INTRODUCTION

Patients with cardiac arrhythmias may come to the attention of their physicians in a variety of ways. An asymptomatic arrhythmia may be fortuitously discovered on a routine electrocardiogram (ECG) or physical exam. Alternatively, a patient may present with a complaint suggestive of arrhythmia, usually palpitations, syncope, or presyncope. Finally, patients who have no history of arrhythmia, but who may be prone to ventricular tachyarrhythmias because of underlying heart disease, may undergo routine testing to evaluate their level of risk. Patients in each category may be evaluated by invasive or noninvasive means. This chapter focuses on the noninvasive evaluation of patients with suspected arrhythmias and discusses indications for invasive testing.

THE INITIAL EVALUATION OF THE PATIENT WITH PALPITATIONS OR SYNCOPE

The initial evaluation of a patient with palpitations, syncope, or presyncope should include a careful history, physical exam, and baseline ECG, all of which may be helpful in defining the need for further evaluation. A clear description of palpitations may help the physician make a diagnosis. A sensation of the heart stopping and then starting...
again, or of a brief “flip-flopping” of the heart, is most often caused by a single premature contraction, either atrial or ventricular in origin. The feeling that the heart has stopped is a result of the pause that follows a premature depolarization, and the “flip-flopping” sensation is caused by the hyperdynamic postextrasystolic beat (1). Patients often notice these beats, particularly when they are lying on their left side, because of the heart’s proximity to the chest wall in that position. A sensation of pulsations in the neck is usually caused by cannon A waves, resulting from contraction of the atria against a closed tricuspid valve. This may occur with a variety of arrhythmias; however, when the pulsations are described as being rapid and regular, the diagnosis of AV nodal reentrant tachycardia (AVNRT) should be considered (1). A sensation of a rapid pounding or fluttering in the chest may be caused by a supraventricular or ventricular arrhythmia. When a patient is able to describe regularity or irregularity of the rhythm, or has taken his or her pulse during an episode, this information may help to narrow the differential diagnosis (1).

Similarly, in patients presenting after a syncopal or presyncopal episode, a careful description of the event may help identify a diagnosis. Vasovagal (neurocardiogenic) syncope is the most common etiology of syncope, particularly among patients with no structural heart disease (2). This is caused by a period of autonomic imbalance during which an excessive vagal response occurs following a period of catecholamine predominance, leading to bradycardia and/or vasodilation. A feeling of warmth, nausea, and lightheadedness classically precedes vasovagal syncope (3). Patients may describe a feeling of fatigue after awakening, and may suffer recurrent syncope if they attempt to arise too quickly. In contrast, arrhythmic syncope often occurs without warning, and a history of injury resulting from syncope may indicate an arrhythmic etiology.

In patients with palpitations or syncope, a situational history may be useful. Vasovagal syncope may occur following a precipitating incident or in a predisposing setting (following a meal, in a restaurant or bar, or another warm, crowded place). Palpitations during exercise or other periods of catecholamine excess may have a triggered mechanism, as occurs with idiopathic ventricular tachycardia (VT) in patients with structurally normal hearts (4). Patients with congenital long QT syndrome (LQTS) may also present with palpitations or syncope, caused by polymorphic VT, during exercise or emotional stress (5).

A personal history of structural heart disease, including prior myocardial infarction (MI), congestive heart failure (CHF), or cardiomyopathy, may identify patients at high risk for ventricular arrhythmias. A family history of sudden death or arrhythmic disease must also be elicited to identify patients with inherited disorders that may predispose them to arrhythmias (see Table 1).

The physical exam is used in the evaluation of patients with palpitations or syncope to aid in the diagnosis of structural heart disease. A physical exam suggestive of previously undiscovered hypertrophic obstructive cardiomyopathy (HOCM), CHF, or a valvular abnormality should prompt the physician to further characterize the abnormality with an echocardiogram. The twelve-lead ECG can also be useful in making a diagnosis of structural heart disease in this patient population. In the occasional situation in which an ECG has been obtained when a patient’s symptoms occur, a diagnosis may be made based on the ECG (6). More often, the only available ECG is obtained during an asymptomatic period. Even a sinus rhythm ECG may offer clues to the cause of a patient’s symptoms. (see Table 2) (1).
Table 1

<table>
<thead>
<tr>
<th>Personal Disorders</th>
<th>Familial Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD (prior MI)</td>
<td>Congenital LQTS</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>Brugada syndrome</td>
</tr>
<tr>
<td>HOCM</td>
<td>Arrhythmogenic right ventricular dysplasia</td>
</tr>
<tr>
<td>Severe valvular disease</td>
<td>HOCM</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>Dilated cardiomyopathy</td>
</tr>
<tr>
<td>Congenital AV block</td>
<td></td>
</tr>
</tbody>
</table>

CAD = coronary artery disease, MI = myocardial infarction; HOCM = hypertrophic obstructive cardiomyopathy; LQTS = long QT syndrome.

Table 2

<table>
<thead>
<tr>
<th>ECG Finding</th>
<th>Suggested Cause of Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short PR interval/delta wave</td>
<td>AVRT related to Wolf-Parkinson-White syndrome</td>
</tr>
<tr>
<td>Q waves</td>
<td>VT or VF related to coronary artery disease/prior infarct</td>
</tr>
<tr>
<td>P mitrale, LVH, frequent atrial ectopy</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Conduction system disease (bundle-branch or fascicular block, PR prolongation)</td>
<td>High-grade or complete heart block</td>
</tr>
<tr>
<td>LVH, apical T-wave inversions, prominent septal Q waves</td>
<td>VT or VF caused by hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Epsilon wave, inverted T waves V1-V3</td>
<td>VT or VF caused by arrhythmogenic right ventricular dysplasia (ARVD)</td>
</tr>
<tr>
<td>Monomorphic VPBs, LBBB, positive axis</td>
<td>Idiopathic VT, RVOT type</td>
</tr>
<tr>
<td>Monomorphic VPBs, RBBB, negative axis</td>
<td>Idiopathic VT, left ventricular type</td>
</tr>
<tr>
<td>Long QT interval</td>
<td>Polymorphic ventricular tachycardia</td>
</tr>
</tbody>
</table>

AVRT = atrioventricular reentrant tachycardia; LVH = left ventricular hypertrophy; VPB = ventricular premature complex; LBBB = left bundle branch block; RBBB = right bundle branch block; VT = ventricular tachycardia; VF = ventricular fibrillation; RVOT = right ventricular outflow tract. Adapted from Zimetbaum et al. (1).

**DIAGNOSTIC TESTING**

After the initial evaluation has been completed, we recommend further testing for three groups of patients with palpitations: those with structural heart disease or a family history of an arrhythmic disorder, those with frequent symptoms that may be amenable to medical or catheter-based treatment, and those who feel compelled to have a specific explanation for their symptoms. We recommend further testing for patients with syncope or presyncope whose history is consistent with an arrhythmic etiology. We do not routinely recommend further testing for those with a history strongly suggestive of neurocardiogenic syncope.
Since 1961, when the Holter monitor was introduced, ambulatory monitoring has been used in the evaluation of palpitations and syncope (7). The diagnosis of cardiac arrhythmias can be safely made in many patients using the variety of ambulatory monitoring devices available today. These include continuous electrocardiographic recorders and intermittent recorders with transtelephonic capabilities. The Holter monitor is the prototype for the continuous recorder. These monitors are typically worn for 24–48 h at a time. They record a continuous ECG tracing in two or three bipolar leads. Data is stored on a cassette or compact disk, and is subsequently digitized for analysis. These devices contain patient-activated event markers that allow patients to indicate the occurrence of symptoms. One advantage of Holter monitors is that they do not require patient activation. Thus, they may be successful in capturing arrhythmias that cause loss of consciousness, and can be used by patients who may have difficulty activating a monitor. These devices offer full disclosure, and will record asymptomatic as well as symptomatic arrhythmias that occur during the monitoring period. The major disadvantage of this system is the relatively short time that these devices are worn. In addition, the devices can be cumbersome and may prevent patients from participating in routine activities, such as exercise, that may be arrhythmic triggers. Asymptomatic arrhythmias that are detected may decrease the specificity of the findings of the test. Although patient event markers and diaries allow correlation between recorded arrhythmias and symptoms, patients often forget to accurately record the time of symptoms.

Intermittent recorders, or event recorders, store a brief ECG tracing when activated by the patient. Some of these devices are applied to the chest wall at the time of symptoms, and record information prospectively for approximately 2 min once activated. Other devices, called loop recorders, are worn continuously by the patient. These devices record continuously, but store data only when activated. This process allows storage of data both preceding and subsequent to device activation. Loop recorders usually consist of two or three chest leads attached to a small monitor the size of a beeper that can be worn on the patient’s belt. These recorders are often worn for up to 1 mo at a time. They have the ability to transmit stored information over the telephone, so that data can be analyzed and interpreted immediately. Because they can be worn for up to 1 mo, event recorders are more likely than continuous monitors to capture infrequent arrhythmias. Information obtained is correlated with patient symptoms, and is thus very specific. The major disadvantage of this system is that patients may be unable to activate the recorder as a result of loss of consciousness, disorientation, or confusion about the activation process.

Recently, implantable loop recorders (ILRs) have become available. These monitors can be left in place for up to 2 yr, and are particularly useful in diagnosing very infrequent arrhythmias (8). These devices are approximately the size of a pacemaker and are implanted subcutaneously to one side of the sternum. Like external loop recorders, they are patient-triggered, and store both prospective and retrospective data when activated. Recordings are initiated by placement of an activator over the device. Unlike external recorders, ILRs are not yet able to transmit tracings over the telephone. The obvious advantage of these devices is that they can conveniently be used even when symptoms rarely occur (less than once per month). Like other loop recorders, most ILRs require patient activation. The most recent devices contain automatic triggers.
Ambulatory Monitoring in the Evaluation of Palpitations

Ambulatory monitoring is a safe and effective way of diagnosing the cause of palpitations (9). Palpitations are usually benign, but may occasionally signify the presence of a significant arrhythmia (1). Although some patients identified during their initial visit as being at risk for dangerous arrhythmias may benefit from an aggressive evaluation including an electrophysiology study, most patients do not fall into this category, and are best evaluated by outpatient monitoring. Loop recorders are approximately twice as effective as Holter monitors when used in the evaluation of palpitations (diagnostic yield 66% vs 33%) (10). Two weeks of monitoring is usually adequate, and little is gained by longer periods of monitoring (11,12). Table 3 lists diagnoses made by event recorders used for the evaluation of palpitations by two authors (13,14). Clearly, the majority of patients monitored are found to have a benign cause of palpitations that does not result in specific treatment. In some cases, however, an arrhythmia requiring treatment is discovered, and often a benign diagnosis offers a patient the reassurance they need.

Our strategy for the diagnostic evaluation of patients with palpitations usually involves 2 wk of ambulatory monitoring using a loop recorder (see Fig. 1). If no symptoms occur during the initial 2 wk of monitoring, another 2 wk may be performed. Occasionally we choose a 24-h Holter monitor rather than a loop recorder for a patient who has very frequent palpitations or who is incapable of activating an event recorder. For a patient whose symptoms are rare, we may choose an ILR (10). Patients whose symptoms are sustained or poorly tolerated, especially those who have evidence of underlying heart disease, may warrant initial evaluation with an electrophysiology study (EPS) rather than ambulatory monitoring (1).

Ambulatory Monitoring in the Evaluation of Syncope and Presyncope

Ambulatory monitoring is also indicated in the evaluation of patients with syncope or presyncope (9). Proven cardiac syncope connotes a 24% 1-yr risk of sudden death (2). Thus, patients at high risk for serious arrhythmias who present with syncope are

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage of patients</th>
<th>Kinlay et al. (14)</th>
<th>Zimetbaum et al. (13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm</td>
<td>35%</td>
<td>39%</td>
<td></td>
</tr>
<tr>
<td>Ventricular premature depolarizations</td>
<td>12%</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>Atrial premature depolarizations</td>
<td>0%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>0%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Sinus tachycardia</td>
<td>29%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>18%</td>
<td>4%</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Zimetbaum et al. (1).
candidates for invasive evaluation, and in some instances implantable cardioverter
defibrillators (ICD) implantation. Syncope is a very common problem, however, and
most patients with syncope do not fall into this category. Ambulatory monitoring can
be a useful tool in the diagnosis of low-risk patients with syncope. The diagnostic yield
of Holter monitoring in the evaluation of syncope is low (15–22%) (15,16). This is a
result of the short duration of monitoring and the relative infrequency of symptoms in
most cases. Several studies have examined the use of external event recorders in patients
with syncope, and have found the diagnostic yield to be similarly low at 6–25% (13,16–18).
Some studies have shown event monitors to have a significantly higher
yield in the evaluation of presyncope than syncope (10,13).

The ILR has proven more effective than both the Holter monitor and the external
loop recorder in diagnosing the cause of syncope. A recently published study of patients
with undiagnosed syncope who underwent monitoring by ILR demonstrated a 59%
diagnostic yield (19). Of 85 patients, 50 recorded a rhythm corresponding with symp-
toms, at an average of 2.3 mo after device implantation. Of these, 16 patients had a
specific arrhythmia diagnosed, 7 were given the diagnosis of neurocardiogenic syncope,
and 27 had an arrhythmic cause of their symptoms excluded. Diagnosis of a specific
arrhythmia was more common among patients who had syncope while being monitored
than among those who had only presyncope (70% vs 24%). There was no incidence
of sudden death during the follow-up period of this study. Another study examined
the cost-effectiveness of the ILR, and found that its cost per diagnosis fell within the
range of those of other diagnostic tests used commonly in the evaluation of syncope.

**Fig. 1.** The evaluation of palpitations. Adapted from Zimetbaum et al. (10).
Incorporation of automatic triggers in the new generation of ILRs will likely improve the diagnostic yield of these devices for syncope. Our strategy for the diagnostic evaluation of the patient with syncope or presyncope involves a careful initial evaluation as described above here (see Fig. 2). If the syncope is believed to be arrhythmic, and the history is not highly suggestive of neurocardiogenic syncope, further evaluation is undertaken. If the initial evaluation suggests the presence of underlying heart disease, an aggressive approach is chosen, and the patient is evaluated by EPS. If there is no evidence of underlying heart disease, we generally proceed with ambulatory monitoring using a loop recorder. If the patient’s symptoms are frequent, we begin with an external loop recorder; if they are infrequent, we start with an ILR.

**Ambulatory Monitoring for Other Symptoms**

Ambulatory monitoring may occasionally be considered for symptoms other than palpitations or syncope, to “rule out” arrhythmia as a cause for chest pain, diaphoresis, dyspnea, or fatigue. In a retrospective analysis of 729 loop recorder reports, we found no diagnostic yield for studies ordered for this indication. As a result, we do not generally recommend ambulatory monitoring for symptoms that are not highly suggestive of arrhythmia. Likewise, the recently published American College of Cardiology/American Heart Association (ACC/AHA) guidelines for ambulatory electrocardiography list unexplained, episodic shortness of breath, fatigue, or chest pain as a class IIIB indication for ambulatory monitoring, or one for which efficacy is not well established.

---

**Fig. 2.** The evaluation of arrhythmic syncope. Adapted from Zimetbaum et al. (10).
Other Noninvasive Diagnostic Tests

Ambulatory monitoring is the mainstay of the noninvasive diagnosis of symptomatic arrhythmias. However, in certain situations other tests may provide added information. Exercise testing can be useful in the evaluation of patients who present with symptoms during or after exercise. Exercise on a treadmill may provoke a patient’s clinical symptoms, and in this case they can be correlated with the obtained rhythm strip. This is particularly useful when the clinical suspicion of a dangerous arrhythmia is not high enough to warrant initial evaluation by EPS, but either the patient or physician feels uncomfortable reinstating an exercise regimen prior to a trial of observed exercise in a controlled setting. In other situations, the use of an event recorder during daily exercise may accomplish the same goals as formal exercise testing.

Tilt table testing can be used to provoke neurocardiogenic syncope, and may be useful in the evaluation of patients with syncope. A test is considered positive if syncope occurs with associated hypotension or bradycardia (21). A positive result may be particularly convincing if a patient reports reproduction of his clinical symptoms during the test. Recently there has been concern about frequent false-positive results in tilt table testing, with some studies finding the specificity of the test to be as low as 50% (22). Kapoor et al. reviewed 23 studies of patients undergoing tilt table testing, and found that specificity varied widely, but seemed to decrease with an increasing tilt angle, and with the use of isoproterenol (23). Reproducibility of positive results varied from 71–87% when tilt table testing was reported after 3 d to 6 wk (23). Because of the relatively low specificity and reproducibility of tilt table testing, and the fact that a diagnosis of neurocardiogenic syncope may not result in specific treatment, tilt table testing is not appropriate for every patient with syncope. Recent ACC guidelines (21) state that tilt table testing is indicated in the evaluation of patients with recurrent or high-risk syncope, who have no underlying heart disease or have had other causes of syncope excluded by appropriate testing. In addition, tilt testing is warranted in the evaluation of recurrent exercise-induced syncope after structural heart disease has been excluded (21).

NONINVASIVE RISK STRATIFICATION AND SURVEILLANCE FOR ASYMPTOMATIC ARRHYTHMIAS

The noninvasive determination of a patient’s risk for developing life-threatening ventricular arrhythmias may be approached using traditional ambulatory monitoring or one of several newer techniques. Holter monitoring for asymptomatic ventricular ectopy has been used in the evaluation of patients with various forms of underlying heart disease, including coronary artery disease (CAD), dilated cardiomyopathy, hypertrophic cardiomyopathy, congenital heart disease, and primary electrophysiologic abnormalities such as congenital heart block and LQTS.

Post-Myocardial Infarction

Patients with nonsustained ventricular tachycardia (NSVT) and left ventricular dysfunction following MI have a 2-yr rate of up to 30% for sudden death (24–27). The Multicenter Automatic Defibrillator Implantation Trial (MADIT) demonstrated significantly improved survival among CAD patients with left ventricular dysfunction, NSVT, and inducible, drug-unresponsive VT who were treated with ICDs (28). More
recently, the Multicenter Unsustained Tachycardia Trial (MUSTT) found that a similar group of patients treated with electrophysiology (EP)-guided therapy (antiarrhythmic medication or ICDs) had decreased mortality compared to those treated with traditional therapy (29). This benefit was entirely attributable to the use of ICDs. These studies, which demonstrate a clear benefit associated with the use of ICDs in the treatment of certain post-MI patients with left ventricular dysfunction, raise the question of whether all such patients should undergo routine ambulatory monitoring to screen for NSVT. Such monitoring would place an enormous burden on the health care system (28,30). It is not clear how many patients enrolled in MADIT and MUSTT were identified by routine ambulatory monitoring. In addition, the optimal timing of initial screening and interval follow-up has not been defined. For these reasons, there are not currently guidelines recommending routine ambulatory monitoring in post-MI patients (9).

**Dilated Cardiomyopathy/Congestive Heart Failure**

Nonsustained VT can be identified by Holter monitoring in more than 50% of patients with idiopathic dilated cardiomyopathy (31–34). Reports differ as to whether NSVT has any prognostic implication in these patients. Several studies have examined the use of empiric antiarrhythmic therapy in patients with cardiomyopathy, and have shown no consistent benefit (31,33,35–37). The presence of CHF clearly increases the risk of sudden death in patients with dilated cardiomyopathy (38–41). There is conflicting evidence as to whether NSVT further increases the mortality risk in this population. In the GESICA study (42), patients with cardiomyopathy, CHF, and NSVT had a 24% 2-yr mortality as compared to a 9% 2-yr mortality among patients without NSVT. In the CHF STAT study (43), 80% of patients with primarily nonischemic cardiomyopathy and CHF had NSVT. In this study, nonsustained VT was not found to be an independent predictor of mortality. Finally, there is no evidence that the use of antiarrhythmic medication to decrease NSVT in this population leads to improved survival (44). Thus routine ambulatory monitoring is not recommended in adults with dilated cardiomyopathy with or without CHF (9). Children with dilated cardiomyopathy are believed to have a higher risk of sudden death than adults, and periodic Holter monitoring is often recommended. Dilated cardiomyopathy is a class I indication for screening Holter monitoring in the pediatric population, according to the most recent ACC/AHA guidelines (9).

**Hypertrophic Cardiomyopathy**

Patients with HOCM are at risk for sudden death; yet, predicting which individuals have the highest risk has proven difficult. Established risk factors in this population include history of syncope and history of sudden death in a first-degree relative (45). NSVT was previously believed to be prognostically important in these patients, and guidelines once advocated routine ambulatory monitoring of patients with HOCM (46). Several subsequent studies found that NSVT was not an independent predictor of death in this population (47–49). Importantly, there is no evidence that antiarrhythmic treatment of patients with HOCM and NSVT has any effect on outcome. Maron et al. again raised the issue of screening for NSVT in their recent retrospective analysis of HOCM patients who had been deemed high-risk and treated with ICDs (50). Although there remains some controversy as to whether adults with HOCM should undergo screening for NSVT, the most recent ACC/AHA guidelines for ambulatory monitoring
do not recommend routine Holter monitoring in this population (9). Hypertrophic HOCM, like dilated cardiomyopathy, is associated with a higher sudden death rate in children than in adults (51), probably because patients who survive to adulthood are selected survivors. Periodic Holter monitoring of children with HOCM is recommended (9).

### Congenital Heart Disease

Patients with complex congenital heart disease who have undergone surgical correction are at risk for ventricular arrhythmias as well as for conduction abnormalities that may lead to heart block (52). It is unclear whether NSVT is prognostically significant in this population (53–55), and there is no data supporting treatment of nonsustained VT once it is discovered. Although some experienced clinicians recommend routine Holter monitoring of patients with corrected tetralogy of Fallot (56), the most recent ACC/AHA guidelines classify asymptomatic corrected congenital heart disease as a class IIB indication for routine monitoring (usefulness not well-established) (9).

It must be emphasized that although routine monitoring of asymptomatic patients with the diseases discussed here is not currently recommended, these patients are at increased risk of dangerous arrhythmias. Palpitations, presyncope, and syncope should be taken very seriously in these populations and should prompt evaluation either with an event recorder or by EPS, depending on the clinical scenario.

### Patients With Congenital Electrophysiologic Abnormalities

Patients with congenital LQTS and congenital heart block are at increased risk for arrhythmic death. Patients with LQTS may develop polymorphic VT (torsades de pointes), causing syncope or sudden death (57,58). These patients may benefit from treatment with beta-blockers and/or implantation of permanent pacemakers or ICDs. Patients who have a family history of sudden death or a personal history of syncope are at particularly high risk for sudden death. Ambulatory monitoring can be used to identify patients with significant bradycardia, periods of QT prolongation, or asymptomatic nonsustained polymorphic VT, which may put patients at increased risk for sudden death (59,60). As a result, many clinicians use annual or biannual Holter monitoring to screen patients with LQTS. There is no available data to support this practice. Evaluation of asymptomatic pediatric patients with known or suspected LQTS is a class I indication for Holter monitoring, according to the most recent ACC/AHA guidelines (9). Whether monitoring should be routinely undertaken in asymptomatic adults, who are likely to be selected survivors, is less certain.

Congenital heart block places patients at risk for left ventricular dysfunction, mitral regurgitation resulting from left ventricular dilation, and sudden death. The likelihood of these complications is diminished by ventricular pacing (61). A recent study showed that in 27 asymptomatic patients followed for 8 ± 3 yr, the presence of a daytime heart rate of less than 50 beats per min, or evidence of an unstable junctional escape (junctional exit block or ventricular arrhythmias) predicted an increased likelihood of complications (62). Another recent study followed 102 patients for up to 30 yr (61). In this study, ventricular response rate decreased with age, with associated increases in ventricular ectopy and worsening of left ventricular function and mitral regurgitation. Only a prolonged corrected QT interval was found to be predictive of syncope. Our practice is to screen these patients yearly by Holter monitor to evaluate their ventricular response,
corrected QT interval, and ventricular ectopic activity. We recommend placement of a permanent pacemaker when patients develop symptomatic bradycardia, exercise intolerance, QT prolongation, frequent ventricular ectopy, or a wide complex escape rhythm. This practice differs from that outlined in the recent ACC/AHA pacing guidelines (63) only because we include QT prolongation among absolute indications for pacing in this population. Holter monitoring is limited by the brief period of time during which the monitor is worn. Consequently, episodic QT prolongation, severe bradycardia, or NSVT may be missed. Patients may develop complications of congenital heart block despite the absence of detectable risk factors, partly because periodic Holter monitoring does not adequately disclose their day-to-day rhythm. As in patients with structural heart disease, palpitations, presyncope and syncope must be taken very seriously in patients who have LQTS or congenital heart block. These conditions should be evaluated by event monitor or invasive testing, depending on the clinical setting.

OTHER TECHNIQUES FOR RISK STRATIFICATION

Several newer techniques, like Holter monitoring, may be useful in predicting the risk of ventricular arrhythmias. These include the signal-averaged ECG (SAECG), heart-rate variability (HRV), T-wave alternans (TWA), and QT dispersion (QTD). There is data to suggest that each of these methods can independently predict risk in certain populations; however, it is not yet clear how information obtained from their use should be clinically applied.

Signal-Averaged ECG

The signal-averaged ECG was developed to identify the existence of substrate for reentrant VT. The goal of the SAECG is to detect late potentials, which represent low amplitude, high-frequency electrical activity occurring in the terminal portion of the QRS. Late potentials are felt to be caused by slow conduction and delayed activation of tissue, and thus to identify the presence of substrate that could potentially cause reentrant ventricular arrhythmias. Because late potentials are very low in amplitude, they are obscured by noise on a regular twelve-lead ECG. Signal averaging improves the signal-to-noise ratio through temporal or spatial averaging, allowing the detection of low-amplitude electrical activity. Unfortunately, the use of this technique is limited because time-domain analysis—the method of analysis most often used—cannot be applied in patients with bundle-branch block or significant intraventricular conduction delay. Atrial fibrillation (AF) and flutter have also been shown to diminish the predictive accuracy of the SAECG (64).

There is strong evidence that the SAECG can identify post-MI patients at risk for ventricular arrhythmias (64–70). There is much less data available on its use in other populations (70). Based on data compiled from 15 studies, 8–48% of post-MI patients who have late potentials detected on SAECG will ultimately experience sustained VT or sudden death (70). A positive SAECG in this population has a positive predictive accuracy of 14–29% when used to predict major arrhythmic events, and a normal SAECG has a negative predictive accuracy of 95–99% (70). Although the presence of late potentials is an independent predictor of major arrhythmic events in the post-MI population, the positive predictive accuracy of the SAECG is not high enough to base clinical decisions regarding treatment of individual patients on this information alone.
Eventually, the SAECG may be used in conjunction with other information to determine which post-MI patients may benefit from invasive evaluation. We do not currently obtain SAECGs on our post-MI patients, as there are no data to support basing management decisions on SAECG results.

**Heart-Rate Variability**

Heart-rate variability analysis is the evaluation of beat-to-beat variability of the R-R interval. Data is obtained from digitized Holter tracings. HRV is believed to be largely a reflection of autonomic tone. There is evidence for a correlation between the risk of sudden cardiac death and autonomic tone, with relatively decreased vagal activity indicating increased susceptibility to lethal arrhythmias. Following MI, HRV is decreased. It is lowest soon after MI, and begins to recover within several weeks. HRV is an independent risk factor for mortality post-MI. In 1987, Kleiger et al. demonstrated a 34% mortality over 4 yr among post-MI patients with depressed HRV, as compared to a 12% mortality among patients with normal HRV. Decreased HRV post-MI has been shown to predict increased mortality, and to specifically predict sudden cardiac death and sustained VT. Although diminished HRV post-MI is an independent risk factor for ventricular arrhythmias and mortality, its predictive accuracy when used alone is low. Information regarding HRV can be used in conjunction with other tests to increase the accuracy of risk stratification post-MI. Bigger et al. and Farrell et al. each demonstrated that the use of multiple risk stratifiers such as left ventricular ejection fraction (LVEF), NSVT, SAECG, and HRV in combination could result in positive predictive accuracy of approx 50%. Thus, HRV analysis may eventually be incorporated into protocols for risk stratification post-MI. It has not yet been determined how HRV analysis should be used in directing therapy to justify its routine use in the post-MI population. There is conflicting data on the relationship between HRV and arrhythmic events in patients with underlying heart disease other than history of MI. Thus, HRV analysis is not recommended in risk stratification of patients with dilated or hypertrophic cardiomyopathy or other underlying disease.

**Microvolt T-Wave Alternans**

Electrical alternans is the variability of the ECG waveform on alternate beats. Repolarization alternans (ST- and T-wave alternans) shows promise as a risk stratifier for ventricular arrhythmias associated with various conditions. T-wave alternans, a marker of heterogeneous electrical repolarization, has been observed on ECG tracings just prior to the onset of ventricular fibrillation (VF) in acutely ischemic animals and humans. In most cases, however, TWA is too subtle to be seen on a basic surface ECG. Recently, techniques have become available to allow visualization of microvolt TWA, which would otherwise be undetectable. TWA is best measured during exercise or atrial pacing with a target heart rate of approx 100 beats per minute (BPM). Slower heart rates and ectopic beats can obscure the detection of alternans. In 1994, Rosenbaum et al. studied TWA during atrial pacing in 83 patients with a variety of underlying conditions who were undergoing EPS. Alternans was predictive of inducibility of VT at EPS, and was also an independent risk factor for spontaneous VT, VF, or sudden cardiac death during 20 mo of follow-up. The relative risk for major arrhythmic events was 9.0 in patients with detectable TWA as compared to those...
without TWA. Other small-scale studies have similarly demonstrated TWA to be predictive of ventricular arrhythmias (88). The clinical implication of TWA has also been evaluated among groups of patients with specific underlying conditions. In patients with HOCM, exercise-induced TWA has been shown to correlate with the presence of traditional risk factors such as a history of syncope or family history of sudden death (89). There is no information yet as to whether exercise-induced TWA will prove to be an independent predictor for ventricular arrhythmias among these patients. In a pilot study of 70 patients with CHF, the presence of TWA at rest or during exercise appeared to be a strong marker for sustained VT, VF arrest, or death during a 1-yr follow-up (82). Although the measurement of TWA is a promising technique for predicting patients’ propensity for ventricular arrhythmias, there is no available information yet as to which patients will benefit from use of this technique, or as to whether patient management should be altered based on a positive test. Thus, we do not currently measure TWA for clinical purposes. In the future, TWA may be used in combination with other markers to improve accuracy in the prediction of ventricular arrhythmias in certain patient populations in order to determine which patients warrant further testing or treatment.

**QT Dispersion**

QT interval dispersion (QTD) is a measure of variability of the QT interval, which, like TWA, is a marker of the heterogeneity of ventricular repolarization. The measurement of QTD is made simply by taking the difference between the longest and shortest QT intervals on a 12-lead ECG. QT dispersion has been found an independent predictor of cardiovascular mortality in two large studies, one examining an elderly population in Rotterdam (90), and the other examining middle-aged and elderly native Americans (the Strong Heart study) (91). In each study, abnormal QTD was associated with an approximately twofold increase in the risk of cardiovascular mortality. The research of de Bruyne et al. also demonstrated a 1.4-fold increase in all cause mortality among patients with abnormal QTD (90). In Okin et al., a corrected QT interval was also an independent predictor of cardiovascular mortality, and corrected QT interval and QTD were additively predictive (91). These large studies examined populations in which the majority of patients had no known heart disease. In addition, QTD seems to be useful in risk stratification of patients with LQTS (92). When other groups of patients who have cardiac disease which places them at risk for sudden death have been evaluated, the results have been variable. In 1994, a retrospective case-control study of patients with CAD showed an association between an abnormal QTD and sudden death (93). Subsequent prospective studies have differed as to whether QTD is predictive of cardiovascular mortality post-MI (94,95). In the study by Spargias et al., although QTD was found to be predictive, it was not a very sensitive or specific marker. Studies have also differed as to whether QTD is of prognostic value in patients with CHF. Barr et al. (96) showed an association between abnormal QTD and sudden death in patients with CHF. However, a larger study (97) failed to demonstrate an independent relationship between QTD and all causes of mortality or sudden death after multivariate analysis. In patients with hypertrophic cardiomyopathy, QTD does not seem to correlate with any of the known risk factors for sudden death (98). Thus, although QTD is predictive of cardiovascular death in a wide population, its clinical usefulness as a risk stratifier in diseases other than LQTS has not yet been demonstrated.
INDICATIONS FOR EPS

When there is high suspicion for a serious arrhythmia, or when an arrhythmia has been diagnosed, but further characterization or catheter-based treatment is desired, invasive testing with an EPS is warranted. Based on the data from MADIT (28) and MUSTT (29), EPS is also indicated for risk stratification in patients who have CAD, LVEF less than 40%, and nonsustained VT occurring more than 96 h after an ischemic event or revascularization. During an EPS, intracardiac recordings are made to document conduction intervals and activation patterns, and programmed electrical stimulation is delivered to attempt reproduction of clinical arrhythmias. The information obtained can be useful in the diagnosis of both bradyarrhythmias and tachyarrhythmias. In symptomatic patients with suspected sinus node disease, information regarding sinus node function can be obtained by measuring sinus node recovery time (99) or sinoatrial conduction time (100,101). In patients with syncope or presyncope and evidence of conduction system disease on ECG, measurement of the HV interval can be used to estimate the likelihood of progression to a heart block (102–104). Electrical stimulation protocols targeting the atria and/or ventricles can be used for induction of supraventricular or ventricular tachyarrhythmias. Induction of a patient’s clinical arrhythmia in the electrophysiology lab enables study of its mechanism, and in some cases catheter ablation of the arrhythmia. Even when the arrhythmia is not ablatable, information obtained during EPS can be used to guide further therapy. In patients with a history of cardiac arrest, EPS can help to define the mechanism for the arrest. Most cardiac arrest patients should be treated with ICDs. Information gathered at EPS can help guide device selection and programming (105). Finally, as previously mentioned, EPS is useful in risk stratification of post-MI patients with poor left ventricular function and nonsustained VT, and in determining which patients in this category should be treated with ICDs (28,29). Detailed information regarding EPS is beyond the scope of this discussion, but can be found elsewhere (106). Some specific indications for EPS based on the 1995 ACC/AHA guidelines for clinical intracardiac electrophysiological and catheter ablation procedures (107) are listed in Table 4.

FUTURE STRATEGIES

Emerging technologies will continue to change the way diagnoses are made in electrophysiology. In particular, advances in ambulatory monitoring will facilitate the diagnosis of arrhythmia in the outpatient setting. As mentioned here, recent technology has allowed loop recorders to self-trigger in the setting of marked changes in heart rate. This feature will likely improve the diagnostic yield of ILRs used in the evaluation of syncope. Systems capable of recording and transmitting blood pressure and oximetry data in addition to ECG data in the ambulatory setting will eventually become available, and will allow more comprehensive monitoring. These systems may provide physicians with an improved understanding of the clinical significance of detected arrhythmias, and will enable more comprehensive monitoring of known disease and prescribed therapy. Increasing information regarding the clinical utility of currently available technology will also change the evaluation of arrhythmias. Emerging techniques for risk stratification such as heart-rate variability, TWA, QTD, and the SAECG may be used routinely once the optimal application of these techniques is understood.
Table 4
Indications for Electrophysiology Study (EPS)

-Class I indications for EPS-

1. Evaluation of suspected sinus node dysfunction in symptomatic patients
2. Evaluation of suspected His-Purkinje system block in symptomatic patients
3. Evaluation of patients with bifascicular block and unexplained symptoms consistent with arrhythmia
4. Frequent or poorly tolerated SVT not adequately controlled with medication or with patient preference for ablation therapy
5. Wide QRS tachycardia when the diagnosis is unclear or information obtained from EPS will help guide therapy
6. WPW in patients undergoing evaluation for accessory pathway ablation with symptomatic tachycardia, or history of unexplained syncope or cardiac arrest
7. Unexplained syncope in the setting of structural heart disease
8. Survivors of cardiac arrest other than in the setting of acute Q-wave MI
9. Palpitations preceding syncope
10. Palpitations with a documented tachycardia by pulse with no ECG documentation of rhythm
11. Patients with documented ventricular or supraventricular tachycardias in whom EPS findings will help guide medical therapy or programming of ICDs
12. Nonsustained VT occurring >96 h post-MI or revascularization in patients with CAD and EF <40%*

SVT = supraventricular tachycardia; WPW = Wolff-Parkinson-White syndrome; MI = myocardial infarction; ICD = implantable cardioverter-defibrillator; CAD = coronary artery disease; LVEF = left ventricular ejection fraction. Guidelines are adapted from the 1995 ACC/AHA. Guidelines for clinical intracardiac electrophysiological and catheter ablation procedures (101). *This recommendation is based on recent data (28,29) and is not included in the 1995 ACC/AHA guidelines.

REFERENCES


88. Estes MNA, Zipes DP, el-Sherif N, et al. Electrical alternans during rest and exercise as a predictor of vulnerability to ventricular arrhythmias. J Am Coll Cardiol 1995; Special Issue:409A.


Management of Cardiac Arrhythmias
Ganz, L.I. (Ed.)
2002, XVI, 527 p. 6 illus. in color., Hardcover
A product of Humana Press