SECTION IV

Arrhythmias

EDITOR

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CHAPTER 21

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Tachyarrhythmias

I. INTRODUCTION. Tachyarrhythmias have been classically categorized by their location and mechanism. Tachyarrhythmias can originate from ventricular tissue (ventricular tachycardia) or, alternatively can originate from or involve supraventricular tissue (supraventricular tachycardia). The three mechanisms of tachyarrhythmias include abnormal automaticity, triggered activity, and reentry.

A. Abnormal automaticity. Automaticity refers to the ability of cardiac tissue to spontaneously generate pacemaker activity. There are both normal and abnormal sources of automaticity.

1. An example of **normal** accelerated automaticity is the rapid firing rates of a normal pacemaker focus, such as the sinus node (SN), atrioventricular (AV) node, or Purkinje system due to ischemia, metabolic disturbance, exercise, or pharmacologic manipulation. A clinical example would be accelerated **sinus tachycardia** or **junctional rhythm**.
2. Abnormal automaticity refers to tissues that under normal circumstances do not demonstrate automaticity, but can become automatic in the setting of ischemia, metabolic disturbance, or pharmacologic manipulation. Overall, abnormal automaticity is responsible for < 10% of tachyarrhythmias. These latent or ectopic loci of cells generate automatic, spontaneous impulses that usurp control of the cardiac rhythm. These usually have a warm-up and cool-down period and cannot be induced by programmed electrical stimulation. A clinical example would be **accelerated idioventricular** rhythm (see Section IV.C.1) or **multifocal atrial tachycardia** (see Section **II.F**).

B. Triggered activity refers to pacemaker activity that is dependent on afterdepolarizations from a prior impulse or series of impulses. Afterdepolarizations are oscillations in the membrane potential. If these reach the critical threshold for depolarization of the surrounding cardiac tissue, they may trigger an action potential, thereby precipitating further afterdepolarizations and perpetuating the pacemaker activity. The two categories of afterdepolarizations are early and delayed.

1. Early afterdepolarizations (EADs) occur before repolarization of the cardiac tissue is completed (during phase 3 of the action potential) and may be the mechanism responsible for the ventricular arrhythmias of the **long QT syndromes (LQTSs)**, as well as **torsade de pointes** ("twisting of the points") produced by class I and class III antiarrhythmics, sympathetic discharge, and hypoxia. Antibiotics such as macrolides, certain azole antifungal agents, some psychotropic medications such as haloperidol, and several nonsedating antihistamines have been shown to produce EADs. Rapid heart rates and the administration of magnesium have been shown to suppress EADs.
2. Delayed afterdepolarizations (DADs) occur after the repolarization of the surrounding tissue is complete (during phase 4 of the action potential) and are thought to be the mechanism of triggered atrial tachycardia, arrhythmias of **digitalis toxicity**, and rare ventricular tachycardias (VTs) responsive to calcium channel blockers. These have been demonstrated in various cardiac issues, including

parts of the conducting system, myocardial cells, and valve tissues. Increases in intracellular calcium are associated with DADs, such as those caused by digitalis preparations or excessive sympathetic stimulation. Drugs that block the influx of calcium (such as calcium channel blockers and β-blockers) and drugs that decrease the sodium current (such as lidocaine and phenytoin) suppress the occurrence of DADs, whereas rapid heart rates augment DADs.

C. Reentry. **Reentry is the most common cause of tachyarrhythmias**. In order for reentry to occur, **three conditions** must be met:

1. Two functionally distinct conducting pathways must connect to form a circuit.
2. Unidirectional conduction block occurs in one of the pathways due to differences in refractory periods (block occurs in pathway with the longer refractory period).
3. Slow conduction occurs down the unblocked pathway (which has the shorter refractory period), allowing the blocked pathway time to recover excitability and sustain the arrhythmia.

Reentrant circuits can occur in the sinus node, the atrium, the AV node, between the atrium and ventricle via bypass tracts, and within the ventricle itself. The typical substrate for malignant reentry in the ventricle is **scar or ischemia**, which can produce regions in the heart that **depolarize and repolarize heterogenously**. Therefore, the impulse can spread to an area that has already repolarized after being previously depolarized. This can set up a circular movement of the impulse resulting in sustained tachyarrhythmias such as VT. Reentry can typically be induced by premature electrical stimulation during electrophysiologic testing.

Elucidation of the mechanisms of tachyarrhythmias has led to the development of catheter-based treatment strategies and more advanced medical therapy.

II. SUPRAVENTRICULAR TACHYARRHYTHMIAS

A. Sinus tachycardia

1. **Clinical presentation.** Sinus tachycardia manifests as sinus rhythm with a rate above 100 beats/min. Although the rate may be as high as 200 beats/min in younger individuals, it is generally **150 beats/min or less in older individuals**.
2. **Pathophysiology**
   - **a.** The SN is an epicardial structure that is located laterally near the junction between the superior vena cava and the right atrium. Under normal circumstances, the rate of SN discharge is governed by sympathetic and vagal stimulation.
   - **b.** Sinus tachycardia generally reflects **an underlying process, metabolic state, or effect of medication**. Fever, hypovolemia, shock, congestive heart failure (CHF), anxiety, pulmonary disease including pulmonary embolism, anemia, thyrotoxicosis, caffeine, nicotine, atropine, catecholamines, or withdrawal from alcohol or drugs (both therapeutic and illicit) can cause sinus tachycardia.
   - **c.** Sinus tachycardia can be appropriate, where it represents a normal physiologic response, **or inappropriate**, as in defects in vagal or sympathetic tone or an intrinsic problem with the SN itself.
   - **d.** The **clinical consequences of sinus tachycardia vary** based on the presence or absence of underlying heart disease. Patients with significant coronary artery disease (CAD), left ventricular (LV) dysfunction, or valve disease may not tolerate sinus tachycardia. Patients with inappropriate sinus tachycardia may experience significant symptoms such as palpitations, dyspnea, and/or chest pain.
3. **Diagnostic testing.** Electrocardiography is the primary diagnostic test. The main differential is between sinus tachycardia, sinus node reentry tachycardia (SNRT) (see Section **II.B**), and inappropriate sinus tachycardia. Inappropriate sinus tachycardia is characterized by the following features: **(a) heart rate > 100 beats/min, (b) P-wave axis and morphology during tachycardia similar or identical to that during sinus rhythm, (c) exclusion of secondary causes**

of sinus tachycardia, (d) exclusion of atrial tachycardias, and (e) symptoms clearly documented to be related to resting or easily provoked sinus tachycardia.

4. Therapy is generally directed at the elimination of the underlying cause whenever possible.
   a. If withdrawal from a therapeutic medication is suspected, then reinstitution or slow tapering of this medication can be attempted, if clinically appropriate.
   b. In the case of **inappropriate sinus tachycardia, β-blockers and calcium channel blockers** may be necessary to control the heart rate.
   c. In **medically refractory cases, catheter ablation for sinoatrial nodal modification** may have to be considered.

B. SNRT accounts for 5% to 10% of all supraventricular tachyarrhythmias.

1. **Clinical presentation.** SNRT is most frequently seen in patients with structural heart disease or CAD, especially in inferior myocardial infarctions (MIs). The rate varies from 80 to 200 beats/min. SNRT's characteristic abrupt onset and termination (paroxysmal nature) along with its ability to be induced and terminated by pacing imply that the underlying mechanism is reentry and distinguish it from sinus tachycardia and inappropriate sinus tachycardia.
2. **Pathophysiology.** Reentry occurs within or adjacent to the SN and then conducts via the normal conduction pathway to the rest of the heart. The morphology of the P wave is identical to the underlying sinus morphology. Block at the AV node may occur, but it does not slow the tachycardia. In fact, a Wenckebach-type block often occurs with this rhythm. The development of a bundle branch block does not affect the cycle length or the PR interval.
3. **Therapy.** Vagal maneuvers or adenosine may successfully terminate this arrhythmia. **Rapid atrial pacing** can be used to induce and terminate this tachycardia. Various agents such as β-blockers, calcium channel blockers, and digoxin may help prevent recurrences. SN ablation or modification is rarely necessary.

C. Atrial fibrillation (AF) is the most common sustained arrhythmia, occurring in up to 1% of the general population. The prevalence of AF increases with age, affecting up to 10% of the population older than 80 years (see Chapter 24).

D. Atrial flutter. Atrial flutter is the **second most common of the atrial tachyarrhythmias**. Its reported incidence varies from 0.4% to 1.2% in hospital reports of electrocardiogram (ECG). The **clinical significance of atrial flutter is generally due to its association with AF** (with all of the attendant risks of AF) and/or its association with rapid rates of ventricular response.

1. **Clinical presentation.** The clinical presentation may vary widely depending on the presence of underlying heart disease, the ventricular rate, and the overall condition of the patient. It is **occasionally reported to persist for days** and, less commonly, for weeks or longer. Careful examination of the jugular venous pulse may reveal **frequent, regular a waves** that correspond to the atrial flutter rate. Like AF, it is **commonly seen after open heart surgery, as well as with other conditions commonly associated with AF**, such as pulmonary disease, thyrotoxicosis, atrial enlargement due to any cause including mitral/tricuspid valve disease, and SN dysfunction.
2. **Pathophysiology.** "Typical" atrial flutter is the **result of a macroreentrant circuit in the right atrium**. Atypical atrial flutter generally involves other macroreentrant circuits around scar tissue or surgical incisions.
   a. **In a typical atrial flutter, the reentrant circuit most commonly travels in a counterclockwise rotation** down the right atrial anterolateral free wall across the cavotricuspid isthmus (area of slow conduction) and up the interatrial septum. Clockwise rotation of this circuit may also be seen.

b. Atrial flutter has been classified into type I and type II based on the following characteristics:

(1) Type I atrial flutter can be terminated with rapid atrial pacing and typically has an atrial rate in the range of 240 to 340 beats/min in the absence of drug therapy.

(2) Type II atrial flutter cannot be terminated with rapid atrial pacing and typically has an atrial rate in the range of 340 to 440 beats/min in the absence of drug therapy.

(3) Types I and II are not synonymous with typical and atypical atrial flutters. Type I atrial flutter can include typical and atypical atrial flutters. Type II atrial flutter is less well characterized than type I with respect to etiology and therapy; therefore, **we refer to type I atrial flutter throughout this discussion**.

3. Laboratory examination

a. The **diagnosis can be difficult when the AV conduction is 2:1**, as the flutter waves may be superimposed on the QRS complex and/or the T waves. When the diagnosis is uncertain, one should **consider maneuvers or medications to slow the ventricular response**, thus revealing the atrial flutter complexes.

(1) Vagal maneuvers include carotid sinus massage and Valsalva maneuver. **Caution must be exercised** when attempting carotid sinus massage **in patients with known or suspected carotid disease** or vagal maneuvers in **patients with CAD who are at risk for ischemia**.

(2) Adenosine can be administered, 6 mg rapid intravenous push, followed by 12 mg if there is no response (a second 12-mg dose can be given if there is no response). The half-life of this medication is very short, approximately 9 seconds. This causes transient (lasting seconds), complete AV block. Alternative agents include the intravenous calcium channel blocking agents **verapamil and diltiazem** and the intravenous β-blockers **esmolol and metoprolol**. Patients should be connected to a transcutaneous pacing device during the administration of this medication for reasons of safety.

(3) The clinician can place and record from a **transesophageal electrode** or record from a **temporary atrial epicardial pacing wire** (placed at open heart surgery). This results in an ECG with clearer atrial complexes and thus simplifies diagnosis. This strategy also allows a method of delivering rapid atrial pacing in an attempt to terminate the atrial flutter.

b. On the surface ECG, typical counterclockwise atrial flutter shows the **classic negatively directed "sawtooth" waveform** in the inferior leads (II, III, and aVF) (Fig. 21.1). Conversely, the atrial depolarizations are positive in these leads in clockwise atrial flutter (Fig. 21.2).

c. The **atrial rate** in the absence of drug therapy is **240 to 340 beats/min**.

d. The **QRS complex should be the same as that seen during sinus rhythm** although aberrant conduction may occur, and the QRS may be slightly distorted by the atrial flutter waves.

e. The **ventricular response** can be irregularly irregular, due to varying degrees of block (2:1, 4:1, and so on), but is more **typically regular as a fixed ratio of the flutter rate**.

4. Therapy

a. Medical therapy differs very little from that for AF (see Chapter 24).

(1) Control of the ventricular response rate with a β-blocker, a calcium channel blocker, or digoxin is critical prior to initiating therapy with agents such as the class IA or IC agents. The class IA or IC agents either enhance AV nodal conduction through their vagolytic effects, thereby enabling 1:1 (AV) conduction, or slow the atrial rate to a point where 1:1 conduction is facilitated.

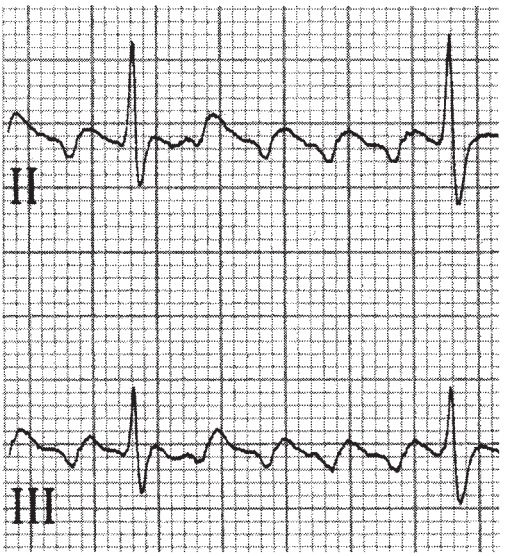


FIGURE 21.1 "Typical" atrial flutter, leads II and III.

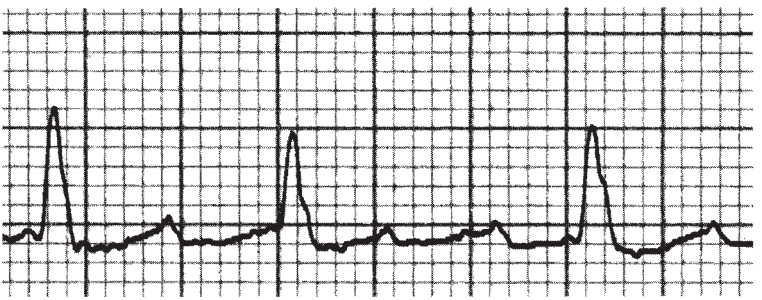


FIGURE 21.2 "Atypical" atrial flutter, lead II.

(2) The conversion from atrial flutter to AF after cardioversion is substantially reduced by the administration of antiarrhythmic drugs prior to direct current cardioversion (DCC), thereby increasing the chance of converting to sinus rhythm.

(3) Anticoagulation. There are no prospective data looking at the incidence of thromboembolic events with atrial flutter. However, retrospective data suggest an increased incidence of thromboembolic events. Recent ACCP (2004) and ACC/AHA/ESC (2006) guidelines recommend managing anticoagulation in atrial flutter in a manner similar to that for AF, including cardioversions. Optimal management is unclear and often needs to be individualized with the patients' profile for thromboembolic risk dictating the type and duration of therapy. We treat atrial flutter in a manner similar to that used for AF with regard to anticoagulation.

b. Direct current cardioversion

(1) DCC is the preferred and most effective therapy for most patients. The procedure is detailed in Chapter 59. A starting energy as low as 25 to 50 J is often effective. Because DCC may result in conversion from atrial flutter to AF, a second shock is sometimes necessary to convert AF to sinus rhythm.

(2) Rapid atrial pacing should be considered as the **first line of therapy for all patients who have epicardial atrial pacing wires in place after open heart surgery**. It may be considered via a transesophageal pacing lead or via a transvenously placed pacing lead in patients for whom DCC fails or who are not candidates for DCC. **Before attempting to rapidly pace the atria, it must be confirmed that ventricular capture is not inadvertently occurring** by first pacing at a relatively slow rate while observing for such a phenomenon. Once this is confirmed, the atrium is paced at a rate of 10 to 20 beats/min faster than the underlying atrial flutter rate. Once atrial capture is attained, the rate is increased steadily until the hallmark negative-sawtooth waveform converts to a positive waveform. The pacing is then either halted abruptly or slowed rapidly to an acceptable atrial pacing rate. In cases that require extremely rapid rates of pacing (> 400 beats/min) or high amplitudes of pacing stimulus strength (> 20 mA), there is an increased tendency for the atrial flutter to convert to AF. **When pacing via a transesophageal lead, a higher stimulus strength (up to 30 mA) may be necessary**. **Because this type of pacing can be quite painful**, a sufficient energy to convert the atrial flutter should be used initially to minimize the conversion attempts.

(3) Percutaneous therapy. Radiofrequency ablation (RFA) of the cavotricuspid isthmus is often curative, with an efficacy > 90% for the long-term elimination of atrial flutter. Despite the high success rate of catheter-based therapy, a significant number of patients may subsequently develop AF.

E. Atrial tachycardias. This term encompasses a number of different types of tachycardias that originate in the atria. These tachycardias account for between10% and 15% of the tachycardias seen in older patients, usually in the setting of structural or ischemic heart disease, chronic obstructive pulmonary disease, electrolyte imbalances, or drug toxicity (particularly digitalis).

1. Clinical presentation. These tachycardias are **infrequently seen in younger, healthy patients without underlying heart disease**. They are **typically paroxysmal**, but if incessant they can lead to a tachycardia-induced cardiomyopathy.

2. Diagnostic testing

a. ECG

(1) The **P-wave axis** or morphology is usually different from that of sinus rhythm. One exception is atrial tachycardias originating from the right superior pulmonary vein, which is anatomically close to SN. The axis can be used to predict the origin of the atrial tachycardia.

(2) Atrial rhythm is regular, except with automatic atrial tachycardia, which displays a warm-up period (see Section **II.E.3.b**).

(3) A **QRS complex that is generally identical to sinus rhythm** (QRS can be wide if aberrant conduction occurs) follows each P wave.

(4) PR interval is within normal limits or prolonged.

(5) Nonspecific ST-T–wave changes may be present.

(6) When an AV block is present, there is an **isoelectric baseline** between P waves in all leads.

b. Electrophysiologic study has become critical in determining the underlying mechanism of these tachycardias, as the clinical differences are subtle and overlapping.

3. **Subclassifications.** The current subclassifications are **based on mechanisms** and include automatic atrial tachycardia, triggered atrial tachycardia, and intra-atrial reentry.
   a. Intra-atrial reentry is usually a disorder **seen in those with underlying heart disease or history of atrial arrhythmia**, such as AF or atrial flutter. The mechanism is not well understood. The ventricular rate is typically 90 to 120 beats/min due to the frequent occurrence of 2:1 AV block, such that hemodynamic effects are generally minimal. This rhythm can be difficult to distinguish from other supraventricular tachyarrhythmias. One clue is that despite any AV conduction block, the rhythm continues. The ability to terminate with adenosine and β-blockers is variable. **RFA may be effective**, with success rates **>** 75%. **Antiarrhythmics** (the same drugs as for AF and atrial flutter) **have been disappointing in the prevention of recurrence**.
   b. Automatic atrial tachycardia appears to be generated by an ectopic atrial focus, which usually arises from regions around the crista terminalis in the right atrium and around the base of the pulmonary veins in the left atrium. The mechanism is not well understood. Automatic atrial tachycardia is **seen more often in younger patients**, displays a **warm-up phenomenon** (the supraventricular tachyarrhythmia accelerates after its initiation), **does not respond to vagal maneuvers, and is more likely to be incessant**. Automatic atrial tachycardia can be induced with treadmill testing or with administration of isoproterenol. Atrial stimulation during electrophysiologic study has no effect on either initiating or terminating this arrhythmia. **Propranolol** has been used successfully to suppress automatic atrial tachycardia. **Catheter ablation is the preferred therapy when the tachycardia is incessant**. Although adenosine may transiently slow automatic atrial tachycardia, it is unlikely to terminate it. Likewise, verapamil has been used without success.
   c. Triggered atrial tachycardia is the least common of the atrial tachycardias and is virtually never incessant. It is more likely to appear in **older individuals**. It can be induced with rapid atrial pacing and is cycle length–dependent. The mechanism of triggered atrial tachycardia is thought to be due to DADs (see Section **I.A.2**) secondary to digitalis toxicity or sympathetic discharge. Catecholamines may play a role in the initiation of this arrhythmia, and thus exercise testing and isoproterenol may provoke it. Verapamil and adenosine have been shown to terminate triggered atrial tachycardia. β-Blockers have been less effective. **RFA** is preferred when the tachycardia is very symptomatic and not responsive to medication.

F. Multifocal atrial tachycardia

1. **Clinical presentation.** This atrial arrhythmia is uncommon and estimated to occur in 0.37% of hospitalized patients. The atrial rate is generally 100 to 130 beats/min. It occurs most often in elderly, critically ill patients and is frequently **associated with concurrent pulmonary disease, particularly chronic obstructive pulmonary disease**. It may also be seen in CHF and can degenerate into AF.
2. **Pathogenesis and diagnostic tests.** The mechanism appears to be abnormal automaticity or triggered activity arising from distinct atrial sites. The diagnosis requires the following criteria: (1) atrial rate > 100 beats/min, (2) P waves with three or more different morphologies, (3) varying P-P, P-R, and R-R intervals, and (4) the P waves separated by isoelectric intervals. Loss of AV conduction of each P wave is uncommon, making it possible to distinguish multifocal atrial tachycardia from AF.
3. **Therapy is directed at the underlying illness, with little role for antiarrhythmics.** Calcium channel blockers in high doses may be useful, or amiodarone when antiarrhythmic therapy is deemed necessary. Maintenance of electrolyte balance, particularly potassium and magnesium, may suppress the occurrence of multifocal atrial tachycardia.

G. Atrioventricular nodal reentrant tachycardia (AVNRT)

1. **Clinical presentation.** AVNRT usually has a narrow QRS complex with a ventricular rate typically in the range of 150 to 250 beats/min, although faster rates are infrequently observed. AVNRT is generally seen in patients without underlying heart disease. Palpitations and dyspnea are common presenting complaints. Angina, CHF, and rarely shock may be seen in those with a history of underlying heart disease. Syncope may occur due to rapid ventricular rates or due to asystole or bradycardia seen occasionally when this tachycardia terminates.
2. **Pathophysiology.** The mechanism in AVNRT appears to be a reentrant circuit composed of separate fast and slow atrial pathways involving the AV node. In 50% to 90% of patients with "typical" AVNRT, the antegrade conduction to the ventricles travels over the slow pathway and the retrograde conduction to the atria occurs over the fast pathway. The initiating event may be either a premature atrial complex (PAC) or a premature ventricular complex (PVC). The PAC blocks the fast pathway antegradely and conducts down the slow pathway, then backs up the fast pathway after it has repolarized. Less commonly, a PVC conducts retrogradely to the atria via the fast pathway and then returns to the ventricles via the slow pathway. In the remaining 5% to 10% of patients, with atypical AVNRT, the antegrade conduction is down the fast pathway and retrograde via the slow pathway. The cycle length is thus dependent on the conduction velocity of the slow pathway, since the fast pathway generally has rapid conduction. Termination of the tachycardia is often the result of a block in the slow pathway. AV dissociation may develop during the tachycardia because the ventricles are not involved in the reentry circuit. This does not affect the rate of tachycardia nor does the development of bundle branch block.
3. **Laboratory features and diagnosis.** P waves are generally hidden within the QRS complex or at the terminal portion of the QRS in typical AVNRT. This may be visible as a small pseudo-R′ in lead V_1 or small negative deflections in the inferior leads, as depolarization of the atria occurs simultaneously with ventricular depolarization. The RP segment is generally < 100 milliseconds. AVNRT is often induced abruptly by a PAC and its termination, which also tends to be abrupt, is often followed by a retrograde P wave. The termination may be followed by a brief period of asystole or bradycardia before the SN recovers from its tachycardia-induced suppression. The cycle length may vary, especially at the beginning and at the end of the tachycardia. This variation reflects the variable antegrade AV nodal conduction time. Vagal maneuvers may slow or terminate this tachycardia.
4. **Therapy.** Presently, the success and safety of percutaneous catheter ablation have allowed this approach to be considered equally with medical therapy as first-line therapy for long-term management of AVNRT. The decision about treatment approach should be individualized according to the characteristics of each patient and his or her arrhythmic patterns.
   a. RFA has the advantage of curing the arrhythmia in the majority of instances and eliminating the need for long-term suppressive therapy with medications. Cure rates with catheter ablation for AVNRT are in excess of 95%.
   b. **Medical therapy.** Medications that suppress AV nodal conduction such as β-blockers, calcium channel blockers, digoxin, and adenosine all slow or block conduction in the antegrade slow pathway, whereas class IA and class IC antiarrhythmic drugs slow the conduction in the retrograde fast pathway. Adenosine may be considered as first-line drug therapy for acute termination of AVNRT. This medication is available in an intravenous form only and has a very short half-life of about 9 seconds. The use of intravenous or oral β-blockers or calcium channel blockers is an alternative if adenosine is unsuccessful. The onset of action of digoxin limits its usefulness in terminating these arrhythmias, although it may be useful to prevent recurrences. Recurrences may be prevented in patients

with frequent sustained episodes with any of the above-mentioned agents except adenosine. Antiarrhythmic drug therapy is not routinely necessary or desirable for AVNRT, given the high success rates and low complication rates for catheter ablation.

c. DCC should be considered for patients whose disease is unstable or highly symptomatic. Low energies of 10 to 50 J are usually sufficient to terminate AVNRT.

H. Atrioventricular reentrant tachycardia (AVRT)

1. **Clinical presentation.** Similar to AVNRT, this is another example of an AV nodal–dependent supraventricular tachycardia (SVT). AVRT usually has a narrow QRS with ventricular rates similar to those of AVNRT, although it more often tends to have a ventricular rate > 200 beats/minute. The clinical features are very similar to those of AVNRT but are distinct on an electrophysiologic basis.
2. **Pathophysiology.** The mechanism in AVRT relies on the presence of an accessory pathway as one portion of the circuit and the AV node as the other portion. The atrium and the ventricle on the same side as the accessory pathway are necessary components of the circuit. AVRT may be orthodromic or antidromic. Orthodromic AVRT usually has a narrow complex that uses the AV node as the antegrade limb and the accessory pathway as the retrograde limb of the circuit. Antidromic AVRT has a wide complex that is the opposite of the orthodromic variety, such that the accessory pathway serves as the antegrade limb and the AV node as the retrograde limb of the circuit. AVRT is most often of the orthodromic type. Accessory pathways may be "concealed" (inapparent by ECG) because of having only retrograde (V to A) conduction properties or "manifest" (apparent on ECG as delta waves, i.e., Wolff-Parkinson-White [WPW] pattern). **Unlike AVNRT, the AVRT circuit must involve one of the ventricles; therefore, the development of bundle branch block on the side ipsilateral to the accessory pathway can prolong the ventricular to atrial conduction time and often the cycle length of the tachycardia**. Bundle branch block, particularly left bundle branch block (LBBB), occurs more commonly in AVRT than in AVNRT. AVRT can be distinguished from AVNRT by electrophysiologic study. The presence of AV or ventriculoatrial (VA) block with continuation of the tachycardia should exclude the presence of an accessory AV pathway.
3. **Laboratory features and diagnosis.** The P waves of AVRT are frequently inscribed on the ST segment or T wave, as the atrial depolarization and ventricular depolarization are in series rather than in parallel. The RP segment is generally > 100 milliseconds. Orthodromic AVRT is more common, accounting for about 95% of all AVRTs, whereas antidromic AVRT accounts for only about 5%. Orthodromic AVRT is usually characterized by a narrow QRS complex as opposed to antidromic AVRT, which is characterized by a wide QRS complex.
4. **Therapy.** See the discussion of therapy for WPW syndrome (Section **I.4**).

I. Preexcitation syndromes. Preexcitation was originally used to describe the premature activation of ventricle in patients with WPW. The term has broadened to include all conditions in which antegrade ventricular activation or retrograde atrial activation occurs partially or totally via an anomalous pathway distinct from the normal cardiac conduction system. The incidence of preexcitation on ECG is approximately 1.5 per 1,000 cases, most of which occur in otherwise healthy subjects without organic heart disease. About 7% to 10% of these patients have associated Ebstein's anomaly and are thus more likely to have multiple accessory pathways. There is a higher rate of preexcitation in males, with the **prevalence** decreasing with age, although the **frequency** of paroxysmal tachycardia increases with age.

1. **Clinical presentation.** Approximately 50% to 60% of patients with preexcitation report symptoms such as **palpitations, anxiety, dyspnea, chest pain or tightness, and syncope**. In approximately 25% of the cases, the disease will

become asymptomatic over time. Those patients older than 40 years whose disease has been asymptomatic are likely to remain symptom free. The absence of preexcitation on ECG despite the discovery of accessory pathways in patients with asymptomatic disease likely identifies a group of patients at low risk for developing symptoms.

2. **Pathophysiology.** Patients with preexcitation generally have an accessory pathway(s) that alters the conduction between the atria and the ventricles. These accessory pathways are likely congenital, as relatives of subjects with preexcitation have an increased incidence of preexcitation. AVRT is the most common mechanism associated with preexcitation (80% to 85%), with permanent junctional reciprocating tachycardia, Mahaim fiber tachycardia, and Lown-Ganong-Levine (LGL) syndrome accounting for the remainder.
   a. **WPW syndrome.** The basic abnormality lies in the existence of an accessory pathway of conducting tissue, outside of the normal conducting system, which connects the atria and the ventricles. This accessory pathway permits the atrial impulse to bypass the normal pathway through the AV node to the ventricles. In the past, these accessory pathways have been referred to as "bundles of Kent." An impulse from the atria can be conducted down both the accessory pathway and the AV node, arriving at the ventricle at nearly the same time. This results in preexcitation of the ventricle, which is really a fusion beat, as a portion of the ventricle is activated via the accessory pathway (giving rise to the delta wave; Fig. 21.3) and the remainder of the ventricle is activated by the normal activation pathway. If antegrade conduction occurs exclusively via the accessory pathway, the resultant QRS is maximally preexcited and is a wide complex. These accessory pathways may conduct rapidly, but frequently have longer refractory periods than the AV node. The inciting event for AVRT is frequently a PAC that is blocked in the accessory pathway and that conducts to the ventricles via the AV node, which has recovered more rapidly. The resultant QRS complex in this instance is normal in appearance. After the QRS complex, the accessory pathway has had sufficient time to recover excitability, and the impulse thus conducts retrogradely to the atria. A small but significant percentage (5% to 10%) of patients have multiple accessory pathways.
   b. Permanent junctional reciprocating tachycardia is a variant of AVRT. It is often an incessant supraventricular tachyarrhythmia with an unusual accessory pathway. Here, the accessory pathway behaves like the AV node in that it displays decremental retrograde conduction properties. Thus, the faster the stimulation of such an accessory pathway, the slower the conduction through the pathway. The accessory pathway is most often located in the posteroseptal region and acts as the retrograde limb of the reentrant circuit. The VA conduction is slowed by the decremental nature of the accessory pathway. Due to the incessant nature of this tachycardia, a tachycardia-induced cardiomyopathy may result.
   c. **Mahaim fiber tachycardias are another variant of reentrant tachycardia.** The two most common varieties that are recognized are **atriofascicular and fasciculoventricular.** In the former, the accessory pathway is located within a few centimeters of the AV node and inserts into the right bundle branch. The reentrant tachycardia conducts antegrade via the accessory pathway, resulting in an LBBB morphology with left-axis deviation. The retrograde circuit is via the AV node. In the second form of Mahaim reentry, the accessory pathway arises in the His-Purkinje fibers and allows bypass of the distal conducting system.
   d. LGL syndrome is diagnosed by the presence of a short PR interval and a normal QRS complex on the surface ECG. LGL syndrome likely represents one

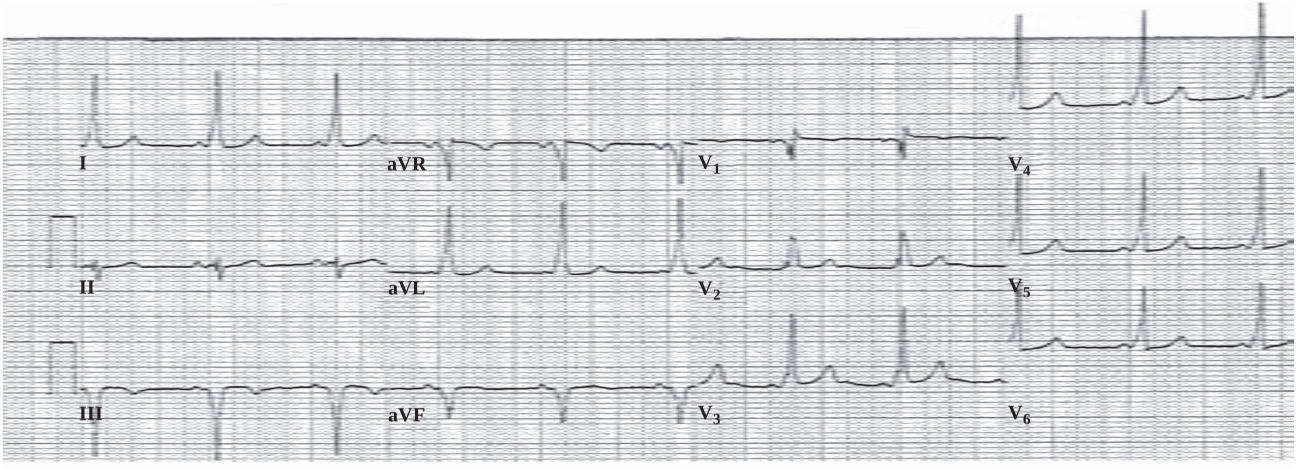


FIGURE 21.3 Wolff-Parkinson-White syndrome, with widespread delta waves seen at the upstroke of the QRS complexes.

end (enhanced) of the normal spectrum of AV nodal conduction properties, but in some cases it is impossible to exclude a distinct perinodal accessory pathway or an abnormality in conduction characteristics of the AV node. It is uncertain if this abnormality in AV conduction is itself associated with arrhythmias.

3. Diagnostic testing

a. The following electrocardiographic criteria are suggestive of an accessory pathway consistent with a WPW pattern. The WPW syndrome occurs in the setting of the WPW pattern and SVT.

(1) The PR interval is short, typically < 120 milliseconds.

(2) The QRS complex exceeds 120 milliseconds, with some leads showing the characteristic slurred upstroke known as a delta wave (Fig. 21.3) and a normal terminal QRS portion.

(3) The ST-T segment is directed opposite to the major delta and QRS vectors.

b. The most commonly seen tachycardia in WPW syndrome is characterized by a normal QRS with a regular rate of 150 to 250 beats/min. Onset and termination are abrupt.

c. Localization of accessory pathway. The **surface ECG** may provide information that allows localization of the accessory pathway. The simplest classification is that of type A or type B. **Type A** has a large R wave in lead V_1. It is due to a left-sided accessory pathway, which permits preexcitation to the posterobasilar segment of the left ventricle. **Type B** has an S or QS in lead V_1 and is due to a right-sided accessory pathway. When present, the morphology of a retrograde P wave can be helpful in predicting the location of the accessory pathway. More elaborate algorithms for localization are available. The **most precise localization method is electrophysiologic study** with ventricular pacing or during orthodromic AVRT (the latter condition is especially helpful as there is VA conduction purely through the accessory pathway, and fusion with VA conduction through the AV node is, therefore, avoided). A positive P wave in lead V_1 during supraventricular tachyarrhythmia suggests a left free wall pathway, whereas a negative P wave suggests a right-sided pathway.

d. Risk stratification should be considered for patients with WPW pattern or ventricular preexcitation according to ECG findings. The appearance or disappearance of preexcitation on **serial ECGs is of no predictive value**. However, **the intermittent loss or appearance of preexcitation on a beat-to-beat basis is indicative of lower risk**. This may be assessed with ambulatory Holter monitoring during usual activities or with formal exercise stress testing. Such intermittent preexcitation suggests a pathway without the ability for rapid AV conduction and, therefore, lower risk of sudden cardiac death (SCD). However, the reverse is not necessarily true in that most patients with persistent preexcitation may still be at low risk for SCD, but these patients cannot be distinguished from those at risk. As the greatest danger to patients with preexcitation may be the development of AF, **the induction of AF may be most useful in risk stratification**. This can be done via transesophageal pacing; however, electrophysiologic study is the procedure of choice for risk stratification in patients with persistent ventricular preexcitation.

4. Therapy

a. Emergency management of acute tachycardia episodes. A patient ***demonstrating hemodynamic instability or extreme symptomatology should be cardioverted rapidly***. Stable patients may be treated medically.

(1) Normal QRS width. Both types of AVRT (orthodromic and antidromic) are AV node–dependent and thus respond to AV nodal blocking therapies. Although it is reasonable to use vagal maneuvers and AV nodal

blocking medications acutely in patients presenting with a narrow QRS (immediate synchronized DCC should be available should the rhythm degenerate), it is not safe in patients when they present with a wide QRS. Atrial pacing, either transvenous or transesophageal, is also quite efficacious for terminating these types of tachycardias. Adenosine, although effective in treating orthodromic and antidromic AVRTs, may induce AF in up to 15% of cases and should, therefore, be used with caution. In patients with WPW syndrome, AF is a potentially life-threatening arrhythmia, especially when the accessory pathway has a short antegrade refractory period capable of rapid ventricular conduction.

(2) **Wide QRS width.** Patients with accessory pathways can present with wide QRS complex resulting from **(1)** orthodromic AVRT with aberrant conduction; **(2)** antidromic AVRT; or, **most importantly**, **(3)** atrial arrhythmias (atrial tachycardia/atrial flutter/atrial fibrillation) with antegrade conduction down an accessory pathway. Since it is often initially impossible to determine the mechanism of a wide QRS complex in patients with an accessory pathway, they should be treated with agents that slow conduction in the accessory pathways (procainamide, flecainide, sotalol, or amiodarone). Because atrial arrhythmias with antegrade accessory pathway conduction are **not** AV node–dependent, AV nodal blocking therapies are ineffective and potentially very dangerous. β-Blockers, calcium channel blockers, digoxin, and adenosine should be avoided in patients presenting with wide complex tachycardias (WCTs), as they may encourage preferential conduction down accessory pathways and accelerate ventricular rates, precipitating ventricular fibrillation (VF). **If the tachycardia persists, synchronized DCC** is the treatment of choice. Energies of at least 200 J are likely to be required.

(3) If the patient develops AF, it has been observed that **definitive therapy for the AV reentrant circuit, such as ablation of the accessory pathway, often results in the prevention of future episodes of AF**.

b. Long-term management

(1) **Priority of therapy.** Patients whose disease is asymptomatic at diagnosis are at low risk for sudden death. As such, it may not be justified to pursue medical or ablative therapy in these patients unless there is a family history of sudden death or the patients are competitive athletes or are in a high-risk occupation. Patients whose disease is symptomatic or who have a history of AF or aborted sudden death may be at higher risk, and such patients warrant further study.

(2) **Medical therapy.** Medical therapy may be **appropriate for those with increased risk but no prior symptoms, those with accessory pathways located near the normal conduction pathway that might develop AV block with RFA**, or those at increased risk from invasive procedures. Single-drug therapy may be attempted with **amiodarone, sotalol, flecainide, or propafenone**. These drugs work to slow conduction in both the accessory pathway and the AV node. **Combination therapy** can be accomplished with drugs that work on the AV node (calcium channel blockers, β-blockers) and with drugs that work exclusively on the accessory pathway (class IA antiarrhythmics).

(3) **Percutaneous therapy.** RFA is effective 85% to 98% of the time, depending on the location of the accessory pathway. Recurrence rates are approximately 5% to 8%. Catheter ablation should be considered for any patient at high risk, patients with symptoms or tachycardias refractory to medical therapy, those who have intolerance to medical therapy, and those with high-risk occupations such as pilots.

J. Atrial premature depolarizations (APDs). APDs are premature depolarizations that arise from a region other than the SN. The P-wave morphology and PR interval may be different from the sinus P wave and normal P interval, depending on the location and timing of the APD.

1. **Clinical presentation.** APDs are usually asymptomatic and in isolation are considered to be benign. Some patients may feel palpitations or skipped beats. If there is atrial bigeminy with each APD causing AV block, patients may develop symptoms of bradycardia. APDs may trigger SVT (AVNRT, AVRT, and atrial tachycardia) or AF in patients with the electrical and structural substrate for these arrhythmias. APDs increase in frequency as patients age and may be more frequent in patients with mitral valve disease, LV dysfunction, hypertrophic cardiomyopathy (HCM), mitral stenosis, pulmonary disease, and renal failure. Stress, alcohol and caffeine consumption, and smoking can promote APDs. However, APDs also occur in healthy individuals with structurally normal hearts and without significant external exposures (caffeine, alcohol, and stress). Although one study showed a correlation between the frequency of APDs within a 24-hour period and the risk of stroke in men, it is unclear what percentage of these men developed AF. Furthermore, in the ARIC (Atherosclerosis Risk in Communities) study which followed patients with APDs and ventricular premature depolarizations (VPDs), patients with APDs only did not have increased incidence of SCD.
2. **Pathophysiology.** APDs may be caused by a variety of mechanisms, including reentry, triggered activity, and increased automaticity. Reentry is thought to be the most common mechanism.
3. **Therapy.** Asymptomatic individuals do not need treatment for APDs. For symptomatic patients, β-blockers and class IA, class IC, and class III antiarrhythmic drugs may be considered, although no randomized controlled trials have been performed in this patient population.

III. VENTRICULAR TACHYARRHYTHMIAS.

Ventricular tachyarrhythmias, including monomorphic VT, polymorphic VT, and VF, account for up to 80% of SCD.

A. Ventricular tachycardia. VT is defined as three or more consecutive QRS complexes of ventricular origin at a rate exceeding 100 beats/min. The various types of VTs and their course of disease are discussed in Section **IV**.

1. **Clinical presentation.** The presentation is variable and depends on the clinical setting, the heart rate, the presence of underlying heart disease, and other medical conditions. Some patients have no or minimal symptoms, whereas others may present with syncope or sudden death. The loss of normal AV synchrony may cause symptoms in patients with decreased cardiac function at baseline. Heart rates < 150 beats/min are surprisingly well tolerated in the short-term, even in the most compromised individuals. Exposure to these rates for more than a few hours is likely to be associated with heart failure in patients with poor ventricular function, whereas those with normal ventricular function may tolerate prolonged periods at such rates. The range of 150 to 200 beats/min is tolerated variably, according to the factors noted previously. Once the rate reaches and exceeds 200 beats/min, there are symptoms in virtually all patients. **Nonsustained ventricular tachycardia** (NSVT) is generally defined as a VT of duration < 30 seconds. VT is **generally regular in rate and appearance**, although it can be polymorphic in appearance, slightly irregular with respect to rate, and may have capture and/or fusion beats within it.
2. **Differential diagnosis.** VT needs to be distinguished from **supraventricular tachyarrhythmia with aberrant intraventricular conduction, bundle branch block, and morphologic changes of the QRS complex secondary to metabolic derangement or pacing**.

a. **Brugada criteria.** Distinguishing VT from **supraventricular tachyarrhythmia with aberrancy** can be challenging. Various criteria have been proposed. A good rule of thumb **is that any WCT in a patient with ischemic heart disease is VT until proven otherwise**. Some have reported that > 80% of WCTs in such patients are VTs. The **algorithm proposed by Brugada may be helpful in making this distinction, and the algorithm is both sensitive** (99%) **and specific** (96.5%) in patients without a preexisting bundle branch block. As shown in Figure 21.4, a stepwise approach is applied. In the first step, the precordial leads are examined for the presence or absence of an RS complex. If an RS is uniformly absent, VT is established. If an RS is present in at least one precordial lead, one moves to the second step, which is measuring the interval from the onset of the QRS complex to the nadir of the S wave. If this distance is > 100 milliseconds in at least one precordial lead, then the diagnosis of VT is made. If there is no RS interval > 100 milliseconds, the third step is used. In the third step, one looks for evidence of AV dissociation. If there are more QRS complexes than P waves, then the diagnosis is VT. If not, then one moves to the fourth step, which involves examining the morphology of the QRS in the precordial leads V_1 and V_6. If the morphology criteria for VT (Fig. 21.5) are present in these leads, then the diagnosis of VT is established. If not, the diagnosis is supraventricular tachyarrhythmia with aberrant intraventricular conduction.

b. The Brugada criteria have been further refined to distinguish between VT and supraventricular tachyarrhythmia with antegrade conduction over an accessory pathway. After applying the preceding criteria, a second stepwise algorithm is applied (Fig. 21.6). This **second algorithm has a sensitivity of 75% and a specificity of 100% to diagnose VT and exclude preexcited tachycardia**. In the first step, leads V_4 to V_6 are examined to see if the QRS is predominantly negative. If so, then VT is favored. If not, then the second step, examining leads V_2 to V_6 for the presence of a QR complex in one or more of these leads, is applied. If there is a QR complex in any of these leads, then the diagnosis is VT. The third criterion, presence of AV dissociation, is 100% specific for VT. If there is no AV dissociation, then supraventricular tachyarrhythmia with antegrade accessory pathway conduction is favored.

c. A new criterion for differentiating VT from SVT was published in 2008 by Vereckei et al. (1), which boasts a > 90% accuracy in their cohort (Fig. 21.7). The rationale to use the new method was to simplify the approach by using one electrocardiographic lead (aVR) in a four-step, tree-like model. The method starts with identifying the presence of an initial R wave in aVR. If present, VT is diagnosed. If not, then the next step is to assess the presence of an initial R or Q wave > 40 milliseconds, and if present, is VT. If this criterion is not satisfied, then the presence of a notch on the descending limb of a negative onset and predominantly negative QRS gives the diagnosis of VT. If this is not present, then one should compare the voltage of the initial 40 milliseconds (V_i) with the voltage of the terminal 40 milliseconds (V_t) of the QRS complex. If $V_i/V_t \leq 1$, then it is VT. If none of these criteria are satisfied, then SVT is diagnosed.

3. **Therapy**

a. **General management.** The treatment of VT may involve DCC, discontinuation of offending proarrhythmic drugs, specific antiarrhythmic therapy with drugs, correction of electrolyte imbalances, implantable devices, ablation, revascularization, and surgery. The appropriate selection of the preceding therapies is aided by the assessment of the patient, an understanding of the etiology and mechanism of the VT, knowledge of any exacerbating medical conditions contributing to the VT, and the risk-to-benefit ratio of the available therapies.

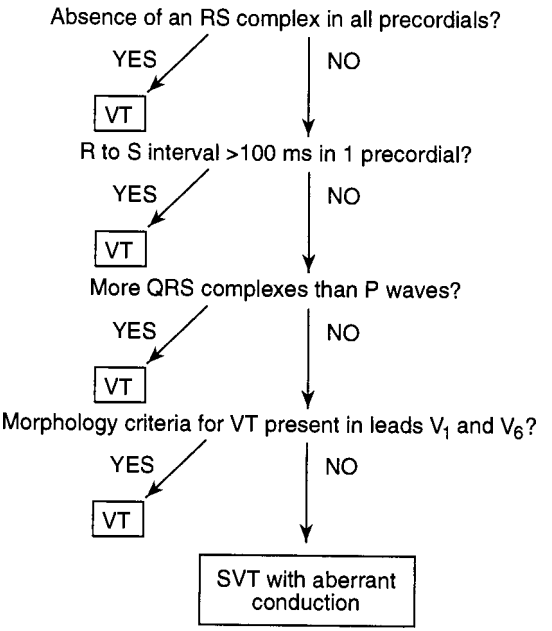
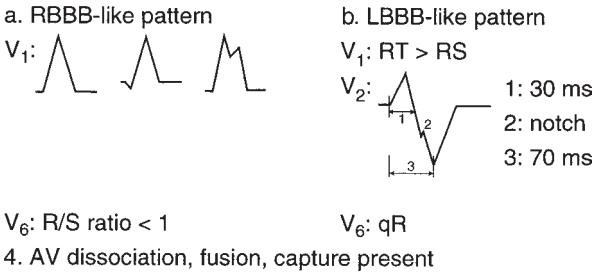


FIGURE 21.4 Brugada criteria for differentiating ventricular tachycardia from supraventricular tachycardia with aberrant intraventricular conduction. VT, ventricular tachycardia; SVT, supraventricular tachycardia.

b. **Priority of therapy.** A patient who has no hemodynamic compromise can be treated medically, at least initially. As with most types of tachyarrhythmias, **the treatment of any unstable patient with VT is rapid DCC**. The treatment for pulseless VT is asynchronous DCC with a starting energy of 200 to 360 J. If the patient is conscious but has unstable vital signs or is extremely symptomatic, **synchronized DCC** is recommended. Current 2011 Advanced Cardiac Life Support (ACLS) guidelines (AHA) currently emphasize the delivery of high-quality cardiopulmonary resuscitation (CPR): effective chest compressions (100/min and compression depth of at least 2″) with minimal interruptions, rescue breaths given over 1 second with visible chest rise while avoiding hyperventilation (30:2 ratio before an advanced airway and 8 to 10 asynchronous breaths/min after airway is secured), and a **single** shock to attempt to defibrillate pulseless VT patients (as opposed to three-stacked shocks) followed by immediate continuation of CPR. (See Section **IV.F.3** for treatment of pulseless VT/VF patients.)

c. **Acute medical therapy.** Intravenous amiodarone, lidocaine, procainamide, β-blockers, and other oral agents may be given initially depending on the clinical scenario. Amiodarone is the agent of choice for resistant VT causing repeated episodes and also for pulseless VT/cardiac arrest. Amiodarone and lidocaine are the preferred agents in patients with LV dysfunction (left ventricular ejection fraction [LVEF] < 40%). Lidocaine is effective when VT is thought to be ischemic in nature. Procainamide is reasonable as the initial treatment in patients with stable monomorphic VT, as it more effectively provides early rate slowing and conversion than amiodarone. β-Blockers may be preferred for acute coronary syndrome, especially if not already being

1. QRS width > 0.14 s
2. Superior QRS axis
3. Morphology in precordial leads:



4. AV dissociation, fusion, capture present

FIGURE 21.5 Classic morphology criteria for ventricular tachycardia.

taken by the patient. Whenever possible, a **reversible cause for VT** should be sought. Elimination of **ischemia** and correction of **electrolyte abnormalities** are recommended. **Bradycardia** may cause frequent premature ventricular contractions or VT. Maneuvers and agents that increase heart rate should be employed for these bradycardias. **Hypotension** should be promptly corrected. Therapy for CHF should be optimized with the agents

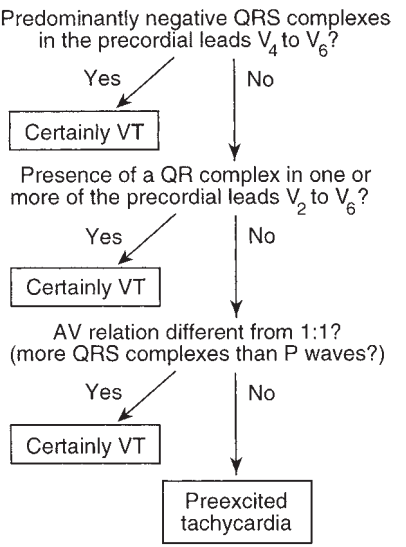


FIGURE 21.6 Brugada criteria for differentiating ventricular tachycardia from antidromic tachycardia over an accessory pathway. VT, ventricular tachycardia; AV, atrioventricular.

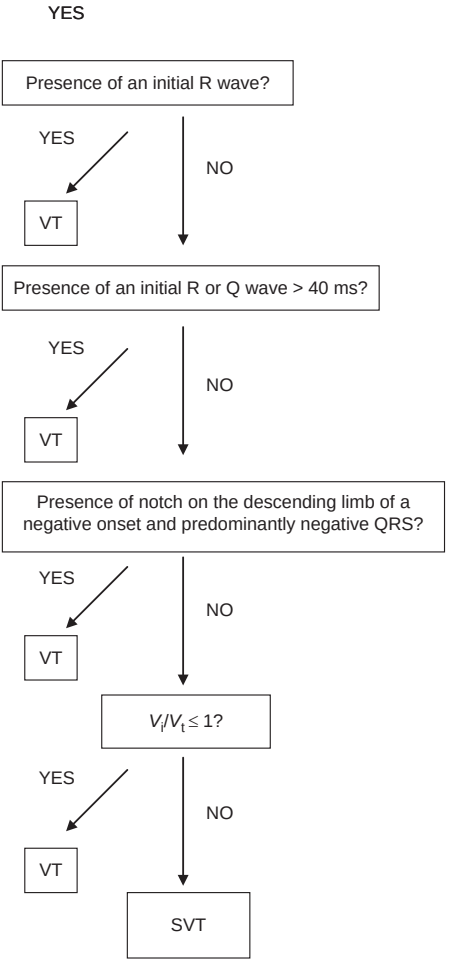


FIGURE 21.7 aVR criteria for diagnosing ventricular tachycardia. Vi = vertical excursion (mV) during initial (V_i) and terminal (V_t) 40 milliseconds of the QRS complex. VT, ventricular tachycardia; SVT, supraventricular tachycardia.

known to promote survival in this disorder. **Offending agents** should be stopped whenever possible, and **antidotes** should be administered in the case of overdosage and poisoning.

4. **Prevention and prophylactic treatment.** All antiarrhythmic agents to date, except β-blockers, have not been shown in randomized clinical trials to be effective as the primary management of patients with life-threatening ventricular arrhythmias or in the prevention of SCD. Since the Cardiac Arrhythmia Suppression Trial (CAST) data have become available, there has been a shift

away from the use of class I agents and toward the **use of class III agents and β-blockers for prophylactic maintenance therapy** of VT. The development of **curative catheter-based therapies and surgical procedures** has somewhat reduced the role of antiarrhythmics in the prevention of recurrence, especially for VT occurring in normal hearts, which has very high cure rates with catheter ablation **(see Section IV.A)**. However, antiarrhythmic drug therapy remains the first-line treatment for VT, particularly for patients with cardiomyopathy. The greatest impact on survival in sudden death has been made by the implantable **cardioverter–defibrillator (ICD)**. Data from the Multicenter Unsustained Tachycardia Trial (MUSTT) investigations have shown that **patients with CAD, an EF < 40% and NSVT who have inducible sustained VT on testing are at substantially increased risk** over those who do not have inducible VT.

a. Medical therapy

(1) Although drug therapy continues to have a role in the prevention of VT and sudden death, this role has become more limited as there has been no decrease in mortality with the use of antiarrhythmic drugs. The Electrophysiologic Studies Versus Electrocardiographic Monitoring (ESVEM) trial studied the efficacy of seven antiarrhythmics (imipramine, mexiletine, pirmenol, procainamide, propafenone, quinidine, and sotalol) in preventing the recurrence of sustained VT. Sotalol was seen to be the most effective, although even with sotalol the recurrence rate was disappointing. The European Myocardial Infarct Amiodarone Trial (EMIAT) and the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT) investigations were designed to study the effectiveness of empiric amiodarone for the prevention of VT after MI. Although both of these trials showed a decrease in arrhythmic deaths, no survival benefit was recorded.

(2) Combination therapy. Drug therapy is becoming **an adjunct to ICD therapy** in this high-risk population. At present, fully half of those with ICDs remain on antiarrhythmic therapy. The rationale for this combined therapy includes preventing atrial tachyarrhythmias and reducing the frequency of VT and thus the frequency of ICD discharge.

(3) Calcium channel blockers are used primarily in the management of supraventricular tachyarrhythmia. However, some of the idiopathic monomorphic VTs, described in Section **IV.A** (the VTs originating in the right ventricular outflow tract [RVOT]), fascicular VT, and the VTs of digitalis toxicity are responsive to calcium channel blocking agents such as verapamil and diltiazem (due to the underlying mechanism of calcium-dependent triggered activity). RFA is potentially curative for idiopathic VTs and should be considered despite effective termination with calcium channel blockers.

(4) β-Blockers may be effective, particularly for outflow tract VT. Idiopathic left VT may respond to calcium channel blockers.

b. Percutaneous therapy

(1) ICDs. Two large trials comparing ICDs with amiodarone in high-risk patients with prior infarction, the Multicenter Automatic Defibrillator Implantation Trial (MADIT) and the Antiarrhythmics Versus Implantable Defibrillator (AVID) trial, have been completed. High risk implies either an EF of 35% or less or the presence of inducible sustained VT at electrophysiologic study. Both trials showed a **decided advantage for ICDs**, with 30% to 50% reductions in mortality with ICDs. In fact, the AVID trial found no survival benefit from amiodarone, β-blockers, or any other antiarrhythmic agent. Newer ICDs often have antitachycardia pacing (ATP) capabilities, can recognize monomorphic ventricular

rhythms with rates < 200 beats/min, and can rapidly pace the ventricles to restore sinus rhythm, aborting the need for countershock (see Chapter 23). In the Primary Prevention Parameters Evaluation (PREPARE) study which evaluated the effects of ICD programming in a patient population receiving ICDs for primary prevention, using ATP as first-line therapy for fast VT (≥ 182 and < 250 beats/min), including a monitoring zone at 167 beats/min, and applying SVT versus VT discriminators for rates < 200 beats/min helped in reducing shocks without negatively affecting the mortality. Data from MADIT II have shown that in patients with a prior MI and an EF < 30%, the implantation of a defibrillator is associated with a significant improvement in survival.

(2) Catheter-based therapy. RFA may be effective for reducing the incidence of VT. The success rate depends on the type of VT, with the highest success rates (> 90%) in structurally normal hearts. VT associated with underlying cardiomyopathy has lower success rates with ablation, particularly those with arrhythmogenic RV cardiomyopathy and ischemic cardiomyopathy. However, catheter ablation still remains an effective and feasible approach, even for these types of VTs. Presently, catheter ablation of VT does not obviate the need for an ICD in a patient with an indication for one.

IV. DIAGNOSTIC EVALUATION OF A PATIENT WITH VT. Once the diagnosis of VT has been established and the patient has been acutely managed with either DCC or medical therapy, further management depends on the underlying cardiac pathology. In broad terms, the substrate can be divided into two categories: the structurally normal heart and the structurally abnormal heart. Various modalities are available to determine the cardiac structure and function, which include electrocardiography, cardiac catheterization, echocardiography, nuclear imaging, and magnetic resonance imaging.

A. VT in a structurally normal heart. About 10% of VT in the United States occurs in structurally normal hearts, the so-called idiopathic VT. These patients have no significant CAD, no family history of arrhythmia or sudden death, and normal surface ECGs. They can be focal VTs or reentry VTs. Focal VTs are a result of triggered activity, abnormal automaticity, or reentry within the Purkinje fibers.

1. Focal VT

a. Mechanism. Focal VTs most commonly arise from the RVOT and account for up to 70% of idiopathic VTs. They may be caused by cAMP-mediated EADs. Of particular importance in the diagnosis of a patient who presents with LBBB VT is to be cognizant of the possibility of arrhythmogenic right ventricular dysplasia (ARVD), which falls into the category of VT/PVCs in the structurally abnormal heart. The clinician should investigate for RV structural abnormalities (fatty infiltration), ask about a family history of ARVD, and review the electrogram for the presence of T-wave inversion across the right precordial leads, and/or epsilon waves (Fig. 21.10). A cardiac MRI or cardiac PET scan may also be useful to rule out the presence of cardiac sarcoidosis, which also would fall into the category of the structurally abnormal heart.

b. ECG. The surface ECG usually demonstrates an LBBB and inferior axis with very positive QRS voltage in inferior leads. Other locations of focal VTs may include the LV outflow tract, aortic cusps, pulmonary artery, mitral and tricuspid annuli, papillary muscles, and epicardium.

c. Treatment. In general focal VTs are benign, carrying a very low risk of SCD. Therefore, the treatment is predominantly guided by symptoms. Given the role of cAMP in inducing this form of VT, adenosine may be effective at acute termination. For longer term therapy in the symptomatic patient,

β-blockers are typically the first-line agents and can be effective in up to 50% of patients. The nondihydropyridine calcium channel blockers may also be effective in 25% to 50% of patients. Very effective medications are sotalol and amiodarone, with up to 90% success rate in eliminating symptoms, but potential side effects may limit their use. Patients who wish to potentially avoid lifelong medications or who are refractory to medical therapy can be considered for ablation, which has variable success rate depending on the location. RVOT VT ablation success rate may be as high as 90%. Ablation procedures, while generally safe, may be associated with infrequent but life-threatening complications, including cardiac perforation and tamponade.

2. **Fascicular VTs.** Fascicular VT involves reentry using the tissue of the LV septum as the antegrade limb and usually the posterior fascicle in the retrograde limb.
   a. **ECG.** This typically produced a right bundle branch block (RBBB) with left-axis deviation pattern. Less commonly, the QRS pattern is an RBBB with right-axis deviation (left anterior fascicular VT).
   b. **Treatment.** This subtype of VT may be verapamil-sensitive, but catheter ablation can be attempted in patients who want to avoid long-term medication or in whom medical therapy is ineffective.

B. VT/VF associated with channelopathies. Various cardiac ion channel disturbances can predispose to ventricular arrhythmias. Patients with these channelopathies have no overt structural heart disease. They are genetically heterogeneous and have variable penetrance. They include LQTS, short QT syndrome, Brugada syndrome, and catecholaminergic polymorphic VT.

1. **Long QT syndrome**
   a. **Pathology and presentation**

This channelopathy is characterized by prolonged cellular repolarization resulting in an increase of the QT interval. Clinical presentation includes syncope or sudden death as a result of torsade de pointes, and usually an autosomal dominant transmission pattern.

While at least 12 mutations have been identified, the most common subtypes of LQTS are LQT1, LQT2, and LQT3, which are characterized by mutations in the I_{Ks}, I_{Kr}, and I_{Na} channels, respectively. Interestingly, a minority of patients with the genetic mutation may actually have "normal" QT intervals. LQT1 and LQT2 mutations result in decreased outward potassium current, while LQT3 mutation results in increased inward sodium current, both of which result in prolonged cellular repolarization. The Jervell and Lange-Nielsen, a clinical syndrome with a constellation of a prolonged QT and sensorineural deafness, is transmitted in an autosomal recessive pattern, and thus far has been localized to the LQT1 or LQT5 mutations.

LQT1 patients typically have broad-based T waves and exercise-induced arrhythmias, especially during swimming. LQT2 syndrome is characterized by low-amplitude or notched T waves and auditory triggers such as sudden loud sounds like alarm clocks or strong emotion, and LQT3 is characterized by a long isoelectric ST segment and arrhythmias during sleep.

   b. **Treatment**

In patients with LQTS, risk stratification involves assessment of age, gender, clinical history, and possibly the QT interval and genetic mutation. While β-blockers have a variable efficacy depending on the type of LQT mutation, typically high doses of propranolol or nadolol are used to prevent clinical symptoms. For the LQT3 patients, there may be a role for flecainide given its effects on the sodium channel inhibition, but this is experimental and has not reached guideline recommendations yet. Patients should be advised against high-intensity sports and should be educated regarding avoidance of QT prolonging drugs. Patient with syncope, history of aborted

sudden death, or torsade de pointes despite β-blocker therapy should undergo ICD implantation. Certain high-risk subgroups such as patients with LQT3 in whom β-blockers may be less effective, patients with QTc > 550 milliseconds, or female LQT2 patients with QTc > 500 milliseconds may benefit from ICD implantation. Left cardiac sympathetic denervation can be used as an adjunctive therapy to reduce recurrence of arrhythmias.

2. **Short QT syndrome.** This syndrome is characterized by gain-of-function mutations in the I_{Ks}, I_{Kr}, and I_{K1} potassium channels or CACNA1 and CACNB2 L-type calcium channel mutations. ICD therapy is the primary treatment modality. However, particular attention needs to be given to the prevention of inappropriate shocks, as patients may have T-wave oversensing (tall T waves) and a high incidence of AF.
3. **Brugada syndrome.** Brugada syndrome is a condition associated with SCD in the setting of a structurally normal heart, characterized by an electrocardiographic pattern of RBBB and ST-segment elevation in leads V_1 to V_3 (Fig. 21.8). It is inherited in an autosomal dominant pattern with a male predominance. It is a genetically heterogeneous disease with many mutations linked to the gene *SCN5A*, which encodes for a cardiac sodium channel, leading to unopposed I_{to} potassium current in the RV epicardium. The diagnosis can be difficult because of the variable expression of the ECGs at baseline, changes in the ECG over time induced by a host of factors (temperature, heart rate, autonomic tone, and medications), and the wide range of clinical manifestations. The diagnosis should be considered in patients who have documented VF, self-terminating polymorphic VT, family members with ST-segment elevation, syncope, or family history of sudden death in the setting of the electrocardiographic findings noted previously. Currently, no medication has proved effective in preventing SCD in these patients, but quinidine, which blocks the I_{to} channel, may be used as an adjunctive therapy to reduce the likelihood of arrhythmias. ICDs are currently the only available treatment and are recommended in patients with previous cardiac arrest (class I), syncope with spontaneous ECG pattern (class IIa), and documented VT that has not resulted in cardiac arrest (class IIa). It is generally recommended to implant an ICD in **symptomatic** patients and clinically follow **asymptomatic** patients with an abnormal ECG only on pharmacologic provocation and no inducible ventricular arrhythmias.
4. **Catecholaminergic polymorphic VT.** This arrhythmia is more common in adolescents and children and may present with SCD or stress-induced syncope. While usually familial, it can also occur due to de novo mutations. Triggers often include emotional or physical stress, and the arrhythmia can be polymorphic, bidirectional, and less commonly, VF. Two culprit genes have been identified thus far: calsequestrin 2 (autosomal recessive pattern) and cardiac ryanodine receptor (autosomal dominant pattern). ICDs are indicated in patients with this syndrome and syncope and/or VT. β-Blockers can reduce the incidence of arrhythmias as well. Flecainide and sympathetic denervation have been used in some patients who are refractory to β-blocker therapy.

C. VT in the structurally abnormal heart

1. **Ischemic VT. Patients with ischemic VT may have acute ischemia leading to MI or a history of ischemic heart disease with scar.** Patients who have VF/VT within 48 hours of an acute MI have a relatively high inhospital and 30-day mortality compared with patients who do not have VF/VT.
   a. **Etiology and pathophysiology.** At the cellular level, ischemia may alter action potentials, prolong refractoriness of cells, and uncouple the cell-to-cell propagation of depolarization. The biochemical milieu in which the cells exist with respect to ion concentrations, acid–base balance, and so forth can be altered. Also, the myocardial damage as a result of infarction is structurally

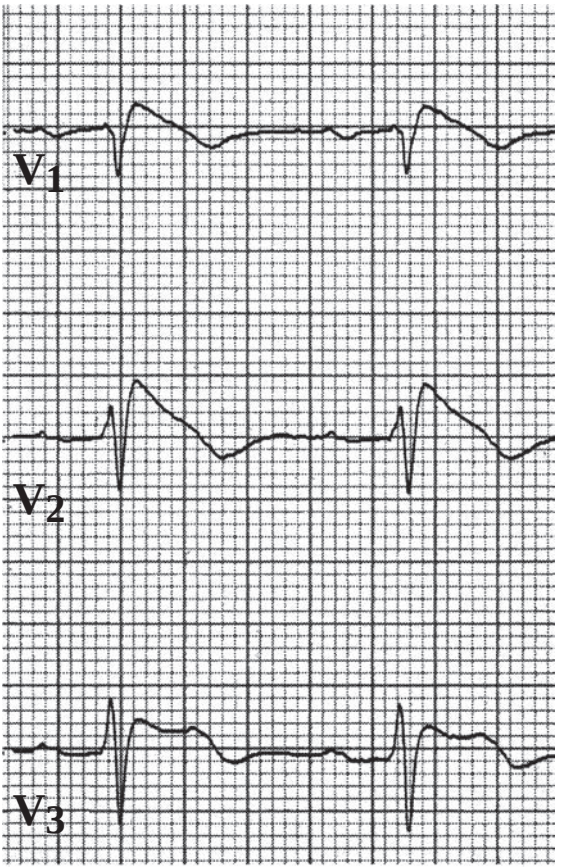


FIGURE 21.8 Leads V_1 through V_3, demonstrating Type 1 Brugada pattern.

heterogeneous. Therefore, scar tissue and healthy tissue are admixed in the region of the infarction. As described before, a reentrant circuit requires two functionally distinct pathways with unidirectional block in one pathway and slowed conduction down a second pathway. The changes associated with ischemia provide the anatomic substrate for reentry. The VT in the setting of ischemia tends to be **polymorphic**, while VT in the setting of established myocardial scar tends to be **monomorphic**. Ischemia has been shown to prolong the QT interval in some subjects, often with associated T-wave inversion. The **QT interval in ischemic-mediated polymorphic VT is not as prolonged** as that in torsade de pointes, another polymorphic VT. Ischemia is by far the **most common cause of polymorphic VT with normal QT interval**.

b. Predictors of VT. As might be expected, **larger infarcts with greater resultant impairment of LV systolic function** are more likely to be associated with VT. In fact, LV systolic function is the single most important predictor of sudden death due to arrhythmia. Similarly, the presence of an **open artery**

appears to reduce the occurrence of VT and other arrhythmias. Other proposed predictors include syncope, abnormal signal-averaged electrocardiogram (SAECG) result, NSVT, absence of heart rate variability, abnormal electrophysiologic study outcome, and T-wave alternans (TWA); however, currently, the LVEF remains the most accurate predictor of sudden death.

c. **Laboratory examination and diagnostic testing.** The various tests for risk stratification (electrophysiologic study, SAECG, heart rate variability, TWA, and so forth) have shown poor specificity and positive predictive value for VT **and thus should not be used alone to guide therapy but in combination with the rest of the clinical information**.

d. **Role for ICD.** In patients who present with a VF/VT arrest in the setting of an acute MI (within 24 to 48 hours of infarction), revascularization should be the primary initial treatment. Given the fact that acute ischemia is considered a "transient or potentially correctable cause" of VF/VT, and such patients were excluded from the AVID trial, based on currently guidelines, an ICD would be indicated 90 days after revascularization if the LVEF is ≤ 35% or after 40 days if no revascularization was performed, but treatment should be guided on a patient-to-patient basis. Of note, patients in the AVID registry who were excluded from the AVID trial due a "transient or potentially correctable cause" had a high mortality risk in follow-up. Of the 278 patients studied, 183 patients were determined to have ischemic causes. Of these, 161 were categorized as new myocardial infarction and 22 were categorized as transient ischemia. Other causes included electrolyte abnormalities, antiarrhythmic drug interaction, and "other (illicit drug use, sepsis, hypoxia, electrocution, drowning)". For patients who are post-MI and are deemed to be at high risk for SCD during the waiting period of 40 to 90 days, a wearable cardioverter–defibrillator (WCD) may provide protection against cardiac arrest, but no randomized clinical trials comparing WCDs with medical therapy in this post-MI period have been completed to date. Patients with late VT/VF (i.e., > 48 hours after acute MI) are deemed to be particularly high risk for recurrent VT/VF and therefore typically receive ICDs before hospital discharge. These patients are considered to meet secondary prevention indications for ICDs.

e. Accelerated idioventricular rhythm (Fig. 21.9) is a form of VT seen almost exclusively in ischemic heart disease, particularly during an MI and especially after reperfusion of an occluded territory. It may be seen with digitalis toxicity, but can also be present in healthy adults and children with no structural heart disease.

   (a) The electrocardiographic features include regular or slightly irregular ventricular rhythm, rate of 60 to 110 beats/min, a QRS morphology resembling that of PVCs, and, often, AV dissociation as well as fusion beats and capture beats.

   (b) **Pathophysiology.** The ectopic ventricular pacing focus competes with the SN and takes control of the ventricular rate when the sinus rate slows or when sinoatrial or AV block occurs. Enhanced automaticity is the likely underlying mechanism.

   (c) Accelerating the sinus rhythm with atropine or atrial pacing can be useful to suppress the accelerated idioventricular rhythm. **Therapy is rarely necessary, unless** the loss of AV synchrony results in hemodynamic compromise, a more rapid VT intervenes, the accelerated idioventricular rhythm falls on the T wave of the preceding beat (R on T phenomenon), the ventricular rate is rapid enough to produce symptoms, or VF occurs.

2. **Dilated cardiomyopathy (DCM).** Risk stratification is particularly difficult in patients with DCM as SAECG, microvolt TWA, and an electrophysiologic study are not reliable predictors in this population, and asymptomatic ventricular arrhythmias are common. The **Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation** (DEFINITE) and Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) have influenced the current guidelines for implanting ICDs in patients with DCM. ICDs are recommended for patients

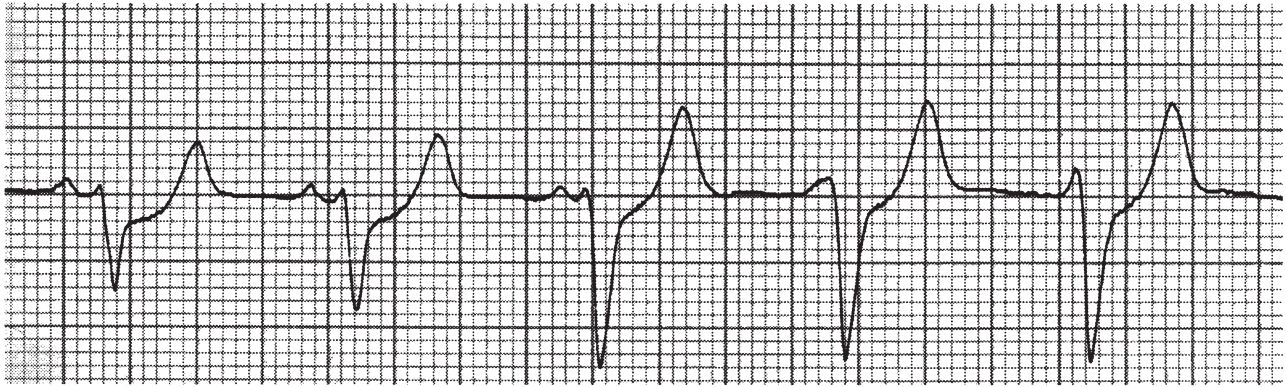


FIGURE 21.9 Accelerated idioventricular rhythm (beats 3 through 5), interspersed with normal sinus rhythm (beats 1 and 2), lead IV.

who manifest life-threatening arrhythmias or syncope and for primary prevention in patients who have an LVEF < 35% and are New York Heart Association (NYHA) classes I–III (less evidence exists for class I). All patients should be receiving chronic optimal medical therapy and have a life expectancy > 1 year. Bundle branch reentrant tachycardia occurs most commonly in patients with DCM for which electrophysiologic testing is helpful in diagnosing and guiding ablative treatment. Although ablation may be curative if bundle branch reentry is the mechanism, such patients should still be considered for ICD implantation.

3. **Hypertrophic cardiomyopathy.** Supraventricular tachyarrhythmia and AF are particularly poorly tolerated by these patients, as is ischemia, and may lead to VT. No prospective randomized trials regarding ICD therapy have been carried out to date in this patient population. Consequently, the precise risk stratification is debated. ICDs are recommended for patients who have sustained VT or VF, or both, and for primary prevention in patients who have either one of the preceding life-threatening arrhythmias or one or more of other major risk factors for SCD (nonsustained spontaneous VT, family history of premature SCD, unexplained syncope, LV thickness ≥ 30 mm, or abnormal exercise blood pressure). Again, all patients should be receiving chronic optimal medical therapy and have a life expectancy > 1 year. Electrophysiologic study may be helpful in stratifying risk for VT and sudden death. Patients at low risk for HCM include those with infrequent or brief episodes that are asymptomatic or mildly symptomatic. Although **amiodarone** may be beneficial in this population, an ICD is increasingly used in those considered to be at high risk.
4. **Muscular dystrophies**, particularly Duchenne's muscular dystrophy and myotonic dystrophy, have been associated with frequent defects in the conduction system. Heart block and bundle branch block as well as sudden death due to ventricular tachyarrhythmias are well-recognized complications of these muscular disorders.
5. **Congenital heart disease.** Structural abnormalities such as **repaired tetralogy of Fallot and mitral valve prolapse** have been associated with increased risk of VT and sudden death. In tetralogy of Fallot, the VT often originates in the RVOT, at the site of a previous repair. Risk of VT and sudden death in this population has been associated with QRS width (and rate of QRS width increase) as well as severity of pulmonary insufficiency. Mitral valve prolapse has been uncommonly linked to sudden death, although ventricular arrhythmias are not uncommon. **The prognosis with respect to VT is quite good in mitral valve prolapse**.
6. **Arrhythmogenic right ventricular cardiomyopathy** is a cardiomyopathy that begins in the right ventricle and often progresses to involve the left ventricle. It results in RV dilation with resultant poor contractile function. The RV muscle becomes increasingly replaced by adipose and fibrous tissues as the disease progresses. VT arising in the right ventricle is often an early manifestation of this disorder. The **VT is a reentrant type and has an LBBB morphology**, although in sinus rhythm there is often inversion of the T waves in the anterior precordial leads and a slurring of the terminal portion of the QRS complex, known as an epsilon wave (Fig. 21.10). These patients frequently have a positive SAECG for late potentials. The combination of the scarring and the late potentials provides the anatomic substrate for reentry. During electrophysiologic study, it may be possible to elicit VT of varying morphologies, due to the prolific scarring of the myocardium. The **risk of VT correlates with the extent of myocardial involvement**. Therapy with sotalol or high-dose amiodarone may be somewhat successful. Ablation via catheters is often successful, but only temporizing, as the generalized involvement tends to give rise to arrhythmias at a different locus later in the disease course. ICDs are often the only reliable therapy to prevent sudden

death in this disorder. Patients are advised against intense exercise, as this may promote the incidence and progression of arrhythmias.

7. Several inflammatory or infectious conditions have been associated with VT.
   - **a.** Sarcoidosis is frequently cited as a cause of heart block and may also cause VT and VF. **Amiodarone** and **sotalol** are the most efficacious agents in this disorder, although an ICD may be necessary in addition to the drug therapy.
   - **b.** Acute myocarditis has been associated with both polymorphic and monomorphic VTs. It may be intractable in giant cell myocarditis. **Antiarrhythmic therapy and anti-inflammatory therapy** are generally combined in the treatment of these patients.
   - **c.** Chagas disease, caused by the parasite *Trypanosoma cruzi*, is a well-known cause of cardiomyopathy, particularly in South and Central America. VT and other arrhythmias due to conduction system involvement are common complications. Therapy involves antiparasitic treatment, standard therapy for CHF, antiarrhythmics, and pacemaker or ICD implantation, as appropriate. Some patients require catheter ablation of refractory VT, which sometimes must be performed epicardially.
8. **Coronary anomalies.** Anomalous aortic origin of the coronary artery is recognized as a cause of sudden death and/or exercise-induced death in young individuals. In an autopsy study of over 200 patients conducted by the Armed Forces Institute of Pathology, the most common coronary anomalies included the right coronary artery and left main coronary artery arising from the left sinus, the left main and right coronary arteries arising from the right sinus, single coronary artery from the aorta, and the left main or left anterior descending artery arising from the pulmonary artery. Patients whose coronary arteries take an interarterial course (between the pulmonary artery and the aorta) may develop exercise-induced ischemia and/or sudden death. Surgical revascularization in patients with symptomatic coronary anomalies has been well described. Surgical treatment for patients with high-risk coronary anomalies who are asymptomatic is controversial.

D. Drug-induced VT. Drugs are a well-known cause of VT, both polymorphic and monomorphic VTs. This is particularly true in ischemic or infarcted hearts. Phenothiazines, tricyclic antidepressants, digitalis, epinephrine, cocaine, nicotine,

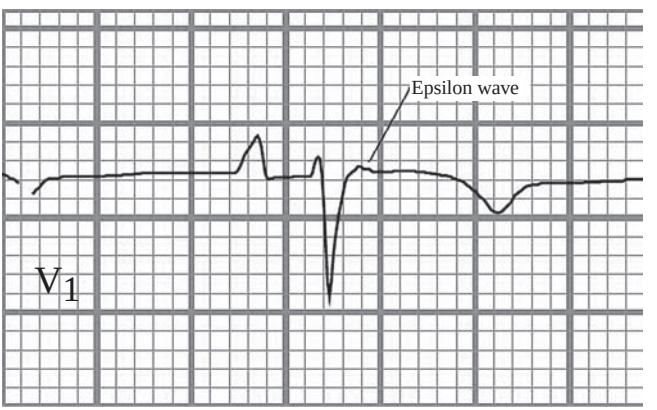


FIGURE 21.10 Epsilon wave in a patient with arrhythmogenic right ventricular dysplasia.

alcohol, and glue (inhaled) are some of the wide variety of drugs that have been implicated in the development of monomorphic VT. The CAST and other trials of the late 1980s showed an increase in mortality resulting from the use of class I antiarrhythmic agents employed to suppress asymptomatic ventricular ectopy after MI. NSVT and depressed LV function remain risk factors for sudden death, and the agents studied in CAST did decrease the occurrence of ventricular ectopy; however, it is believed that these drugs (flecainide, encainide, and moricizine) generated VT, causing sudden death in recipients. These agents all have in common their sodium channel blocking activities. Other drugs in this class, including procainamide, quinidine, disopyramide, lidocaine, tocainide, and mexiletine, have all been shown either experimentally or clinically to be associated with increased mortality compared with controls in the periinfarction period. The results of CAST caused a major shift away from the sodium channel blocking agents (class I antiarrhythmics) in the periinfarction period.

1. The generation of torsade de pointes due to effects on the QT interval is discussed in Section **IV.D.2**.
2. Digitalis toxicity can propagate DADs, which generate action potentials, leading to VT. The VT of digitalis toxicity is typically monomorphic and often responds to calcium channel blockers. Rarely, digitalis toxicity manifests as a bidirectional VT, meaning that it has a regular rhythm with an axis that alternates from −60 to −90° to +120 to +130°, with a ventricular rate from 140 to 200 beats/min. Because digitalis toxicity may have a narrow QRS complex and may respond to calcium channel blockers, it may be confused with supraventricular tachyarrhythmia. This type of VT is best managed by removing the offending agent, digoxin, with its binding antibody. The treatment for digitalis toxicity is the same in the face of bidirectional VT.
   a. Torsade de pointes is a type of polymorphic VT associated with delayed myocardial repolarization, most often manifested as a prolonged QT interval. Although the duration of torsade de pointes is typically brief (< 20 seconds), it can be sustained and can degenerate into VF. It generally has an irregular ventricular rate (> 200 beats/min) and displays a polymorphic structure with an undulating appearance. The QRS complexes appear to twist around an isoelectric axis. Characteristics that distinguish torsade de pointes from other forms of VT include (1) prolonged QT interval, (2) initiation with a short–long–short sequence, and (3) typical "twisting of the points" appearance of the VT.
      (1) **Etiology.** QT prolongation can be congenital or acquired.
         (a) The **congenital** forms are seen in the LQTS, discussed in Chapter 23.
         (b) The **acquired forms are most often drug induced**, although polymorphic VT with a prolonged QT can be caused by electrolyte abnormalities, hypothyroidism, cerebrovascular events, MI or ischemia, starvation diets, organophosphate poisoning, myocarditis, severe CHF, and mitral valve prolapse.

      The **most commonly implicated drugs have been the class IA drugs**, although less frequent occurrences have been reported with all subclasses of class I antiarrhythmics. The class III drugs, such as sotalol, dofetilide, and, less commonly, amiodarone, have been implicated. The incidence of torsade de pointes with sotalol is in the range of 2% to 5% and with dofetilide it is < 1%. Ibutilide is an antiarrhythmic agent for supraventricular tachyarrhythmias that is associated with an incidence of torsade de pointes at least as high as that of sotalol. Other drugs implicated include the phenothiazines, haloperidol, and the tricyclic antidepressants. Antibiotics, including erythromycin and other macrolides, as well as trimethoprim–sulfamethoxazole combinations, have been implicated. The macrolides are particularly prone to cause torsade de pointes when combined with certain antihistamines such

as astemizole and terfenadine. These antihistamines have also been found to cause torsade de pointes when combined with certain azole antifungal agents such as ketoconazole. Ionic contrast and promotility agents such as cisapride have also been associated with torsade de pointes. Medications associated with increasing QT interval are listed on the following website: www.torsades.org. It is maintained by the University of Arizona Center for Education and Research on Therapeutics.

Bradycardia can promote torsade de pointes in patients with prolonged QT intervals, although it is not clear if bradycardia by itself predisposes to torsade de pointes. Specifically, pause-dependent VT occurs in the setting of bradycardia and a prolonged QT interval. Usually a long RR interval followed by a short RR interval followed by another long RR interval initiates the VT.

Electrolyte disorders. **Hypokalemia** is the electrolyte disorder most reliably linked to torsade de pointes. **Hypomagnesemia** has been proposed as a logical cause, as the administration of magnesium frequently terminates torsade de pointes. However, there is scant evidence to confirm this. Likewise, although **hypocalcemia** is associated with prolongation of the QT interval, there are only rare reports of torsade de pointes associated with hypocalcemia.

Short coupled VT. Polymorphic VT is initiated < 400 milliseconds following the preceding QRS complex.

R-on-T phenomenon occurs when a defibrillation or pacing current or spike is delivered simultaneously with occurrence of the electrocardiographic T wave resulting in polymorphic VT.

A variety of **cerebrovascular events** have been associated with torsade de pointes, most notably subarachnoid hemorrhage. The prolongation of the QT interval sometimes seen with intracranial bleeding is usually transient, resolving within weeks.

(2) Therapy. Acute management is aimed at terminating the arrhythmia.

(a) If torsade de pointes is sustained or associated with hemodynamic compromise, prompt DCC should be carried out. Starting voltages are generally 50 to 100 J and can be advanced to 360 J if necessary.

(b) Correction of hypokalemia, hypomagnesemia, and hypocalcemia should be undertaken promptly. Magnesium can be given in a bolus form at a dose of 1 to 2 g, with a total dose of 2 to 4 g given over 10 to 15 minutes. This successfully terminates torsade de pointes within 5 minutes in up to 75% of patients and within 15 minutes in virtually all patients.

(c) Bradycardia can be corrected with either isoproterenol infusion or temporary transvenous pacing. Pacing may be preferable when readily available, due to the potential complications of isoproterenol therapy (worsened ischemia and hypertension). Offending agents should be discontinued.

E. Miscellaneous

Commotio cordis. Commotio cordis is the sudden ventricular arrhythmia occurring as a result of a blunt, nonpenetrating impact to the precordial region, which is most commonly observed in young healthy persons during participation in sports. The blow likely falls within a small 10- to 30-millisecond window of ventricular vulnerability just prior to the peak of the T wave that results in polymorphic VT and sudden death. A 2002 case series of 128 individuals showed that only 16% of patients survived an episode of commotio cordis, with most returning to a baseline level of function. Prompt CPR/defibrillation was the only identifiable factor associated with a favorable outcome.

F. Ventricular fibrillation

1. VF is a **chaotic ventricular rhythm that reflects no organized electrical activity and hence no cardiac output** from the ventricle. It is devoid of the distinct elements that makeup the usual electrical complex of ventricular activity. It is a **rapidly fatal rhythm, and if resuscitation is not begun within 5 to 7 minutes, death is virtually certain**. VF is often preceded by VT. Virtually all of the risk factors and conditions discussed for VT are applicable to VF. It may arise without any inciting cardiac rhythm or event.
2. **Course of disease.** Of patients who experience an out-of-hospital cardiac arrest, 75% have VF as their initial cardiac rhythm. Of those successfully resuscitated, 75% have significant CAD and 20% to 30% have a transmural infarction. Patients without an ischemic etiology have an increased risk of further episodes of sudden death, whereas those who have an MI associated with sudden death have a 1-year recurrence rate of 2%. Anterior MI complicated by VF represents a subgroup at high risk for recurrence of sudden death. Predictors of SCD include evidence of ischemia, decreased LV systolic function, 10 or more PVCs per hour on telemetry, inducible or spontaneous VT, hypertension and LV hypertrophy, smoking, male sex, obesity, elevated cholesterol, advanced age, and excessive alcohol use.
3. **Therapy.** As noted previously, VF is a rapidly fatal rhythm, which virtually never terminates spontaneously. CPR must be initiated promptly and rapid, asynchronous DCC performed as soon as possible. A **single** shock of 200 to 360 J (biphasic devices, 200 J; monophasic devices, 360 J) should be given initially followed by immediate resumption of CPR for 2 minutes before checking for a pulse. If VF/pulseless VT persists, an immediate **second** shock (biphasic devices, ≥ 200 J; monophasic devices, 360 J) should be given followed by a vasopressor (1 mg of epinephrine every 3 to 5 minutes; single dose of 40 units of vasopressin may replace first or second dose of epinephrine). If VF/pulseless VT persists after two or three shocks, CPR, and a vasopressor, administration of an antiarrhythmic should be considered (amiodarone is preferred and lidocaine as an alternative). The emphasis should be on performing high-quality CPR with interruptions in chest compressions **only** for ventilation (until an advanced airway is established), rhythm checks (pulse checks only if an organized rhythm is observed), and shocks.

   See Chapter 23 for a discussion about the long-term treatment of survivors of VF.

G. Ventricular premature depolarizations and nonsustained ventricular tachycardia.

1. **VPDs** are common in patients with both structurally normal and structurally abnormal hearts. They are usually not hemodynamically significant, except in patients with depressed EF or in patients with frequent VPDs and/or bradycardia. Whether or not VPDs increase risk of subsequent cardiovascular events depends on the study. In the ARIC study, after controlling for cardiovascular risk factors, patients with a single VPD on a 2-minute Holter had over a two-fold incidence of dying of CAD over a 10-year follow-up period compared with patients who had no VPDs. However, in the Baltimore Longitudinal Study on Aging which evaluated ambulatory ECGs on apparently healthy subjects ≥ 60 years of age, VPDs on ambulatory ECG monitoring did not predict the development of coronary events. One main difference between the ARIC study and the Baltimore Longitudinal Study was that in the latter, inclusion criteria were more strict, requiring a normal exercise stress test, and therefore, likely had less patients with subclinical CAD.

   Although patients post-MI with VPDs have a higher mortality than patients post-MI without VPDs, suppression of VPDs with antiarrhythmic medication is associated with increased mortality. For patients with symptomatic VPDs, β-blockers or calcium channel blockers should be the first-line agent. If this fails and the patient has no structural heart disease, class IC

agents may be effective; however, potential risks and benefits of the antiarrhythmic drug should be explained to the patient. Sotalol has been shown to reduce the frequency of VPDs by 70% to 80%. In CAMIAT, amiodarone reduced VPDs and arrhythmic deaths, but did not reduce overall mortality. **A very high burden of VPDs (> 20,000/d) may be associated with reduced** EF**, although it may be difficult to determine if the VPDs caused the cardiomyopathy or vice versa**. However, in some patients with a high burden of VPDs and idiopathic DCM, treating the VPDs either with medication or with catheter ablation may improve the LVEF. Ablation can be an alternative approach to treatment in patients with very symptomatic VPDs refractory to medical therapy and/or patients with reduced EF thought to be a result of the VPDs.

2. **NSVT** is defined as VT of duration < 30 seconds. It can occur in up to 4% of healthy adults and increases in frequency as people age, and NSVT during exercise is not associated with a poor cardiovascular prognosis. The approach to NSVT is based on the cardiac substrate. However, patients with frequent polymorphic NSVT should undergo an evaluation for LQTS and catecholaminergic VT (Sections **IV.B.1** and **IV.B.4**, respectively). One should also be mindful of repetitive monomorphic NSVT that may be of LBBB morphology in patients who have a family history of arrhythmias or sudden death, which may suggest ARVD. Monomorphic NSVT may also be a part of the spectrum of the outflow tract VTs (Section **IV.A.1**).
   a. In patients in whom structural heart disease has been excluded, NSVT does not carry prognostic significance. Treatment should therefore only be guided by symptoms. A similar approach to NSVT with regard to medication choices is used as with symptomatic VPDs (Section **IV.G.1.**)
   b. Structural heart disease. In patients with MI, NSVT within the first 24 to 48 hours has little prognostic significance. However, NSVT > 48 hours after acute MI may increase the risk of sudden death by almost twofold, and the risk is even higher in patients with reduced LV function. **Patients with CAD, an EF < 40%, and NSVT who have inducible sustained VT on testing are at substantially increased risk** over those who do not have inducible VT. In patients with HCM, NSVT on Holter monitoring is one of the major risk factors of SCD. Patients with mitral valve prolapse and aortic stenosis who have NSVT are not at increased risk for SCD compared with those without NSVT. In patients with nonischemic DCM, NSVT is not an independent predictor of sudden death.

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CHAPTER 22

Santosh S. Oommen

Bradyarrhythmias, Atrioventricular Block, Asystole, and Pulseless Electrical Activity

I. INTRODUCTION. Bradyarrhythmias and **conduction blocks** are common electrocardiographic findings. Many of these arrhythmias are asymptomatic and do not require specific therapy, whereas others can be life threatening, requiring rapid intervention. **Myocardial ischemia** is an important cause of acute and potentially dangerous bradyarrhythmia.

II. ANATOMY

A. Sinoatrial node. The sinus beat originates in the **sinoatrial (SA) node**, a focus of automatic cells near the junction of the superior vena cava and right atrium.

1. The blood supply to the SA node is from the **sinus node artery**, which arises from the proximal **right coronary artery** in 55% of the population (Fig. 22.1) and from the **circumflex artery** in 35%. The SA node receives a dual supply of blood from both the right coronary artery and the circumflex artery in 10% of the population.
2. The automaticity of the SA node is affected by both the parasympathetic and sympathetic nervous systems. If the SA node fails to generate an impulse, other foci in the atrium, atrioventricular (AV) node, or ventricle can act as "backup" pacemaker sites.

B. AV node. The AV node is located in the anteromedial portion of the right atrium just anterior to the coronary sinus.

1. The impulse generated by the SA node progresses through the atrium to the AV node. The AV node is also innervated by both the parasympathetic and sympathetic nervous systems.
2. The AV node receives its blood supply from the AV node artery, which arises from the posterior descending artery in 80% of the population (Fig. 22.1), from the circumflex artery in 10%, and from both arteries in 10%.
3. Collateral blood supply from the left anterior descending artery makes the AV node somewhat less prone to ischemic damage than the SA node.

C. His bundle and bundle branches

1. After a delay of < 200 milliseconds in the AV node, the electrical impulse is propagated down the His bundle to the right and left bundle branches. The **left bundle branch splits further into anterior and posterior fascicles**. The autonomic nervous system does not have a major effect on conduction below the AV node.
2. The **His bundle and right bundle branch** receive their blood supply from the AV nodal artery and from septal penetrating branches of the left anterior descending artery. The anterior fascicle of the **left bundle branch** receives blood from the septal perforating branches of the left anterior descending

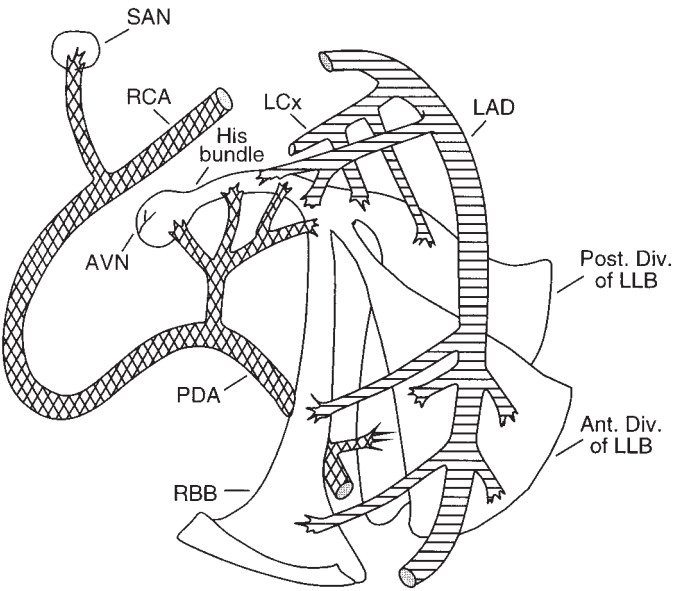

FIGURE 22.1 Diagrammatic representation of the conduction system and its blood supply. SAN, sinoatrial node; RCA, right coronary artery; AVN, atrioventricular node; PDA, patent ductus arteriosus; RBB, right bundle branch; LCx, left circumflex artery; LAD, left anterior descending; LLB, left lateral branch.

artery. The posterior fascicle has a dual blood supply: from the septal perforating branches of the left anterior descending artery and branches of the posterior descending artery.

III. SINUS NODE DYSFUNCTION. Sinus node dysfunction encompasses any dysfunction of the sinus node and includes **inappropriate sinus bradycardia**, SA **exit block**, SA **arrest, and tachycardia–bradycardia syndrome**.

A. Clinical presentation. There is a wide range of presentations, and some patients' disease may be asymptomatic.

1. Syncope and **presyncope** are the most dramatic presenting symptoms. **Fatigue, angina, and shortness of breath** are more subtle consequences of sinus node dysfunction.
2. In the tachycardia–bradycardia syndrome, the primary complaint may be palpitation. Documentation of the arrhythmia may be difficult because of the sporadic and fleeting nature of the problem.

B. Etiology. The intrinsic and extrinsic causes of sinus node dysfunction are listed in Table 22.1. **Idiopathic degenerative disease** is the most common cause of intrinsic sinus node dysfunction, and the incidence increases with age. **Acute coronary syndromes** are a common cause of bradyarrhythmias, occurring in 25% to 30% of patients with myocardial infarction (MI) (Table 22.2).

C. Electrocardiographic findings

1. Inappropriate sinus bradycardia, also known as "chronotropic incompetence," is defined as a sinus rate of < 60 beats/min that does not increase appropriately

TABLE 22.1 Etiologies of Sinus Node Dysfunction

Intrinsic causes
Idiopathic degenerative disease
Coronary artery disease
Cardiomyopathy
Hypertension
Infiltrative disorders (amyloidosis, hemochromatosis, and tumors)
Collagen vascular disease (scleroderma and systemic lupus erythematosus)
Inflammatory processes (myocarditis and pericarditis)
Surgical trauma (valve surgery and transplantation)
Musculoskeletal disorders (myotonic dystrophy and Friedreich's ataxia)
Congenital heart disease (postoperative or in the absence of surgical correction)
Extrinsic causes
Drug effects
β-Blocking agents
Calcium channel blocking agents
Digoxin
Sympatholytic antihypertensives (clonidine, methyldopa, and reserpine)
Antiarrhythmic drugs
Type IA (quinidine, procainamide, and disopyramide)
Type IC (flecainide and propafenone)
Type III (sotalol and amiodarone)
Others (lithium, cimetidine, amitriptyline, and phenytoin)
Autonomic influences
Excessive vagal tone
Carotid sinus syndrome
Vasovagal syncope
Well-trained athletes (normal variant and not dysfunction)
Electrolyte abnormalities
Hyperkalemia
Hypercarbia
Endocrine disorders—hypothyroidism
Increased intracranial pressure
Hypothermia
Sepsis

From Topol EJ, ed. *Textbook of Cardiovascular Medicine.* Philadelphia, PA: Lippincott–Raven; 1998, with permission.

TABLE 22.2 Incidence of Bradyarrhythmia in the Setting of Acute Myocardial Infarction

Rhythm	Incidence (%)
Sinus bradycardia	25
Junctional escape rhythm	20
Idioventricular escape rhythm	15
First-degree AV block	15
Second-degree, Mobitz type I AV block	12
Second-degree, Mobitz type II AV block	4
Third-degree AV block	15
Right bundle branch block	7
Left bundle branch block	5
Left anterior fascicular block	8
Left posterior fascicular block	0.5

AV, atrioventricular.

with exercise. Inappropriate sinus bradycardia must be differentiated from a low resting heart rate, which may be normal in athletes and sleeping individuals.

2. Sinus arrest, or sinus pause, occurs when the sinus node fails to depolarize on time. Pauses of < 3 seconds may be seen on Holter monitoring in up to 11% of normal adults (especially athletes) and are not a cause for concern. However, **pauses lasting longer than 3 seconds are generally considered abnormal and are suggestive of underlying pathology**, especially if the patient is awake when they occur.
3. SA exit block, although similar to sinus arrest on the electrocardiographic tracing, may be distinguished by the fact that the **duration of the pause is a multiple of the sinus PP** interval. High-grade SA exit block cannot be differentiated from prolonged sinus arrest and is treated in the same manner.
4. Tachycardia–bradycardia syndrome, also referred to as "sick sinus syndrome," is characterized by episodes of sinus or junctional bradycardia interspersed with an atrial tachycardia, usually paroxysmal atrial fibrillation.

D. Diagnostic testing. Invasive testing is used when noninvasive methods have failed to yield a diagnosis and sinus node dysfunction is still strongly suspected.

1. **Noninvasive testing**
   a. **Electrocardiogram (ECG).** In evaluating sinus node dysfunction, the initial workup should include a 12-lead ECG, followed by a 24-hour to 48-hour ambulatory ECG monitoring, if necessary. Use of a diary during the recording period can help correlate symptoms with the cardiac rhythm. For less frequent events, a loop recorder or an event recorder may be used to assess symptoms over a 2-week to 4-week period. Stress testing can help document the severity of chronotropic incompetence.
   b. Autonomic testing includes physical maneuvers, such as carotid sinus massage and tilt table testing, as well as pharmacologic interventions to test the autonomic reflexes.
      (1) Carotid sinus massage distinguishes intrinsic sinus pause/sinus arrest from a pause due to **carotid sinus hypersensitivity**, which is a 3-second

or longer pause and/or a ≥ 50 mm Hg or greater drop in blood pressure that occurs with massage of the carotid sinus (firm pressure applied to one carotid sinus at a time for 5 seconds). **Carotid sinus massage should not normally precipitate sinus pause/sinus arrest**, although it will decrease the rate of depolarization of the SA node and slow conduction in the AV node.

(2) Tilt table testing may help differentiate between syncope caused by sinus node dysfunction and that due to autonomic dysfunction. **Bradycardic episodes precipitated by tilt table testing are usually caused by autonomic dysfunction and not by sinus node dysfunction**.

(3) Pharmacologic testing may be used to differentiate between sinus node dysfunction and autonomic dysfunction. Total autonomic blockade is achieved after administration of atropine 0.04 mg/kg and propranolol 0.2 mg/kg. The resulting intrinsic heart rate represents the sinus node rate, devoid of autonomic influences. Assuming that the normal intrinsic heart rate (in beats/min) is defined by the formula

$$\text{Intrinsic heart rate} = 118.1 - (0.57 \times \text{age})$$

then an intrinsic heart rate lower than predicted using this formula is consistent with sinus node dysfunction; an intrinsic heart rate close to the predicted rate in a patient with a clinical presentation of sinus node dysfunction is suggestive of an autonomic dysfunction as a cause of the bradyarrhythmia.

2. Invasive testing. The two most common tests use indirect measurements of SA node function. Direct measurement of SA node function is laborious and rarely performed.

a. Sinus node recovery time (SNRT) is the time it takes the SA node to recover following paced overdrive suppression of the node.

(1) A delay of longer than 1,400 milliseconds is considered abnormal. This measurement may be corrected by subtracting the intrinsic sinus cycle length (in milliseconds) from the recovery time. **A corrected SNRT > 550 milliseconds is suggestive of sinus node dysfunction**.

(2) The limitations of this test are as follows:

(a) It is an indirect measurement of SA node function and reflects both sinoatrial node conduction time(SACT) and automaticity.

(b) It may be falsely shortened by an SA node entrance block during atrial pacing (due to failure of the paced impulse to reset the sinus node) or falsely prolonged by an SA node exit block (the sinus node is normal but the impulse cannot leave the node), which affects its specificity.

(c) The SNRT is not prolonged in all patients with sinus node dysfunction, which affects its sensitivity.

b. Sinoatrial node conduction time

(1) The steady-state atrial rate is determined (A_1–A_1 interval or the time between P waves). Then premature atrial **extra stimuli** (A_2) are introduced by pacing high in the right atrium, starting in late diastole at progressively shorter intervals until atrial refractoriness is found (i.e., A_2 does not result in a P wave). The duration before the next spontaneous atrial impulse (A_3) is measured and the baseline rate is subtracted.

$$\text{SACT} = (A_2 - A_3 \text{ interval}) - (A_1 - A_1 \text{ interval})$$

(2) The test assumes that SA node automaticity is not affected by pacing, that conduction time into the node is equal to conduction time out of the node, and that there is no shift in the principal pacemaker site.

E. Therapy. Treatment for symptomatic sinus node dysfunction may be pharmacologic, pacing, or a combination of both.

1. Indications for pacing in sinus node dysfunction are determined by symptoms (e.g., correlation with a documented arrhythmia; Table 22.3). Another common indication is when drug therapy that causes sinus node dysfunction cannot be stopped or changed.
2. Medications that suppress sinus node automaticity should be stopped if possible. If this is not possible, it may be necessary to place a temporary or permanent pacemaker (Table 22.3).
3. For patients with **tachycardia–bradycardia syndrome**, a pacemaker is often placed for management of the bradyarrhythmia, and antiarrhythmic drugs are added for treatment of the tachycardia episodes.
4. Acute treatment for patients with **symptomatic sinus node dysfunction** includes the following:
   (a) Atropine (0.04 mg/kg intravenous bolus)
   (b) Temporary pacing for patients whose conditions fail to respond to drug therapy
   (c) Isoproterenol (starting at 1 μg/min intravenously), which may be used as a bridge to pacemaker placement. Isoproterenol is not indicated in most patients with cardiac arrest

IV. AV CONDUCTION DISTURBANCES. These disturbances are classified as first-degree, second-degree, or third-degree block, depending on the severity of the conduction abnormality.

A. Classification

1. First-degree AV block is characterized by the prolongation of the PR interval beyond 200 milliseconds. This finding may occur as a normal variant in 0.5% of asymptomatic young adults without overt heart disease. In older individuals, it is most often caused by idiopathic degenerative disease of the conducting system.
2. **Second-degree** AV **block**
   a. Second-degree AV block is characterized by **a failure of one or more, but not all, atrial impulses to conduct to the ventricles**. The block may be at any level of the AV conduction system.
   b. When more than one atrial impulse is present for each ventricular complex, the rhythm may be described as a ratio of the number of atrial impulses to the number of ventricular complexes (for three P waves preceding each QRS complex, 3:1 second-degree AV block is present).
      (1) Lesser degrees of AV block (i.e., 4:3 or 3:2) with a prolonging PR interval prior to a nonconducted atrial impulse are described as **Mobitz type I AV block** (also known as Wenckebach block).
         (a) The conducted impulse of a **Mobitz type I block** will generally be narrow, and the site of block is often in the AV node above the His bundle.
         (b) A Mobitz type I block with a bundle branch block is still likely to be above the His bundle, but a His bundle ECG is needed to confirm the level of block.
      (2) High-grade AV block (3:1, 4:1, or greater) is typically described as **Mobitz type II AV block**. The conducted impulses will generally be preceded by constant PR intervals and have a wide QRS morphology (right bundle branch block [RBBB] or left bundle branch block [LBBB] pattern). The site of block is often below the AV node. A **Mobitz type II block** is usually intra-Hisian or infra-Hisian and has a greater propensity for progressing to third-degree AV block.
      (3) Pure 2:1 conduction patterns cannot be reliably classified as Mobitz type I or type II, and if diagnostic maneuvers (such as exercise) are not able to elucidate one type of second-degree block versus the other, an electrophysiology study may be warranted.

TABLE 22.3 Indications for Permanent Pacing

Indication	Class I	Class II	Class III
SND	1. SND documented in association with symptomatic bradycardia and due to factors that are irreversible or due to essential drug therapy 2. Symptomatic chronotropic incompetence	IIa. No clear association between SND with heart rate < 40 beats/min and symptoms can be documented IIb. In minimally symptomatic patients, chronic heart rate < 40 beats/min while awake	1. SND with marked sinus bradycardia or pauses but no associated symptoms including that due to long-term drug therapy 2. SND in patients with symptoms suggestive of bradycardia that are clearly documented as *not* associated with a slow heart rate 3. SND with symptomatic bradycardia due to nonessential drug therapy
Acquired AV block	1. Third-degree AV block at any anatomic level, associated with any one of the following conditions: a. Bradycardia with symptoms presumed to be due to AV block b. Arrhythmias and other medical conditions that require drugs that result in symptomatic bradycardia c. Documented periods of asystole ≥ 3.0 s, or an escape rhythm below the AV node, or any escape rate < 40 beats/min in awake, symptom-free individuals in sinus rhythm d. Documented pauses > 5 s in awake, symptom-free patients who are in atrial fibrillation	IIa. 1. Asymptomatic third-degree AV block at any anatomic site with average awake ventricular rates ≥ 40 beats/min 2. Asymptomatic type II second-degree AV block. Of note, when type II second-degree AV block occurs with a wide QRS, including isolated right bundle branch block, pacing becomes a class I recommendation 3. Asymptomatic type I second-degree AV block at intra-His or infra-His levels found incidentally at EP study performed for other indications	1. Asymptomatic one-degree AV block 2. Asymptomatic type I second-degree AV block at the supra-His (AV node) level or not known to be intra-Hisian or infra-Hisian 3. AV block expected to resolve and unlikely to recur (e.g., drug toxicity and Lyme disease)

Indication	Class I	Class II	Class III
	e. After catheter ablation of the AV junction f. Postoperative AV block that is not expected to resolve g. Neuromuscular diseases with AV block such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb's dystrophy (limb girdle), and peroneal muscular dystrophy h. Permanent pacemaker implantation is indicated for asymptomatic persistent third-degree AV block at any anatomic site with average awake ventricular rates of 40 beats/min or faster if cardiomegaly or LV dysfunction is present or if the site of block is below the AV node. i. Permanent pacemaker implantation is indicated for second-degree or third-degree AV block during exercise in the absence of myocardial ischemia 2. Second-degree AV block regardless of type or site of block, with associated symptomatic bradycardia	4. First-degree AV block with symptoms suggestive of pacemaker syndrome and documented alleviation of symptoms with temporary AV pacing	
Post–myocardial infarction	1. Persistent second-degree AV block in the His-Purkinje system with bilateral bundle branch block or third-degree AV block within or below the His-Purkinje system after acute myocardial infarction	IIa. None IIb. 1. Persistent second-degree or third-degree AV block at the AV node level, even in the absence of symptoms	1. Transient AV block without intraventricular conduction defect 2. Transient AV block in the presence of isolated left anterior fascicular block

(Continued)

TABLE 22.3 Indications for Permanent Pacing (*Continued*)

Indication	Class I	Class II	Class III
	2. Transient advanced (second-degree or third-degree) infranodal AV block and associated bundle branch block. If the site of block is uncertain, an EP study may be necessary 3. Persistent and symptomatic second-degree or third-degree AV block		3. Acquired left anterior fascicular block in the absence of AV block 4. Persistent first-degree AV block in the presence of bundle branch block that is old or age indeterminate
Chronic bifascicular and trifascicular blocks	1. Intermittent third-degree AV block 2. Type II second-degree AV block 3. Alternating bundle branch block	IIa. 1. Syncope not proved to be due to AV block when other likely causes have been excluded, specifically ventricular tachycardia 2. HV interval > 100 milliseconds 3. Pacing-induced block below the His that is not physiologic	1. Fascicular block without AV block or symptoms 2. Fascicular block with first-degree AV block without symptoms
Carotid sinus hypersensitivity (carotid sinus irritability) and neurally mediated syncope	1. Recurrent syncope caused by carotid sinus stimulation; minimal carotid sinus pressure induces ventricular asystole of > 3 s duration in the absence of any medication that depresses the sinus node or AV conduction	IIb. None IIa. 1. Recurrent syncope without clear, provocative events and with a hypersensitive cardioinhibitory response 2. Syncope of unexplained origin when major abnormalities of sinus node function or AV conduction are discovered or provoked in EP studies	1. A hyperactive cardioinhibitory response to carotid sinus stimulation in the absence of symptoms 2. A hyperactive cardioinhibitory response to carotid sinus stimulation in the absence of symptoms A hyperactive cardioinhibitory response to carotid sinus stimulation in the presence of vague symptoms such as dizziness, light-headedness, or both

Indication	Class I	Class II	Class III
		IIb. 1. Neurally mediated syncope with significant bradycardia reproduced by a head-up tilt with or without isoproterenol and other provocative maneuvers	3. Recurrent syncope, light-headedness, or dizziness in the absence of a hyperactive cardioinhibitory response 4. Situational vasovagal syncope in which avoidance behavior is effective

Class I: conditions for which there is evidence and/or general agreement that pacing is beneficial, useful, and effective.
Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of pacing.
Class IIa: weight of evidence/opinion is in favor of usefulness/efficacy.
Class IIb: usefulness/efficacy is less well established by evidence/opinion.
Class III: conditions for which there is evidence and/or general agreement that pacing is not useful/effective and in some cases may be harmful.
SND, sinus node dysfunction; AV, atrioventricular; LV, left ventricular; EP, electrophysiologic; HV, half-value.

Adapted from Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (writing committee to revise the ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices). *J Am Coll Cardiol*. 2008; 51:2085-2105.

3. Third-degree AV block, or **complete heart block**, may be acquired or congenital.
   a. Of patients with **congenital complete heart block**, 60% are female. Of children with congenital complete heart block, 30% to 50% of their mothers have connective tissue disease, usually systemic lupus erythematosus.
   b. Acquired AV block occurs most frequently in the seventh decade and more commonly affects males.

B. Clinical presentation

1. **Signs and symptoms**
   a. First-degree AV block is generally not a cause of symptoms.
   b. Second-degree AV block sometimes results in symptoms; however, high-grade second-degree AV block may progress to third-degree AV block, which can frequently cause symptoms.
   c. Depending on the ventricular escape rate, patients with **third-degree** AV **block** may experience **fatigue** or **syncope**.
2. **Physical findings.** The amplitude of the arterial pulse and venous waveform varies, depending on the timing of atrial filling of the ventricles.
   a. Second-degree AV block is associated with a periodic change in amplitude. In patients with **third-degree AV block**, amplitude is constantly changing, for example, periodic appearance of cannon *a* waves (large-amplitude waves in the venous pulsations seen in the neck when the atria contracts against a closed tricuspid valve).
   b. Heart sounds are similarly affected by the change in filling duration of the ventricles.
      (1) **The first heart sound** (S_1) becomes softer as the PR interval is prolonged, resulting in a soft S_1 in first-degree AV block, a progressive softening of S_1 in type I second-degree AV block, and a constantly changing S_1 in third-degree AV block.
      (2) Third-degree AV block may also result in a functional systolic ejection murmur.

C. Etiology. The causes of AV block are listed in Table 22.4; the most common cause is **idiopathic fibrosis. Acute MI** results in AV block in 14% of patients with inferior infarction and 2% of those with anterior infarction, usually within the first 24 hours.

D. Diagnostic testing

1. **First-degree AV block.** Measuring a PR interval longer than 200 milliseconds in adults and 180 milliseconds in children makes up the diagnosis. A P wave precedes each QRS, and both the P and the QRS are morphologically normal.
2. **Second-degree AV block**
   a. The diagnosis of **Mobitz type I** is made when the following criteria are met on the ECG:
      (1) Sequential and gradual prolongation of the PR interval terminated by a nonconducted P wave
      (2) Prolongation of the PR interval occurring in progressively shorter increments in "typical" Wenckebach, which results in progressive shortening of the RR intervals prior to the nonconducted atrial impulse
      (3) Duration of the pause following the nonconducted P wave is less than the sum of any two consecutively conducted beats
      (4) Decreased PR interval following the pause when compared with the prepause PR interval
      (5) "Grouped beating," a pattern of repeated groups of QRS complexes characteristic of Wenckebach block
   b. Mobitz type II second-degree AV block is less common than type I.
      (1) The PR interval is constant with a sudden nonconducted P wave (Fig. 22.2), in contrast to nonconducted premature atrial contractions that have a varying PR interval.

TABLE 22.4 Causes of Atrioventricular Block

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

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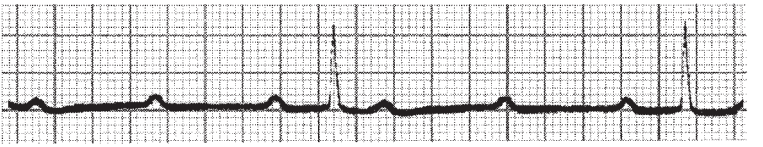

FIGURE 22.2 Mobitz type II second-degree atrioventricular block with 3:1 conduction.

(2) Each QRS complex may have multiple P waves, which are designated by the number of P waves before each conducted QRS (3:1, 4:1, etc.). The QRS complex is typically not narrow (a narrow QRS complex is suggestive of a Mobitz type I block).

3. **Third-degree AV block** (Fig. 22.3)
   a. Third-degree AV block is characterized by the identification of **complete dissociation of the atrial and ventricular electrical activities** (no temporal relationship exists between the P waves and the QRS complexes), with atrial activity more rapid than ventricular activity. Using calipers, it is possible to march out the progression of the P waves to determine the atrial rate.
   b. Third-degree AV block is only one cause of AV dissociation; **not all AV dissociation is third-degree AV block.** For example, conditions where the ventricles are depolarizing faster than the atria—such as accelerated junctional rhythm or ventricular tachycardia—also result in AV dissociation if there is a lack of retrograde conduction over the AV node.

E. **Therapy.** Patients with first-degree AV block and Mobitz type I AV block usually do not require therapy. Permanent pacing is indicated for Mobitz type II AV block and third-degree AV block. (See Table 22.3 for complete indications for pacing.)

1. Medical therapy may be used as a bridge to pacing but it has no role in long-term treatment.
   a. The principal drug used as a bridge to pacing is **atropine**,
      (1) which reduces heart block due to hypervagotonia but not due to AV nodal ischemia;
      (2) which is more useful for AV block in inferior MI than anterior MI;
      (3) which does not increase infranodal conduction (will not improve second-degree or third-degree AV block that is below the AV node);
      (4) which is ineffective in the denervated hearts of transplant patients;
      (5) which is used with caution (if at all) in Mobitz type II AV block due to a possible paradoxical decrease in heart rate (as atrial rate increases, AV conduction decreases, and a 2:1 block with an atrial rate of 80 beats/min and a ventricular rate of 40 beats/min may be converted to a 3:1 block with an atrial rate of 90 beats/min and a ventricular rate of 30 beats/min).
   b. Digoxin-specific Fab fragments may be used to treat patients with symptomatic AV blocks related to the use of digitalis. The number of vials = weight (kg) × digoxin serum concentration (ng/mL)/100.
2. **Pacing**
   a. Third-degree AV block as a complication of inferior MI is usually temporary and thus usually only requires **temporary pacing**.
   b. However, complete heart block as a result of anterior MI often requires **permanent pacing** (Table 22.3).
   c. Acquired third-degree AV block usually requires pacing, but patients with congenital third-degree AV block often have a sufficiently rapid escape rhythm to prevent symptoms and avoid permanent pacemaker implantation.

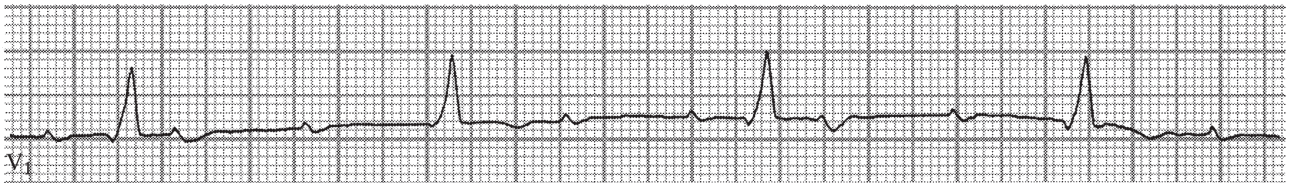

FIGURE 22.3 Third-degree atrioventricular block with sinus tachycardia and right bundle branch block.

V. JUNCTIONAL RHYTHMS. Junctional rhythms arise from the area surrounding the AV node, including the approaches to the node, the node itself, and the bundle of His. This area has an intrinsic rate of 30 to 60 beats/min and serves as an escape mechanism to prevent ventricular asystole in case of complete AV block. Junctional rhythm that is faster than the sinus rhythm is referred to as **accelerated junctional rhythm**.

A. Clinical presentation. Patients usually do not develop symptoms that are directly attributable to accelerated junctional rhythm. The **physical findings of AV dissociation may be noted** and are the same as those seen in third-degree AV block.

B. Etiology

1. Accelerated junctional rhythm is seen in approximately **10% of patients with acute MI**. More than one-half of these patients have inferior MI and about one-third have anterior infarctions.
2. Digitalis toxicity by itself does not seem to cause accelerated junctional rhythm, as evidenced in persons with normal hearts who take accidental overdoses of digoxin. **Concomitant heart disease** is required to develop accelerated junctional rhythm.
3. Other causes of accelerated junctional rhythm are valve surgery, acute rheumatic fever, direct current cardioversion, cardiac catheterization, serious infection, chronic obstructive pulmonary disease, systemic amyloidosis, and uremia with hyperkalemia.

C. ECG findings

1. **Accelerated junctional rhythm**
   a. **Unless the junctional rhythm causes retrograde activation of the atria**, the P wave is normal in morphologic characteristics. The QRS complex has a normal duration, unless there is concomitant bundle branch block. The distinguishing characteristic of accelerated junctional rhythm is the AV dissociation and changing PR interval (Fig. 22.4).
   b. **The difference between accelerated junctional rhythm and third-degree AV block is the fact that the ventricular rate is faster than the atrial rate in accelerated junctional rhythm and slower than the atrial rate in third-degree AV block**.
2. **Junctional rhythm.** In the absence of a sinus beat, the AV node can act as a backup pacemaker. The ECG findings are an absence of P waves (or retrograde P waves immediately before or after the QRS complex), a narrow QRS complex, and a rate of 30 to 60 beats/min.

D. Therapy

1. Therapy for junctional rhythm secondary to SA node failure or AV block is as previously outlined for AV conduction disturbances.
2. Patients with accelerated junctional rhythm do not usually require therapy for the arrhythmia, although management of the underlying cause is indicated.
3. Suppression of accelerated junctional rhythm may be achieved by **increasing the atrial rate with drugs** (e.g., atropine and adrenergics) or **pacing**.
4. Digoxin-induced accelerated junctional rhythm is an indication to stop digoxin but it does not usually require administration of digoxin-specific Fab fragments.

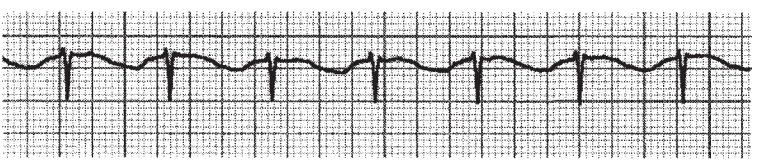

FIGURE 22.4 Accelerated junctional rhythm.

VI. INTRAVENTRICULAR CONDUCTION DISTURBANCES. Conduction disturbances due to blockage below the AV node are classified on the basis of the intraventricular conduction system. An intraventricular conduction disturbance (IVCD) does not itself cause bradyarrhythmia, but it may be associated with any of the other rhythms that cause bradycardia. When associated with an acute MI, an IVCD predicts a worse outcome.

A. Etiology

1. The causes of IVCDs are similar to those that cause AV block (Table 22.4); **idiopathic degenerative conduction disease** and **acute ischemic syndromes** are the most common causes.
2. IVCDs increase with age and affect up to 2% of individuals older than 60 years.
3. The incidence of IVCDs is increased in persons with structural heart disease, especially those with coronary artery disease.

B. ECG findings

1. The ECG findings of IVCDs are summarized in Table 22.5 and examples are presented in Figures 22.5 to 22.8. As shown, **IVCDs may be further classified by the number of fascicles they affect**.
2. **Fascicular blocks**
   a. Unifascicular blocks affect only one of the three fascicles. Examples are RBBB, left anterior fascicular block, and left posterior fascicular block (LPFB).
   b. Bifascicular block is present when conduction disturbances affect two of the fascicles, most commonly the right bundle branch and the left anterior fascicle. Approximately, 6% of these patients progress to complete heart block. RBBB with LPFB is less common, but the progression to complete heart block is more common.
   c. "Trifascicular block" is said to be present when there is a combination of bifascicular block and first-degree AV block (Fig. 22.8).

C. Therapy. Pacing is indicated in patients with bifascicular block who have intermittent symptomatic complete heart block and in patients with bifascicular or trifascicular block with asymptomatic intermittent Mobitz type II AV block (Table 22.3).

TABLE 22.5 Electrocardiographic Features for the Fascicular and Bifascicular Blocks

ECG finding	LBBB	LAFB	LPFB	RBBB	RBBB and LAFB	RBBB and LPFB
QRS axis		≥ – 45°	+90° to +120°		–60° to –120°	≥ +120°
QRS duration Leads I/aVL	≥ 120 milliseconds broad monophasic R	Normal qR	Normal rS	≥ 120 milliseconds qRS with wide terminal S	≥ 120 milliseconds qR	≥ 120 milliseconds rS
Leads II, III, and aVF		rS	qR		rS	qR
Leads V_1 and V_2	rS or QS			rsR′ or rSR′	rsR′ or rSR′	rsR′ or rSR′
Leads V_5 and V_6		S	no Q's	qRS		

ECG, electrocardiogram; LAFB, left anterior fascicular block; LBBB, left bundle branch block; LPFB, left posterior fascicular block; RBBB, right bundle branch block.

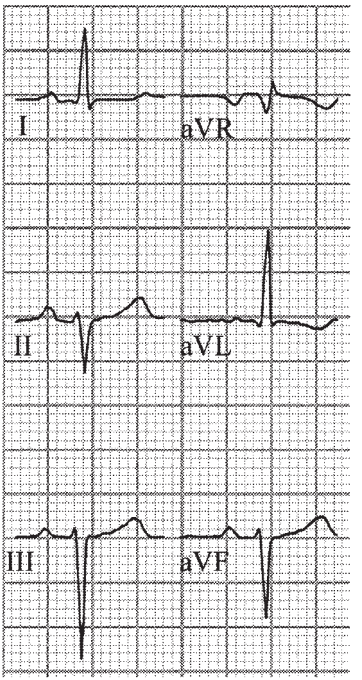

FIGURE 22.5 Left anterior hemiblock.

VII. POSTSURGICAL BRADYARRHYTHMIAS

A. Etiology. Bradyarrhythmias following cardiac surgery are common.

1. Valvular surgery and septal myectomy can cause mechanical damage to the conduction system, leading to AV blocks and IVCDs. For example, there is an approximately 7% incidence of postoperative permanent pacemaker implantation for high-grade AV block after conventional aortic valve replacement in patients with severe calcific aortic stenosis (this may be partly due to a higher prevalence of infranodal conduction system disease at baseline). Also, there is a high incidence of LBBB after septal myectomy, due to the presence of the left bundle branch in the myocardium being excised.
2. Prolonged ischemic time during cardiac transplantation can lead to sinus node damage.

B. Therapy. Because postsurgical bradyarrhythmias may be only temporary, the decision to proceed to **permanent pacing** should be made after 5 to 7 days. The same criteria listed in Table 22.3 are used to determine the need for a pacemaker. Permanent pacing is required in 2% to 3% of patients following valve surgery (when considering all types) and in upward of 10% of transplant patients.

VIII. PULSELESS ELECTRICAL ACTIVITY.

Pulseless electrical activity is defined as the absence of a pulse or blood pressure measured by usual methods, with the continued presence of electrical activity of the heart.

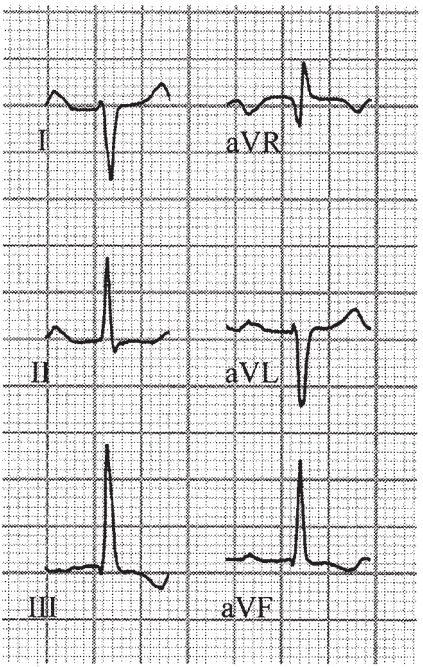

FIGURE 22.6 Left posterior hemiblock.

A. Etiology

1. Pulseless electrical activity may result from a variety of **rhythm disturbances**, such as electrical–mechanical dissociation, idioventricular rhythms, and ventricular tachycardias. When the electrical activity is organized and within the physiologic range, the term **electrical–mechanical dissociation** is used.
2. A variety of clinical situations are also associated with pulseless electrical activity, a potentially manageable condition if certain actions are undertaken rapidly (Table 22.6).

B. Therapy

1. Specific management of the underlying cause is most likely to result in a successful outcome (Table 22.6).
2. Emergency intervention should be initiated at once, including the following:
   - **(a)** Effective cardiopulmonary resuscitation (CPR) and airway management
   - **(b)** Epinephrine, 1 mg intravenous push every 3 to 5 minutes
   - **(c)** A one-time intravenous push of 40 IU of vasopressin may be considered as an alternative to epinephrine during the first or second round of advanced cardiac life support
   - **(d)** Atropine is no longer recommended for routine administration during advanced cardiac life support for pulseless electrical activity, as per 2010 ACC/AHA guidelines.
   - **(e)** Discovery and correction of the underlying reason for the pulseless electrical activity (see Table 22.6) remains the paramount concern along with performing

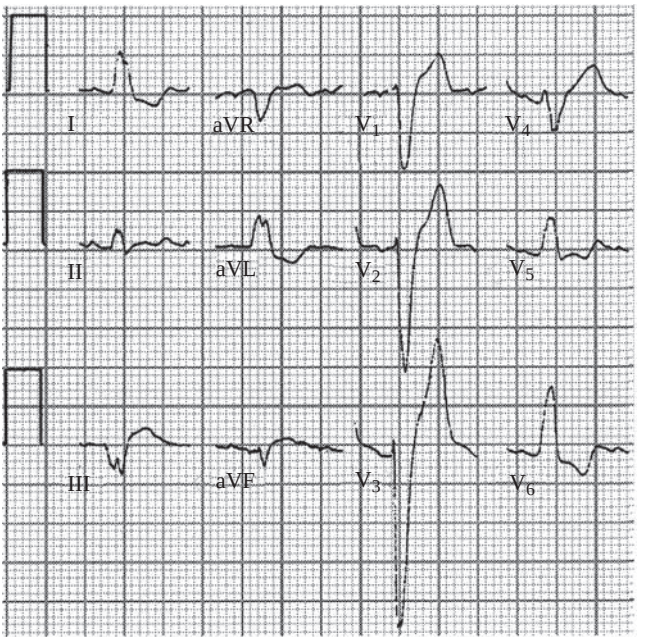

FIGURE 22.7 Left bundle branch block.

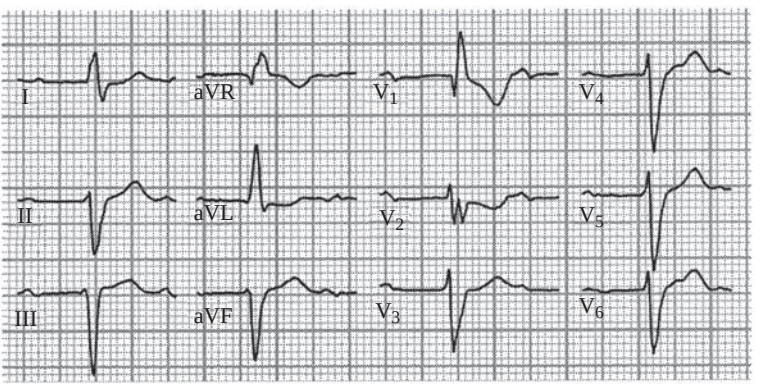

FIGURE 22.8 First-degree atrioventricular block with right bundle branch block and left anterior hemiblock.

effective CPR. The "H's and T's" of hypoxia, hypovolemia, hypothermia, hyperkalemia, acidosis ("hyper-H+"), tension pneumothorax, thrombosis (coronary or pulmonary), tamponade, and toxins must be considered and addressed as soon as possible.

TABLE 22.6 Conditions That Cause Pulseless Electrical Activity

Condition	Clues	Management
Hypovolemia	History and flat neck veins	Volume infusion
Hypoxia	Cyanosis, blood gases, and airway problems	Ventilation
Cardiac tamponade	History (trauma, renal failure, and malignancy), no pulse with CPR, vein distention; impending tamponade—tachycardia, hypotension, and low pulse pressure	Pericardiocentesis
Tension pneumothorax	History (asthma, ventilator, chronic obstructive pulmonary disease, and trauma), no pulse with CPR, neck vein distention, and tracheal deviation	Needle decompression
Hypothermia	History of exposure to cold, central body temperature, and ECG	Gradual warming
Massive pulmonary embolism	History and no pulse felt with CPR	Pulmonary arteriogram, surgical embolectomy, and thrombolytics
Drug overdose (tricyclics, digoxin, β-blockers, and calcium channel blockers)	Bradycardia, history of ingestion, empty bottles at the scene, pupils, and neurologic examination	Drug screens, intubation, lavage, activated charcoal, and lactulose per local protocols
Hyperkalemia	History of renal failure, diabetes, recent dialysis, medications, and ECG	Calcium chloride (immediate); then combination of insulin, glucose, and sodium bicarbonate; then sodium polystyrene sulfonate/sorbitol; and dialysis (long term)
Preexisting acidosis	Renal failure	Sodium bicarbonate and hyperventilation
Acute massive MI	History, ECG and enzymes	Treatment for cardiogenic shock

CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; MI, myocardial infarction.

IX. ASYSTOLE

A. Clinical presentation. Asystole is defined as the absence of myocardial electrical activity. *It should be confirmed by switching between several leads or changing the position of the defibrillation paddles.*

1. Most patients with asystole present in a code situation. Persons outside of the hospital who are found to have asystole by the initial responding team usually have it as a result of **profound myocardial ischemia**. The possibility of a successful outcome in this situation is extremely small.

2. Hospital inpatients monitored by telemetry, on the other hand, may have a favorable outcome.

B. Etiology. Asystole may be due to profound parasympathetic suppression of both atrial and ventricular activities, stunning of the myocardium due to electrical defibrillation, complete heart block, or prolonged myocardial ischemia. Also, many of the causes of pulseless electrical activity may also lead to asystole, and the same search for obvious and immediately reversible causes is warranted (Table 22.6).

C. Therapy. Management consists of effective **CPR, airway protection**, and **a similar management algorithm to** pulseless electrical activity.

1. Routine shocking is strongly discouraged. Electrical shocks have not been demonstrated to have any benefit in the management of asystole and may in fact produce a stunned myocardium, leading to a delay in the return of a rhythm.
2. Pacing for asystole is controversial. If pacing is to have any effect, it must be initiated early. Patients with asystole due to myocardial ischemia are unlikely to respond to pacing, but those with asystole due to other causes might respond.
3. As with the 2010 revised guidelines for management of pulseless electrical activity, atropine is no longer recommended for routine use in the resuscitation of the asystolic patient.

X. CAROTID SINUS HYPERSENSITIVITY.

Carotid sinus hypersensitivity, defined as a sinus pause of 3 seconds or more and/or a drop in blood pressure of 50 mm Hg or more with carotid sinus massage, is common, affecting up to one-third of older men with coronary artery disease. Carotid sinus hypersensitivity may be purely cardioinhibitory, purely vasodepressive, or a combination of both. **Carotid sinus syndrome** is present when carotid sinus hypersensitivity is accompanied by syncope or near syncope.

A. Etiology and pathophysiology

1. The **cause of carotid sinus hypersensitivity and carotid sinus syndrome is unknown**. It is more common in older individuals, particularly those with atherosclerotic disease. Carotid sinus syndrome may be precipitated by the patient stretching his or her neck (such as with shaving or turning the head) or wearing a tight collar, but often a precipitating event cannot be found.
2. Sites of potential lesions causing carotid sinus hypersensitivity are the sternocleidomastoid muscle, the central nervous system, and the feedback loops between the cardiovascular and the central nervous systems.
3. It has been demonstrated that the **carotid sinus function is intact** and the sinus is not hypersensitive in the true sense. Some investigators have suggested that carotid sinus syndrome be renamed carotid sinus irritability to better reflect its pathophysiology.

B. Diagnostic testing. A patient with suspected carotid sinus hypersensitivity/carotid sinus syndrome should be tested lying down with ECG and blood pressure monitoring.

1. Carotid sinus massage is performed by placing firm manual pressure over the carotid sinus located at the bifurcation of the carotid artery for not more than 5 seconds. Only one sinus at a time is compressed, and the temporal artery should be lightly palpated to ensure that complete occlusion of the artery does not occur.
2. Potential risks of carotid sinus massage are transient ischemic attack and stroke. This test should not be performed if a carotid bruit is present. Tilting the patient to an upright position will increase the diagnostic yield of the test but it may also result in false-positive outcomes.

C. Therapy

1. Carotid sinus hypersensitivity by itself generally does not require treatment. However, therapy is warranted if carotid sinus hypersensitivity is demonstrated to be the cause of syncope or near syncope.

2. For purely cardioinhibitory or the mixed type of carotid sinus syndrome, the therapy of choice is pacing (Table 22.3).
3. Management of vasodepressive carotid sinus syndrome is more difficult, and pacing is generally ineffective.

ACKNOWLEDGMENTS: *The author thanks Drs. Christopher Cole, Gregory Bashian, and Oussama Wazni for their significant contributions to earlier editions of this chapter.*

LANDMARK ARTICLES

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CHAPTER 23

Edmond M. Cronin

Sudden Cardiac Death

I. DEFINITION AND EPIDEMIOLOGY. Sudden cardiac death (SCD) is defined as death following cardiac arrest in a patient with or without known preexisting heart disease in whom the mode and time of death are unexpected (1). The generally accepted timeframe between the onset of symptoms and loss of consciousness is 1 hour, although some patients who receive medical interventions may live for much longer after the initiating event before expiring. If the patient survives the event, due to defibrillation or spontaneous recovery, it is labeled sudden cardiac arrest (SCA). The incidence of SCD in the United States is estimated at 460,000 cases per annum, accounting for 10% to 15% of all deaths from natural causes and about 50% of all cardiac deaths. SCD exhibits a bimodal age distribution with peaks between birth and 6 months of age and then rises steadily from age 30. A male preponderance is observed in all age groups, narrowing after age 65, and is attributable to an increased incidence of coronary artery disease (CAD). While the absolute risk of SCD is greater among high-risk populations, most SCDs occur in patients who have not been identified as being at risk, being the first presentation of cardiovascular disease in approximately 25% of patients.

It is likely that ventricular fibrillation (VF) or ventricular tachycardia (VT) is the initiating rhythm in most cases of SCA. As the time from onset and rhythm identification increases, the proportion of VF decreases. This suggests that asystole and pulseless electrical activity (PEA) are frequently the result of prolonged VF and resultant ischemia and hypoxia. However, a significant proportion of SCA is due to bradyarrhythmias and pump failure. The proportion of these deaths is slightly higher in patients with advanced heart failure, although tachyarrhythmias still predominate.

II. CAUSES OF SCD

A. Coronary artery disease accounts for 80% or more of episodes of SCD in Western societies, and SCD is the first presentation of CAD in 20% to 25% of patients. However, the extent to which acute ischemia plays a role in initiating a trigger for SCD is unclear. Autopsy data have demonstrated a recent occlusive thrombus in only about 15% to 20% of patients, while evidence of a remote infarct is identified in 40% to 70% of cases. The majority (80%) of SCD episodes in patients with CAD are considered to be primary (i.e., no precipitating factor can be identified), whereas secondary causes like myocardial ischemia/infarction, drug toxicity or proarrhythmia, decompensated heart failure, or electrolyte imbalance can be identified in the minority. Patients with reduced left ventricular ejection fraction (LVEF) and frequent premature ventricular contractions (PVCs) are identified as a particularly high-risk subgroup. A study of patients implanted with a loop recorder with recent myocardial infarction (MI) and ejection fraction (EF) ≤ 40% found that the terminal rhythm was VF in 86% of sudden deaths, and 50% of all deaths, with bradyarrhythmias in the remaining 50%.

B. Cardiomyopathies

1. **Dilated cardiomyopathy (DCM).** Patients with DCM represent the second largest group of patients who experience SCD, accounting for approximately 10% of cases. The annual mortality from DCM is 11% to 15%, with SCD accounting for about 30% of all deaths in this population. The presence of reduced LVEF and syncope are markers of a high risk of SCD in these patients. There is also a higher incidence of sudden deaths related to bradyarrhythmias and PEA in patients with advanced disease.
2. **Hypertrophic cardiomyopathy (HCM).** The incidence of SCD in patients with *HCM* is 2% to 4% per year in adults and 4% to 6% per year in children and adolescents. Risk factors that identify a high-risk population in patients with HCM include prior SCA, family history of SCD, sustained or nonsustained VT (NSVT), syncope, a drop in blood pressure with exercise, and septal hypertrophy ≥ 30 mm. Myocardial scar, detected by late gadolinium enhancement on magnetic resonance imaging (MRI), is also emerging as a predictor of risk. SCD usually results from ventricular arrhythmias, but occasionally it may be precipitated by atrial fibrillation, bradyarrhythmias, or myocardial ischemia.
3. **Arrhythmogenic right ventricular dysplasia (ARVD).** *ARVD* is a rare genetic disorder characterized by heart failure, ventricular arrhythmias, and SCD. Mutations involving the desmosome are manifested by fibrofatty infiltration of the right ventricle. The incidence of SCD is approximately 2% per year and is mainly due to ventricular tachyarrhythmia. Patients are identifiable by right bundle branch block (RBBB), T-wave inversion in V_1 through V_3 and epsilon waves on the electrocardiogram (ECG), regional right ventricular akinesia, dyskinesia, or aneurysm on echo or MRI, and findings on endomyocardial biopsy.

C. The channelopathies

1. **The congenital long QT syndrome (LQTS).** *LQTS* is a familial disease with a prevalence of about 1:2,000, characterized by an abnormally long QT interval, leading to the development of early afterdepolarizations and torsades de pointes.

The two variants of the syndrome include the more common autosomal dominant form (Romano-Ward syndrome) and the less common recessive form (Jervell and Lange-Nielsen syndrome), which is associated with congenital deafness. To date, mutations at 12 different LQTS susceptibility genes have been identified. The most common, accounting for over 50% of cases, is a mutation in *KCNQ1*, which encodes the α-subunit of the potassium channel conducting the slow delayed rectifier current (I_{Ks}). This mutation produces LQT1, which is characterized clinically by broad-based T waves and exercise-induced arrhythmic events (especially swimming). LQT2 (35% to 40% of cases) is caused by mutations in the *KCNH2* gene encoding the HERG protein (I_{Kr} current) and presents with low-amplitude, notched T waves and auditory arrhythmogenic triggers. LQT3 is caused by a gain-of-function mutation in the sodium channel gene *SCN5A* and manifests a long, isoelectric ST segment and SCD events during sleep.

The mortality rate for LQTS is estimated to be about 1% per year. High-risk patients include those with a corrected QT interval > 500 milliseconds, a history of syncope or SCA, male sex in children and female sex in adults (especially after menopause), and the LQT2 or LQT3 genotype. It has been postulated that 11% to 13% of sudden infant death syndrome cases could be caused by LQTS. All patients are treated with β-blocker therapy; however, genotype-specific and individualized therapies are evolving. Symptomatic patients who are either refractory to or intolerant of medical therapy, or who have other high-risk markers for SCD, should be considered for implantable cardioverter–defibrillator (ICD) implantation and left cardiac sympathetic denervation. It seems increasingly likely that many patients who suffer cardiac events due to drug-induced or other acquired QT prolongation have a *forme fruste* of LQTS.

The very rare *short QT syndrome* is caused by mutations in genes encoding the potassium channel, resulting in shortening of the action potential duration and vulnerability to VF.

2. **Brugada syndrome.** The *Brugada syndrome* is an autosomal dominant arrhythmogenic disorder caused by mutations in the *SCN5A* gene encoding the cardiac sodium channel, which predisposes patients to develop polymorphic VT or VF. The arrhythmias commonly occur at rest or during sleep, and the risk of SCA is up to 30% at 3 years in untreated symptomatic patients. Incomplete RBBB with coved ST elevation in the right precordial leads is diagnostic and, although often transient, may be elicited by a drug challenge. Atrial fibrillation and conduction abnormalities are frequently associated. Symptomatic patients (syncope or SCA) should undergo ICD implantation; risk stratification for asymptomatic patients is controversial.
3. **Catecholaminergic polymorphic ventricular tachycardia (CPVT)** is due to mutations in the ryanodine receptor and calsequestrin and results in a malignant phenotype of bidirectional VT during emotional or physical stress. Treatment is with β-blockers and ICD, and recent evidence suggests an emerging role for flecainide.

D. Others. The risk of SCD is also higher in patients with *Wolff-Parkinson-White (WPW) syndrome*, especially if they have rapidly conducting accessory pathways, when atrial fibrillation can be associated with very rapid ventricular rates and degeneration to VF. An RR interval ≤ 220 milliseconds during spontaneous AF indicates a higher risk. The incidence of SCD is 0.05% to 0.1% per year and is higher in males in their second and third decades, but the phenomenon is easily identifiable and manageable. When no cause of SCA can be found, the label *idiopathic VF* is applied. In some cases, VF is triggered by a PVC which is amenable to catheter ablation. Recent evidence suggests that *early repolarization* on ECG denotes a higher risk of SCD in the presence of proarrhythmic triggers, and the clinical implications of this are still being clarified. Some of the other cardiac and noncardiac causes of SCD are presented in Table 23.1.

TABLE 23.1 Some Other Conditions with an Increased Risk of Sudden Cardiac Death

Cardiac	Noncardiac
Cardiac vascular	Neurologic
Coronary artery anomalies	Epilepsy
Coronary artery embolism	Hereditary muscular dystrophies
Coronary arteritis (polyarteritis nodosa and Kawasaki syndrome)	Friedreich's ataxia
Coronary artery dissection	Central nervous system injury
Coronary spasm	Respiratory
Myocardial bridging	Asthma
Valvular and great vessels	Obstructive sleep apnea
Severe aortic stenosis	Massive pulmonary embolism
Severe mitral regurgitation	Pulmonary hypertension
Prosthetic valvular obstruction or dehiscence	Endocrine and metabolic
Ruptured sinus of Valsalva aneurysm	Diabetes mellitus
Aortic dissection	Acromegaly
Electrophysiologic	Electrolyte disturbances
Progressive cardiac conduction disease (Lev-Lenegre disease)	Acid–base disturbances
Myocardial	Renal
Left ventricular hypertrophy	Chronic kidney disease
Infiltrative disease (sarcoid and amyloid)	Hemodialysis
Apical ballooning syndrome	Psychiatric/psychological
Myocarditis	Depression
Congenital	Anxiety
Eisenmenger physiology	Anorexia nervosa
Late after surgical repair, especially of tetralogy of Fallot	Intense emotion
Trauma	Situational
Cardiac tamponade	Intense exercise and athletes
Commotio cordis	Drugs
	Antiarrhythmic drugs
	Typical and atypical antipsychotics
	Other QT-prolonging drugs
	Drug–drug interactions
	Cigarette smoking
	Cocaine

III. DIAGNOSTIC AND PROGNOSTIC TESTING. Survivors of SCA should have a detailed cardiovascular evaluation. Reversible precipitating factors must be identified and corrected. Underlying diseases must be identified and managed, and the risk of recurrent SCD must be determined. Diagnostic and prognostic testing appropriate for the survivor of SCA includes the following:

A. ECG for the evidence of MI or ischemia, intraventricular conduction delay, accessory pathway (WPW syndrome), prolonged QT interval, epsilon waves, Brugada pattern, and left ventricular hypertrophy.

B. Laboratory data to rule out reversible causes, such as cardiac biomarkers (creatine kinase–myocardial band, troponin T, and troponin I), abnormal electrolytes, antiarrhythmic drug levels for toxicity, and urine screening for illicit drugs such as cocaine.

C. ECG monitoring to assess frequency, duration, and symptomatology of arrhythmias.

D. **Twenty-four-hour ambulatory electrocardiography** during normal activities can be useful in predicting the risk of recurrent SCA.

E. **Echocardiography** for the assessment of left ventricular function, valvular disease, cardiomyopathy, and hypertrophy. Nuclear or angiographic determinations of left ventricular function may be used but do not provide as much information as echocardiography. The LVEF continues to be the most potent predictor of SCD, behaving as a continuous variable with markedly increased risk < 40%. However, nonsudden death also increases with declining EF, meaning that the likely mode of death cannot be predicted. LVEF is also limited by poor sensitivity—from 22% to 59% in studies in the last decade.

F. **Coronary angiography** for the assessment of CAD or coronary anomalies.

G. **Exercise or pharmacologic stress testing** with radionuclide imaging or echocardiography if CAD is present and myocardial ischemia and/or viability is in question.

H. **Electrophysiologic (EP) testing** has a limited role in assessing the survivor of SCA. Given its low sensitivity, a negative test does not exclude recurrent SCA, and almost all patients who survive SCA are in any case candidates for an ICD. Although EP testing can be performed to guide programming of the ICD, this is rarely done in practice. Voltage mapping has been used to corroborate a diagnosis of ARVD, and mapping and ablation are essential in the management of patients with WPW and selected patients with cardiomyopathy and VT. Emerging applications of ablation in ARVD and Brugada syndrome deserve further study.

I. **Cardiac MRI.** Particularly for the patient with normal left ventricular function, cardiac MRI may be useful to evaluate for arrhythmogenic right ventricular cardiomyopathy and to investigate left ventricular hypertrophy.

J. Drug challenge with flecainide, procainamide, or ajmaline to provoke the Brugada pattern should be considered in all SCA survivors where the above tests do not reveal a cause. Epinephrine infusion or exercise testing has been used to diagnose LQT1 and CPVT.

K. Genetic testing for the channelopathies, HCM, and ARVD is becoming increasingly comprehensive; however, many as yet unidentified mutations are postulated to exist. At present, only 21% of patients with Brugada syndrome and 52% with ARVD have an identifiable causative mutation. Testing in cases where a clear phenotype has not been established, or is not suggestive of a genetic disorder, is discouraged, as many variants are of uncertain significance. A positive genetic test is useful and facilitates family screening, but a negative test is not.

IV. THERAPY

A. Acute therapy for SCA

1. **Cardiopulmonary resuscitation (CPR).** Early response is crucial. The two most critical components of out-of-hospital cardiac resuscitation are the availability of a rapid response system and citizen bystander CPR. Survivors of SCA are more likely to be discharged from the hospital if the arrest is witnessed and they receive early CPR from bystanders. There is an increasing drive to train police personnel, students, and the general public in resuscitation techniques, focusing on high-quality, uninterrupted chest compressions.
2. **Automated external defibrillator (AED) and public access defibrillation.** An AED is designed to be used by emergency personnel and lay rescuers with minimal or no training, particularly for victims of out-of-hospital SCA. The device monitors the patient's ECG via self-adhesive defibrillation electrode pads applied to the chest wall and is programmed with a VF detection algorithm. When the device detects VF, an alarm is emitted, followed by delivery of a defibrillation shock or an indicator for the rescuer to press a button to deliver the shock. Availability of these devices results in more rapid delivery of defibrillation and improved survival to hospital discharge in several large trials. Provision of AEDs for public access defibrillation in airports, sporting facilities, and shopping

malls has the potential to have a significant impact on survival of out-of-hospital SCA. Home AEDs have not been shown to increase survival.

3. **Advanced cardiac life support (ACLS).** Unlike AEDs, incorporation of ACLS techniques into prehospital care has not been shown to improve survival in out-of-hospital SCA. Continuous refinements in ACLS algorithms continue to be made, including an emphasis on high-quality CPR with minimal interruption.
4. **Post–cardiac arrest hospital care.** Initial management is focused on establishing and maintaining hemodynamic stability and supportive care. Amiodarone or lidocaine (especially if ischemia is suspected as the trigger) is often used to prevent further ventricular tachyarrhythmias. Therapeutic hypothermia for patients who remain unconscious after resuscitation confers a modest improvement in neurologic outcome. Immediate coronary angiography, with revascularization if indicated, may improve survival in patients in whom an ischemic etiology is suspected. Further diagnostic testing is described above.

B. Primary prevention of SCD

1. **Identifying individuals at risk for SCD.** No single factor has been identified that accurately predicts the occurrence of SCD, although combinations of factors have been more useful. In general, the specificity and positive predictive value of these tests are poor, whereas the negative predictive value is much better (particularly for combinations of tests). Overall, the most potent predictor of survival continues to be LVEF, but other factors may aid prognostication and guide subsequent therapy. Other tools for predicting the risk of SCD, such as EP testing, ambulatory electrocardiography, signal-averaged electrocardiography (SAECG), baroreflex sensitivity, heart rate variability (HRV), and T-wave alternans, have been used to identify high-risk groups, but none have been shown to be of convincing value. Although a combination of different tests can improve sensitivity and specificity, the positive predictive value remains modest.
2. **Pharmacologic agents and surgical/percutaneous revascularization.** Because the majority of episodes of SCD occur in patients with CAD, agents that reduce myocardial ischemia (β-blockers), prevent or limit the extent of MI, and alter ventricular remodeling after MI (ACE inhibitors and aldosterone antagonists) have all been shown to reduce the incidence of SCD. Although there is no direct evidence of a role for antiplatelets or statins in reducing SCD, such an effect is likely, given the reduction in mortality in several broad populations. Early studies of surgical myocardial revascularization showed a reduction in SCD for patients with triple-vessel CAD and left ventricular dysfunction compared with those patients treated medically. Fibrinolysis and percutaneous coronary intervention also reduce SCD in patients with MI. Catheter ablation of VT has a role in select patient populations, particularly in patients with incessant arrhythmias, despite antiarrhythmic drug and/or implantable device therapy.

   More than 40 years ago, complex ventricular ectopy in survivors of MI was recognized as a risk factor for SCD. Suppression of ventricular ectopy with antiarrhythmic drugs in such patients was, therefore, thought to be beneficial. However, the Cardiac Arrhythmia Suppression Trial (CAST) demonstrated that the proarrhythmic effects of class Ic antiarrhythmic drugs are greater than the benefit achieved through ectopy suppression in the post-MI population, resulting in a 2.6-fold increased mortality. Excess mortality was also demonstrated in survivors of MI with poor left ventricular function taking the class II/III agent sotalol in the Survival With Oral *d*-Sotalol (SWORD) study and with mexiletine.

   To date, of all the antiarrhythmic drugs only amiodarone has been shown to reduce SCD in some populations. Initial small trials of amiodarone therapy for survivors of MI, and meta-analyses of these trials, suggested reduced SCD mortality and the larger but unblinded Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA) study appeared to corroborate

this finding. However, several prospective, placebo-controlled trials did not. The Survival Trial of Amiodarone in Patients with Congestive Heart Failure (CHF-STAT) failed to demonstrate a significant reduction in either SCD or all-cause mortality in a largely male population with heart failure, EF ≤ 40%, and frequent PVCs. Although the European Myocardial Infarct Amiodarone Trial (EMIAT) demonstrated a 35% reduction in arrhythmic deaths in a population with recent MI, there was no difference in all-cause mortality. The Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT) similarly reported a reduction in resuscitated VF or arrhythmic death in survivors of MI with frequent ventricular ectopy, but no difference in all-cause mortality. Lastly, there was no difference in the primary end point of all-cause mortality between amiodarone and placebo in the medical treatment arm of the large Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). The newer benzofuran derivative, dronedarone, also reduced SCD in the pivotal ATHENA trial of patients with atrial fibrillation and additional risk factors, but increased all-cause mortality in patients with severe heart failure in the Antiarrhythmic Trial with Dronedarone in Moderate to Severe CHF Evaluating Morbidity Decrease (ANDROMEDA). Mexiletine showed a trend toward increased mortality, and dofetilide and azimilide had no effect on all-cause mortality or SCD in patients with recent MI in large controlled studies.

In summary, amiodarone reduces SCD but not all-cause mortality in patients with heart failure or recent MI, and several other antiarrhythmics, including class Ic agents, mexiletine, dronedarone, and sotalol, may increase mortality in this population.

3. **Implantable devices.** In light of the inefficacy and even hazards of antiarrhythmic drugs for the prevention of SCD, attention has shifted to the ICD. Since its introduction by Mirowski in 1980, technical refinements have paralleled a series of clinical trials which extended indications to primary prevention in select populations. The Multicenter Automatic Defibrillator Implantation Trial (MADIT) demonstrated a 54% relative risk reduction in all-cause death versus usual care in 196 patients with prior MI, New York Heart Association (NYHA) class I–III heart failure, EF ≤ 35%, NSVT, and inducible, nonsuppressible, ventricular arrhythmia during EP study (EPS). The Multicenter Unsustained Tachycardia Trial (MUSTT) randomized patients with coronary artery disease, EF ≤ 40%, NSVT, and inducible VT/VF to receive EP-guided antiarrhythmic drug therapy, with or without an ICD, or no therapy. The 27% reduction in arrhythmic death or cardiac arrest in the EP-guided drug therapy arm was entirely driven by a 76% reduction in patients with ICDs, with no difference between drug therapy and no therapy. Given the modest predictive value of EPS, MADIT II dispensed with inducible VT as an inclusion criterion and enrolled patients with prior MI on the basis of an EF ≤ 30%. This randomized comparison of ICD with usual care demonstrated a 31% relative risk reduction in all-cause mortality over an average follow-up of 20 months. MADIT, MUSTT, and MADIT II all enrolled patients with prior MI. While the underpowered Amiodarone Versus Implantable Cardioverter-Defibrillator (AMIOVIRT) and Cardiomyopathy Trial (CAT) failed to show a benefit of ICDs over medical therapy in patients with nonischemic cardiomyopathy (NICM), the results of the Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial extended primary prevention ICD therapy to these patients. In patients with NICM, heart failure, EF ≤ 35%, and NSVT or frequent PVCs, a nonsignificant reduction in all-cause mortality was observed, with a significant reduction in SCD. The larger SCD-HeFT randomized 2,521 patients with ischemic cardiomyopathy (52%) or NICM (48%), EF ≤ 35%, and NYHA functional class II or III heart failure to receive conventional therapy plus placebo,

amiodarone, or a single lead ICD. ICD therapy reduced all-cause mortality by 23% compared with placebo, whereas amiodarone was not associated with any benefit. These trials, and SCD-HeFT in particular, ushered in the current era of primary prevention ICDs for patients risk-stratified largely on the basis of EF.

The limitations of ICDs have also been defined by clinical trials. The Coronary Artery Bypass Graft (CABG) Patch Trial demonstrated that primary prevention ICD implantation at the time of CABG in patients with preoperative left ventricular dysfunction (EF ≤ 35%) and an abnormal SAECG did not improve the overall survival, despite reducing arrhythmic deaths. The lower event rates in the CABG Patch Trial were consistent with earlier evidence that CABG reduces the risk of SCD in this population, negating the protective effect of the ICD.

MADIT, MUSTT, and MADIT II studied patients with remote (> 3 weeks) ischemic events. The Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) assessed whether the benefits of ICD therapy would also be seen early after MI. The trial enrolled patients 6 to 40 days post-MI with EF < 35% and impaired HRV or elevated average 24-hour heart rate and randomized them to receive an ICD or no ICD. Although ICD therapy reduced arrhythmic death, this was offset by an increase in nonarrhythmic death in the ICD group, so there was no difference in all-cause mortality over 30 months of follow-up. These results were confirmed by the larger Immediate Risk Stratification Improves Survival (IRIS) trial, which enrolled a similar population. Taken together, IRIS and DINAMIT suggest that while ICDs prevent SCD in high-risk patients early post-MI, this merely changes the mode of death to nonsudden death, without affecting the overall survival. This is supported by a secondary analysis of DINAMIT, which showed that the risk of nonsudden death in the ICD group was 4.8-fold higher in those who had received an appropriate shock. The above findings have been incorporated into the Centers for Medicare and Medicaid Services (CMS) coverage determination for ICDs, which excludes patients with MI within 40 days and surgical or percutaneous revascularization within 3 months of ICD implantation. A wearable defibrillator is available for temporary use, while diagnostic testing is ongoing, or during periods of transient elevated risk.

4. **Cardiac resynchronization therapy (CRT).** Approximately 30% of patients with advanced heart failure (EF ≤ 35%) have an associated ventricular conduction delay resulting in a QRS duration ≥ 120 milliseconds and are candidates for CRT. Biventricular pacing has been shown to improve survival, quality of life, exercise capacity, and EF in patients with advanced CHF. Extended follow-up data from the Cardiac Resynchronization in Heart Failure (CARE-HF) trial also reported a significant 46% reduction in SCD in patients with CRT without a defibrillator when compared with no CRT. However, a significant number of SCDs occurred in the CRT group, some of which might conceivably have been prevented by a defibrillator. The only large randomized trial comparing CRT with a defibrillator (CRT-D), CRT without (CRT-P), and no device was the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial. While not powered to detect a difference between CRT-D and CRT-P, a nonsignificant 50% decrease in SCD was seen with CRT-D in patients with NYHA class III or IV CHF, EF ≤ 35%, and a QRS duration ≥ 120 milliseconds. These data suggest that CRT-D should be considered for most patients eligible for biventricular pacing.

C. Secondary prevention

1. **Pharmacologic agents.** As with primary prevention of SCD, the disappointing efficacy and safety of class I antiarrhythmic drugs shifted attention to other antiarrhythmic drugs for the secondary prevention of SCD. In the Cardiac Arrest in Seattle Conventional Versus Amiodarone Drug Evaluation (CASCADE) study,

amiodarone reduced cardiac death, arrest, and ICD shocks compared with conventional class I antiarrhythmic drugs in a secondary prevention population. In addition, the Electrophysiologic Study Versus Electrocardiographic Monitoring (ESVEM) trial demonstrated that the class II/III antiarrhythmic drug sotalol was superior to six class I agents guided by EP testing or Holter monitoring in preventing all-cause, cardiac, and arrhythmic mortality in patients with a history of VT/VF, SCA, or syncope. However, emergence of the ICD led to randomized trials comparing the efficacy of best medical therapy and ICDs for the secondary prevention of SCD.

2. **Implantable devices.** The Antiarrhythmics Versus Implantable Defibrillators (AVID) trial studied the efficacy of ICD therapy versus the antiarrhythmic drugs amiodarone or sotalol for the secondary prevention of SCD in patients with resuscitated VF or sustained VT plus either syncope or EF ≤ 40% and hemodynamic compromise during VT. Inducible arrhythmias were not required for inclusion, and only sotalol therapy was guided by EP testing (only 2.6% of patients randomized to antiarrhythmic drug therapy were discharged on sotalol). ICDs reduced all-cause mortality by 31% at 3 years of follow-up.

   Two other large trials of ICDs for secondary prevention of SCD that ran concurrently with AVID reported similar results. The Cardiac Arrest Study Hamburg (CASH) found that ICDs conferred a nonsignificant 23% reduction in all-cause mortality when compared with amiodarone or metoprolol in patients with resuscitated cardiac arrest due to documented VT/VF. The propafenone arm of the study was terminated early after an interim analysis showed excess mortality compared with the ICD group. The Canadian Implantable Defibrillator Study (CIDS) enrolled a similar population as the AVID trial randomizing patients with resuscitated VF, sustained VT with syncope or hemodynamic compromise and EF ≤ 35%, or unmonitored syncope with subsequent spontaneous or induced VT to ICD or amiodarone therapy. Over a mean follow-up period of 3 years, a nonsignificant 19.7% relative risk reduction in all-cause mortality was observed, as well as a nonsignificant 32.8% reduction in SCD. Each of the above studies excluded patients with a transient or reversible cause of ventricular arrhythmias, such as MI within 72 hours, or electrolyte imbalances. A meta-analysis of these three trials confirmed a significant 28% reduction in the relative risk of death with the ICD, which was due largely to a 50% reduction in SCD.

   Of considerable interest is evidence that patients screened for the AVID trial but thought to have a transient or reversible cause of SCA, and who were not entered in the trial but followed in a registry, had poor long-term survival similar to those patients who were also ineligible for the trial but known to be at high risk for SCD. These data emphasize the need for meticulous evaluation of every SCA survivor and careful consideration of whether SCA was due to a cause that was not only transient and reversible but also preventable in the future.

D. Summary: antiarrhythmic drugs versus ICDs. Current guidelines for ICD therapy are summarized in Table 23.2. From the available data, there is good evidence that many antiarrhythmic drugs are not efficacious and may be harmful in the primary prevention of SCD, and antiarrhythmic drugs (apart from β-blockers) are not indicated for this purpose. ICD therapy has been proven to be highly effective in the termination of malignant ventricular arrhythmias and is more effective than antiarrhythmic medications for the prevention of SCD in patients with ischemic or nonischemic heart failure and an EF ≤ 35%. Patients with prolonged QRS duration, especially with LBBB, should also be considered for CRT. The most powerful predictor of SCD risk in this population remains LVEF, and other methods such as EP testing and SAECG may give additional information but are neither sensitive nor specific enough to select patients for ICD therapy. Specific antiarrhythmics may have niche uses in high-risk patients with genetic diseases predisposing

TABLE 23.2 Indications for Implantable Cardioverter–Defibrillator Therapy

Class I

1. Survivors of cardiac arrest due to VF or hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes
2. Structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable
3. Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced during electrophysiologic study
4. LVEF ≤ 35% due to prior MI, at least 40 d post-MI, and NYHA class II or III
5. Nonischemic DCM, LVEF ≤ 35%, and NYHA class II or III
6. LV dysfunction due to prior MI, at least 40 d post-MI, LVEF ≤ 30%, and NYHA class I
7. Nonsustained VT due to prior MI, LVEF ≤ 40%, and inducible VF or sustained VT during electrophysiologic study
8. Symptomatic sustained VT in association with congenital heart disease after hemodynamic and electrophysiologic evaluation

Class IIa

1. Unexplained syncope, significant LV dysfunction, and nonischemic DCM
2. Sustained VT and normal or near-normal ventricular function
3. Hypertrophic cardiomyopathy with one or more major risk factors for SCD
4. ARVD/C with one or more risk factors for SCD
5. Long QT syndrome with syncope and/or VT while receiving β-blockers
6. Nonhospitalized patients awaiting heart transplantation
7. Brugada syndrome with syncope
8. Brugada syndrome with documented VT that has not resulted in cardiac arrest
9. Catecholaminergic polymorphic VT with syncope and/or documented sustained VT while receiving β-blockers
10. Cardiac sarcoidosis, giant cell myocarditis, or Chagas disease
11. Congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias during electrophysiologic study

Class IIb

1. Nonischemic heart disease, LVEF ≤ 35%, and NYHA class I
2. Long QT syndrome with risk factors for SCD
3. Syncope and advanced structural heart disease where thorough invasive and noninvasive investigations have failed to define a cause
4. Familial cardiomyopathy associated with sudden death
5. LV noncompaction

TABLE 23.2 Indications for Implantable Cardioverter–Defibrillator Therapy (Continued)

6. Recurrent syncope associated with complex congenital heart disease and advanced systemic ventricular dysfunction when thorough invasive and noninvasive investigations have failed to define a cause

Class III

1. Patients who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 y
2. Incessant VT or VF
3. Patients with significant psychiatric illnesses that may be aggravated by device implantation or that may preclude systematic follow-up
4. NYHA class IV patients with drug-refractory congestive heart failure who are not candidates for cardiac transplantation or CRT-D
5. Syncope of undetermined cause without inducible ventricular tachyarrhythmias and without structural heart disease
6. VF or VT that is amenable to surgical or catheter ablation (e.g., atrial arrhythmias associated with the Wolff-Parkinson-White syndrome, RV or LV outflow tract VT, idiopathic VT, or fascicular VT in the absence of structural heart disease)
7. Ventricular tachyarrhythmias due to a completely reversible disorder in the absence of structural heart disease (e.g., electrolyte imbalance, drugs, or trauma)

VF, ventricular fibrillation; VT, ventricular tachycardia; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; DCM, Dilated cardiomyopathy; SCD, sudden cardiac death; ARVD/C, arrhythmogenic right ventricular dysplasia/cardiomyopathy; CRT-D, cardiac resynchronization therapy with a defibrillator; RV, right ventricle; LV, left ventricle.

Adapted from the 2008 ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities.

to SCD, such as HCM, ARVD, Brugada syndrome, and LQTS, and an ICD is also indicated in select patients. The bradyarrhythmias respond well to pacemaker therapy. Radiofrequency catheter ablation is the therapy of first choice in patients with WPW syndrome and is an effective synergistic therapy in patients with VT who have recurrent ICD shocks.

Evidence from several recent randomized trials demonstrates the superiority of the ICD over antiarrhythmic drugs for the population requiring secondary prophylaxis. Antiarrhythmic drugs such as amiodarone, sotalol, and mexiletine may be of use in those patients who experience frequent ICD shocks.

V. PROGNOSIS

A. VF and pulseless VT ("shockable rhythms") are the initial rhythm in approximately one-quarter of SCA victims and are associated with more favorable outcomes than asystole or PEA. VT/VF incidence declines by ~10% with each minute since the onset of SCA; therefore, witnessed SCA and prompt recognition and defibrillation are associated with improved survival. Only one-third of SCA victims receive bystander CPR. A recent large study of cardiac arrest incidence and outcomes in North America found that of the 58% of patients in whom resuscitation was attempted, 7.6% survived to hospital discharge, with wide regional

variation. This proportion rose to 21% if the initial rhythm was VF. A number of factors have been identified to aid prognostication post arrest, including preexisting comorbidities, absent pupillary and corneal reflexes, extensor or no motor response to pain on day 3, and myoclonus status epilepticus; however, none are definitive.

VI. FUTURE. Large population studies are needed to better define the incidence of SCD across ethnic/racial groups and elucidate the mechanisms. Discovery of risk markers of SCD in the general population, such as clinical, molecular, and genetic factors, will facilitate targeting of evaluation and therapy to those who need it. Coronary artery disease and its consequences account for 80% of SCD, often occurring as the first presentation of CAD. Given the difficulty in identifying those with subclinical disease who are ostensibly at low risk, focus has recently moved to primordial prevention—the prevention of the development of risk factors for CAD. This will likely have the most impact on SCD at the population level, but its effects are difficult to measure. In those at established risk, improved risk markers that refine the current LVEF-based approach will allow better targeting of ICD therapy.

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CHAPTER 24

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Atrial Fibrillation

I. INTRODUCTION. Atrial fibrillation (AF) is the most common sustained tachyarrhythmia and is associated with increased cardiovascular morbidity, mortality, and preventable stroke, accounting for approximately one-third of cardiac hospitalizations for cardiac rhythm disturbances. The incidence and prevalence of AF increase with age, with a prevalence of 0.4% to 1% in the general population and as high as 8% in patients older than 80 years. In addition, the age-adjusted incidence in the Framingham study has increased significantly from the 1960s to the present. It is estimated that 3 million people in America and 6 million people in Europe have either paroxysmal AF or persistent AF. AF is associated with increased risk of stroke, heart failure exacerbation, and all-cause mortality, especially in women. The mortality rate in patients with AF is about twice that of patients with normal sinus rhythm (NSR).

A. Classification. AF may be classified as lone, idiopathic, first detected, recurrent, paroxysmal, persistent, long-standing persistent, and permanent. **Lone AF** is used to describe patients experiencing AF without clinical or echocardiographic evidence of cardiopulmonary disease. **Idiopathic AF** refers to the uncertainty of AF origin without considering age or underlying cardiovascular pathology. During a patient's first detected episode of AF, it should be noted whether it is self-limited or the patient symptomatic with the arrhythmia. When a person has experienced two or more episodes of AF it is considered **recurrent**, and once recurrent AF is terminated it is referred to as **paroxysmal**. Paroxysmal episodes are usually self-terminating and, at least initially, do not usually require direct current cardioversion (DCC). **Persistent AF** usually lasts longer than 7 days and requires cardioversion for its termination. **Long-standing persistent** is when AF has lasted for > 1 year. AF becomes **permanent** once cardioversion, either electrical or chemical, is unsuccessful and presence of arrhythmia is accepted by the patient and physician and hence rhythm control interventions are not pursued.

B. Clinical presentation. As with all arrhythmias, the clinical presentation of AF can vary widely and **patients may be asymptomatic**, despite rapid rates of ventricular response. Common symptoms include **palpitations, fatigue, dyspnea and/or shortness of breath, dizziness, and diaphoresis**. Less commonly, patients may present with extreme manifestations of hemodynamic compromise, such as **chest pain, pulmonary edema, and syncope**. AF is often noted in patients presenting with a new thromboembolic stroke, with reported rates of 10% to 40%.

C. Differential diagnosis. AF needs to be distinguished from multifocal atrial tachycardia (MAT), frequent premature atrial contractions, and automatic atrial tachycardias.

D. Etiology. AF is most commonly associated with advanced age, hypertension, valvular heart disease, congestive heart failure (CHF), and coronary artery disease (CAD). The pathophysiology is dependent on the interaction between atrial anatomic and physiologic factors that favor the initiation and maintenance of the arrhythmia. Pathophysiologically, these entities result in left atrial fibrosis, pulmonary vein dilation, and reduced atrial contractility, which in turn result at a cellular

level in abnormal intracellular calcium handling, atrial myolysis, connexin down-regulation, and altered sympathetic innervation. Structural remodeling results in electrical dissociation between muscle bundles and local conduction heterogeneities facilitating the initiation and perpetuation of AF. This electroanatomical substrate permits multiple small reentrant circuits that can stabilize the arrhythmia and lead to the establishment of AF.

AF has been associated with physiologic stress, drugs, pulmonary embolism, chronic lung disease, hyperthyroidism, caffeine, infectious processes, and various metabolic disturbances. AF has also been linked with obesity and likely underlying sleep-disordered breathing. This phenomenon seems to be mediated by left atrial dilation. Other less common cardiac associations include Wolff-Parkinson-White (WPW) syndrome, pericarditis, and cardiomyopathy. Surgery, particularly **cardiac surgery, is associated with a high risk of postoperative AF** that depends on the type of cardiac surgery and is highest for mitral valve surgery, which may reach 35% to 50%. Persistence of AF has been correlated with elevated C-reactive protein levels, which raises the question of a role for inflammation in this condition, and atrial natriuretic peptide has been found to be elevated in people with acute AF. This hormone, which is released by myocardial tissue in response to increased wall stress, promotes diuresis and vasodilation. However, with long-standing AF, atrial natriuretic peptide levels remain within the normal range and patients do not experience its useful hemodynamic effects.

E. Pathophysiology

1. The role of the pulmonary veins as a source of triggers and/or drivers in AF is increasingly appreciated. A previous model proposed by Moe et al. in 1962 had described multiple reentrant wavelets within the atrial tissue (substrate) that contributed to the maintenance of AF. Recent data support **a focal mechanism involving both increased automaticity and multiple reentrant wavelets, occurring predominantly in the left atrium around the pulmonary veins**. A new model incorporates these mechanisms of initiators/drivers of AF and atrial substrate conditions for AF maintenance. This in turn may be affected by various modulating factors, such as autonomic tone, medications, atrial pressure, and catecholamine levels. AF is a very complex arrhythmia, and this mechanistic model simply serves to provide a conceptual framework from which to gain insight into it.
2. Paroxysmal, persistent, or chronic AF presents a **considerable risk for thromboembolism;** lone AF is presently thought to also increase the risk, but to a lesser extent. **The risk of stroke becomes more pronounced with increased age.** An increased risk of stroke has been shown to be associated with AF in the presence of any of the following: **age > 65 years, history of diabetes, history of hypertension, history of CHF, history of prior stroke, or transient ischemic attacks (TIAs)**. Left ventricular (LV) systolic dysfunction predicts ischemic stroke in patients with AF who do not receive antithrombotic therapy.

F. Laboratory examination and diagnostic testing. The initial evaluation of a patient with new-onset AF includes at a minimum a detailed history including enquiry about family history of AF and physical examination to define the clinical type of AF—frequency, duration, and precipitating factors—and to delineate the presence and nature of symptoms associated with AF. In addition, evaluation should include the following:

1. **A 12-lead electrocardiogram** (ECG) to identify the rhythm (that is to verify AF), underlying LV hypertrophy, and presence of preexcitation, and to diagnose the existence of CAD and any other atrial arrhythmias. A 12-lead ECG may also be used to measure and follow PR, QRS, and QT intervals during the treatment with antiarrhythmic agents. In AF the P waves are absent. Atrial activity is chaotic and fibrillatory **(F) waves are present**. The baseline of the ECG is often

undulating and may occasionally have coarse, irregular activity that can resemble atrial flutter, but it is not as stereotypical from wave to wave as atrial flutter. AF is distinguished from MAT by the presence in MAT of at least three different morphologic types of P waves. **Ventricular rhythm is usually irregularly irregular, and if AF is suspected with a regular ventricular response, then heart block with a junctional or ventricular escape should be considered**. The **atrial rate** is generally in the **range of 400 to 700 beats/min,** while the ventricular response is generally in the range of 120 to 180 beats/min in the absence of drug therapy. Ventricular response may be 180 beats/min or greater in the presence of an accessory pathway.

2. **Transthoracic echocardiogram** is usually performed to identify the presence of valvular heart disease, to assess atrial and ventricular size and function, and to document coexistent pulmonary hypertension. Echocardiography is also used as a prognostic tool to predict the development of systemic complications from AF and to help in the decision to initiate antithrombotic therapy. **Echocardiographic predictors of increased thromboembolic risk include mitral stenosis, left atrial enlargement, reduced LV systolic function, decreased left atrial appendage emptying velocities, and evidence of spontaneous contrast ("smoke") or thrombus in the left atrium or left atrial appendage**.
3. **Tests of thyroid, renal, and hepatic function.** Hyperthyroidism should always be considered, especially when the ventricular rate is difficult to control.
4. Additional investigation in selected patients with AF may include ambulatory ECG monitoring (e.g., Holter), or a 6-minute treadmill walk test to document heart rate response to exercise and an evaluation of sleep-disordered breathing should be considered especially in obese patients.

G. Therapy. The therapy of choice in any unstable patient where AF is recent in onset and contributing to the instability is immediate DCC. The term "unstable" should include the patient who is highly symptomatic (e.g., chest pain and pulmonary edema), as well as the patient who is hemodynamically unstable. **General management of AF centers on three areas: control of the ventricular response, minimization of the thromboembolic risk, and restoration and maintenance of sinus rhythm**.

1. **Control of the ventricular response.** The ventricular response is generally **controlled through drugs** that slow conduction through the atrioventricular (AV) node. AF that presents in the setting of WPW syndrome usually has evidence of preexcitation on ECG and is treated differently from AF conducting down the AV node alone. As noted previously, **intravenous calcium channel blockers, β-blockers, adenosine, and lidocaine are contraindicated in patients with AF and WPW syndrome associated with preexcitation because they facilitate conduction down the accessory pathway, causing acceleration of the ventricular rate, hypotension, and ventricular fibrillation**. In the hemodynamically stable patient, class I antiarrhythmic medications such as procainamide may be administered intravenously, which diminishes antegrade conduction down the accessory pathway and decreases the degree of preexcitation and may convert the AF. For patients without evidence of preexcitation, the following agents are available to control the ventricular rate.
   a. β-Blockers have a **rapid onset of action,** as well as **short half-lives in both the oral and intravenous forms.** These medications should be used cautiously in patients who have known decreased systolic function or evidence of heart failure. Intravenous preparations of metoprolol, esmolol, and propranolol have their onset of action in approximately 5 minutes. Orally available β-blockers of varying durations of action can be used for rate control. These include metoprolol and propranolol, as well as atenolol, nadolol, and a number of less commonly used agents. Amiodarone is an antiarrhythmic

medication with β-blocking properties and can be used for both rate and rhythm control in the acute setting. Sotalol is another class III antiarrhythmic medication with β-blocking properties, which can be used for both rate and rhythm control; however, this medication is available in oral form only and is more proarrhythmic than amiodarone.

b. Calcium channel blockers such as diltiazem and verapamil are available in both intravenous and oral forms. The intravenous forms are rapidly effective and have a short duration of effect. **In appropriate patients, they provide rapid control of the ventricular response**. Both oral diltiazem and verapamil are available in short-acting and sustained-release preparations.

c. Digitalis has long been used for rate control. Given its relatively long onset of action, **digoxin is ideally used in patients with decreased LV function or where a contraindication exists to the use of β-blockers or calcium channel blockers** (e.g., bronchospastic airway disease, asthma, or hemodynamic instability). It may be used as an adjunct to β-blockers or calcium channel blockers in patients in whom these medicines alone do not provide sufficient control of the heart rate. Digoxin is usually **effective at controlling the resting heart rate;** however, it is **less effective at lowering the ventricular response to activity**. Because of this it is recommended that if digoxin alone is used in rate control, the patient should undergo monitored exercise and the exertional heart rate verified to be < 110 beats/min.

Digoxin can be administered intravenously or orally. The **onset of action of digoxin is slow** (1 to 4 hours). Initially dosing of digoxin is 0.25 mg intravenously every 6 hours for a total of 1 mg every 24 hours. Then a maintenance dose is given, which is based on the patient's renal function. Digoxin is **generally well tolerated, although it is associated with adverse effects**, such as gastrointestinal toxicity and neurotoxicity, and because of its long half-life (38 to 48 hours) is more likely to be associated with symptomatic bradycardia requiring intervention such as temporary pacing.

d. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor antagonists may decrease the incidence of AF by decreasing left atrial pressure and by reducing the frequency of atrial premature beats. These medications may also reduce atrial fibrosis and decrease the recurrence of AF. Withdrawal from ACE inhibitors is associated with postoperative AF in patients undergoing coronary artery bypass grafting (CABG) surgery, and concurrent therapy with ACE inhibitors and antiarrhythmic agents enhances the maintenance of sinus rhythm.

e. HMG-CoA reductase inhibitors: statin drugs decrease the risk of AF recurrence following cardioversion. The mechanisms underlying this are poorly understood but probably include an inhibitory effect on the progression of coronary disease as well as their pleiotropic anti-inflammatory and antioxidant properties.

f. Antiarrhythmic agents such as dofetilide and ibutilide are effective for conversion of atrial flutter and AF but are not effective for the control of ventricular rate alone. Propafenone, which is a class IC antiarrhythmic drug, exerts additional mild β-blocking effects and may slow conduction across the AV node, although this is seldom sufficient to control the rate in patients with AF and may paradoxically cause an increase in AV nodal conduction and accelerate the ventricular rate response. Flecainide is another class IC agent that is very effective in converting AF in structurally normal hearts but like propafenone requires concomitant AV nodal blockage.

2. Thromboembolic risk management

a. Current recommendations regarding the use of antithrombotic therapy to prevent the development of thromboembolism in patients with AF are to

use antithrombotic therapy in all patients with AF except those with lone AF or with contraindications to antithrombotic agents. **Lone AF is defined as that occurring in a structurally normal heart, in a patient younger than 65 years**. The American Heart Association (AHA) recommends that the individualized selection of appropriate antithrombotic agents **associated with the highest risk of stroke in patients with AF include a history of prior thromboembolism (stroke, TIA, and systemic embolism) and rheumatic mitral stenosis**. Moderate risk factors for stroke include age older than 65 years, CAD, CHF, female gender, hypertension, diabetes mellitus, and renal insufficiency. Presence of more than one moderate risk factor suggests the use of a vitamin K antagonist with a goal international normalized ratio (INR) of 2.0 to 3.0 or or alternative anticoagulation with dabigatran, rivaroxaban or apixaban. Aspirin in doses of 81 to 325 mg daily is recommended as an alternative to vitamin K antagonism in low-risk patients or in those with contraindications to oral anticoagulation, and more recent evidence suggests that combination of aspirin and clopidogrel is superior to the use of either agent alone in patients who are unable to tolerate warfarin therapy. The guidelines also suggest similar use of antithrombotic therapy in patients with atrial flutter. Table 24.1 outlines one method of selecting the appropriate antithrombotic therapy for any given patient.

Based on the multivariate analysis from randomized controlled trials (RCTs), there have been several clinical scores developed to stratify the risk of systemic complications. The most well known of these is called the **CHADS** (*C*ardiac Failure, *H*ypertension, *A*ge, *D*iabetes, and *S*troke) risk index, which is a point system and assigns two points for history of TIA or stroke and one point for

TABLE 24.1 Selection of Appropriate Antithrombotic Therapy

Risk category	Recommended therapy	
No risk factors	Aspirin, 81–325 mg daily	
One moderate risk factor	Aspirin, 81–325 mg daily or warfarin (INR 2.0–3.0, target 2.5)	
Any high risk factor or more than one moderate risk factor	Warfarin (INR 2.0–3.0, target 2.5)[a]	
Less validated or weaker risk factors	**Moderate risk factors**	**High risk factors**
Gender (female)	Age ≥ 75 y	Previous stroke, TIA, or embolism
Age (65–74 y)	Hypertension	Mitral stenosis
Coronary artery disease	Heart failure	Prosthetic heart valve[b]
Thyrotoxicosis	LV ejection fraction 35% or less	
	Diabetes mellitus	

[a]If mechanical valve, target INR > 2.5.
[b]Mechanical prosethetic heart valve especially if in the mitral position to replace "prosthetic heart valve"
INR, international normalized ratio; LV, left ventricular; and TIA, transient ischemic attack.
Adapted from ACC/AHA practice guidelines.

each of the following risk factors: age older than 75 years, hypertension, diabetes, or recent heart failure. This risk factor index was evaluated retrospectively in patients older than 65 years and with nonvalvular AF, and the stroke risk varied from 1.8% per year in the lowest risk group with a CHADS score of 0, to 18.2% per year for those with an index score of 6. Another thromboembolic risk factor scoring system is the CHA2DS2-VASc, which assigns two points for age > 75 years and prior history of TIA or stroke and one point for each of the *following* risk factors: CHF, hypertension, diabetes, stroke, vascular disease, age 65 to 74 years, and female gender. Thus, this risk stratification scheme extends the CHADS2 scheme by considering additional stroke risk factors that may influence the decision on whether or not to anticoagulate with a threshold for therapy that is similar to the CHADS scheme. An assessment of bleeding risk is an integral part of patient evaluation prior to initiating anticoagulation. A simple bleeding risk score (HAS-BLED: hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly [age > 65 years], drugs/alcohol concomitantly) has been used to assess the risk of bleeding while on anticoagulant therapy. A score of ≥ 3 indicates higher risk and suggests caution and regular review of the patient following the initiation of anticoagulant therapy.

Following cardioversion, therapeutic anticoagulation should be continued until sinus rhythm has been maintained for at least 4 weeks to allow for recovery of the atrial transport mechanism and for the recurrence of AF. The decision to anticoagulate beyond 4 weeks will be dependent on the CHADS2 score of the patient with long-term anticoagulation being recommended for all patients with a CHADS2 score ≥ 2. For patients with a CHADS2 score of 1, the physician and patient should discuss the merits and risks of long-term anticoagulation versus the use of aspirin alone. **If cardioversion cannot be postponed for 3 weeks and the AF has been present for > 48 hours, patients should be anticoagulated (Table 24.2) with intravenous unfractionated heparin or subcutaneous low-molecular-weight heparin as a bridge to therapeutic INR or alternatively dabigatran, rivaroxaban or apixaban could be used and the patient should undergo transesophageal echocardiography (TEE)** to rule out atrial thrombus; **then anticoagulation should be** used for at least 4 weeks after cardioversion.

b. A number of major trials have attempted to compare the benefits of aspirin and warfarin in minimizing the stroke risk in patients with AF. Overall, warfarin has shown an annual average reduction of 68% in relative risk for stroke, with aspirin showing a reduction anywhere from 0% to 44% (mean, ~30%). A recent trial has shown that clopidogrel reduces the risk of embolic stroke similar to that of aspirin and the combination of aspirin and clopidogrel is superior to either agent alone but inferior to warfarin therapy.

The decision to anticoagulate patients with AF depends on both the risk of thromboembolic complications and the risk of bleeding. In younger patients at low risk for stroke (younger than 65 years, without other risk factors), and who generally lead active lifestyles that place them at increased risk for bleeding, **aspirin** may be an acceptable alternative to warfarin. **Older patients at greater risk for stroke (age 65 and older, with or without other risk factors)** should be anticoagulated with **warfarin to maintain an INR of 2 to 3 or alternative anticoagulation with dabigatran, rivaroxaban or apixaban. The risk of thromboembolism increases rapidly at INR levels even slightly < 2, and the risk of bleeding increases at INR levels > 3**. Studies of fixed low-dose warfarin and aspirin have shown ineffective protection from thromboembolic risk as compared with anticoagulation with warfarin to maintain an INR of 2 to 3, and thus are not recommended. **Patients who have contraindications to warfarin** therapy should be treated with **aspirin or the combination of aspirin and clopidogrel should be considered if the patients can tolerate it**.

TABLE 24.2 Anticoagulation Strategies in Patients Who Require Cardioversion

Length of time in atrial fibrillation	Elective cardioversion?	Timing and anticoagulation strategy
< 48 h	Yes	Depends on the presence of risk factors for thromboembolism
< 48 h	No	Immediate DCC may be performed without delay or need to start anticoagulation
> 48 h or unknown	Yes	A goal INR 2.0–3.0 or alternative anticoagulation with dabigatran, rivaroxaban or apixaban for at least 3 weeks prior to and 4 weeks following DCC
> 48 h or unknown	Yes	A TEE can be performed while the patient is on IV heparin with a goal aPTT ratio of 1.5–2.0, and if no identifiable thrombus is present, DCC can safely be performed, followed by 4 weeks of oral coumadin with goal INR of 2.0–3.0 or alternative anticoagulation with dabigatran, rivaroxaban or apixaban
> 48 h or unknown	Yes	If the TEE demonstrates a thrombus, then anticoagulation with coumadin with a goal INR of 2.0–3.0 or alternative anticoagulation with dabigatran, rivaroxaban or apixaban for a period of 3 weeks prior to a repeat TEE to assess for thrombus resolution. If no identifiable thrombus is visible on repeat TEE, then DCC should be followed by at least 4 weeks of anticoagulation with INR of 2.0–3.0 or alternative anticoagulation with dabigatran, rivaroxaban or apixaban post DCC

DCC, direct current cardioversion; INR, international normalized ratio; TEE, transesophageal echocardiography; IV, intravenous.

The **risk of thromboembolism increases with longer duration of AF. Current guidelines recommend that patients who have been in AF for longer than 48 hours should be systemically anticoagulated** whenever possible. This can be accomplished quickly with intravenous unfractionated heparin, subcutaneous low-molecular-weight heparin, or oral dabigatran, rivaroxaban or apixaban. Cardioversion should be delayed in patients with AF of > 48 hours duration who have not been anticoagulated as described in the AHA guidelines discussed previously unless a patient is sufficiently unstable that more rapid cardioversion is necessary, in which case screening of the atria for the presence of thrombus with TEE is appropriate.

c. TEE is highly effective in the detection of thrombus in the atria and in the left atrial appendage and is more sensitive in this regard than transthoracic echocardiography. The Assessment of Cardioversion using Transesophageal

Echocardiogram (ACUTE) study compared the use of TEE screening of patients with AF prior to cardioversion with a conventional approach based on 3 weeks of anticoagulation therapy. In the TEE group, those patients without thrombus on TEE underwent immediate cardioversion after therapeutic anticoagulation had been initiated and without waiting for 3 weeks. Patients were continued on warfarin for 4 weeks after the cardioversion as in the conventional group. No significant difference was noted in the embolic event rate or in the likelihood of maintenance of normal rhythm. TEE cardioversion is now considered an acceptable alternative when the conventional approach is not possible.

d. Cardiac output may be decreased after cardioversion in up to one-third of patients, and this can persist for as long as a week. Rarely, this leads to pulmonary edema as soon as 3 hours after cardioversion. Atrial function also declines immediately after cardioversion, even after that occurring spontaneously or pharmacologically. Cardiac output should return to baseline within 4 weeks. The risk of thromboembolism is thus still increased during this time period, and that is why systemic anticoagulation is recommended for a minimum of 4 weeks after cardioversion.

e. After 4 weeks of therapy, the decision to continue anticoagulation is based on each patient's individual risk for recurrence of AF. **Patients who cannot be successfully cardioverted should be anticoagulated long-term**, as should patients with frequent recurrences/paroxysms.

f. In addition to the expanding number of pharmacologic options for anticoagulation, there are now nonpharmacologic methods for reducing thromboembolic risk. In the Embolic Protection in Patients with Atrial Fibrillation Trial (PROTECT trial), the WATCHMAN left atrial appendage occlusion system was noninferior to anticoagulation with warfarin in terms of thromboembolic outcomes. More data are needed on the long term safety and efficacy of this device.

3. **Rate control during AF.** Patients with AF may have controlled heart rates at rest, but they accelerate even with mild exercise. Hence, it is useful in patients with chronic AF to evaluate the heart rate response to submaximal or maximal exercise or to monitor the heart rate over an extended period (such as a 24-hour Holter monitor). The traditional criteria defining that adequate rate control varies with age but usually involves achieving a ventricular rate between 60 and 80 beats/min at rest and between 90 and 110 beats/min during moderate exercise have not been shown to be beneficial over a more lenient approach to achieve a resting heart rate of < 110 beats/min in patients with persistent or continuous AF and stable LV systolic function.

4. **Restoration and maintenance of sinus rhythm.** There is debate whether restoration to sinus rhythm is beneficial for patients whose disease is asymptomatic as compared with a combined strategy of simply controlling the ventricular response and minimizing the thromboembolic risk. Data from nonrandomized trials show an increase in mortality in patients on long-term antiarrhythmic therapy for AF. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial compared two treatment strategies in patients with asymptomatic or tolerable AF. One group was treated with antiarrhythmic drugs and cardioversion as necessary to maintain sinus rhythm. The other group was allowed to remain in AF and the ventricular rate alone was controlled. Both groups received anticoagulation therapy. There was no difference in survival or embolic event rate between the two groups.

a. Direct current cardioversion. When restoration of sinus rhythm is deemed necessary, this is most effectively carried out with DCC. **DCC is successful at least 80% of the time**, whereas pharmacologic rates of successful cardioversion are lower and depend on the antiarrhythmic drug used and the clinical scenario. Whenever possible, **DCC should be carried out under sedation, with appropriate cardiac and hemodynamic monitoring, and**

in the presence of personnel skilled in airway control/management. See Chapter 59 for details of DCC, including sedation and methods.

b. Pharmacologic cardioversion

(1) The "drugs first" approach may promote more successful DCC and/or maintenance of sinus rhythm after DCC, if the attempt at pharmacologic cardioversion is unsuccessful. Similarly, it is reasonable to **attempt chemical cardioversion on any patient who fails DCC**, especially before repeated attempts at DCC.

(2) Table 24.3 shows the currently available intravenous agents available for the pharmacologic cardioversion of AF to sinus rhythm.

(i) Procainamide is a class IA antiarrhythmic drug that is often considered **the first line of therapy** for the pharmacologic conversion of AF occurring in the postoperative period after cardiac surgery.

TABLE 24.3 Intravenous Medications Used for the Cardioversion of Atrial Fibrillation

Drug name	Vaughan Williams class	Dose	Adverse side effects
Amiodarone	III	5–7 mg/kg over 30–60 min, followed by 1.2–1.8 g/d until 10 g, then 200–400 mg daily for maintenance	Hypotension, bradycardia, hyperthyroidism, hepatitis, skin discoloration, and phlebitis
Ibutilide	III	1 mg over 10 min, repeat as needed	Torsade de pointes, increased QTc
Propafenone	IC	1.5–2.0 mg/kg over 20 min	Hypotension and atrial flutter with RVR
Flecainide	IC	1.5–3.0 mg/kg over 10–20 min	Hypotension and atrial flutter with RVR
Vernakalant (approved in Europe but not yet in United States)	III	3 mg/kg IV infusion over 10 min. Second infusion of 2 mg/kg IV over 10 min after 15 min of rest	Vernakalant is contraindicated in patients with systolic blood pressure < 100 mm Hg, severe aortic stenosis, heart failure (NYHA classes III and IV), ACS within the previous 30 d, or QT interval prolongation. Before its use, the patients should be adequately hydrated. ECG and hemodynamic monitoring should be used, and the infusion can be followed by DCC if necessary. The drug is not contraindicated in patients with stable coronary artery disease, hypertensive heart disease, or mild heart failure

RVR, rapid ventricular response; ACS, acute coronary syndrome; ECG, electrocardiogram; DCC, direct current cardioversion.

(ii) Amiodarone is considered a class III antiarrhythmic drug, although it has properties of all of the four Vaughan Williams classes. Like procainamide, amiodarone is commonly used intravenously in the postoperative period for AF after cardiac surgery, particularly for those patients with renal insufficiency or failure who are not candidates for procainamide.

(iii) Ibutilide is an agent approved for the pharmacologic conversion of AF. The incidence of torsade de pointes is at least 1% to 2% with ibutilide, which is higher than that seen with procainamide or amiodarone. Ibutilide is available only in the intravenous form and is, therefore, not an option for long-term maintenance of sinus rhythm.

(iv) Vernakalant is an agent that was recently approved in Europe for chemical cardioversion but has not yet been approved by the US Food and Drug Administration (FDA). It is more effective than amiodarone for conversion of AF to sinus rhythm. Vernakalant is contraindicated in patients with systolic blood pressure < 100 mm Hg, severe aortic stenosis, heart failure (NYHA classes III and IV), acute coronary syndrome (ACS) within the previous 30 days, or QT interval prolongation. Before its use, patients should be adequately hydrated. ECG and hemodynamic monitoring are mandatory, and the infusion can be followed by DCC if necessary. The drug is not contraindicated in patients with stable CAD, hypertensive heart disease, or mild heart failure. The clinical positioning of this drug has not yet been determined, but it is likely to be used for acute termination of recent-onset AF in patients with lone AF or AF associated with hypertension, CAD, or mild to moderate (NYHA classes I and II) heart failure.

(3) A number of **oral agents** are available for the pharmacologic cardioversion of AF. **In appropriate patients the class IC agents, such as flecainide and propafenone, may be particularly effective for pharmacologic cardioversion**. In the text to follow are mentioned some other agents that may be used in the long-term for maintenance of sinus rhythm in patients with AF. It should be kept in mind that initiation or upward dose titration of antiarrhythmic drugs should be done with caution and, in many instances, should be performed in a hospital setting with a cardiac monitor. This is particularly true for the class III agents sotalol and dofetilide. On the other hand, in patients without structural heart disease, the class IC agents flecainide and propafenone may be considered for initiation on an outpatient basis. Table 24.4 outlines the presently available orally acting medications to treat AF.

(i) **Class IA agents.** These agents have seen a decline in their use, primarily due to a high incidence of intolerance because of side effects but also due to evidence of possible increased mortality for those patients with structural heart disease.

- **Procainamide.** This medication has not been used as frequently now for long-term treatment of AF, especially due to the potential for gastrointestinal, hematologic, and immunologic (e.g., lupus-like syndrome) side effects. An active metabolite of this drug, *n*-acetylprocainamide (NAPA), is cleared renally and has class III antiarrhythmic properties. Blood levels of both procainamide and NAPA need to be monitored to prevent toxicity, especially in the setting of renal and/or hepatic insufficiency.
- **Quinidine** is another class IA drug that has not been used as frequently in recent years, again primarily due to a relatively high

TABLE 24.4 Oral Agents Available for Rhythm Control in Atrial Fibrillation

Drug name	Vaughan Williams class	Cardioversion dose		Daily maintenance dose
Amiodarone	III	400–800 tid dosing daily until 10 g, then		200–400 mg
Dofetilide	III	Based on CrCl (mL/min):	Dose: (μg bid)	Same. Dosing also adjusted for adjusted QTc
		> 60 mL/min	500	
		40–60	250	
		20–40	125	
		< 20	Contraindicated	
Propafenone	IC	600 mg		450–900 mg
Flecainide	IC	200–300 mg		Same
Sotalol	III	160–320 mg		Same
Dronedarone	III		Contraindicated if CrCl < 30 and patient with class IV heart failure, admission for CHF in preceding 4 weeks especially if EF < 35%	400 mg bid

CHF, congestive heart failure; EF, ejection fraction; IV, intravenous.

incidence of gastrointestinal, hematologic, and neurologic side effects. In addition, quinidine interacts with several cardiac and noncardiac medications.

- **Disopyramide.** This antiarrhythmic medication may have a "niche" for the treatment of vagally mediated AF or AF that occurs in the setting of hypertrophic cardiomyopathy. However, its **negative inotropic effects** are greater than those of other class IA drugs, and it is associated with **greater anticholinergic effects** such as constipation and urinary retention.

(ii) Class IC agents. This group has become the preferred antiarrhythmic drugs for the management of AF in patients without structural heart disease, especially those patients with "lone" AF. These medications should not be used in patients with structural heart disease, especially patients with known or suspected ischemic heart disease. **Flecainide** was shown in the Cardiac Arrhythmia Suppression Trial (CAST) to be associated with increased mortality when used for suppression of ventricular arrhythmias in patients with LV dysfunction

following myocardial infarction (MI). This has led to much concern over the use of the class IC agents in any patient with CAD and even in other types of structural heart disease.

- **Flecainide.** This is a well-tolerated medication that has a low incidence of neurologic side effects. This medication is approved in both oral and intravenous forms for the acute cardioversion of AF. Randomized trials with this drug show that it converts 60% to 70% of patients with new-onset AF at 4 hours and close to 90% at 8 hours. Oral administration and intravenous administration were equally efficacious, but the average response to the intravenous loading is seen within 1 hour, whereas it is 3 hours with the oral loading dose.
- **Propafenone.** This is also a well-tolerated medication. Its β-blocking properties limit its use in patients intolerant of such medications. Like sotalol, this property allows for its use as a single agent for AF suppression and ventricular rate control.

(iii) Class III agents. This group has become the preferred treatment for AF in patients with structural heart disease.

- Sotalol also has β-blocking properties, which makes it useful as a **single-agent therapy** for AF suppression and ventricular rate control. However, these properties are also responsible for the intolerance seen with this drug and may contribute to exacerbation of heart failure in some patients. **The dose must be reduced with renal insufficiency**.
- **Dofetilide.** This is the latest antiarrhythmic drug to be approved by the FDA for management of AF. This drug is generally well tolerated and has been shown to be safe for patients with structural heart disease, in particular those patients who have had an MI and those with CHF. **This drug has been associated with proarrhythmia, especially in the setting of renal dysfunction. The prescription of the drug is tightly controlled, and only those certified in its use may prescribe it**.
- **Amiodarone.** This is a unique medication in that it has properties of all four Vaughan Williams classes. It is also unique with regard to its very long elimination half-life (up to 120 days). Amiodarone is effective for the management of AF but is generally reserved for patients in whom other antiarrhythmic drugs have been ineffective or poorly tolerated, due to the important potential organ toxicities that may occur, predominantly in the liver, lungs, thyroid, and eyes. It is recommended that patients treated with amiodarone have baseline and then regular screening tests such as ophthalmologic examination, pulmonary function study, chest x-ray, and blood tests for liver and thyroid function.
- **Dronedarone** is a multichannel blocker that inhibits the sodium, potassium, and calcium channels and has noncompetitive antiadrenergic activity. It is **similar to amiodarone with a much better side-effect profile, though it is less effective than amiodarone**. Contraindicated in NYHA classes III and IV or unstable heart failure, during concomitant therapy with QT-prolonging drugs, powerful CYP3A4 inhibitors, and creatinine clearance < 30 mg/mL. There is potential for serious liver toxicity with dronedarone and liver function tests have to be monitored closely when patients are on this medication.
- **Azimilide.** New class III antiarrhythmic drug that is not yet FDA approved for the management of AF.

(4) Figure 24.1, adapted from American Heart Association/American College of Cardiology/European Society of Cardiology (AHA/ACC/ESC) guidelines, outlines strategies used in the maintenance of sinus rhythm.

c. AV nodal ablation in conjunction with permanent pacemaker.

(1) Symptomatic refractory AF, especially when the ventricular rate is uncontrollable or such control is limited by underlying bradycardia, may be amenable to ablation of the AV node and implantation of a **rate-responsive single-chamber permanent pacemaker**. These patients still require systemic anticoagulation. A recent meta-analysis of 21 studies that included 1,100 patients who underwent AV nodal ablation for highly symptomatic AF concluded that AV nodal ablation and subsequent pacemaker implantation significantly improved the quality of life, exercise capacity, and LV function and decreased symptoms of AF. In a small subset of 56 patients who had impaired LV function (an ejection fraction < 40%) and AV nodal ablation, permanent pacemaker implantation caused an average improvement in ejection fraction of 8% and complete normalization of the ejection fraction in one-third of the patients. The remaining patients with persistent LV dysfunction after AV nodal ablation had a 5-year survival rate of <40%. The 1-year mortality rate after AV nodal ablation and permanent pacemaker implantation is approximately 6.3%, which includes a high 2% risk of sudden cardiac death (SCD), which is thought to be related to early post pacemaker implantation R-on-T phenomenon caused by pacemaker-induced bradycardia. For this reason, it has been suggested, without a great deal of support in the published literature, that pacemakers be programmed with a minimum heart rate of 90 beats/min for the first month after the AV nodal ablation procedure.

(2) **Indications for permanent pacemaker for AF.** A permanent pacemaker may be needed in patients who develop symptomatic bradycardia, which may be exacerbated by therapy for AF. This may occur because of an underlying sinus node dysfunction or perhaps poor AV conduction leading to slow ventricular rates during AF. Modern pacemakers have **"mode switching"** capabilities, so that the pacing mode changes from dual-chamber to single-chamber ventricular pacing at the onset of AF to avoid rapid ventricular pacing rates due to the pacemaker responding to the atrial activity.

(3) **Limitations.** Although, as mentioned earlier, AV nodal ablation has been shown to cause symptomatic improvement in patients with refractory and very symptomatic AF, its limitations include the potential lifelong need for anticoagulation, the loss of AV synchrony, and the lifelong pacemaker dependence with its attendant risks.

Several recent pacemaker trials have shown worsening hemodynamic effects of right ventricular (RV) apical pacing compared with biventricular pacing. The Post AV Nodal Ablation Evaluation (PAVE) trial randomized patients to RV apical pacing versus biventricular pacing following AV nodal ablation for permanent AF. At an average follow-up of 6 months, the biventricular-paced group had longer 6-minute walk times and increased peak oxygen consumption and reported improved quality of life. Although LV ejection fraction did not differ between the groups at baseline, at follow-up, the ejection fraction in the biventricular pacing group stabilized, whereas the ejection fraction in the RV apically paced group had declined significantly.

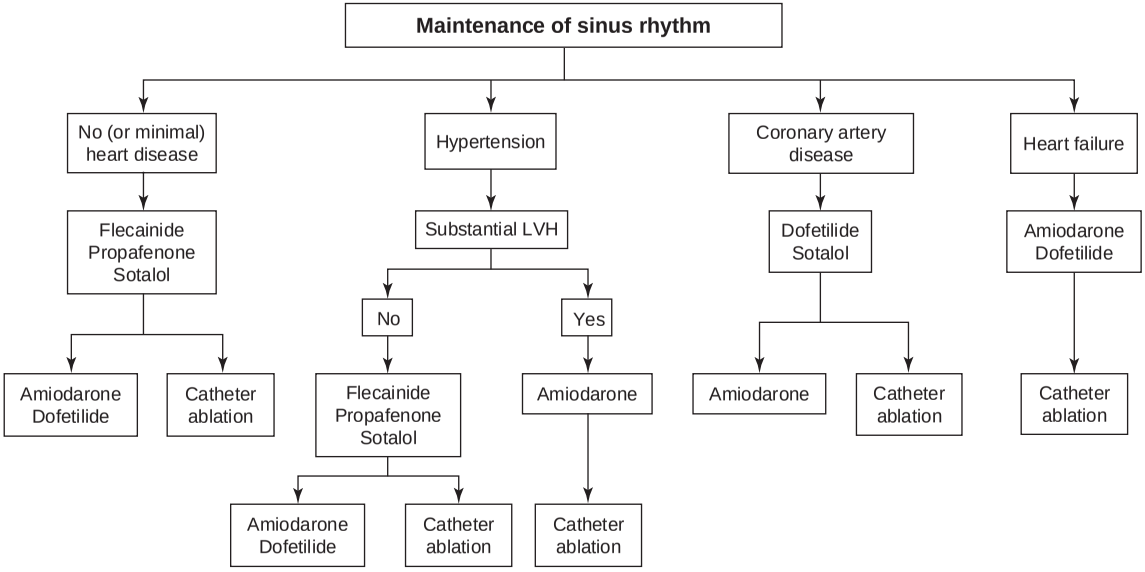

FIGURE 24.1 Therapeutic approach to the maintenance of sinus rhythm. Adapted from American College of Cardiology/American Heart Association (ACC/AHA) practice guidelines. LVH, left ventricular hypertrophy.

Current recommendations regarding the choice of pacemaker following AV nodal ablation suggest the use of RV pacing devices in patients with normal LV function or in those thought to have reversible LV dysfunction secondary to AF with poor rate control. In patients with impaired LV function not caused by AF, a biventricular pacemaker with or without defibrillator capability should be considered. In patients who have undergone AV nodal ablation and developed heart failure symptoms following RV apical pacing, an upgrade from an RV apical system to biventricular system should be considered.

d. Implantable devices with treatment and suppressive strategies for AF are now available for selected patients. Some devices may terminate AF with a rapid atrial burst pacing or a cardioversion shock. Pacemakers that have pacing algorithms aimed at preventing AF episodes have become available. The use of such pacemakers in patients without an indication for pacing is still under investigation. A difficulty in their implementation is the frequency of episodes of AF in patients requiring device activation and the discomfort associated with shock delivery.

e. Invasive curative therapies. There are two major interventional approaches for the management or cure of AF, one based on a percutaneous approach and the other on a surgical approach. These approaches are not yet first-line therapy, but in recent years have become a much more attractive option for patients with troublesome AF in whom antiarrhythmic treatment has been ineffective or poorly tolerated.

(1) Catheter ablation of AF with pulmonary vein isolation (PVI). In 1998, Haissaguerre and colleagues described the presence of isolated foci in the left atrium and pulmonary veins and their role in the initiation of AF. They were also able to demonstrate that ablation of these foci could successfully terminate AF. Based on this early work, the field of AF ablation was born. Initial experiences with AF ablation attempted to mimic the surgical Maze procedure. Since that time, ablation has undergone various changes in both philosophy and technique.

Approaches to AF ablation can vary widely. Purely anatomic approaches may focus on the creation of linear lesions around the pulmonary veins and may not require demonstration of entrance or exit block. Other techniques focus on ablation of sites of autonomic ganglia or areas of complex fractionated electrograms. Electrogram-based approaches make use of a mapping catheter to help identify electrograms in areas targeted for isolation but may vary in the scope of the area targeted for isolation. Anatomic ablation techniques use recently developed three-dimensional (3D) mapping systems to demonstrate the anatomy of the left atrium and the pulmonary veins. Various anatomic techniques including the isolation of each of the four veins, individually or via isolation of two veins at a time, have been developed. In addition, anatomic lines extended to the mitral isthmus or involving the room of the left atrium have been utilized. Exit block is often used as an end point in the anatomic approach.

Electrogram-based techniques require the use of a second (ring) mapping catheter. After circumferential isolation, the mapping catheter is used to evaluate for the presence of gaps in the ablation line and these gaps are then ablated. There have also been experiences using electrogram-based approaches to perform additional ablation points in other areas of the heart, including the coronary sinus, the superior vena cava, and the right atrium, after performing PVI. Additionally, drug testing with adenosine and isoproterenol to provoke AF and thereby identify potential triggers for ablation is sometimes used.

Advances in techniques have improved the efficacy and safety of the procedure. One major advance has been the development of protocols that ablate outside the ostia of the pulmonary veins to help reduce the incidence of postprocedure pulmonary vein stenosis. Catheter ablation is now considered a reasonable alternative to pharmacologic therapy to prevent recurrent AF in symptomatic patients with little or no left atrium enlargement with a class I recommendation in the most recent guideline update. In addition, catheter ablation performed in experienced centers is useful in maintaining sinus rhythm in selected patients with significantly symptomatic, paroxysmal AF who have failed treatment with an antiarrhythmic drug and have normal or mildly dilated left atria, normal or mildly reduced LV function, and no severe pulmonary disease.

Patient preparation and procedural considerations. Prior to ablation, considerations including access, conscious sedation, and choice of anticoagulation regimen should be made on an individual patient basis. The presence of multiple catheters in the left atrium requires patients to be given full anticoagulation. Prior to the procedure, some centers require patients to be therapeutic on warfarin for 4 to 6 weeks. Patients not anticoagulated prior to the procedure should undergo transesophageal echocardiogram to exclude the presence of left atrial thrombus. Regardless of preprocedural anticoagulation status, patients are fully anticoagulated with unfractionated heparin during the procedure to achieve a prespecified targeted activated clotting time.

Catheters are placed in the right atrium and coronary sinus, typically via sheaths in the right and left femoral veins, and an additional sheath is often needed if intracardiac echo is used. The left atrium is accessed via transeptal puncture. Great care is needed, using fluoroscopic guidance to assure successful transeptal puncture, and many centers use intracardiac echo to assist in safely achieving transeptal puncture. After placement in the left atrium, circular "lasso" mapping and ablation catheters are used to approach the pulmonary veins. If used, intracardiac echo can assist 3D mapping techniques in identifying the pulmonary vein ostia.

End point for ablation differs depending on the technique used. On completion of electrogram-based ablation, success is demonstrated by the development of entry block in the antrum of the pulmonary veins. However, anatomic-based procedures do not require the demonstration of block.

Centers performing ablation should have backup available of physicians experienced in pericardiocentesis and cardiothoracic surgery, secondary to the development of hemorrhagic pericardial effusion or atrial appendage rupture.

The identification of the pulmonary veins as the predominant source of ectopic foci that trigger AF has led to catheter-based ablation strategies to electrically isolate the pulmonary veins by delivering radiofrequency energy at their ostium. In the initial series, foci of increased automaticity within the pulmonary veins were targeted and ablated. In one early series of 45 patients with AF, 62% became free of symptomatic AF over a mean follow-up of 8 months. However 70% of the patients required multiple procedures. In a subsequent study using the same approach, the success rate (defined as the absence of return of symptomatic AF) was 86% over a 6-month follow-up.

Continued research into the substrate for AF has demonstrated that there are many potentials that can contribute to the initiation and maintenance of AF and that these may arise in multiple areas of the right and left atria. Thus, catheter ablation procedures have been developed to

incorporate linear lesions in the roof of the left atrium and mitral valve isthmus ablation to account for these. Using this approach in a series of 70 patients with symptomatic AF, 70% of the patients were found to be free from AF following PVI without antiarrhythmic medications at 4 months of follow-up. The procedure continued to advance with the development of the circular mapping catheter, which allowed for more accurate mapping and isolation of the pulmonary veins.

At the time of this writing, the accumulated published experience in PVI suggests an approximately 70% to 90% success rate in patients with paroxysmal AF and 40% to 80% success rate in patients with persistent AF. It must be noted that the success rates in patients with depressed ejection fraction are much lower than that in patients with normal systolic function.

A newer approach to radiofrequency catheter ablation of AF involves the ablation of complex fractionated electrograms, which has a 91% efficacy reported at 1 year. This study also showed that restoration of sinus rhythm following catheter-based ablation of AF caused a significant improvement in exercise capacity, quality of life, and LV systolic function.

Presently, the long-term efficacy of catheter-based ablation is not known and requires further study. Long-term follow-ups from RCTs are presently either lacking in patient numbers or marred by high crossover rates or by antiarrhythmic use. The current ACC/AHA/HRS guidelines allow for the use of PVI in the treatment of symptomatic AF following intolerance to, depending on the substrate, at least one drug and as many as three antiarrhythmic drugs.

Complications. Major complications from catheter-based ablation have been reported in about 2% to 3% of patients and include pulmonary vein stenosis, systemic thromboembolism, atrial esophageal fistula, and the development of atypical left atrial flutter.

The incidence of **pulmonary vein stenosis** has diminished by the judicious use of radiofrequency ablation energy to target areas just outside the pulmonary veins so as to isolate the ostia of the pulmonary veins from the remainder of the left atrium. The use of intracardiac echocardiography to detect microbubble formation as a means to measure the magnitude of radiofrequency energy delivered has been reported to reduce the instance of pulmonary vein stenosis. This complication often presents as dyspnea and breathlessness in the weeks to months following catheter-based ablation, with radiographic evidence of asymmetric pulmonary edema or pulmonary emboli, as it results in obstructive venous outflow from a single pulmonary lobe. This diagnosis is best made by the use of computed tomography venography, but it can also be made through the use of TEE with the finding of high-velocity flow in the affected pulmonary vein.

Systemic embolic events, including embolic stroke, are among the most serious complications of catheter-based ablation of AF, and the reported incidence varies from 0% to 5%. A trial comparing heparin-dosing regimens found that increasing the intensity of anticoagulation reduces the probability of forming left atrial thrombi from 11% to 3%, when the activated clotting time was increased from 250 to > 3 00 seconds.

Atrial esophageal fistula is a relatively rare complication of PVI, and it is more likely to occur when extensive ablation occurs over the posterior left atrial wall where it abuts the esophagus. Typical symptoms include nausea, vomiting, fever, and sudden neurologic deterioration

(from systemic embolization), which occur in the days to weeks following ablation. Successful treatment of this condition requires prompt recognition of its clinical signs, as delay in the treatment often leads to death.

The development of **atypical left atrial flutter** is thought to be related to the development of scar in the left atrium, which creates the substrate for reentry required for this arrhythmia. The most important predictor of the development of left atrial flutter is the presence of an incomplete line of ablation, and it has been found that extending the ablation line to the mitral valve annulus may reduce the frequency of this complication. This arrhythmia, as is the case with right atrial flutter, is amenable to further catheter-based ablation.

(2) Cox-Maze procedure is a surgical approach that has been developed over the last 25 years and that tested the original hypothesis that reentry is the predominant mechanism for the development and maintenance of AF. It has undergone multiple revisions through the years, and now it has evolved to include techniques that surgically isolate the pulmonary veins and connect these dividing lines to the mitral valve annulus. The surgical procedure uses atrial incisions in critical locations to create barriers to the propagating wavelets that are responsible for the initiation and maintenance of AF and that consequently eliminate the macroreentrant circuits in the atrium necessary to maintain AF.

The Maze procedure has changed over the last two decades, and present techniques use transmural lesions to isolate the pulmonary veins and to connect these dividing lines to the mitral valve annulus, as well as lesions to create barriers in the right atrium. The reported success of the combined three developmental stages of the Cox-Maze procedure is 93% in patients with symptomatic AF who were intolerant of antiarrhythmic drugs. This long-term report included 178 patients, and there was a 2.2% risk of periprocedure death and a 6% risk of pacemaker requirement in the patients undergoing a Cox-Maze I procedure. Other, more current studies have reported lower success rate of around 70%. This procedure maintains the atrial transport function, and especially when allied with left atrial appendage ligation substantially reduces the risk of postoperative thromboembolic events.

Procedure risks include **death** risk, which is dependent on the patient's comorbidities but is usually estimated to be < 1% as an isolated procedure, the need for a **pacemaker**, **impaired atrial transport function**, and delayed **atrial arrhythmias** including atrial flutter.

The Maze procedure has not had widespread acceptance as a means of treatment for AF, except in patients undergoing open heart surgery. Even in these patients, the additional intraoperative time and complexity of the procedure have limited its widespread surgical application. Currently under development are less invasive approaches, including thoracoscopic and catheter-based epicardial techniques.

The Maze procedure is often associated with significant edema formation, probably due to atrial natriuretic peptide derangements. This is effectively mitigated by the use of aldosterone antagonists such as spironolactone for the first 4 to 6 weeks postoperatively. All procedures used to restore NSR in patients with AF have had a variable effect on the restoration of atrial transport function, depending on the duration of fibrillation before the procedure and the rhythm maintained following the procedure. The need for long-term anticoagulation therapy following these procedures is generally assessed on an individual basis.

II. SPECIAL CONSIDERATIONS

A. Postoperative AF. AF is common postoperatively. The incidence of AF postoperatively varies with the type of surgery and is highest following open heart surgery, during which time it ranges between 20% and 50%. It usually occurs in the first 5 days. Risk factors for perioperative AF include age, a history of AF, chronic obstructive pulmonary disease (COPD), valvular heart disease (especially mitral valve disease), atrial enlargement, perioperative heart failure, and withdrawal from a β-blocker or an ACE inhibitor. Postoperative AF is a major determinant of length of stay and thus of cost. It is associated with all the risks associated with AF in the nonpostoperative setting including hemodynamic compromise and thromboembolism.

1. **Therapy.** Postoperative AF is usually self-limited, and DCC is usually not needed. There are a variety of antiarrhythmic agents available for cardioversion in postoperative patients. In a small trial, ibutilide was found to be more effective than placebo for the treatment of postoperative AF. Sotalol is particularly acutely effective in patients with preserved LV systolic function, because the risk of proarrhythmic toxicity is small and also because its β-blocker action contributes to slowing the ventricular rate.

   AF carries an increased risk of stroke in post-CABG patients, and so anticoagulation with heparin followed by oral anticoagulants is recommended if AF persists for longer than 48 hours. The choice of antiarrhythmic therapy, choice of AV nodal blocking agents, and the use of either heparin and/or oral anticoagulants depend on the individual patient, the time from surgery, and the specific type of surgery.

2. **Prevention.** There is evidence supporting the prophylactic administration of β-blocker medications in patients undergoing cardiac surgery to prevent the development of AF. Sotalol has also been studied, but there is at present conflicting evidence regarding its effectiveness. Amiodarone, when given either prophylactically before cardiac surgery or following open heart surgery, has been found to significantly reduce the incidence of postoperative AF. In the Prophylactic Oral Amiodarone for the Prevention of Arrhythmias that Began Early After Revascularization (PAPABEAR) trial, oral amiodarone, dosed at 10 mg/kg beginning 6 days before and continuing for 6 days after surgery, decreased the incidence of postoperative AF by 50%. This efficacy was present in patients irrespective of whether CABG, valve surgery, or a combination was performed. Preoperative treatment with procainamide has yielded inconsistent results, as has treatment with either digoxin or verapamil.

   At present there are limited data supporting the use of atrial overdrive pacing as opposed to single-chamber pacing in the prevention of postoperative AF. In a randomized trial involving 132 patients undergoing CABG, postoperative biatrial pacing significantly reduced incidence of AF by 12.5% compared with left atrial pacing, right atrial pacing, or no pacing. A meta-analysis of 10 randomized trials also concluded that biatrial pacing, atrial pacing, and right atrial pacing reduced the incidence of AF after CABG surgery.

B. AF in acute MI. The incidence of AF following acute MI varies depending on the population sampled as well as the type of MI but ranges between 10% and 20% at 30 days. AF is more commonly associated with acute MI in older patients as well as those with a higher Killip class and more severe LV dysfunction. Patients with AF in the setting of an acute MI have a worse outcome at 30 days than those in sinus rhythm (29.3% with AF vs. 19% with NSR). Stroke rates are also increased in patients with post-MI AF.

The guidelines presently recommend urgent DCC in patients with acute MI who present with AF, especially if in rapid ventricular response with intractable ischemia or evidence of hemodynamic instability including CHF. Intravenous β-blockade is indicated for rate control to reduce myocardial oxygen consumption and demand, and digoxin is an alternative in patients with severe left surgical dysfunction and

heart failure. Anticoagulation is recommended in patients with large anterior MIs and those in which the AF becomes persistent. Post-MI ACE inhibitors seem to reduce the incidence of AF in patients with significant LV dysfunction. Post-MI use of carvedilol also seems to diminish the incidence of AF and atrial flutter.

C. AF and WPW syndrome. The most feared complication of the WPW syndrome is the development of ventricular fibrillation and SCD secondary to antegrade conduction of the AF into the ventricles. The incidence of SCD in patients with a WPW syndrome is around 0.6% per year, and risk factors for SCD include having a short antegrade bypass tract refractory period (< 250 milliseconds), short RR intervals during preexcited AF, and the presence of multiple accessory pathways.

It is important to avoid AV nodal blocking agents in a patient who presents with a preexcited tachycardia, as this has the potential to increase the refractory period of the AV node and facilitate conduction down the accessory pathway. Administration of AV nodal blocking agents such as verapamil, diltiazem, and digoxin is contraindicated in this setting. Intravenous β-blockers are ineffective in this setting and may have adverse hemodynamic consequences.

Flecainide, a class IC antiarrhythmic agent, can be used to slow the ventricular rate in patients who have AF with rapid ventricular rates associated with preexcitation by shortening the shortest preexcited cycle length during AF.

Patients with WPW syndrome and syncope or with a short antegrade bypass tract refractory period require immediate DCC followed by catheter-based ablation of the accessory pathway as the preferred therapy. Ablation of the bypass tract does not necessarily prevent recurrence of the AF, but it should be noted that following this ablation the management of AF is similar to that of patients without preexcitation.

D. AF in pregnancy. AF occurs infrequently during pregnancy and when it does it usually has an identifiable cause, such as mitral valve disease, thyroid disease, or pulmonary processes. The ventricular rate can be controlled with digoxin, β-blockers, or a nondihydropyridine calcium channel blocker. Currently available antiarrhythmic medications cross the placenta and are excreted in breast milk and should be avoided if possible in the pregnant and lactating individuals, but amiodarone, sotalol, and flecainide have all been used successfully during pregnancy in selected instances. Quinidine has the longest safety record of any antiarrhythmic agent in pregnancy and remains the agent of choice for pharmacologic conversion of AF. In the hemodynamically unstable patient, DCC can be performed without any concerns of fetal damage.

Anticoagulation should also be given high priority during pregnancy, given the risk of thromboembolic disease during pregnancy, and only those patients with lone AF at low risk for thromboembolic complications do not require anticoagulants.

The oral anticoagulant warfarin is generally avoided during the first trimester of pregnancy because of teratogenic effects and also during the last month of pregnancy because of bleeding concerns during delivery. Administration of unfractionated heparin either by continuous intravenous infusion in a dose sufficient to increase the activated partial thromboplastin time (aPTT) to 1.5 to 2 times control or by intermittent subcutaneous injection of 10,000 to 20,000 units every 12 hours adjusted to prolong the midinterval aPTT to 1.5 times control is appropriate. Low-molecular-weight heparin may also be considered during the first trimester and last month of pregnancy, although there are limited data on clinical outcomes with its use.

E. AF and hypertrophic obstructive cardiomyopathy (HOCM). Patients with AF and HOCM have a high risk of systemic embolic events. For this reason, it is recommended to maintain oral anticoagulation therapy in the range of an INR of 2.0 to 3.0 or alternative anticoagulation with dabigatran, rivaroxaban or apixaban in patients with HOCM and AF regardless of what the CHADS2 score is. Antiarrhythmic medications can be used to prevent recurrent episodes of AF, and although there are insufficient data comparing the various antiarrhythmics, anecdotal evidence seems to support the use of disopyramide in combination with a β-blocker or a nondihydropyridine calcium channel blocker.

F. AF and pulmonary disease. AF commonly develops in patients with COPD exacerbations. General recommendations include the treatment of the underlying lung process, correction of hypoxia, and of the acid–base imbalances. Medications commonly used to treat bronchospastic airway disease such as theophylline and β-adrenergic agonists can precipitate AF and decrease the ability of medications to control the ventricular rate. Antiarrhythmic medications with β-blocking properties such as sotalol, propafenone, and adenosine can worsen bronchospasm and are contraindicated in patients with severe bronchospastic airway disease. Ventricular rate control is usually achieved with nondihydropyridine calcium channel blockers such as verapamil and diltiazem.

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