraoperative electrophysiologic mapping during surgery for the Wolff–Parkinson–White syndrome. These pioneered interventions help establish principles that still stand today.

(a) Therapeutic targets can be designed as follows: (1) the earliest activation site during ventricular tachycardia was recognized as the marker of the critical exit site from the arrhythmogenic substrate of the reentrant activation [8]; and (2) the anatomic arrhythmogenic [12] substrate was delineated as the site of low and/or delayed and/or fractionated potentials recorded during diastole, which have been described under multiple names.

(b) Surgical rationales were based on either *ablation or exclusion of the targeted arrhythmogenic sites (Figure 12.2)*, depending on their anatomy and physiology: The goal was to neutralize the arrhythmogenic substrate without jeopardizing the heart's contractile function or valvular function.

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(c) The third principle was to reduced the mortality of open heart surgery, in patients with ventricular tachycardia after myocardial infarction associated with left ventricular dysfunction because of early ventricular aneurysm formation. During the pioneer years, surgery was associated with excessive mortality. In consequence, patient selection was aimed at reducing surgical risk (mortality) to an acceptable level, but without the supporting evidence that the reduced risk [13–23] was associated with increased benefit, that is, longer life expectancy.

These difficult challenges were to be addressed in the following years. Randomized clinical trials comparing surgical therapy and medical therapy in the eighties had to be interrupted because of high mortality in the surgical arm (Nobert van Hemel, personal communication). In the early eighties, when the first ICDs were implanted using a surgical approach, the impact of ventricular arrhythmia control on life expectancy could not be documented [24]. Only, when ICDs were implanted using a transvenous approach with dramatically reduced procedural risk, randomized clinical trials could document that control of ventricular tachycardia prolonged life in patients with an altered left ventricular ejection fraction of less than 35%: a population at high risk for direct surgical approach [25–30]. Even low surgical mortality is unwarranted because it nullifies the benefit of arrhythmia control. In this patient population with multiple risk factors, control of risk of arrhythmia death cannot be replaced by surgical death.

The "historical" selection of patients with lower surgical risk might have been flawed because in most of them the surgical risk might have been too high compared to the benefit.

Conclusion

In the current state of interventional therapies for ventricular tachycardia, surgery can be considered an option only when highly effective, that is, equivalent to a cure, while associated with minimal morbidity.

Surgical indications are based on the "no failure–no complication principle," although the side effects of uncomplicated surgery might be considered too high in many cases. This statement is consistent with accepted wisdom that a true alternate to minimally invasive approach should not be more invasive.

The handicap of conventional open heart surgery is not a lack of effectiveness but excessive morbidity [31].

General recommendations

- The skill, experience, and proficiency of a well-established pluridisciplinary team with a keen interest is the key argument in selecting and performing the surgery for ventricular tachycardia.
- Surgery for ventricular tachycardia should be considered only when other less invasive therapeutic interventions have failed.

• Surgery must yield high success rate. The ideal outcome should be the equivalent of a cure, without the need for any other invasive treatment, such as ICD.
• Surgery must be associated with minimal side effects, using off-pump technique when possible, and minimal access, in particular epicardial access or newly described beating heart intracardiac access.
Open heart surgery may be considered in rare cases of ventricular arrhythmia associated with imminent life threat, such as an electrical storm.

Surgical indications

Ventricular tachycardia after myocardial infarction

Surgery can be considered under the following conditions:
(1) In low-risk patient, with a discrete scar, preserved left ventricular function, and persistence of problematic monomorphic sustained ventricular tachycardia after failed catheter ablation. A well-selected surgery can offer a cure that will eliminate the need for ICD and antiarrhythmic drugs, with the benefit of a better quality of life.
(2) Surgery may be an option for life-threatening electric storm after failed catheter ablation [32–39], as a life-saving procedure, but only after careful consideration of the patient left ventricular anatomy and function and the severity of comorbidity.
(3) When, after attempted catheter ablation, there is good evidence that the arrhythmogenic targets are not endocardial but epicardial. The surgical epicardial approach can be performed as an alternate to attempted catheter-based epicardial ablation [40–43] because of contraindication to this access (Dr. Paolo Della Bella, personal communication, 2008).
(4) Well-experienced teams may offer surgical curative surgery, with minimal morbidity.

Nonischemic ventricular tachycardia

Problematic nonischemic ventricular tachycardia has long been an ideal surgical indication, before the advent of catheter-based interventions. The main indications were idiopathic left ventricular aneurysm, idiopathic left ventricular tachycardia, right ventricular outflow tract tachycardia, and arrhythmogenic right ventricular dysplasia. Catheter ablation is now associated with good control of tachycardia. An epicardial access via a median sternotomy may be considered in few patients who failed catheter ablation via the vascular or transthoracic route.

A special case can be made for ARVD after failed catheter ablation and frequent ICD shocks. Epicardial access for cryoablation can be a reasonable minimally invasive option in selected patients [44], while more invasive right ventricular free wall disconnection (RVFD) may be an option too (Figure 12.3). RVFD has given excellent long-term results, accounting for a cure when the

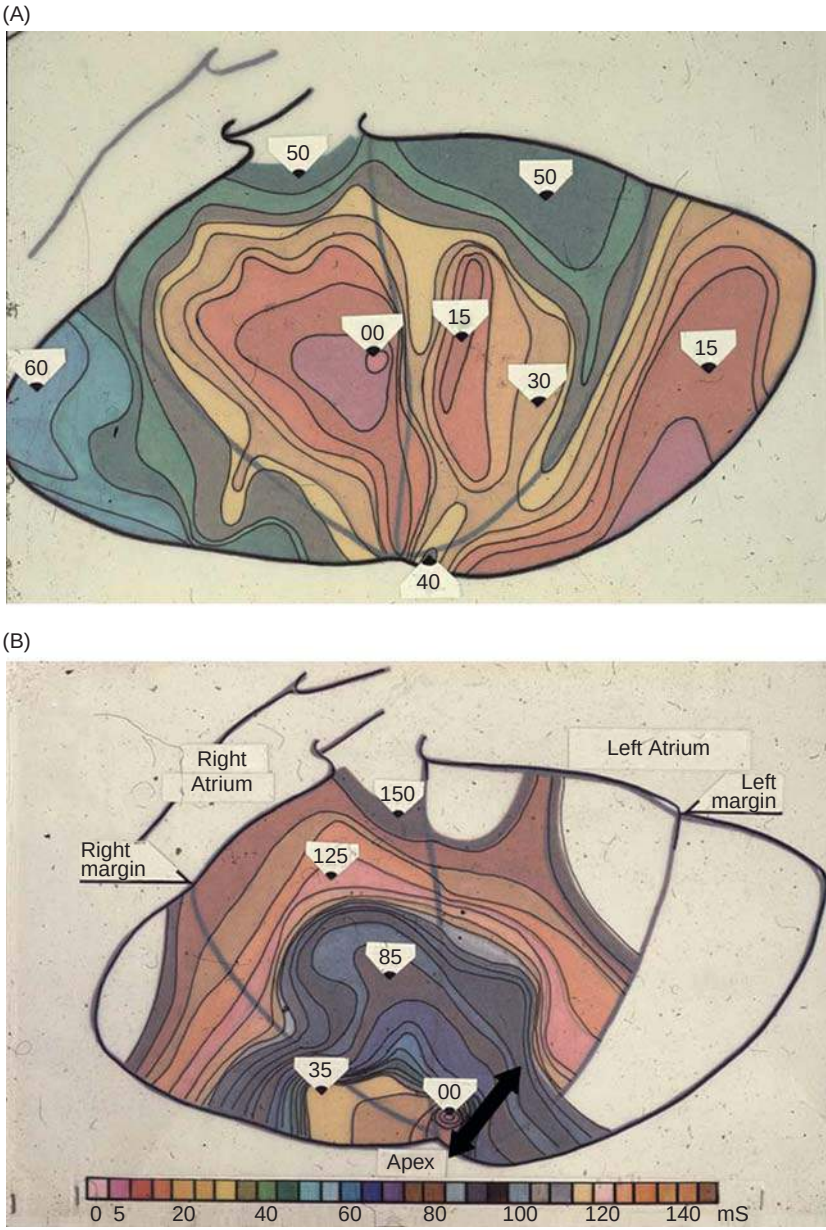

Figure 12.1 Epicardial map of the first patient operated for ventricular tachycardia using map-guided direct surgery [3]. (A) Map during sinus rhythm; (B) map during one tachycardia. Originating from the LV apex and interrupted using a simple ventriculotomy (arrow) .

arrhythmia are refractory to conventional minimally invasive approaches, and when there is evidence that the dysplasia is limited to the free wall. Modern imaging techniques provide reliable diagnostic tools [45,46]. Excellent long-term control with preserved cardiac function has been reported under these conditions [47–56].

Indications for combined interventions

Combined surgery for ventricular tachycardia is not justified based on the simple but wrong argument that the surgeon is already here. It should be submitted to the same scrutiny as the primary indication, with an exception when surgery for repair of a LV aneurysm is a primary or routine adjunct in the institution, although there is still lack of strong evidence to support this strategy [57,58].

Surgical after manual

Patients should have an extensive preoperative workup including EP study to document the number, site of origin of various VT morphologies, low-amplitude mapping to delineate the area of scar tissue with special attention to areas outside the main endocardial scar, as well as attempts of an RF catheter ablation.

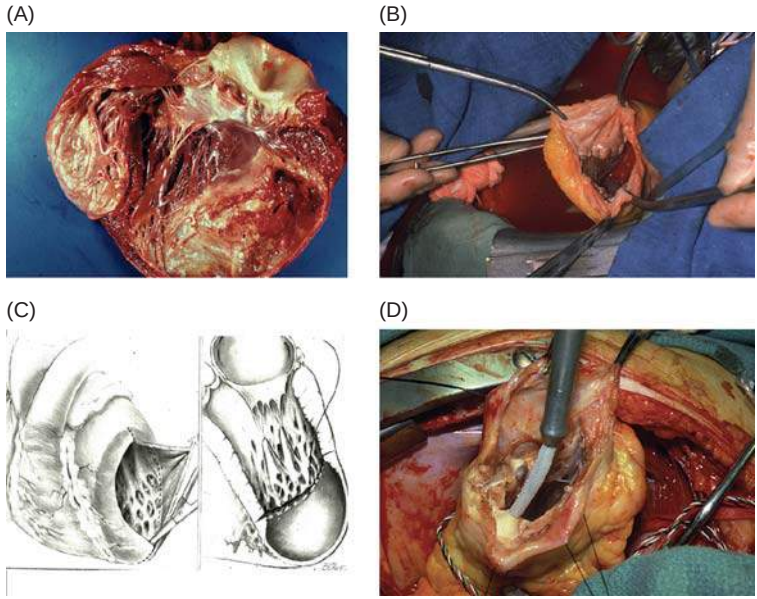

Figure 12.2 Illustration of the endocardial encircling ventriculotomy (EEV). (A) Pathology of a LV apical aneurysm; (B) operative view of the EEV; (C) schematic representation of the EEV; (D) encircling cryoablation proved as effective as, and safer than, the encircling ventriculotomy.

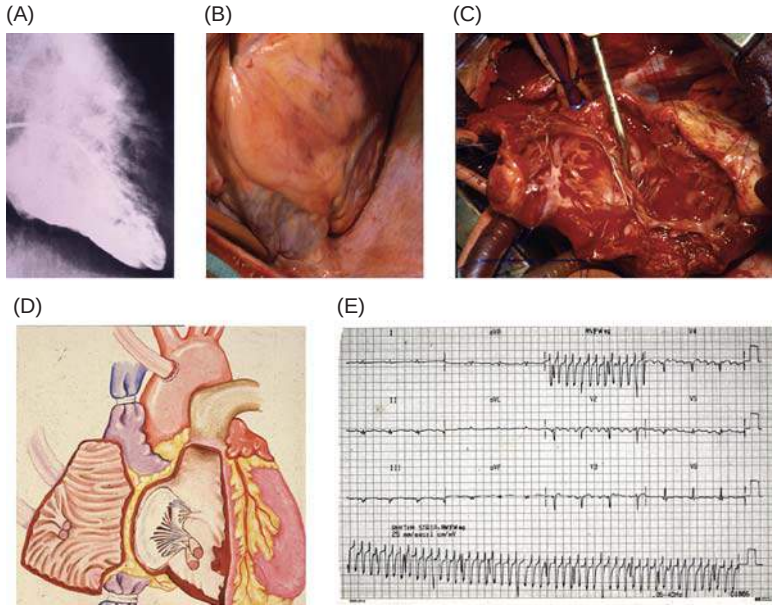

Figure 12.3 Right ventricular free wall disconnection for ARVD. (A) RV angiogram; (B) operative view of the RV inferior wall with fatty infiltration; (C) operative view with the RV free wall disconnected from the rest of the heart; (D) schematic representation of the RV disconnection; and (E) postoperative EKG showing RV free wall flutter dissociated from the rest of the ventricles.

Surgery should follow the rationales of established surgery for VTs.

The surgical team must comprise a well-experienced group of experts in surgery and electrophysiology ready to demonstrate an excellent teamwork.

A detailed, comprehensive plan must be prepared and agreed upon, with all potential unexpected or variant situations. This plan will be modified only on strong intraoperative evidence.

Intraoperative EP study should include all sophisticated mapping, catheter, and surgical techniques.

Ablation should use the best and more efficient energy with the best designed surgical tools.

Before entering the LV aneurysm, comprehensive epicardial mapping should be performed to identify early epicardial breakthroughs during tachycardia.

Ablation should be guided by electrophysiologic mapping during sinus rhythm and VT, as well as by cardiac pathology; all areas of endocardial fibrosis should be ablated or excluded.

The surgery can be performed on the arrested heart or beating heart.

Closure of the LV can use LV remodeling techniques, with which the surgeon is comfortable.

Conclusions

Nowadays, there is still a niche for surgery for ventricular tachycardia. These few selected patients may have the opportunity to get the best patient-specific intervention. The missed *opportunities for cure* demand a revision of the therapeutic spectrum and the development *of surgical and electrophysiologic expertise and interest*.

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CHAPTER 13

Indications to Ventricular Tachycardia/ Ventricular Fibrillation Ablation and Hybrid Therapy

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The indications for catheter ablation in general have evolved rapidly since the first application in humans in 1986 with ongoing improvement of technology and increase in experience. However, as with other technology-based approaches, progress is rapid which, among other reasons, has prevented the performance of large randomized multicenter clinical trials with long recruitment periods during which technology usually will have changed. Therefore, almost all indications even when considered as strong (Class I and IIa) have a low level of evidence.

Indications for ablation of idiopathic right ventricle/left ventricle ventricular tachycardia

Right ventricular outflow tract tachycardia

Ventricular arrhythmias originating from the right ventricular outflow tract (RVOT) are the most frequent ones seen in patients with normal ventricles. When occurring in an otherwise normal heart, these arrhythmias, even sustained monomorphic ventricular tachycardia (VT), are typically benign and rarely cause sudden cardiac death (SCD). There is a malignant form of RVOT that usually has either early-coupled ventricular extrasystoles or a more rapid VT cycle length [1,2]. The mechanism of RVOT tachycardia is likely

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multifactorial, but a substantial amount of data suggest that it is secondary to triggered activity rather than reentry [1,3,4]. Likewise, left ventricular outflow tract tachycardia appears to have a similar mechanism [4,5].

The RVOT arrhythmias have several distinct morphologies to help locate the site of origin of tachycardia, but there is a considerable overlap. Typically, there is a left bundle branch block pattern with an inferior axis. Lee *et al*. [6] demonstrated successful ablation when the precordial transition zone was at lead V4, whereas failed ablations occurred when the precordial transition zone was at lead V3. It is now well appreciated that arrhythmias with an earlier transition zone often require ablation in the left ventricular outflow tract or neighboring structures [7]. Tanner *et al*. [7] analyzed 33 successfully ablated patients with outflow tract tachycardia. A transition in V3 was present in 58% of all patients, and in 11 of 19 such patients, the tachycardia could be successfully ablated from the RVOT; the other patients required ablation from other areas. The pulmonary artery may be the site of origin of "apparent" RVOT ventricular arrhythmias [8]. Arrhythmias from the para-Hisian area have a distinct pattern [9]. Yamauchi *et al*. [9] evaluated 90 patients undergoing mapping and ablation in the RVOT and 10 were identified who had foci near the bundle of His. In such patients, the R-wave amplitude in the inferior ECG leads was lower than that noted in other areas of the RVOT, and ECG lead I showed a significantly taller R-wave than in other RVOT sites.

The success rate for ablating RVOT ventricular arrhythmias is high, from greater than 80% to 95% [2,6–9]. However, long-term late reoccurrences have been reported to be relatively common [10]. Of note, with more recent sophisticated mapping and ablation approaches, the serious complication of cardiac perforation and tamponade during ablation in this area has been reported to be $<1\%$.

The RVOT premature ventricular contractions (PVCs) and VT occurring with substantial frequency on a 24-h ECG recording can amazingly "disappear" when the patient is in the electrophysiology laboratory, even in the absence of sedation or anesthesia. Infusions of isoproterenol or epinephrine may initiate tachycardia, but in some patients, nothing seems to work and the patient reverts to a quiescent stage. Thus, whenever possible, prior to bringing the patient to the electrophysiology laboratory, an effort should be made to characterize the 12-lead ECG morphology of the patient's spontaneous arrhythmia so that at least pace mapping can be attempted in an electrophysiology study.

It is very important to differentiate arrhythmias from the RVOT, which occur in a normal ventricle, from those in patients with subtle forms of right ventricular cardiomyopathy. Similar VT morphologies can occur in right ventricular dysplasia and even cardiac sarcoid [11,12]. Some investigations suggest the use of endomyocardial biopsy guided by voltage mapping to help with this differential in certain cases that are unclear [11,12].

Ventricular tachycardia originating from the aortic sinus of Valsalva

An unusual form of VT with left bundle branch block, inferior axis may originate from the aortic sinus of Valsalva. Kanagaratnam *et al*. [13] evaluated ablation of 12 such patients in whom tachycardia could not be ablated from either the right or left ventricular outflow tract areas. These patients were all successfully ablated and typically demonstrated an early precordial transition with a prominent R-wave in electrocardiographic leads V2 or V3. The origin of these unusual forms of VT are most frequently from the left coronary cusp but can also be found in the right coronary cusp and the noncoronary cusp [13,14]. Ablation success rates from very experienced laboratories have been high, greater than 80%, with minimal complications. However, a dire consequence can be acute occlusion of the coronary artery, which has been reported.

Left ventricle fascicular ventricular tachycardia

Verapamil-sensitive idiopathic left ventricle (LV) VT occurs primarily as a result of reentry involving the fascicles of the left bundle branch [15–17]. Areas of slow conduction are identifiable as early diastolic potentials during VT and sinus rhythm in fascicular and Purkinje system. Three varieties may occur: (a) left posterior fascicular VT with a right bundle branch block (RBBB) and superior electrocardiographic axis; (b) left anterior fascicular VT with an RBBB and right axis; and (c) high septal fascicular VT with relatively narrow QRS complex and normal axis. Majority have an RBBB with left axis deviation electrocardiographic pattern indicating its most frequent site of origin—the posterior fascicles of the left bundle branch. Medical therapy with verapamil or beta-blockers can be effective in some patients. Antiarrhythmic drug therapy with Class Ic agents or Class III agents may be attempted in resistant cases. As a result of the excellent clinical prognosis of these arrhythmias, ICD therapy is generally unwarranted. Radio frequency ablation is highly effective (>80%) and should be considered in patients in whom medical therapy is unsuccessful or poorly tolerated. Different targets of ablation have been described including early diastolic Purkinje potentials during VT, sites of mechanical termination of VT, or diastolic sinus rhythm potentials [15–17]. Electroanatomic mapping may be helpful in localizing the area of slow conduction and creating a line of lesion in such areas.

Other left ventricle ventricular tachycardia

Mitral Annular VT: In a series of 352 patients with symptomatic idiopathic VT or PVCs, 5% arose from mitral annulus [18]. Of these, majority (58%) originated from the antero-lateral portion of the mitral annulus. In all patients, radio frequency ablation eliminated the arrhythmia, with no recurrences

during follow-up for 21 months. In another series, the success of ablation of these arrhythmias was also high [19].

Epicardial VT: Epicardial foci of VT are characterized by a slurred QRS onset giving a pseudo-delta wave appearance. The slowed initial QRS activation was quantified by Daniels *et al*. [20] and a delayed precordial maximum deflection index of ⩾0.55 identified epicardial VTs with high specificity and sensitivity. Perivascular sites (adjacent to epicardial veins or arteries) on the LV epicardium are common sites. It is amenable to ablation either by a percutaneous pericardial approach or transvenously via the coronary sinus. Some cases may require surgical approach because of proximity to critical epicardial coronary arteries.

Recommendations

The indications of ablation for idiopathic right ventricle (RV)/LV VT are summarized in Table 13.1.

Table 13.1 Indications of ablation for idiopathic right ventricle/left ventricle ventricular tachycardia

Class I:
1 Symptomatic ventricular tachycardia/premature ventricular contractions (VT/PVCs) of right ventricular origin unresponsive to medical therapy with beta-blockers and calcium channel blockers
2 Symptomatic VT/PVCs of left ventricular fascicular or endocardial origin remote from aortic sinus of Valsalva, unresponsive to medical therapy with beta-blockers and calcium channel blockers
3 Symptomatic or asymptomatic VT/PVCs of right ventricular or left ventricular origin thought to be causing cardiomyopathy and unresponsive to medical therapy

Class IIa: Asymptomatic sustained VT of right ventricular origin unresponsive to medical therapy

Class IIb:
1 Symptomatic VT/PVCs originating from uncommon left ventricular sites (aortic sinus of Valsalva, epicardium) that are unresponsive to medical therapy including Class I/III agents
2 Asymptomatic sustained VT of left ventricular origin unresponsive to medical therapy

Class III: Asymptomatic PVCs of right or left ventricular origin not thought to be causing cardiomyopathy

Indications for ablation of nonischemic ventricular tachycardia

In general, VT complicating structural heart disease is treated with ICD. Catheter ablation is considered adjunctive or palliative therapy most of the time. VT ablation is recommended for patients with an ICD who receive

multiple shocks as a result of sustained VT that is not manageable by reprogramming or optimization of drug therapy. In patients at low risk of SCD otherwise and sustained monomorphic VT when drug therapy is not effective, not tolerated, or not preferred, catheter ablation is also recommended. In patients at low risk of SCD and symptomatic nonsustained monomorphic VT, catheter ablation may be useful as an alternate to medical treatment.

Although the safety and efficacy of prophylactic catheter ablation for prevention of ICD therapy had been evaluated in a highly selected group of patients with a history of myocardial infarction, the role of prophylactic ablation is not established in any form of nonischemic VT. The indications of ablation in nonischemic VT and VF as recommended by ACC/AHA/ESC are summarized in Table 13.2 [21].

Nonischemic dilated cardiomyopathy

Catheter ablation is recommended as standard treatment in patients with bundle branch reentry VT [21]. This form of VT is a macro-reentrant tachycardia incorporating the His bundle, right bundle branch, left bundle branch, and septal myocardial conduction as critical components. Ablation of the right bundle branch or left bundle branch alternately is curative for bundle branch reentry VT [22]. However, if the patient is at high risk of SCD, or if there is symptomatic heart failure with depressed left ventricular ejection fraction ⩽30–35%, ICD implantation may still be indicated for primary prevention. In nonischemic dilated cardiomyopathy, presence of more extensive epicardial scarring in association with smaller endocardial scar is identified in its arrhythmogenic substrate in contrast to ischemic VT. A novel approach for VT ablation has been established to target the epicardial VT origin, which contributes 25–30% of all VT in nonischemic dilated cardiomyopathy [23,24]. When VT ablation in nonischemic dilated cardiomyopathy is contemplated, epicardial approach may be considered in case there are ECG features suggestive of an epicardial VT origin. These include presence of pseudo-delta wave, prolonged intrinsicoid deflection, and prolonged time to earliest QRS nadir [25]. Epicardial approach may also be attempted when endocardial approach fails, or when presence of left ventricular thrombus precludes endocardial approach.

Arrhythmogenic right ventricular cardiomyopathy

Catheter ablation is currently considered useful adjunctive therapy to decrease ICD shock, despite optimal medical treatment in arrhythmogenic right ventricular cardiomyopathy (ARVC) patients. Successful radio frequency catheter ablation of VT complicating ARVC was reported more than 10 years ago [26]. However, all reported series involved only small number of patients. Dalal *et al*. [27] recently published a series of 24 patients

with ARVC who underwent catheter ablation for VT. With techniques of pace-mapping, activation mapping, entrainment, and three-dimenional electromagnetic mapping, the successful rate was low (46%) and recurrence was high (85%). The cumulative VT recurrence-free survival was 75%, 50%, and 25% after 1.5, 5, and 14 months, respectively. More than half of the patients required more than one attempt of catheter ablation, and acute procedural success was not predictive of freedom from future recurrence. There was one procedure-related death. In view of the diffuse fibrosis and progressive disease in the right or potentially both ventricles, the authors cautioned the role of catheter ablation in management of VT in ARVC. Of additional concern is the fact that thinning of the right ventricular myocardium and replacement with fibrofatty infiltrates in ARVC patients may increase the risk of perforation and pericardial tamponade during ablation.

Hypertrophic cardiomyopathy

Very little is published in catheter ablation of VT in hypertrophic cardiomyopathy, with the exception of VT associated with an apical aneurysm. Apical aneurysms and the contiguous regions of myocardial fibrosis have been associated with monomorphic VT and increased risk for adverse clinical outcome [28]. Similar to ischemic VT complicating left ventricular aneurysm post-myocardial infarction, mechanism of the VT may be reentry within the aneurysm, or microreentry within the neck of the aneurysm. Radio frequency catheter ablation may be performed with three-dimensional electromagnetic mapping in addition to conventional techniques like pace mapping and entrainment.

Cardiac sarcoidosis

Ventricular arrhythmias and SCD are hallmarks of cardiac sarcoidosis, which often involves a small portion of the heart and may be clinically silent otherwise. Without histological evidence of noncaseating granuloma on endomyocardial biopsy, patients are sometimes diagnosed and managed as idiopathic VT or ARVC. Ventricular myocardial scarring and fiber disruption associated with granulomatous infiltration and fibrosis form the substrate of arrhythmogenesis. In 2006, Koplan *et al*. [29] reported eight patients with cardiac sarcoidosis that underwent VT ablation. Electrophysiology study revealed evidence of scar-related reentry with multiple monomorphic VT induced. Although they abolished one or more VT in six out of eight patients, some forms of VT remained inducible in all but one patient. Six patients had clinical recurrence, and four patients had VT despite antiarrhythmic drug and immunosuppressive therapy. Cardiac transplantation was eventually performed in five patients because of VT or heart failure. In 2009, Jefic *et al*. [30] reported another series of endocardial VT ablation in 9 among 42 patients with

cardiac sarcoidosis treated with a stepwise approach of ICD implantation, immunosuppressive medications, antiarrhythmic agents, and then catheter ablation. They were able to identify and ablate the reentry circuit in the peri-tricuspid area in most patients. Elimination of VT was achieved in five patients and decreased VT burden was possible in four. The authors attributed their better results to early use of steroid and immunosuppressants during the course of disease. As a result, their patients had better preserved left ventricular function and long-term outcome. Also, the arrhythmogenic substrate appeared to be more localized and amenable to catheter ablation. It is postulated that ICD in combination with catheter ablation may improve the outcome in patients with cardiac sarcoidosis if left ventricular function is still preserved. On the other hand, in sarcoidosis with advanced and diffuse cardiac involvement, prognosis is poor regardless of outcome of catheter ablation.

Chagas disease

Chagas disease is the major cause of protozoal myocarditis in Central and South America. After the causative agent *Trypanosoma cruzi* is transmitted to humans via the insect vector, a nonischemic cardiomyopathy typically develops years afterwards. The anatomic substrate for ventricular arrhythmia is characterized by segmental wall motion abnormality that is often located at the inferolateral wall of the left ventricle. Focal and interstitial fibrosis of the myocardium is usually subepicardial, with surviving myocardial fibers arranged in a random fashion favoring nonuniform anisotropic conduction. Epicardial circuits of VT were commonly found. In the small series and case reports published, epicardial mapping and ablation of VT in Chagas disease appeared to result in slightly better acute procedural success and long-term outcome [24,31]. However, as the underlying electrophysiological mechanism is scar related, and the disease process is progressive with substrate remodeling, catheter ablation is again not a primary treatment strategy but an adjunctive treatment.

Idiopathic ventricular fibrillation and other congenital syndromes

Haissaguerre *et al*. [32] first reported on the role of Purkinje conduction system in triggering of VF. Catheter ablation targeting the ventricular ectopics or Purkinje potentials as triggering mechanism of VF was shown to be successful in eliminating VF recurrence in a small series of patients with idiopathic VF [32]. All patients enrolled had very frequent spontaneous PVCs, which allowed endocardial mapping of these ectopics. The site of earliest local activation during an ectopic beat having an identical ECG morphology as those responsible for initiation of VF clinically was mapped. A sharp

Purkinje potential preceding the ventricular electrogram was identified at the origin of the ventricular ectopy in most patients. Radio frequency ablation targeting this location was successful in abolishing the PVCs and preventing VF recurrence on long-term follow-up. There have been some reports of success in similar approaches in mapping and ablation of the triggering ectopy in VF among patients with Brugada syndrome, long and short QT syndromes, malignant early repolarization, and ischemic heart disease [33]. Therefore, catheter ablation may be considered in patients presenting with VF storm having consistent triggering ectopy. However, long-term results from larger clinical trials are required for routine recommendation in clinical practice.

Wolff–Parkinson–White syndrome

Catheter ablation of the accessory pathway is indicated in Wolff–Parkinson–White (WPW) syndrome with rapid preexcited AF causing VF or when the refractory period of the accessory pathway is very short and preexcited AF is likely to result in VF. In addition, catheter ablation of an accessory pathway involved in symptomatic reentrant supraventricular tachycardia is a standard therapy that offers arrhythmia cure in otherwise healthy individuals.

Premature ventricular complexes

Extremely frequent and repetitive PVC may cause a reversible form of dilated cardiomyopathy. In patients who presented with dilated cardiomyopathy of uncertain etiology and very heavy PVC burden (>15–20%), this entity should be considered. It has been reported that ablation of the PVC was associated with improvement in left ventricular function so that ICD was no longer indicated for primary prevention of sudden death [34]. It is therefore reasonable to consider catheter ablation of frequent PVC with a view to cure or prevent tachycardia-induced cardiomyopathy.

Conclusions

Catheter ablation of VT or VF in nonischemic substrate is limited predominantly to patients with ICD and recurrent arrhythmia. The role is palliative in majority of patients. There is no evidence to show that catheter ablation may impact the mortality in patients with advanced structural heart disease who develop VT storm. However, appropriate patient selection for catheter ablation performed with sophisticated mapping tools and technique, as well as device therapy, may reduce arrhythmia recurrence and improve short-term outcome and quality of life.

Recommendations

Table 13.2 Indications of ablation for nonischemic ventricular tachycardia (VT) and ventricular fibrillation (VF)

Class I:
1 Sustained monomorphic VT in patients at low risk of sudden death when drug therapy is not effective, not tolerated, or not preferred (level of evidence C)
2 Bundle branch reentrant VT (level of evidence C)
3 Adjunctive treatment for VT storm in patients with an ICD (level of evidence C)
4 Accessory pathway ablation in ventricular fibrillation (VF) caused by preexcited AF in Wolff–Parkinson–White (WPW) syndrome (level of evidence B)

Class IIa:
1 Symptomatic nonsustained VT in patients at low risk of sudden death when drug therapy is not effective, not tolerated, or not preferred (level of evidence C)
2 Frequent symptomatic premature ventricular contractions (PVCs) in patients at low risk of sudden death when drug therapy is not effective, not tolerated, or not preferred (level of evidence C)
3 Ablation of accessory pathway to prevent VF in symptomatic patients with WPW syndrome in whom the refractory period of the accessory pathway is less than 240 ms (level of evidence B)

Class IIb:
1 Ablation of Purkinje fiber potentials in VT/VF storm consistently triggered by ectopics of a similar morphology (level of evidence C)
2 Ablation of asymptomatic PVCs to avoid or treat tachycardia-induced cardiomyopathy (level of evidence C)

Class III:
1 Ablation of asymptomatic and infrequent PVCs is not indicated (level of evidence C)

Indications for ablation of ischemic ventricular tachycardia

"Ischemic" VT may present itself in different forms [35]. In the acute phase of myocardial infarction, mostly large ones, during ongoing ischemia and necrosis, repetitive episodes of ventricular tachyarrhythmias, mostly polymorphic and degenerating to VF, may occur. In the chronic stage after myocardial infarction when scar tissue has developed and stable reentrant circuits may be present, stable monomorphic VT at different rates is the typical presentation. In advanced stages of LV dysfunction and heart failure, "ischemic" VT may again manifest itself as monomorphic or polymorphic VT. Thus, "ischemic" VT or VF is not always the direct consequence of ischemia but depends on its sequelae like scarring. VT may occur as single or multiple episodes such as in incessant VT/VF or electrical storm (ES), which either are hemodynamically well tolerated or may lead to severe hemodynamic compromise.

ICD are first-line therapy in patients with VT after myocardial infarction. However, of patients who receive an ICD after a spontaneous sustained VT, 40–60% will experience recurrent episodes [36]. ES defined as at least three separate episodes of sustained VT within 24 h, occurs in up to 20% of patients [37]. In addition, in patients with an ICD implanted for primary prevention of SCD, 20% will experience at least one VT episode within 3–5 years after ICD implantation [38].

Catheter ablation is able to abolish the propensity to a specific form of VT based on a single reentrant circuit. Catheter ablation has a high acute success rate in eliminating the dominant (clinical) type of VT. Several factors make catheter ablation of VT more difficult than ablation of supraventricular tachyarrhythmias. The infarct region is often large. The induced VT can be unstable or hemodynamically only poorly tolerated and therefore "unmappable." Although the critical VT zone is most commonly located in the subendocardium, it can occasionally be epicardial or intramural. In many cases, several reentrant circuits may coexist making ablation of a single form of VT a palliative procedure, which does not obviate the risk of SCD. The aim of ablation may be to get rid of the dominant form of VT, although attempts may be made to abolish also other forms of not clinically relevant but inducible VT. These nonclinical types of VT may be left behind for the sake of keeping the procedure short because these patients frequently are already protected by an ICD or will receive one afterward anyhow. No prior study has shown that catheter ablation of VT in any of the three settings described in the preceding text has improved long-term prognosis, albeit able to stabilize the patient and apparently being of immediate benefit. Thus, catheter ablation of sustained VT in the setting of acute or chronic myocardial infarction can only be considered as an adjunctive therapy, which in general will require the ICD as the underlying modality.

Catheter ablation is generally proposed for drug-resistant VT but what constitutes a drug-resistant arrhythmia is poorly defined. This is partly because of the emergency situation where no protocol can be used to evaluate drug resistance. The definition of drug resistance should include the selection of an adequate antiarrhythmic drug with a proper duration of administration and dosage to achieve adequate blood levels. This may require some patience on behalf of the treating physicians and the patient; otherwise, a drug that may not yet have achieved its adequate dosage and time of administration may be stopped because of a recurrence that is carelessly interpreted as inefficacy of the drug instead of inefficacy of its administration.

Indications for ablation of monomorphic ventricular tachycardia after myocardial infarction

The following text presents recommendations for management of patients with monomorphic VT after myocardial infarction that are repetitive but not occurring with high frequency to fall into the category of incessant

VT/VF or of ES. This also excludes ischemia-triggered VT or VF early during myocardial infarction that may occur as a single episode requiring immediate termination or as ischemia-induced ES or incessant VT/VF in this early setting.

When considering a given patient, the urgency of the arrhythmia itself and the patient's longevity and comorbidities have to be taken into account when considering catheter ablation of VT to solve an acute problem and the issue of subsequent ICD implantation if not already existing. In elderly patients with heart failure, especially in the presence of significantly impaired renal function, overall mortality is high but death is less frequently from a purely arrhythmic cause negating any benefit of ICD therapy. On the other hand, even an elderly patient without such major comorbidities will derive a benefit from ICD therapy although survival after implantation is shorter among the elderly than among younger patients. Whether this also applies to a patient presenting with frequent drug-resistant VT after myocardial infarction has not been studied because such situations are rare. Mostly, the patient will have already received an ICD before for primary or secondary prevention and will develop repetitive episodes later.

The elderly patient with comorbidities may be more a candidate for VT ablation to solve the clinical problem of the arrhythmia but not with the aim to prolong life. This has to be balanced against the potentially higher risk of the access to the LV for postmyocardial infarction ablation as a result of potential vascular changes.

Many patients who develop repeated episodes of VT or VF, at least when beyond the acute phase of myocardial infarction, will have an indication for an ICD based on the underlying poor LV function or will already be on ICD therapy as primary or secondary preventive measure. The specific setting will guide the therapeutic strategy that has the first aim to stabilize the rhythm, and thus the hemodynamics by any means, and then to decide upon long-term management including implantation of an ICD if not yet done.

The typical patient considered for VT ablation has frequent VT episodes resulting in ICD shocks because of rapid VT or ineffective antitachycardia pacing (ATP) or has severe symptoms (e.g., presyncope) despite effective ATP therapy. In order to plan VT ablation, careful review of the ICD electrogram morphologies recorded during spontaneous VT episodes or ECG recordings of VT episodes is necessary. Prior to ablation the actual status of the underlying heart disease should be known. The potential for ischemia that may contribute to instability during the ablation procedure should be assessed. An echocardiogram should be obtained to exclude left ventricular thrombi that might increase the risk for embolization during mapping.

The classification system used here (Table 13.3) is analogous to the recent ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of SCD [21].

Recommendations

Table 13.3 Indications of ablation for ischemic ventricular tachycardia (VT)

Class I:
1 Patients after myocardial infarction with an ICD who present with repetitive monomorphic VT that leads to multiple shocks or who present with drug-refractory incessant VT or "electrical storms" (ES) that can be neither avoided despite adequate reprogramming of the antitachycardia pacing mode nor prevented by beta-blocker and/or antiarrhythmic drug therapy or when patients are intolerant of these drugs (level C)
2 Patients after myocardial infarction with an ICD who present with repetitive sustained VT, which made mandatory the therapy with antiarrhythmic drugs that decreased the rate of VT below an acceptable intervention rate into the range of exercise-induced sinus rhythm despite concomitant beta-blocker therapy (level C)
Patients with bundle branch reentry after myocardial infarction (level C)

Class IIa:
1 Patients after myocardial infarction with an ICD who present with infrequent monomorphic VTs that have been terminated successfully by more than one electrical shock that most probably cannot be avoided in the long-term future despite adequate reprogramming of the antitachycardia pacing mode and where it is difficult to predict whether future events can be avoided by beta-blocker and/or antiarrhythmic drug therapy or when patients are not willing to take long-term drugs, the efficacy of which cannot be predicted beforehand (level C)

Class IIb:
1 As the sole procedure, that is, without an ICD, in patients after myocardial infarction who have relatively well-preserved LV function (above 35–40%) and in whom VT is monomorphic, relatively slow and well tolerated, who are considered to have a good long-term prognosis, and who are either drug resistant, do not tolerate an antiarrhythmic drug, or do not accept long-term therapy (level C)
2 Patients after myocardial infarction who present with frequent self-terminating monomorphic VT that may cause shock intervention by the ICD that potentially cannot be avoided by changing the intervention rate of the ICD (level C)
3 Patients with markedly reduced longevity and comorbidities (e.g., heart failure, reduced renal function) where VT cannot be prevented by antiarrhythmic drug therapy or drugs have not been tolerated and where an ICD would not be indicated because of the overall conditions of the patient
4 Patients with more than one intervention of the ICD by a shock that causes severe anxiety and psychological distress

Indications for ablation of ventricular fibrillation and electrical storm

The term ES has been adopted to describe a period of severe cardiac electrical instability manifested by recurrent ventricular arrhythmias. Before the widespread use of ICD, the definition of ES was occurrence of two and more episodes of hemodynamically unstable VT or VF within 24-h period, requiring usually repeated electrical cardioversion or defibrillation [39–41]. In the ICD era, ES has been more frequently observed. The fact that ICD

can terminate ventricular arrhythmias before development of symptoms or signs of hemodynamic instability has urged modification of definition [42–45]. Current definition of ES is the occurrence of three or more distinct episodes of VT and/or VF within a 24-h period resulting in device intervention (either antitachycardia pacing and/or shock delivery). The matter of discussion remains whether incessant VT should be included in the scope of ES or whether arbitrary 5-min time interval between episodes of VT/VF should be part of the definition of ES [37,46].

Although the data on acute causes and risks for ES are far from conclusive, they imply that ES is a result of complex interplay between arrhythmogenic substrate and acute perturbations in autonomic tone and cellular milieu [47]. This has practical consequences for selection of appropriate treatment strategy that includes correction of precipitating causes, decrease of sympathetic tone, and modification of the substrate. Catheter ablation should be considered whenever ES is persistent and drug refractory (or occurs in patients on chronic antiarrhythmic therapy). For the purpose of ablation strategy, it is important to differentiate between recurrent monomorphic VT and polymorphic VT or VF.

Electrical storm due to monomorphic ventricular tachycardia

In patients with ES because of recurrent monomorphic VT, strategy of catheter ablation does not differ from strategies used for ablation of monomorphic VTs in general [35,48,49]. Activation sequence mapping and pace mapping are mostly used when ablating focal VTs. Entrainment mapping is an important technique in ablation of mappable, tolerated VT of reentrant origin. Substrate mapping supported by three-dimensional electroanatomic mapping systems is frequently employed for ablation of unmappable monomorphic VTs. Such mapping systems could be also useful to differentiate between less advanced structural heart disease and idiopathic VT [12,50]. Alternately, noncontact mapping can be employed to accomplish catheter ablation of nonmappable monomorphic VTs [51]. Another alternate could be a combination of contact and noncontact mapping for ablation of multiple and fast VTs. In this approach, exit sites of fast VTs are identified by noncontact mapping and located within the border zone of the scar defined by electroanatomic substrate mapping [52].

The efficacy of catheter ablation of monomorphic VT as an underlying cause for ES was initially demonstrated in smaller series when ablation was used as a bail-out therapy [53–55]. Recent, larger single-center study confirmed efficacy and safety of catheter ablation in ES refractory to antiarrhythmic therapy in patients with structural heart disease [56]. Accumulated evidence suggests that suppression of clinical VTs in ES can be achieved in approximately 90% of patients. In a subset of patients, epicardial approach had to be employed to increase success of catheter ablation [56–58]. Anecdotal

reports imply that catheter ablation could be also considered as treatment of choice in patients with ES triggered by cardiac resynchronization therapy [59,60]. The optimal end point of catheter ablation should be prevention of inducibility of any VT [56]. Failure to suppress at least one clinical VT is associated with high risk of ES recurrence and increased mortality.

Optimal long-term strategy in patients in whom ES was successfully managed without emergency catheter ablation is unknown. In this population, the relative benefits and risks of the long-term antiarrhythmic therapy should be weighted against prophylactic catheter ablation. Early evidence suggests that prophylactic substrate modification in patients with ischemic cardiomyopathy can significantly reduce recurrences of VT episodes and thus decrease probability of ES recurrence [61].

The indications of ablation for ES because of monomorphic VT are reported in Table 13.4.

Recommendations

Table 13.4 Indications for catheter ablation of electrical storm (ES) because of monomorphic ventricular tachycardia (VT)

Class I:
1 Patients with ES and no apparent structural heart disease who present with ES because of recurrences of monomorphic VT (or incessant VT) without apparent correctable cause despite adequate sedation, administration of beta-blockers, and/or antiarrhythmic drugs (level C)
2 Patients with ES after myocardial infarction or with other cardiopathies with or without ICD who present with ES because of recurrences of monomorphic VT without apparent correctable cause despite adequate sedation, administration of beta-blockers, and/or antiarrhythmic drugs (ICD backup should be provided even after successful catheter ablation in patients without previous ICD implant) (level C)
Class II:
1 Ablation is indicated in patients with an ICD and ischemic cardiomyopathy after ES is treated conservatively to avoid frequent recurrences of VT and/or ES (level B)

Electrical storm due to polymorphic ventricular tachycardia or ventricular fibrillation

Idiopathic polymorphic ventricular tachycardia/ventricular fibrillation

Based on anecdotal experience from several centers about feasibility of catheter ablation in eliminating PVCs that triggered frequent episodes of polymorphic VT/VF in subjects without structural heart disease, the analysis of pooled data revealed that Purkinje system plays predominant role in initiation of these arrhythmias [32,62]. In a landmark study, 23 of 27 subjects with frequent episodes of idiopathic VF had origin of triggering focus in

Purkinje network and elimination of this ectopic focus by catheter ablation was demonstrated to abolish VF and its recurrences. In these patients, the site of earliest activation is preceded by early, sharp potential that is recorded at this spot also in sinus rhythm, confirming the origin in peripheral Purkinje network [62]. Only in a minority of patients, the origin of ectopic activity was in the myocardium of the RVOT. Both subgroups of patients differed in length of coupling interval of the PVCs (280 ms for Purkinje origin and 355 ms for RVOT origin) and duration of the QRS complex (126 ± 18 and 145 ± 12 ms, respectively). Significantly longer coupling intervals of triggering foci from the RVOT have been confirmed in other studies [2]. The concept of catheter ablation of triggering ectopic focus has been successfully applied in other subsets of patients without structural heart disease such as long QT or Brugada syndrome [63,64]. Compared to patients with idiopathic VF, Purkinje system plays probably less important role in initiating ES in Brugada syndrome. The site of origin of triggering PVCs was in all reported Brugada syndrome cases the RVOT.

To identify triggering focus, conventional activation sequence mapping is the most frequently used mapping technique. However, noncontact mapping could be used to locate the site of ectopy, especially when infrequent PVCs occur [65].

Ischemic polymorphic ventricular tachycardia/ventricular fibrillation

Similar strategy of eliminating triggering focus was subsequently used as life-saving procedure in subjects with ES early after myocardial infarction [66–68]. In contrast to catheter ablation of idiopathic VF, activation time between Purkinje fibers and ventricular muscle was in these patients substantially longer (38 ± 28 ms during ectopic activity in normals versus 126–160 ms in postinfarction patients). In addition, a considerable number of applications of RF energy were necessary in these postinfarction patients to abolish local Purkinje potentials and suppress ectopic activity. This suggests that the triggering fibers cover larger area and may have various connections to surrounding tissue. This finding is consistent with experimental data on selective survival of the Purkinje tissue cells within the infarcted area because of their increased resistance to ischemia and their proximity to endocardium and possible exposition to endocavitary oxygenated blood [69,70]. Triggering ventricular ectopy from Purkinje system appears to play the role even in ES later, after myocardial infarction (more than 6 months) [71]. Importantly, there is evidence that ectopic foci triggering VF both early and late after myocardial infarction are located predominantly close to the border zone of the scar. Three-dimensional electroanatomic mapping system is useful in this situation because it allows delineation of the scar and the conduction system. It may help to ablate triggering tissue even in a period of transient loss of ectopic activity during the mapping [71]. Intraaortic balloon pump can be used to provide hemodynamic support [67].

There have been case reports on successful catheter ablation of ectopic foci triggering VF in patients with other underlying structural heart diseases such as aortic valve repair or cardiac amyloidosis [72,73].

Technical considerations

In order to map and ablate polymorphic VT/VF, accurate documentation of triggering ectopy on 12-lead ECG is essential. Because of unpredictable nature of ectopic activity, the optimal time for catheter ablation is often during ES when ectopy is frequent. The procedure is expected to be less successful when there are no clinical ectopic beats at the time of mapping and ablation [62]. When mapping, mechanical bumping into the right or left bundle should be avoided, as the resulting transient block will conceal ipsilateral Purkinje activation.

The indications of ablation for ES because of polymorphic VT/VF are summarized in Table 13.5.

Recommendations

Table 13.5 Indications for catheter ablation of electrical storm (ES) because of polymorphic ventricular tachycardia/ventricular fibrillation (VT/VF)

Class I:
1 Patients with ES and no apparent structural heart disease with or without ICD who present with ES because of recurrences of polymorphic VT/VF without apparent correctable cause despite adequate sedation, administration of beta-blockers, and/or antiarrhythmic drugs (ICD backup should be considered even after successful catheter ablation in patients without previous ICD implant) (level B)
2 Patients with ES after myocardial infarction or with other cardiopathies with or without ICD who present with ES because of recurrences of polymorphic VT/VF without apparent correctable cause despite adequate sedation, administration of beta-blockers, and/or antiarrhythmic drugs (ICD backup should be provided even after successful catheter ablation in patients without previous ICD implant) (level C)

Hybrid therapy: ablation and ICD

In patients with a history of sustained VT or VF, the ICD is the mainstay of therapy to prevent SCD. However, ICD shocks are painful, can result in clinical depression, and do not offer complete protection against death from arrhythmia. To reduce the incidence of VT or VF, catheter ablation of the substrates involved in the genesis of VT may be useful with the ICD serving as a backup device. This is opposite to most situations nowadays where a patient with ES or incessant VT or VF has already been equipped with an ICD and catheter ablation is the secondary measure (i.e., ICD *plus* ablation). However, in some cases, this emergency situation may occur in a given patient without a prior ICD (ablation *plus* ICD).

Previous work had shown that surgical ablation with the use of the substrate-based approach can successfully control both VT and VF [70–75]. Therefore, the Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia (SMASH-VT) study examined the hypothesis that prophylactic catheter ablation (ablation after defibrillator implantation to prevent the occurrence of future shocks) can safely decrease the likelihood of subsequent ICD therapy in patients with myocardial infarction who receive an ICD after surviving a life-threatening ventricular arrhythmic event [61]. In 128 randomized patients, prophylactic substrate-based catheter ablation reduced the incidence of ICD therapy (shocks or antitachycardia pacing) from 33% (ICD alone) to 12% (ablation plus ICD) (hazard ratio in the ablation group, 0.35; 95% confidence interval, 0.15–0.78; $P = 0.007$). Among these patients, 20 in the control group (31%) and 6 in the ablation group (9%) received shocks ($P = 0.003$). Mortality was not increased in the group assigned to ablation as compared with the control group (9% vs 17%, $P = 0.29$).

In the near future, other ongoing studies will give further insights into the efficacy and safety of this approach.

The indications of a hybrid therapy consisting of ablation and ICD are reported in Table 13.6.

Recommendations

Table 13.6 Indications of ablation and ICD for ventricular tachycardia/ventricular fibrillation (VT/VF)

Class IIa:
To reduce the burden of VT recurrences in patients receiving an ICD for secondary indication, catheter ablation may be considered (level C)

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CHAPTER 14

Future Tools and Treatment Options for Catheter Ablation of Ventricular Tachycardia/Ventricular Fibrillation

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Image-integration-based mapping

Future progress in mapping and ablation of ventricular tachycardia/ventricular fibrillation (VT/VF) will require the extension of currently available tools and technologies and the development of new approaches. It is anticipated that scar delineation will be one of these increasingly applied techniques [1]. Classically, this has been based on voltage mapping, but it has received renewed emphasis with the application of electroanatomic mapping in experimental myocardial infarction [2,3]. This subsequently was confirmed by establishing the 95th percentile distribution of bipolar EGM voltage amplitude in normal subjects [1,4]. Myocardial areas with low (<1.5 mV) bipolar EGM voltage have been confirmed to correspond to infarcted zones. Substrate mapping to identify ventricular scars was first used in postinfarct patients, and then in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy [5], idiopathic dilated cardiomyopathy [6], or congenital heart diseases [7]. Obtaining an accurate three-dimensional (3D) reconstruction of the ventricles with a precise demarcation of the scar zones is however time-consuming. In addition, poor catheter tip/wall contact—as is commonly the case on the left ventricular septum—produces low EGM voltages and, consequently, "false" scar zones.

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Cardiac MRI with delayed contrast enhancement (DCE) analysis has emerged as the noninvasive, gold standard, diagnostic tool to analyze the topography and transmural extent of myocardial infarction [8–10]. Retention of gadolinium contrast in scar zones results in increased signal intensity on T1-weighted images relative to that of the normal myocardium. It is important, however, to recognize that delayed myocardial enhancement is not specific to myocardial infarction and can occur in a variety of other disorders, such as inflammatory or infectious diseases of the myocardium, cardiomyopathy, cardiac neoplasms, and congenital or genetic cardiac pathologic conditions. There are, however, differences in terms of scar location as well as transmural scar extent according to the underlying heart disease [11]. As a consequence, DCE-MRI may ultimately aid diagnosis. Finally, scar/fibrosis data on MRI has been shown to be associated with ventricular arrhythmogenicity in different cardiac pathologic conditions [12,13].

Integration of 3D CT-scan or MRI cardiac images into a 3D mapping system is becoming popular during supraventricular tachycardia ablation [14–15]. Such integration would be of great interest for guiding VT ablation if information regarding the arrhythmogenic substrate is available from the 3D image.

As compared to MRI scar definition, a recent study [16] showed that 3D electroanatomic mapping only provides a rough delineation of infarct areas. A clear mismatch in scar delineation was observed on the Carto map in one-third of the scars. This typically occurred in regions (basal LV posterior wall and basal LV septum) where achievement of both catheter stability and good wall contact were technically challenging via the transaortic approach. Merging a preacquired MRI dataset into the mapping system can also provide a precise anatomical context and may help identifying postinfarct VT circuits.

Application in congenital heart disease

The anticipated future multimodality imaging/mapping systems will capitalize on enhanced tissue characterization available in delayed MR imaging. This is likely in the assessment and treatment of congenital heart disease.

Three-dimensional mapping systems, both sequential and simultaneous, have made a great impact on the effectiveness of catheter ablation of ventricular arrhythmias in patients with congenital heart disease. Merging the acquired 3D mapping information with preacquired images from MRI or CT scans is the standard of care in many ablation centers treating atrial arrhythmias, but only partially applied in patients with nonischemic myopathies.

The next-generation mapping systems will allow a quicker creation of an accurate 3D while depicting diagnostic catheters without distortion. Combination of this data with intracardiac echo, rotational angiography, or other imaging data will allow better imaging of real-time substrate within a broader structural context [17,18].

Future systems in general will not only facilitate the understanding of the underlying tachycardia substrate, but also enhance the ability to assess lesion formation during the energy delivery to make the ablation itself more efficient. This will be particularly true in the much thicker ventricular myocardium, where assessment of the formation of lesions during the actual ablation will be valuable. The implementation of remote navigation systems will require integration of mapping, recording, and imaging systems.

Future risk stratification

Although SCD has been recognized as a limiting factor in the otherwise good or even excellent postoperative long-term outcome of patients undergoing corrective cardiac surgery for a variety of congenital heart defects, little information is available on how to risk stratify these patients [19]. The risk of SCD seems to be high after corrective cardiac surgery for double-outlet right ventricle, moderate in patients with transposition of the great arteries managed with Mustard or Senning procedure, and relatively low in patients after tetralogy of Fallot repair [20–22].

Because devices such as PM and ICD have a higher failure rate in ACHD patients [23,24], future improvements to correctly identify patients with ACHD at risk for SCD is a foremost task. Recent studies have demonstrated that addition of the morphologic information of a given patient, that is, the amount of ventricular scar in postsurgical Fallot patients, allows improved risk stratification [25]. In patients with defects in which the RV carries out the workload of the systemic circulation (e.g., in TGAs with Mustard or Senning operation), improved functional imaging of the "overworked" ventricle may allow identifying the optimal time to recommend ICD implantation. In a large study including 534 patients, survival estimates were 89% at 5 years and 76% at 20 years of age [21]. SCD was the most frequent mode of death. Especially in previously operated patients, distinct reentrant circuits can be postulated if the applied surgical technique (e.g., patches) is known [26].

Late gadolinium enhancement MRI provides scar image information that will be integrated into 3D mapping systems to allow preprocedural identification of potential reentrant circuits. Extensive sequential mapping could be shortened with enhanced aiming at critical isthmus or exit sites at the scar borders. Automated pace-map comparisons around a preidentified scar in hemodynamically poorly tolerated VTs may represent an alternate over preprocedural imaging. Identification of the site of the scar (endocardial—mid-wall—epicardial) may facilitate the adequate mapping approach for a given VT [27].

Future tools and treatment options for epicardial ventricular tachycardia ablation

Most VTs occurring in the setting of structural heart diseases are 3D macroreentrant circuits related to surviving myocyte arrangement in a dense

ventricular scar and evolving subendocardial, subepicardial, and intramyocardial layers of the ventricles [28–30]. It follows that electrophysiologists might be able to more precisely access and safely ablate subepicardial structures during VT ablation procedures.

Safe access of the pericardial space

There are two techniques usually performed by the electrophysiologists to access the subepicardial fibers during VT ablation: transcatheter exploration of the great cardiac vein and its branches, as well as the direct access to the pericardial space through a percutaneous subxyphoid puncture. The transvenous approach has been facilitated in recent years by the development of very thin catheters that are able to explore and delivery RF energy along the branches of great cardiac vein [31]. However, the paucity of veins on the ventricle surface limits this technique for just specific cases. Accessing the pericardial space allows the exploration of extensive areas of epicardial ventricles using standard catheters [32,33]. However, there is still concern about the safety of percutaneous pericardial puncture because of pericardial bleeding and/or ventricular perforation [33].

Thus, technical development is still needed to access the pericardial space. A specific device has been constructed aiming to aspirate the parietal pericardium to facilitate the introduction of a needle and a guidewire in the pericardial space [34]. Mahapatra *et al*. [35] also recently constructed a device capable of measuring the pressure–frequency components observed at the needle tip during introduction (Figure 14.1). The observed pressure cycle related to respiratory rate is long while the needle is in the thorax in that cycle, and becomes shorter in relation to the heart rate when the needle is in the pericardial space. The previously unreported finding could give more confidence when accessing the pericardial space.

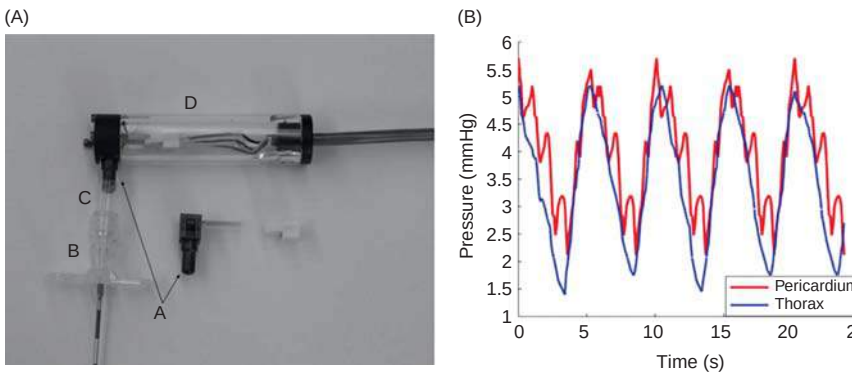

Figure 14.1 (A) Device prototype for pressure–frequency measurements. (B) Pressure–frequency waveforms comparing records obtained in the thorax (blue) and in the pericardial space (red) during catheter ablation of a sustained VT

Intracardiac approaches to accessing the pericardial space have also been proposed. Verrier *et al*. first described a percutaneous approach via the right atrial appendage [36]. Since this approach was proposed, no attempts for epicardial mapping and ablation have been performed as regular sheaths and electrophysiologic catheters are larger than used in such preliminary studies. Preliminary data obtained revealed that pericardial space can be accessed by regular electrophysiologic catheters introduced via transatrial approach and hemopericardium was not observed after downsizing sheath and catheters during their withdrawal (Figure 14.2). However, developing a system that could close and stitch the right appendage after sheath withdrawal would add even more safety and confidence while performing such pericardial access.

Catheter ablation on the epicardial surface of the ventricles

Additional epicardial ablation development will take advantage of coronary artery or vein access. The coronary vessels are natural barriers for epicardial

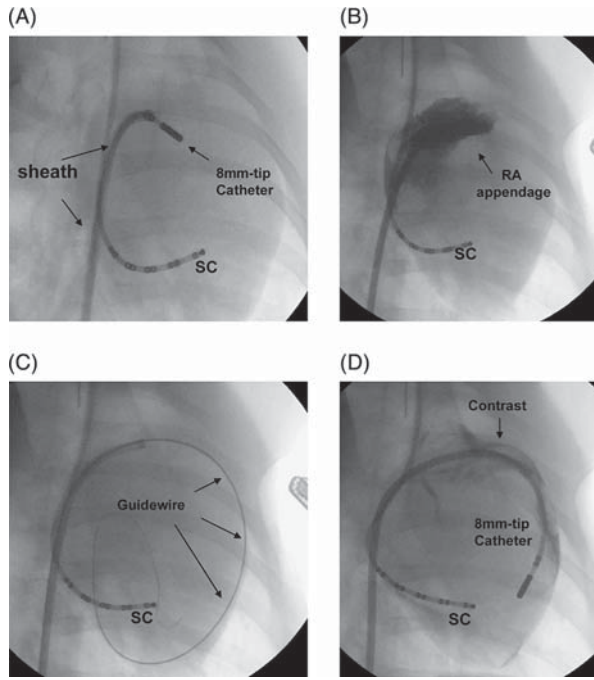

Figure 14.2 Transatrial access to the pericardial space in a pig model. (A) Location of the ablation catheter in the right atrial appendage. (B) Right atrial appendage angiography. (C) Introduction of the guidewire into the pericardial space. (D) Introduction of the sheath and the 8-mm-tip catheter in the pericardial space

ablation. RF pulses delivered near an artery may result in intima hyperplasia and thrombosis [37]. In contrast, ablation near large vessels, with increased arterial and venous flow, might preclude myocardial lesion development underneath the vessels that could be involved in the reentrant circuit [38]. Therefore, accessing the coronary venous system should be a good alternate in case of a perivascular VT substrate [39–41]. Direct visualization of the epicardial surface through a customized pericardial endoscope might also facilitate a safer epicardial RF delivery [41].

The epicardial fat thickness is also an important barrier to RF epicardial ablation. Cooled-tip catheters [42] and ultrasound energy create larger lesions despite the presence of fat interposed between the catheter tip and the epicardium, although there may persist the risk that a coronary artery could be occluded. Thus, more investigations are needed to safely ablate in that area. There is also an intrinsic risk for collateral tissue injury involving the phrenic nerve, parietal pericardium, pleural membrane, and lungs. Intrapericardial balloons or injection of fluid and air [43–45] have been used to prevent phrenic nerve injury; however, a specific device should be developed to facilitate access to divergent areas of the pericardial space. Another way to prevent neighboring structure injury is through an epicardial customized thermally shielded catheter. Fenelon *et al*. compared lesion sizes obtained via regular irrigation-tip electrodes and thermally shielded electrodes in dogs. The thermally shielded approach promoted the same creation of similar lesion size as regular catheters, but prevented injury to the contiguous tissue [46]. In summary, many new strategies and tools are under evaluation, giving expectation that epicardial and endocardial VT mapping and ablation might be performed in combination with more reliable pericardial access, under direct visualization, and with specific catheters and sources of energy in the future.

Ultrasound and laser energy for endocardial and epicardial catheter ablation of ventricular tachycardia/ventricular fibrillation

Future tools for ablating the ventricular myocardium will undoubtedly leverage alternate energy sources. Deeper lesions are desirable for catheter ablation of VT, especially VT associated with prior myocardial infarction or arrhythmogenic right ventricular cardiomyopathy.

There are several limitations of radiofrequency (RF) energy for ablation: (1) the need for stable contact between the ablation electrode and the ventricle [47]; (2) the risk of thrombus formation when the electrode–tissue interface temperature exceeds 75–80ºC (while the electrode temperature may be <55–60ºC [48–50]); (3) the risk of cardiac perforation associated with a steam pop (especially when applying higher RF power with excessive contact force using a saline-irrigated electrode [47,49,51] (Figure 14.3); and (4) limitations for use during percutaneous epicardial access, which include restriction of

RF power because of lack of cooling, poor penetration through the epicardial fat, and lack of directionality that can lead to collateral damage of a coronary artery and phrenic nerve.

Ultrasound and laser energy may have several advantages for endocardial and/or epicardial catheter ablation of VT.

Ultrasound energy

Ultrasound energy is only minimally absorbed by blood. Therefore, there is little or no direct heating of blood during endocardial ablation, resulting in a lower risk of thrombus than for RF energy [52–54]. Ultrasound energy decays as the inverse of distance from the source. In contrast, RF energy decays as the inverse of the square of the distance. The reduced decay allows ultrasound energy to produce a more homogeneous pattern of tissue heating with less focal hot spots in the tissue, a lower risk of steam pop, and deeper lesions (Figure 14.3).

Ultrasound penetration into the myocardium is dependent on frequency (higher the frequency, less the depth of penetration). Ablation using ultrasound at 20, 9, and 1 MHz would be expected to have a depth of active heating of 1–2, 5–6, and 25–30 mm, respectively. In a preliminary study, ablation using a 9 MHz ultrasound catheter created long (>14 mm) and deep (>8 mm)

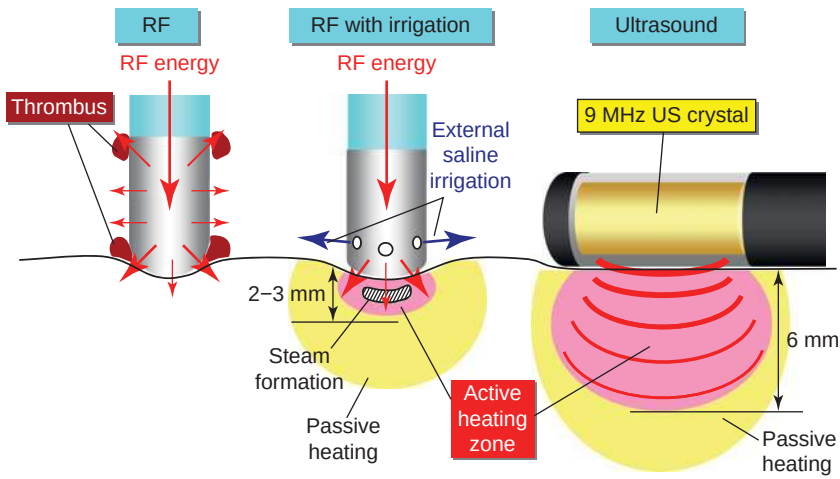

Figure 14.3 Comparison of radiofrequency (RF) energy and ultrasound energy for lesion formation and risk of steam pop and thrombus. Left panel: RF ablation using a nonirrigated electrode results in thrombus formation when the interface temperature between the electrode and the tissue or the electrode and blood reaches 75–80°C, even though the electrode temperature may be <55–60°C. Center panel: RF ablation using a saline-irrigated electrode prevents thrombus. However, a higher RF power application produces a focal hot spot 2–3 mm below the surface, resulting in steam formation within the tissue and a steam pop. Right panel: Ultrasound energy at 9 MHz penetrates myocardial tissue to a depth of 5–6 mm and produces a homogenous active tissue heating, resulting in a deeper lesion with a lower risk of steam pop and thrombus

lesions without thrombus or steam pop in a canine thigh muscle preparation (Figure 14.4) [53].

The advantages of ultrasound energy for percutaneous epicardial ablation are the ability to penetrate epicardial fat and no requirement for additional external cooling. The limitations for epicardial ablation are as follows: (1) acoustic insulation may be required to prevent collateral damage to a coronary artery and phrenic nerve; and (2) injection of saline into the pericardial space may be required to ensure an air-free interface between the catheter and the epicardium.

Laser energy

A major advantage of laser energy for ablation of VT is the ability to use an endoscopic fiber to allow direct visualization of the ablation target. Because the laser energy is absorbed by blood, lasing into blood may produce thrombus. This can be avoided by using a balloon filled with clear fluid, generally

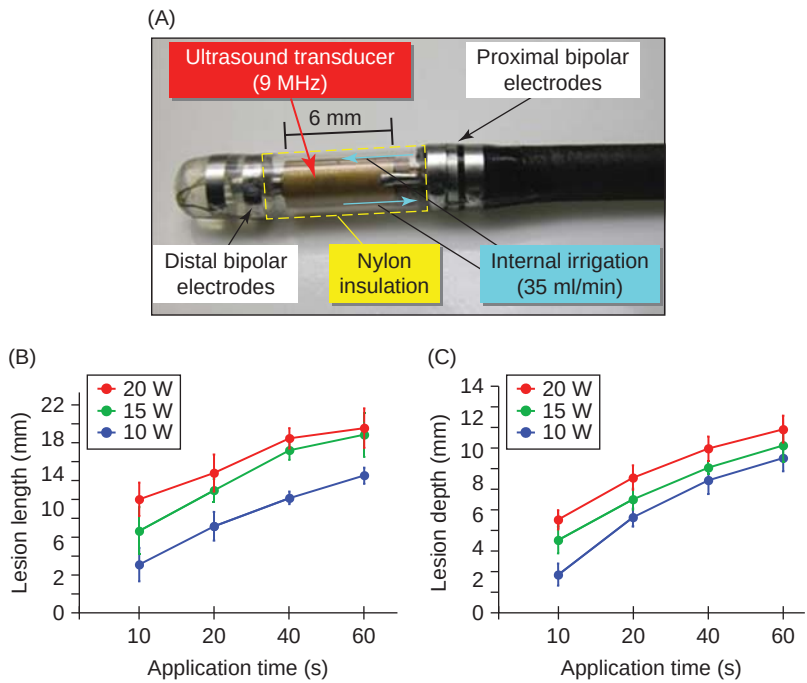

Figure 14.4 A prototype 10.5 Fr deflectable catheter (ProRhythm, Inc) has a 9-MHz ultrasound transducer, which is 6 mm in length (panel A). The transducer is irrigated internally at 35 ml/min to maintain a transducer temperature <43°C. There are two close bipolar electrodes on either side of the transducer. In a canine thigh muscle preparation, single ultrasound applications using this ablation catheter consistently created long (usually >14 mm in length measured perpendicular to the catheter, panel B) and deep lesions (usually >8 mm in depth, panel C) without thrombus or steam pop

D_2O (heavy water), and visualizing the ablation filed through the endoscopic fiber [54]. Another advantage of endoscopic visualization is that scar and scar border can be easily seen for scar localization. Laser energy may not be well absorbed by fibrous tissue. This may result in refraction of the laser light until reaching myocardial cells for improved ablation of surviving myocardial bundles (arrhythmogenic channels) within the scar.

The advantages of laser energy for percutaneous epicardial ablation are (1) penetration of epicardial fat, (2) the ability to penetrate through air in the pericardial space, and (3) directional focus to prevent collateral damage to a coronary artery and phrenic nerve.

Future ablation using new tools such as ultrasound and laser energy sources, combined with new localization techniques such as direct visualization using endoscopy, may improve the ease, efficacy, and safety for endocardial and epicardial catheter ablation of VT/VF.

Virtual electrode and cellular ablation

A substantial amount of progress in the development of these new energy technologies has been made over the past 10 years. These enable the creation of larger lesions that may be more effective in penetrating through underlying tissue abnormalities such as infarct scar. Large and irrigation-tip electrodes allow tissue cooling through internal flow or convective means, thereby fostering the delivery of higher power with less chance of an impedance pop or scar formation. Nevertheless, these approaches remain limited in reaching circuits embedded in thick scar.

As a result, needle tip electrodes have been developed for the delivery of both energy and higher ionic strength solutions such as normal saline into the tissue [55,56]. The combination of this delivery results in a synergistic effect to create a larger "virtual electrode." Recent studies [55,56] have demonstrated the utility of such a system for creating large linear lesions in infarcted myocardium. In studies abating normal and abnormal infarcted myocardium, these investigators demonstrated that up to 90% of embedded tissue strands relevant for reentrant circuit in an infarct were effectively eliminated. Additional studies demonstrated the creation of contiguous linear lesions extending through the entire myocardium. Sapp *et al*. [56] have also demonstrated higher delivery of power within tissue, providing more full thickness energy delivery than possible with standard irrigation-tip catheters.

While these data provide new insight into the generation of larger lesions, additional efforts will be required to produce controllable lesions of narrower width. To date, the safety of these approaches has also been understudied. Nevertheless, in normal myocardium, recent preliminary studies show little effect on chamber volumes or LV function as measured in the ejection fraction. Undoubtedly, the application of this technology would require careful targeting of infarcted areas rather than residual healthy myocardium.

Cell therapies

Another avenue for investigation of novel treatment modalities is that of cell therapy for arrhythmias. Extensive studies detail the utility of delivery of either stem cells or bone marrow progenator cells to the enhancement of myocardial contractility [57]. A variety of recent clinical trials have also demonstrated additional benefit, although these have not demonstrated mortality benefit. There have also been questions regarding the occurrence of proarrhythmic events. Progenator cells may be less likely to create this problem. The complex electrophysiology involved in the tissue engraftment of these cells has been reviewed in other sources.

The issue of whether or not these approaches serve an antiarrhythmic purpose has been less completely explored. Recently, Bunch *et al*. [58]

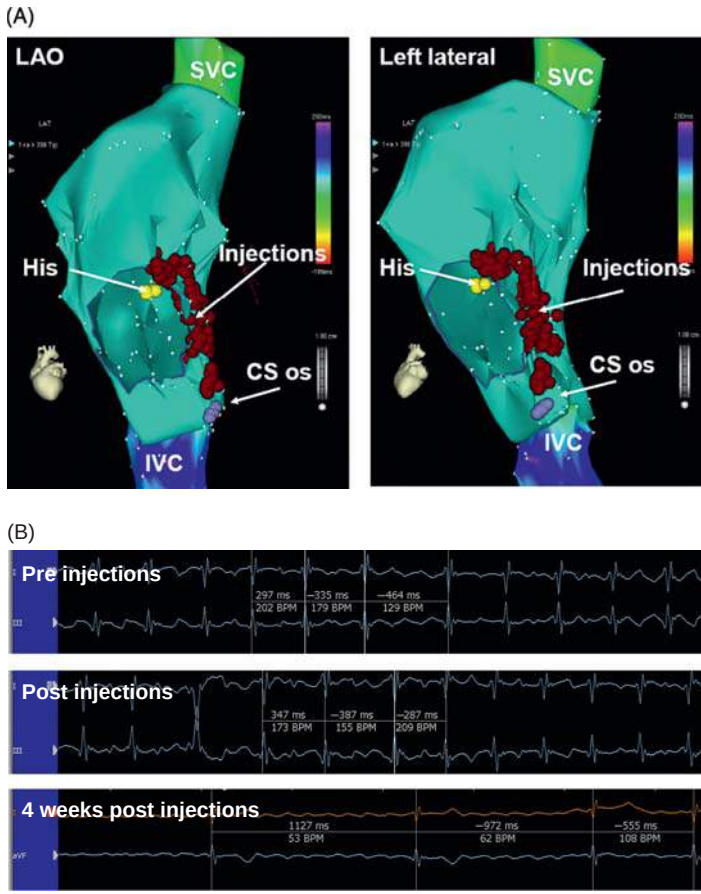

Figure 14.5 Panel A shows a left anterior oblique and a left lateral view of a 3D map of the right atrium with the sites of fibroblast injection (red dots) around the His bundle region (yellow dots). In panel B from top to bottom, the ventricular response during atrial fibrillation is shown before, after, and 4 weeks postfibroblast injection.

demonstrated that injection of autologous fibroblasts, cultured from the dermis of canines, could be injected into peri-AV nodal tissue to modulate conduction during atrial fibrillation in an intact canine model (Figure 14.5A). While the effect was pronounced with cells alone, fibroblasts incubated with TGF-β 1 grew to a much larger extent, resulting in greater prolongation in AV nodal conduction time, also reducing the ventricular response rate during atrial fibrillation (Figure 14.5B). Others have shown similar findings in porcine models [59]. These data suggest that cell injection might critically alter conduction to reduce AV nodal transit in the setting of this arrhythmia. It has also been hypothesized that similar cellular injections would more homogenize the periphery of infarcts, perhaps leading to a decrease in infarct-related ventricular arrhythmias [60].

Whether or not cellular injection might have a beneficial effect on impulse formation or propagation has been less completely studied. A variety of studies have now demonstrated the possibility of the creation of automatic tissue capable of generating sinus node-type impulses [61]. The use for enhancing conduction elsewhere in the myocardium has not been examined, but should serve as an important area of subsequent research. While each of these areas are exciting, much additional work will be required to bring these to a level permitting full application in the clinical arena.

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Index