SECTION 2
CARDIOVASCULAR DISORDERS

CHAPTER 13

Cardiovascular Testing

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KEY CONCEPTS

1. A careful patient history and physical examination are extremely important in diagnosing cardiovascular disease and should be done prior to any test.
2. Heart sounds and heart murmurs are important in identifying heart valve abnormalities and other structural cardiac defects.
3. Elevated jugular venous pressure is an important sign of heart failure and may be used to assess severity and response to therapy.
4. Electrocardiography is useful for determining rhythm disturbances (tachy- or bradyarrhythmias) and changes in ventricular and atrial size.
5. Exercise stress testing provides important information concerning the likelihood and severity of coronary artery disease; changes in the electrocardiogram, blood pressure, and heart rate are used to assess the response to exercise.
6. Cardiac catheterization and angiography are used to assess coronary anatomy and ventricular performance.
7. Echocardiography is used to assess valve structure and function as well as ventricular wall motion; transesophogeal echocardiography is more sensitive for detecting thrombus and vegetations than transthoracic echocardiography.
8. Radionuclides such as technetium-99m and thallium-201 are used to assess wall motion and myocardial viability in patients with coronary artery disease and heart failure.
9. Pharmacologic stress testing is used when patients cannot perform physical exercise to assess the likelihood of coronary artery disease.

Learning objectives, review questions, and other resources can be found at **www.pharmacotherapyonline.com.**

Every 36 seconds 1 person dies from cardiovascular disease and each day about 2,500 people die in the United States. Cardiovascular disease exceeds the next four leading causes of death combined (cancer, lung disease, accidents, and diabetes).[1] Another important factor in cardiovascular disease is that greater than 60% of unexpected cardiac deaths occur *without* prior history of heart disease and 70% of patients having a myocardial infarction have coronary artery blockages of about 40% to 60% (Fig. 13–1).

Cardiovascular disease affects 71,300,000 Americans, with one-third being older than age 65 years based on the National Health and Nutrition Examination Survey.[2] The current increase in patients older than age 65 years with cardiovascular disease will undoubtedly generate a large financial burden on the economy and families. Adding to the increasing burden of cardiovascular disease is information from Centers for Disease Control and Prevention revealing a marked increase in the number of patients with obesity; additionally, the projected 2050 growth rate in both obesity and diabetes is staggering. In 1997, the percentage of patient with obesity was approximately 19.5% of the U.S. population, and in 2004 it was found to have increased by 25% (24.3%). Along with this increase in obesity there was a 30% increase in diabetes from 5.3% to 6.9% over this same period of time.[3] The rise of obesity and diabetes will undoubtedly lead to increases in heart disease prevalence.

Another area of concern in cardiovascular disease is illustrated by the Framingham Heart Study, which has followed patients for more than 40 years and found that the average annual rate of first major cardiovascular events increase significantly with age. Patients ages 35 to 44 years were found to have 7 major cardiovascular events per 1,000 men and to increase to 68 per 1,000 men by age 85 years, a 9-fold increase.[4]

In summary, one of the most important pieces of information that patients need to know is that lifestyle changes, that is, healthy-smart eating with reasonable caloric intake and frequent exercise, are major keys to a productive healthy life. The importance of lifestyle in saving lives is well illustrated from a recent study by Chiuve et al., which studied 42,847 men in the Health Professionals Follow-up Study (cohort) who were 40 to 75 years of age and free of disease in 1986.[5] The healthy lifestyle was defined as no smoking, body mass index <25 kg/m^2, moderate to vigorous activity >30 min/day, moderate alcohol consumption (5 to 30 g/day), and a healthy diet score. Tracking nonfatal myocardial infarctions and fatal coronary heart disease using a multivariate-adjusted Cox proportional hazards model, men complying with these five lifestyle factors had a

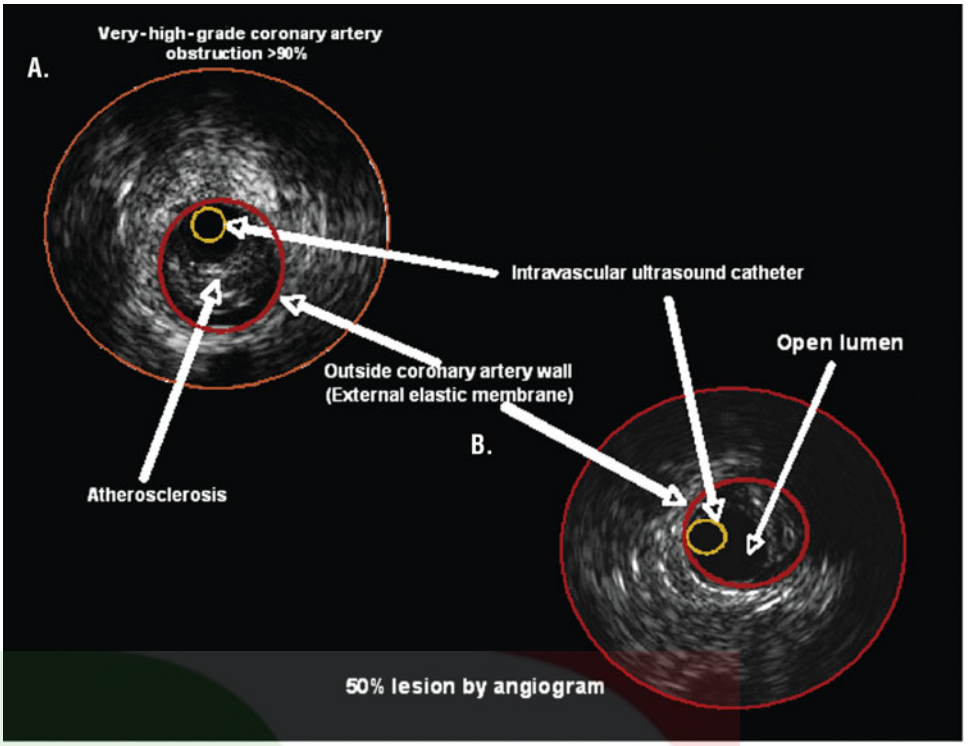

FIGURE 13-1. Intravascular ultrasound (IVUS) of a coronary artery. *A.* High-grade obstruction which on angiogram was thought to be only approximately 50% stenotic. *B.* Another coronary artery segment with 50% stenosis but more prone to rupture.

lower risk of coronary heart disease (relative risk: 0.13; 95% confidence interval [CI]: 0.09 to 0.19) compared with men who were at low risk with no lifestyle factors. Using population-attributable risk calculations (proportion of cases within the population that could have been avoided had all the men adhered to the low-risk lifestyle) adherence to five lifestyle changes could prevent 62% of men from having a coronary event. If patients were taking medication for hypertension or hypercholesterolemia they still would have a 57% reduction ([95% confidence interval (CI) 0.07 to 0.43]).

THE HISTORY

A comprehensive history is the cornerstone of a cardiovascular workup. The value of the history depends on the clinician's ability to elicit relevant information. Family history is very important because of the genetic links involved in many cardiovascular diseases from early myocardial infarction, strokes, diabetes, valvular heart disease, hypertension and familial hypercholesterolemia. The elements of a comprehensive history include the chief complaint, present problems, past medical history, review of systems, and social history.

The chief complaint needs to be narrowed down and focused if possible. Usually the chief complaint/main concern is a short brief statement as to the reason why the patient seeks medical care (get to the point). The duration of the chief complaint is important, along with any prior history of the same problem, the severity of the problem, and whether there are any limitations on the patient's daily activities. Other areas that need to be addressed are character, any types of motion or other things that increase or decrease the discomfort, any association with additional signs or symptoms, and whether the discomfort is increasing in frequency or duration. All these and many other matters need to be considered as the clinician does the intake interview with a new patient.

CARDIOVASCULAR HISTORY

1 Ischemic heart disease is the most common cardiovascular disease seen in clinical practice. A focus on chest pain history is very important. The clinical syndrome of angina is frequently described by patients as a discomfort from chest ache, pain, or pressure, to dull pain in the jaw, back, shoulder, or either arm. Many research studies have found that family/work stress or exertion brings on increased symptoms of angina and rest or nitroglycerin frequently relieves it.[6] Another important consideration when one considers angina is that in addition to epicardial large-vessel coronary artery disease (CAD), angina can develop in patients with valvular heart disease, obstructive cardiomyopathies, and hypertension. Symptoms of angina can occur in patients with noncardiac conditions such as gastrointestinal (esophageal), chest wall, or pulmonary disease (see Chap. 17). Angina does not necessarily relate to the severity or extent of CAD obstruction. Angina that is increasing in severity, longer in duration or occurring at rest is consistent with unstable angina and should be evaluated immediately.[7]

Initial evaluation of chest pain requires a good history and physical examination.[8,9] The quality of chest pain, its location and duration, and factors that provoke or relieve the chest pain are important elements. Rarely do patients with ischemic heart disease describe their pain as sharp or stabbing. Commonly, patients state they do not have chest pain but a heaviness or pressure in the chest. Ischemic chest pain typically lasts only a few minutes and is generally brought on by exertion or emotional stress, and is commonly relieved by rest or nitroglycerin. Based on the history, classify the patient's symptoms. Three characteristics to consider are (a) whether the substernal chest discomfort has a classic quality and duration that is (b) provoked by exertion or emotional stress and (c) relieved by rest or nitroglycerin. If all three of these conditions are met, then the patient has classical angina; if only two of these conditions exist, the pain is considered to be atypical or probably angina; and if none are met, it is considered to be noncardiac chest pain. It is equally important that the patient inform the healthcare professional that the discomfort the patient is experiencing, which could be atypical, is the patient's "angina equivalent." Important information when taking a history of patients with angina is being aware of the grading of angina pectoris by the Canadian Cardiovascular Society (see Chap. 17).

It is important in an ischemic chest to differentiate angina from acute coronary syndrome. Acute coronary syndrome is more frequent, dramatic, and severe (see Chap. 18).

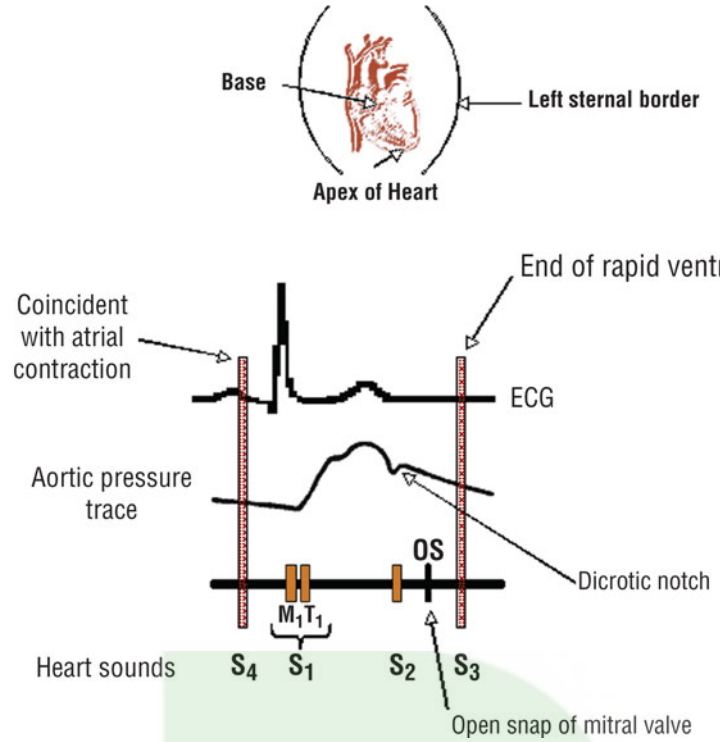

FIGURE 13-2. Correlation of the electrocardiogram (ECG) with an aortic pressure tracing and heart sounds. Normal heart sounds are S_1 and S_2; S_3 and S_4 are abnormal, as is an opening snap (OS), which is heard with mitral stenosis. S_1 may be split in some conditions (M_1, mitral; T_1, tricuspid.)

PHYSICAL EXAMINATION

The cardiovascular physical examination is divided into four categories:

1. Global examination of the patient for signs of cardiovascular disease (CVD) and a review of all body systems.
2. Observation and assessment of physical findings (e.g., jugular venous pressure).
3. Measurement of parameters of CVD function (pulse, blood pressure).
4. Auscultation, percussion, and palpation of the chest and related cardiac structures.

The initial part of the physical examination consists of inspection of the precordium for normal patterns of rise and fall and any abnormal markings or shape. The chest is then palpated for normal pulses, thrills (humming vibrations like the throat of a purring cat), and heaves (lifting of the chest wall). Thrills may indicate murmurs, and heaves may indicate enlargement of one of the heart chambers or an abnormal vessel such as an aneurysm. The apical pulse (also known as the *point of maximum impulse*) is helpful to estimate heart size and rotation. This is usually located in the fifth intercostal space in the midsternal line and radiates in an arc of 1 to 2 cm. Heightened intensity and/or displacement laterally suggests left or right ventricle enlargement, and reduced intensity may be a sign of fluid overload or pericardial effusion. Factors such as obesity, large breasts, muscularity, and pulmonary disease can interfere with determination of the apical pulse. The carotid pulse is examined for its intensity and, concurrently with the apical pulse, for concordance within the cardiac cycle. Decreased carotid pulsations may be a result of reduced stroke volume or atherosclerotic narrowing of the carotid artery.

Important physical correlations need to be carefully noted, as shown in Figs. 13–2 and 13–3. These critical associations are basic facts needed to understanding the physical examination of the human heart.

HEART SOUNDS

2 Auscultation with a stethoscope is used to characterize heart sounds. Auscultation is conducted in a systematic manner to ensure that all sites where normal and abnormal sounds are heard are reviewed. Respiratory pattern, various maneuvers such as handgrip and the Valsalva maneuver, sitting versus standing, and pharmacologic agents (e.g., amyl nitrate) also may be used in the evaluation of heart sounds to accentuate or diminish the intensity of these sounds. Auscultation is an acquired art and requires considerable practice to become competent.

The normal heart sounds include S_1 (first heart sound—closure of the mitral and tricuspid valves) and S_2 (second heart sound—aortic and pulmonic valves). Normally the second heart sound becomes split during inspiration because of delayed closure of the pulmonic valve (prolongation of right ventricle systole secondary to an increase in venous return) or because of an inspiratory decrease in impedance of the pulmonary bed.

Other sounds, such as S_3 (third heart sound) and S_4 (fourth heart sound) and murmurs, are not considered normal but provide important diagnostic information. Initially, the patient is examined lying partially on the left side to accentuate left-sided S_3 and S_4 and mitral murmurs, with the bell on the point of maximum impulse. To identify S_1 and S_2, the patient can be examined lying or sitting. The other areas that are auscultated are the apex or base of the heart (mitral sounds), the lower left sternal border (tricuspid sounds), the second left interspace (pulmonic sounds), and the second right interspace (aortic sounds). At each of these locations, S_1 and S_2 should be heard (Fig. 13–4).

Heart sounds are characterized by location, pitch, intensity, duration, and timing within the cardiac cycle. High-pitched sounds such as S_1 and S_2, murmurs of aortic and mitral regurgitation, and pericardial friction rubs are best heard with the diaphragm. The bell is preferred for low-pitched sounds such as S_3 and S_4. S_1 is heard as a click at the end of diastole and usually is synchronous with the apical pulse. The intensity of S_1 can be increased if systole begins

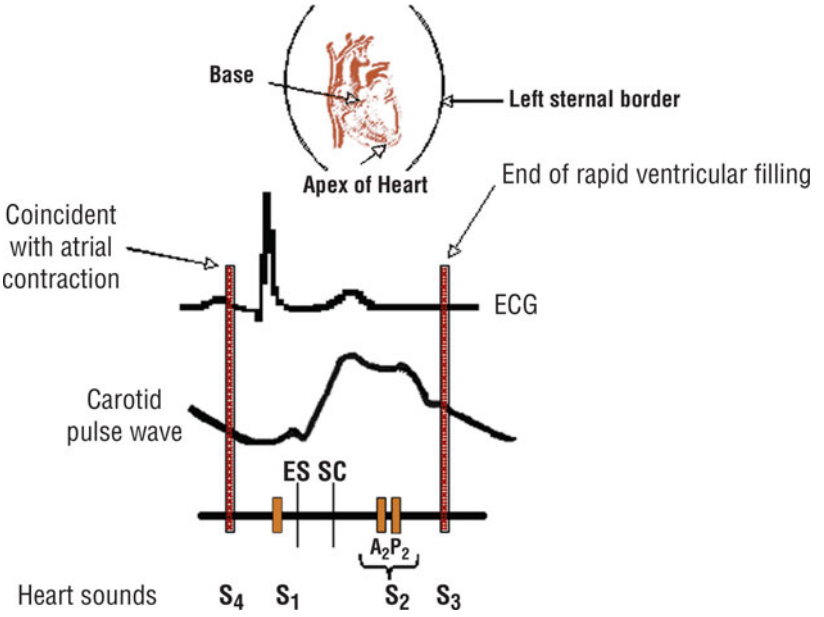

FIGURE 13-3. Correlation of the electrocardiogram (ECG) with a carotid pulse pressure tracing and heart sounds. A split S_2 is heard in some conditions (A_2, aortic; P_2, pulmonic).

prior to the mitral valve closing, which may occur in high-output states (e.g., exercise, tachycardia, anemia, or hyperthyroidism) and mitral valve stenosis. S_1 intensity is decreased in first-degree heart block, mitral regurgitation, states of reduced myocardial contractility (such as heart failure or coronary artery disease), obesity (difficult to hear), and systemic or pulmonary hypertension. S_2 is heard at the end of systole and is best heard at the tricuspid and mitral areas. Most of the sound arises from aortic valve closure. Heart sounds may be "spilt" if the two valves do not close synchronously. Physiologic splitting of S_1 or S_2 is accentuated by inspiration and may disappear with expiration. Splitting of S_2 creates a pulmonic (P_2) and aortic (A_2) sound. S_2 frequently is heard as a split sound and is most predominant at the height of inspiration. Although S_1 also may be split, this is often difficult to hear.

Pathologic splitting of S_2 during expiration is described as *wide splitting, fixed splitting,* and *paradoxical splitting* and may be indicative of both stenosis and regurgitation. With right-sided heart failure, right bundle-branch block, pulmonic stenosis, or atrial septal defects, S_2 may be split owing to delayed closure of the pulmonic valve. Fixed splitting of S_2 is associated with large atrial septal defects and right ventricular failure. Increased intensity of P_2 is seen in pulmonary hypertension and dilated pulmonary arteries and with atrial septal defects. Decreased or absent P_2 occurs with aging and in pulmonic stenosis. Extra heart sounds in systole include early systolic ejection sounds and clicks and midsystolic clicks. Early ejection sounds such as aortic or pulmonic ejection sounds often are associated with valvular disease. Midsystolic to late systolic clicks usually are a result of mitral valve prolapse. Mitral valve prolapse is best heard at or medial to the apex, but also may be heard at the left lower sternal border.

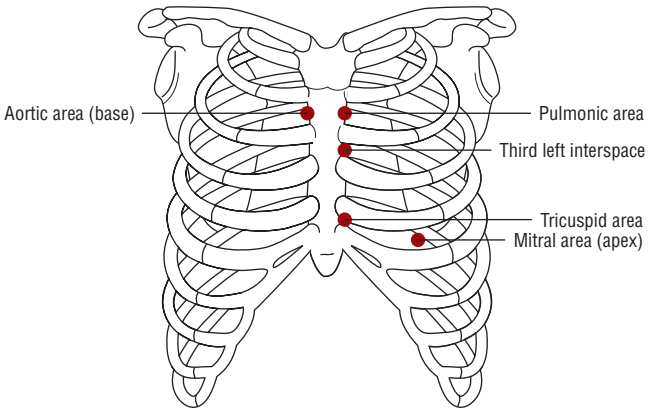

FIGURE 13-4. Schematic illustrations of topographic areas on the precordium for cardiac auscultation. Auscultatory areas do not correspond to anatomic locations of the valves but to the sites at which particular valves are heard best. *(Redrawn from Kinney MR, Packa DR, eds. Andreoli's Comprehensive Cardiac Care, 8th ed. St. Louis: Mosby, 1996, with permission.)*

The S_3 heart sound, or ventricular gallop, is an abnormal low-pitched sound usually heard at the apex of the heart. It is thought to be caused by rapid filling and stretching of the left ventricle when the left ventricle is somewhat noncompliant. This heart sound is characteristic of volume overloading, such as in congestive heart failure (especially left-sided heart failure), tricuspid or mitral valve insufficiency, and atrial and/or ventricular septal defects. A physiologic S_3 is heard commonly in children and may persist into young adulthood. Localization of S_3 is helpful for determining heart rotation within the chest cavity.

The S_4 diastolic sound is a dull, low-pitched postsystolic atrial gallop (rapid blood flow) usually caused by reduced ventricular compliance. It is best heard at the apex in the left lateral position. Like S_3, it occurs with reduced ventricular compliance and is present in conditions such as aortic stenosis, hypertension, hypertrophic cardiomyopathies, and coronary artery disease. It is less specific for congestive heart failure than S_3.

The frequency range of S_3 and S_4 is below 100 Hz and requires the bell of the stethoscope to be used most of the time. This should be lightly touched to the skin to obtain the best results.

HEART MURMURS

Murmurs are auditory vibrations heard on auscultation, and they occur because of turbulent blood flow within the heart chambers or through the valves.[10] They are classified by timing and duration within the cardiac cycle (systolic, diastolic, and continuous), location, intensity, shape (configuration or pattern), pitch (frequency), quality, and radiation (Table 13–1). It is important to first note where it is heard best and where it radiates for example from apex to left axilla. Using S_1 and S_2 as a marker for timing, ask yourself this

TABLE 13-1 Characteristics of Heart Sounds

Type of Murmur	Examples	Location	Pitch	Radiation	Quality
Midsystolic	Aortic stenosis	2nd RICS	Medium	Neck, left sternal border	Harsh
	Pulmonic stenosis	2nd and 3rd LICS	Medium	Left shoulder and neck	Harsh
	Hypertrophic cardiomyopathy	3rd and 4th LICS	Medium	Left sternal border to apex	Harsh
Pansystolic	Mitral regurgitation	Apex	Medium to high	Left axilla	Blowing
	Tricuspid regurgitation	Lower left sternal border	Medium	Right sternum, xiphoid	Blowing
	Ventricular septal defect	3rd, 4th, and 5th LICS	High		Often harsh
Diastolic	Aortic regurgitation	2nd to 4th LICS	High	Apex	Blowing
	Mitral stenosis	Apex	Low	Little or none	

LICS, left intercostal space; RICS, right intercostal space.

question: Does the murmur occur in systole or diastole? Next carefully listen to see if the murmur completely fills that phase of the systolic cycle (i.e., holosystolic), or if it has discrete start and end points. Murmurs that occur after second heart sound are considered diastolic murmurs and most commonly relate to mitral stenosis or aortic insufficiency; however there are many other possibilities. Regurgitant murmurs for example, mitral valve insufficiency, usually fill the entire phase, while ejection murmurs, like aortic stenosis, usually have discrete beginning and end points within systole (between S_1 and S_2). Next the shape and quality of the murmur should be described along with descriptive terms about the murmur, that is, blowing, harsh, rumbling, machinery, musical, and others.

Some murmurs are considered innocent or physiologic and result from rapid, turbulent flow of blood into the left ventricle during atrial systole and through the aorta during ventricular systole. Fever, anxiety, anemia, hyperthyroidism, and pregnancy exacerbate physiologic murmurs, and these murmurs need to be distinguished from those suggestive of valvular abnormalities. Another important consideration is the grading of heart murmurs. The intensity or loudness of a murmur is graded using a scale of I to VI. Below are the different grades.

- I — Lowest intensity; difficult to hear even by expert listeners
- II — Low intensity, but usually audible by all listeners
- III — Medium intensity; easy to hear even by inexperienced listeners but without a palpable thrill
- IV — Medium intensity with a palpable thrill
- V — Loud intensity with a palpable thrill; audible even with the stethoscope placed on the chest with the edge of the diaphragm
- VI — Loudest intensity with a palpable thrill; audible even with the stethoscope raised above the chest

Multiple factors determine the grade, which includes the amount of blood ejected across a valve, severity of the lesion, and chest anatomy.

Systolic murmurs begin with or after S_1 and end at or before S_2, depending on the origin of the murmur. They are classified based on time of onset and termination within systole: midsystolic, holosystolic (pansystolic), early, or late. Some examples of pathologic midsystolic murmurs are pulmonic stenosis, aortic stenosis, and hypertrophic cardiomyopathy. Midsystolic murmurs may include obstruction to ventricular outflow (a common example is aortic stenosis; Fig. 13–5), dilation of the aortic root or pulmonary trunk, an increased flow in the great arteries, anatomic changes in the semilunar valves, and some forms of regurgitation. Holosystolic murmurs occur when blood flows from a chamber of higher pressure to one of lower pressure, such as with mitral or tricuspid regurgitation and ventricular septal defects. Early systolic murmurs can be decrescendo and may be associated with ventricular septal defects, mitral regurgitation, or tricuspid regurgitation. A late systolic murmur preceded by one or more midsystolic to late systolic clicks is the hallmark of mitral valve

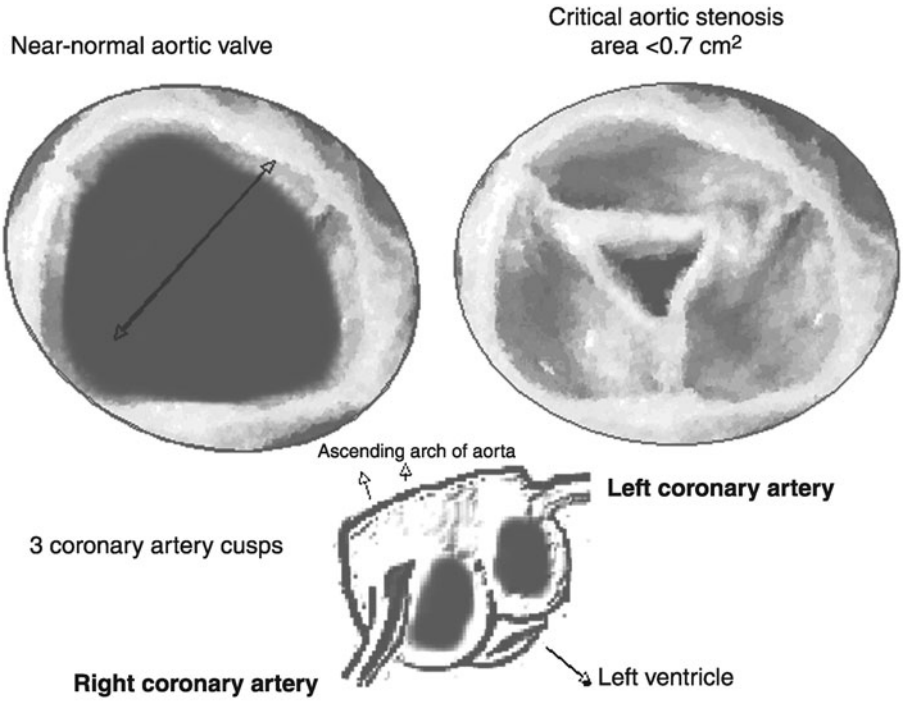

FIGURE 13-5. Aortic valve anatomy. A near-normal aortic valve is shown on the left and critical stenosis is shown on the right. The relationship of the aortic valve to coronary artery anatomy is shown below.

prolapse, which classically moves during changes in ventricular volume. Atherosclerotic obstruction of the carotid, subclavicular, or iliofemoral artery can give rise to a crescendo–decrescendo extracardiac systolic arterial murmur.

Early diastolic murmurs that are heard more commonly are mitral stenosis and aortic regurgitation. Aortic regurgitation begins with A_2 and generally is decrescendo, reflecting the progressive decline in volume and rate of regurgitant flow during diastole. Aortic regurgitation is best heard by having the patient lean forward while holding his or her breath and listening with the diaphragm along the mid left sternal border. Pulmonary hypertension (Graham Steell murmur: an early diastolic murmur caused by pulmonary insufficiency secondary to pulmonary hypertension) also may cause an early diastolic murmur. Middiastolic murmurs occur across the atrioventricular valves (mitral or tricuspid) during rapid filling and are consistent with mitral stenosis or mitral stenosis along with a ventricular septal defect or tricuspid regurgitation with an atrial septal defect. The Austin Flint murmur is a consequence of blood jets from the aortic regurgitation hitting the anterior leaflet of the mitral valve, leading to a middiastolic, low-pitched rumbling best heard at the cardiac apex that results in early mitral valve closure because of simultaneous rapid left ventricular filling (volume overload) from aortic regurgitation. Continuous murmurs begin in systole and continue without interruption into all or part of diastole. Such murmurs are mainly a result of aortopulmonary connections (e.g., patent ductus arteriosus), arteriovenous connections (e.g., arteriovenous fistula, coronary artery fistula), and disturbances of flow patterns in arteries or veins.

Anatomic correlation of murmurs may require cardiac catheterization or echocardiography with Doppler, where direct visualization of the blood flow abnormality and calculation of flow and chamber pressures can be obtained. In special cases the use of positron emission tomography (PET) and magnetic resonance imaging (MRI) are also possible options to evaluate flow patterns and gradients of murmurs across heart valves.

JUGULAR VENOUS PRESSURE

3 The jugular venous pressure (JVP) is used as an indirect measure of right atrial pressure.[10] The JVP is measured in centimeters from the sternal angle and is best visualized with the patient's head rotated to the left. The JVP is described for its quality and character, effects of respiration, and patient position-induced changes. When reporting a JVP, both the extent of elevation and the patient position must be reported. The JVP can be reported as centimeters above the manubrium, or this value plus 5 to 7 cm to indicate the rise of the JVP above the right ventricle. For persons in whom the central venous pressure is normal, JVP is observed in the right internal jugular vein with the patient supine at 30° or less. In the presence of an elevated central venous pressure, the JVP is measured at 60 to 90°. In patients with poor myocardial function, the accuracy of the JVP as a measure of central venous pressure is reduced, and central venous pressure is best measured directly by means of a Swan-Ganz catheter.

The normal JVP is a *v* wave 1 to 2 cm above the sternal ridge. Elevation in JVP more than halfway to the jaw angle are elevated. Both the degree of elevation of the JVP and its wave flow in conjunction with the heartbeat are noted. The first wave, or *a* wave, represents atrial contraction and occurs just prior to S_1, giving rise to increased pressure. It is seen as an undulating pulsation in the internal jugular vein. The second and much larger wave, the *v* wave, represents the increased venous pressure that occurs during venous filling. To interpret the JVP accurately, the carotid pulse is palpated concurrently. The *a* wave occurs just before the pulse and the *v* wave just after. Jugular venous pressure is often elevated in heart failure, and the degree of elevation can be used to assess the severity of heart failure, and diminution of JVP can be used to assess therapy.

PERIPHERAL CIRCULATION AND ARTERIAL PULSES

In recent years the recognition of peripheral arterial disease (PAD) has become very important because of the marked number of patients with asymptomatic disease. PAD affects about 8 million Americans and is associated with significant morbidity and mortality.[11,12] PAD affects 12% to 20% of Americans age 65 years and older. Despite its prevalence and cardiovascular risk implications, only 25% of PAD patients are undergoing treatment.[13] Approximately 40% do not complain of leg pain and only approximately 10% of persons with PAD have the classic symptoms of intermittent claudication (see Chap. 24).

It includes a variety of arterial syndromes (noncoronary artery) that are caused by pathobiologic changes of the arteries that supply the brain, visceral organs, and the limbs. Terminology is also important in discussing this area of arterial disease. Peripheral arterial disease includes an assorted group of disorders that lead to progressive stenosis or occlusion, or aneurysmal dilation, of the aorta and its noncoronary branch arteries, including the carotid, upper extremity, visceral, and lower extremity arterial branches. PAD is the preferred clinical term that should be used to denote stenotic, occlusive, and aneurysmal diseases of the aorta and its branch arteries, exclusive of the coronary arteries. Peripheral vascular disease includes pathophysiologic syndromes that affect the arterial, venous, and lymphatic circulations.

Current American College of Cardiologists/American Heart Association (ACC/AHA) guidelines[11] for the management of peripheral artery disease recommend a vascular history and physical examination (class I) for patients who are at risk for lower extremity PAD, age less than 50 years with diabetes and one other atherosclerosis risk factor (smoking, dyslipidemia, hypertension, or hyperhomocysteinemia), age 50 to 69 years and a history of smoking or diabetes, age 70 years and older, ischemic leg symptoms with exertion (intermittent claudication) or ischemic rest pain, abnormal lower extremity pulse examination, or known atherosclerotic coronary, carotid, or renal artery disease. They also recommend that patients older than 50 years of age should be asked if they have a family history of a first-degree relative with an abdominal aortic aneurysm.

One of the most important tests that can be easily done in patients suspected of PAD is to do an ankle–brachial index. An ankle–brachial index of <0.90 is 90% sensitive and 95% specific for PAD. Severe PAD causing rest pain or ulceration generally occurs with ankle–brachial indices of <0.40. This is easily calculated by measuring the systolic blood pressure in the ankle and dividing it by the systolic blood pressure in the arm (brachial). Normally the lower extremity blood pressure is higher than the arm. To appreciate the significance of PAD, one only needs to recognize that over a 5-year period in patients with PAD the mortality is 30%.[14]

Arterial pulses are evaluated and characterized bilaterally by observation, palpation, and auscultation for presence, character, pattern, and rhythm. Various arterial pulse patterns are described: pulsus alternans (variation in amplitude beat to beat), bisferiens pulse (increased arterial pulse with a double systolic peak), bigeminal pulse (reduced amplitude associated with premature ventricular beats), and paradoxical pulse (decrease in amplitude with inspiration). Although each may be associated with certain disorders (e.g., bigeminal pulse in premature ventricular contractions), none is sensitive or specific enough to be diagnostic. The status of the patient's overall peripheral circulation is recorded, especially the presence and degree of edema or skin changes suggestive of venous or arterial insufficiency. Color, condition, and integrity of the skin are also recorded, including signs of thrombophlebitis, tenderness, or swelling. Capillary refill (normal less than 2 seconds) is assessed by depressing the nail bed until it blanches and then releasing pressure and watching for the return of color, indicating blood flow.

HEART RATE

Heart rate is described by both rate and rhythm. The arterial pulse usually is taken at the radius, but carotid or other arterial pulses may be used. In healthy individuals, the heart rate is usually assessed by counting the pulse for 15 seconds and multiplying by 4. In patients with irregular rhythms, the pulse should be taken over an extended period, approximately 1 to 2 minutes, to try to determine the patient's average pulse and rhythm.

Arterial pulses are an accurate measure of the ventricular rate in healthy persons with good ventricular function. In patients with a rapid ventricular rate—because of supraventricular tachyarrhythmias such as atrial flutter or fibrillation or rapid ventricular rates (e.g., ventricular tachycardia or premature ventricular beats)—extremity pulses (e.g., radial pulse) may be considerably slower than the true ventricular rate. A more accurate ventricular rate is determined by listening to the ventricles with the stethoscope (usually at the apex) or counting from an electrocardiogram (ECG). In patients with atrial fibrillation and a fast ventricular rate, a pulse deficit (measure of the difference in true ventricular rate and peripheral pulse rate) may exist. This may be as much as 10 to 20 beats per minute. Consequently, the location of the pulse (radial or apical) should be recorded. The pulse deficit will be reduced as the ventricular rate is controlled with drug therapy or normal sinus rhythm is restored.

PRACTICE GUIDELINES FOR DIAGNOSTIC AND PROGNOSTIC TESTING IN CARDIOVASCULAR DISEASE TESTING

The American Heart Association (AHA) and American College of Cardiology (ACC) task force on practice guidelines publishes guidelines as to the recommended uses for many diagnostic testing methods. Such guidelines were first developed in the 1980s and are updated as more information is available. These are evidence-based recommendations that rank the indications and uses of tests into three primary classes. Class I indications are those where there is evidence or agreement that the specific procedure is useful and effective. Class II indications are those situations where there is divergence of opinion as to the usefulness of the method. Class III indications are those where there is evidence or agreement that a diagnostic test is not useful. Each class (usually class II) may be broken down into two or three subcategories. Class IIa indications are those where there is evidence or opinion in favor of the test, whereas class IIb indications are those where there is less evidence favoring the test. With each class of recommendation for a specific clinical scenario, the guidelines indicate the level of evidence for the recommendation. Level A evidence is given if the recommendation is based on the availability of multiple randomized clinical trials. Level B evidence is given if only a single randomized trial or multiple nonrandomized trials exist. Level C evidence is given if the recommendation is afforded based on expert opinion only.

Each guideline provides a preamble to indicate how it was constructed and the peer review process. These documents provide the clinician with an extensive database on the testing methodologies and are endorsed by both organizations as acceptable standards of practice.

TESTING MODALITIES

CHEST RADIOGRAPHY

The chest radiograph provides supplemental information to the physical examination and is usually the first diagnostic test in a cardiac workup. It does not provide details of internal cardiac structures but gives global information about position and size of the heart and chambers and surrounding anatomy. The standard chest radiographs for evaluation of lungs and heart are standing postero-anterior and lateral views taken at maximal inspiration. Portable chest radiographs usually are less satisfactory because of penetration difficulties, patient rotation, and poor inspiratory effort.

Initial assessment of the chest radiograph evaluates the quality of the film for patient rotation, inspiratory effort, and penetration. Rotation is assessed by evaluating symmetry of the clavicles and central placement of the carina. Inspiratory effect is considered adequate if the diaphragms are pulled below the ninth rib. Lack of inspiratory effort and obesity lead to a poor-quality chest radiograph, which makes it more difficult to assess the presence of pleural effusions and fluid in the costophrenic angles. Where possible, comparison with previous or baseline films is done to determine the quality of film and comparison of structures.

The posteroanterior view chest radiograph outlines the superior vena cava, right atrium on the right and left sides, aortic knob, main pulmonary artery, left atrial appendage (especially if enlarged), and left ventricle. In the lateral view, the chest radiograph visualizes the right ventricle, inferior vena cava, and left ventricle. These structures are visualized as shadows of differing density rather than discrete structures.

The chest radiograph is approached from two perspectives: (a) observation and (b) clinical correlation. Observation notes gross anatomic features such as size and placement of the cardiac silhouette, definition of the cardiac border, chamber enlargement, pulmonary vasculature, air–fluid levels, and diaphragm. Cardiac enlargement is determined by the cardiothoracic ratio, which is the maximal transverse diameter of the heart divided by the maximal transverse diameter of the thorax of a posteroanterior view. Normal averages 0.45, but it may be up to 0.55 in subjects with large stroke volumes (e.g., highly trained athletes). Heart conditions, such as heart failure and hypertension, may enlarge the heart and so the cardiothoracic ratio. Individual chamber enlargement can be seen on the chest radiograph. Right ventricle enlargement is best seen on the lateral film, where the heart appears to occupy the retrosternal space. Left atrial enlargement is suspected if there is elevation of the left bronchus or an increase in the atrial appendage bulge. Left ventricular enlargement is the most common feature identified on chest radiograph and is seen as an elongation and downward displacement of the apex of the heart. Sometimes a characteristic "boot" or "water bottle" outline is seen with left ventricular enlargement, as in heart failure.

The pulmonary vessels are examined for plumpness and definition of vessel walls. Decreased pulmonary flow (e.g., tetralogy of Fallot) causes central and peripheral vessels to be decreased in size. Increased pulmonary flow is associated with high-output states such as hyperthyroidism and atrial septal defects. This may lead to enlargement and tortuosity of the central and peripheral vessels. Pulmonary arterial hypertension (increased pulmonary resistance) is identified by enlargement of the central vessels and diminished peripheral vessels. Pulmonary venous hypertension usually is caused by mitral stenosis or left ventricular failure. This is characterized by larger-than-normal vessels in the upper lung zones owing to recruitment of upper vessels from blood diverted from the lower constricted vessels (cephalization of flow).

Heart failure causes Kerley B lines (edema of interlobular septa), which appear as thin, horizontal reticular lines in the costophrenic angles. At higher pressures, alveolar edema and pleural effusions appear in the pleural space or as blunting of the costophrenic angles. Pericardial effusions also may appear as a large heart, but because it usually occurs rapidly, there is no evidence of pulmonary venous congestion.

ELECTROCARDIOGRAM

4 Measurement of electrical activity in the heart, now known as the ECG, was introduced about 75 years ago by Willem Einthoven. The

TABLE 13-2 Drugs That May Affect the Electrocardiogram

Digoxin	Pentamidine
Antiarrhythmics–classes I–IV	Lithium
Tricyclic antidepressants	Catecholamines (e.g., dopamine, albuterol)
H_1 antagonists	Diuretics (electrolyte abnormalities)
Methylxanthines	
Doxorubicin	

ECG is simple to perform and is the most frequently used, least invasive, and cheapest cardiovascular test.[15,16] It remains the procedure of first choice for evaluation of chest pain, dizziness, or syncope. In its simplest interpretation, the ECG characterizes rhythms and conduction abnormalities. However, the ECG also provides, by inference, information about the anatomy and structures of the heart, pathophysiologic changes, and hemodynamics of the CVD system.[17] ECG abnormalities are often the earliest sign of adverse drug effects, ischemia, and electrolyte abnormalities.

Although few ECG recordings are highly specific or sensitive to a disease state, correlation of findings with clinical and pathologic states affords the ECG significant diagnostic and prognostic capabilities. Sensitivity and specificity of ECG changes depend primarily on the clinical setting, recording technique, and skill of interpreters. Sensitivity and specificity of findings are increased by interpretation in conjunction with patient information such as age, gender, medical history, and medications. Additionally, prior and/or serial ECGs should be obtained for comparison prior to identifying new findings on a current ECG as diagnostic. This is particularly important in patients with significant cardiac disease or on medications that alter the ECG (Table 13–2). The ECG is sensitive in detecting rhythm abnormalities, but it does not record the actual activity of the conduction tissue.[18,19]

The ECG can be used to evaluate ischemia following angioplasty or other surgical interventions and to monitor responses to antiarrhythmic agents or in patients receiving drugs with potential cardiac effects.

Electrocardiography is based on the measurement of change in summated three-dimensional electrical vectors or forces that result from depolarization and repolarization of cells in the conduction system and heart muscle. The standard external 12-lead ECG uses two sets of leads: limb and chest (Fig. 13–6). The six limb leads look at the heart in a single frontal plane. Limb lead nomenclature is as follows: lead I, right arm/left arm; lead II, right arm/left leg; lead III, left arm/left leg. Altering resistances create the augmented limb leads, which are called aVR, aVL, and aVF. Unipolar chest leads are positioned across the chest and labeled V_1 to V_6. V_1 is positioned slightly to the right of the midline, and V_6 is positioned in the left midaxillary line (Fig. 13–7). Leads aVR and V_1 are considered right-sided leads, so they appear inverted, and leads aVL, I, II, V_5 and V_6 are left-sided leads, so they appear upright on the ECG. Leads II, III, and aVF are inferior leads. Leads V_1 to V_4 are anterior wall leads. Single-lead ECGs or ECG monitors frequently use lead II.

Recording of the ECG has several standard features. The paper is divided into squares of 1 mm; each 10 mm (10 small boxes) is equivalent to 1 mV. Paper speed is 25 mm per second. Each small box on the tracing paper equals 0.04 second (40 milliseconds), and each big box is 0.2 second. If there is one QRS complex per six big boxes (6×0.20 second), the patient has a heart rate of 50 beats per minute, whereas one QRS per big box indicates a heart rate of 300 beats per minute.

The ECG pattern is named alphabetically and is read from left to right, beginning with the P wave. Electrical activation (depolarization) of the right and then the left atrium as a result of discharge from the sinoatrial nodes causes an upward or positive deflection in lead II called the *P wave.* The normal duration of the P wave is up

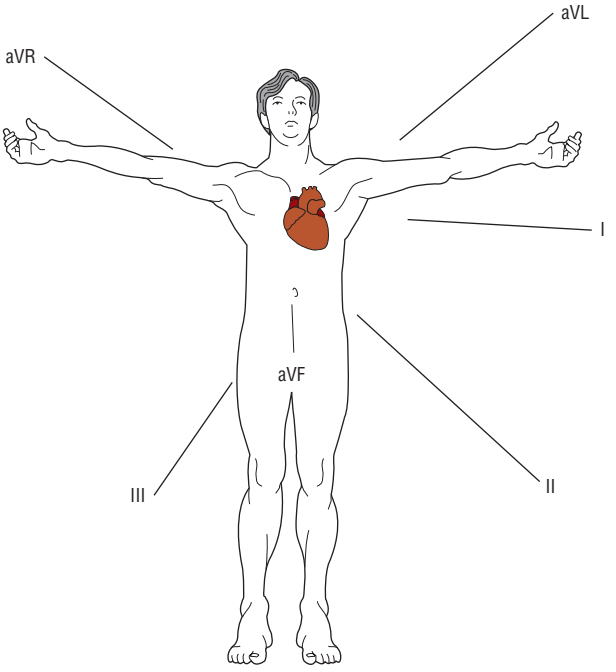

FIGURE 13-6. The torso with the six limb leads in a single frontal plane.

to 0.12 second, and it has an amplitude of 0.25 mV (i.e., 2.5 small boxes). The *PR segment* is created by passage of the impulse through the atrioventricular node and the bundle of His and its branches, and it has a duration of 0.12 to 0.21 second. The *QRS complex* primarily traces the electrical depolarization of the ventricles. Initially, there is a negative deflection, the *Q wave,* followed by a positive deflection, the *R wave,* and finally a negative deflection, the *S wave.* Q-wave duration is normally 0.4 second or less, and the amplitude is 25% or less of the overall height of the QRS complex. Normal duration of the QRS complex is 0.12 second. The QRS complex is positive in left-sided leads and negative in right-sided leads because the left ventricle is much thicker than the right, and the forces going left during depolarization dominate.

Following the QRS complex is a plateau phase called the *ST segment,* which extends from the end of the QRS complex (called the *J point*) to the beginning of the T wave. The ST segment is evaluated from its position relevant to the baseline, configuration, and leads where changes occur. The ST segment is normally on or slightly above the baseline. Configuration changes, convexity upward or downward, identify the presence of myocardial ischemia. Lead localization of ST-segment changes indicates the area of ischemia. The *QT interval* is measured from the start of the QRS complex to the end of the T wave. This varies with heart rate and is corrected (QTc) for heart rates greater than 60 beats per minute. The normal QTc is less than 0.42 second in men and 0.43 second in women.

Repolarization of the ventricle leads to the *T wave.* The T wave usually goes in the same direction as the QRS complex. The normal axis of the ECG is 30° (above the horizontal) to +110° (away from the horizontal) (see Fig. 13–7). The six frontal plane (A) and the six horizontal plane (B) leads provide a three-dimensional representation of cardiac electrical activity.

The ECG is evaluated in a systematic manner to avoid omission of important characteristics. All ECGs are interpreted for the following elements: rate, general rhythm, intervals, voltage, axis, waveforms, abnormal features (e.g., Q waves), and technical aspects such as adequacy of lead placement and calibration.[20] The number of P waves and QRS complexes (*RR interval*) is also used to determine rate. QRS complexes may be more useful if heart block exists. The rhythm from the ECG is identified by the following features:

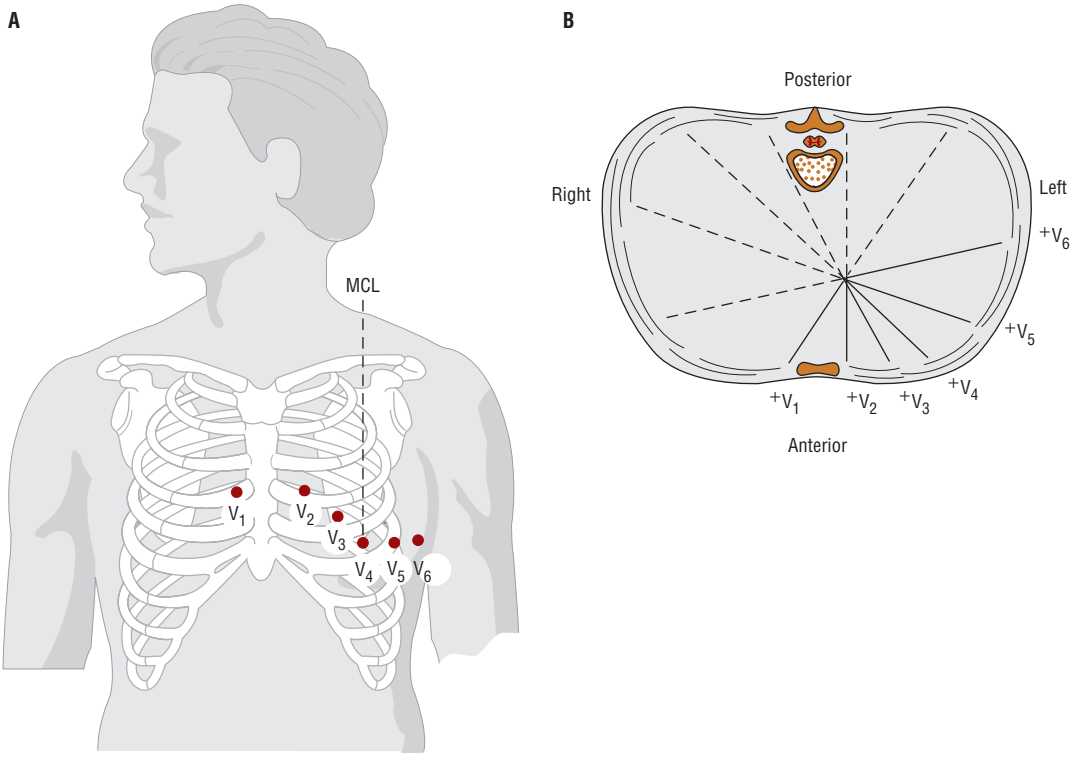

FIGURE 13-7. *A.* Electrode positions of the precordial leads. (MCL, midclavicular line; V_1, fourth intercostal space at the right sternal border; V_2, fourth intercostal space at the left sternal border; V_3, halfway between V_2 and V_4; V_4, fifth intercostal space at the midclavicular line; V_5, anterior axillary line directly lateral to V_4; V_6, anterior axillary space directly lateral V_5.) *B.* The precordial reference figure. Leads V_1 and V_2 are called right-sided precordial leads; leads V_3 and V_4, midprecordial leads; and leads V_5 and V_6, left-sided precordial leads. *(Redrawn from Kinney MR, Packa DR, eds. Andreoli's Comprehensive Cardiac Care, 8th ed. St. Louis: Mosby, 1996, with permission.)*

1. The rate of the QRS (>100/min is tachycardia and <60/min is bradycardia).
2. The regularity of the QRS. (The presence or absence of the QRS complex with each P wave helps to identify if the rhythm is atrial or ventricular in origin and if each atrial beat [P wave] is being conducted to the ventricles. The regularity of the QRS identifies conditions such as atrial fibrillation and extra beats.)
3. Configuration of the QRS—wide or narrow—indicating if it is generated from electrical activity that arose in the atria or ventricles.

Always reported are the RR, PR, QRS, and QT intervals and the duration, magnitude, and configuration of the P waves, QRS complexes, ST segments, T waves, and U waves.[21] Computer interpretation of the ECG provides a standardized reading and records and calculates basic rhythm patterns, heart rate, and intervals but does not interpret arrhythmias. Independent review of the ECG is necessary for accurate translation of findings. In epidemiologic studies, the ECG is used to assess physical fitness, document the prevalence of ischemic heart disease (IHD), and identify subclinical heart disease. The sensitivity and specificity of ECG changes are highly dependent on the pretest probability of heart disease. As the pretest probability of heart disease increases, the sensitivity and specificity of ECG findings increase. The use and value of the ECG as a screening tool are controversial. It is only used where the diagnosis of heart disease would preclude active employment, such as in airline pilots. The ECG frequently is used in conjunction with other diagnostic tests to provide additional data, to monitor the patient, and to identify if abnormalities detected during tests correlate with ECG changes.[20–22]

Gating, or linkage of and simultaneous recording of an ECG and other diagnostic tests, such as echocardiography and computed tomography (CT) scans, allow for correlation of images with the cardiac cycle. Gating is either prospective, where a certain portion of the cardiac cycle is predetermined as the time during which the images are obtained, or retrospective, where the ECG and image are recorded simultaneously but independently and later matched for concurrent events. This allows multiple cardiac cycles to be overlaid, thus increasing the sensitivity to detect abnormalities.

Anomalies on the ECG include abnormal intervals, altered waveform configurations, and rate variability. Other findings give evidence for various forms of heart block, ischemia, infarction, atrial and ventricular enlargement and hypertrophy, atrial and ventricular rhythm disorders, pericarditis, metabolic abnormalities, drug-induced changes, and pacemaker-related changes. ECG patterns found on consecutive leads can help to identify where a particular conduction defect or impulse generation is occurring or anatomic problem is located. For example, ST-segment elevation in V_2 to V_6 is indicative of anterior wall myocardial infarction from occlusion of the left anterior descending coronary artery. Single-lead abnormalities most frequently are attributed to poor lead placement, position of the patient, or recording artifacts.[22]

Examples of some common findings will be discussed briefly. Short PR intervals are associated with the Wolff-Parkinson-White and Lown-Ganong-Levine syndromes and reflect the presence of accessory pathways. Long PR intervals are measures of heart block. The presence of a Q wave is a marker for loss of electrically functioning myocardium and suggests a prior myocardial infarction. It also may be present in congenital heart disorders, hypertrophic cardiomyopathy, left ventricular hypertrophy, conduction defects such as Wolff-Parkinson-White syndrome, and intraventricular conduction defects. U waves are relatively nonspecific, the most common cause being hypertension. Bundle-branch blocks are frequent findings and indicate conduction defects in one of the bundles of His. Their presence confounds the interpretation of important ECG findings such as

ischemia. Right bundle-branch block is associated with an R wave and the following abnormalities: QRS complex greater than or equal to 12 milliseconds, delayed right ventricular forces resulting in terminal R waves in the right-sided leads and S wave in the left-sided lead, and right-sided ST-segment depression and T-wave inversion. Left bundle-branch block is characterized by the following: QRS complex greater than or equal to 12 milliseconds, delayed left ventricular activation, loss of the normal "septal Q wave" in the left-sided leads, and left-sided ST-segment depression and T-wave inversion. Intraventricular conduction delay usually causes a wide QRS complex, and generally there are ST-segment–T-wave abnormalities.

Myocardial ischemia, ranging from injury to necrosis, results in T-wave changes, ST-segment abnormalities, and changes in the QRS complex. Myocardial infarction results in a typical pattern of ECG changes that begins with tall, peaked T waves persisting up to several hours, followed by ST-segment elevation with a coved (convexity upward) configuration, and inverted T waves. Development of a new Q wave has a high specificity but low sensitivity for acute myocardial ischemia. Q waves that are 4 milliseconds or longer in duration and 25% or greater of the overall QRS height are considered diagnostic and occur within minutes to hours of occlusion. Although Q waves usually evolve within hours of infarction, they may not become evident for several days. The finding of new and significant Q waves on an ECG is indicative of a previous infarction. Q waves persist indefinitely in 80% to 90% of myocardial infarctions. The location of Q waves identifies the region of myocardium affected and the coronary artery blocked (e.g., inferior infarction will result in Q waves in II, III, and aVF associated with blockage in the right coronary artery). Non–Q-wave (subendocardial) myocardial infarction implies that the Q wave does not meet the diagnostic criteria for Q-wave infarction. ST-segment depression may be present.

ST-segment changes are very common and always should be compared with a previous ECG. ST-segment elevation may be seen in persons with no known coronary disease but is usually indicative of hyperacute ischemia. ST-segment depression is never considered a normal finding. ST-segment scooping (convexity downward) may be normal, but coving (convexity upward) is abnormal. Depression of the ST segment that does not return quickly to normal and changes in multiple leads suggests clinically significant heart disease. Diffuse ST-segment elevation in all leads except V_1 and aVR suggests the diagnosis of pericarditis. Exertion in normal individuals may cause J-point depression with a rapid rise of the ST segment, and this may be confused with ST-segment depression because of the configuration. Poor R-wave progression (usually increase in size moving from V_1 to V_6) suggests anterior myocardial infarction, but smaller R waves also can occur in diseases such as chronic obstructive pulmonary disease. T-wave changes are the most frequent and most sensitive abnormality on the ECG but are also the least specific and frequently are found in persons with no heart disease.

Left atrial enlargement is characterized by a P wave that is ≥12 mV in lead II, or the negative component of the biphasic P wave is 4 mV in duration and 0.1 mV in depth in lead V_1. In right atrial enlargement, the P wave in lead II can exceed 0.25 mV and usually has a vertical axis. Ventricular hypertrophy results in increased deflection of the QRS complex because of the increased muscle mass. Left ventricular hypertrophy (LVH) is diagnosed from the ECG using several different sets of criteria; none are considered highly sensitive or specific. LVH often is indicative of hypertension and resulting ventricular enlargement and strain. Commonly used voltage criteria indicating LVH are summation of the S wave in V_1 and the R wave in V_5 or the S wave in V_2 and the R wave in V_6 that exceeds 3.5 mV (35 small boxes) or the R wave in lead aVL that exceeds 1.1 mV (11 small boxes). Right ventricular hypertrophy is characterized by an R wave in V_1 that is equal to or greater than the S wave in that lead. In persons who are obese, increased voltage may not be apparent, making voltage criteria a less useful tool to identify hypertrophy. LVH also may be assessed using echocardiography.

Electrolyte abnormalities have characteristic signs on the ECG and can be used as monitoring parameters. Hypokalemia may increase ventricular ectopic beats and causes ST-segment depression, T-wave flattening, and the appearance of a U wave (usually when the serum potassium concentration is less than 3.0 mEq/L). Hyperkalemia results in very characteristic changes in the ECG. Potassium concentrations above 6.0 mEq/L produce tall, peaked T waves. As the concentration rises further, intraventricular conduction becomes blocked, with widening of the QRS complex, and ultimately, a sine wave develops. Hypercalcemia causes a short QT interval and, occasionally, ST-segment depression, sinus arrest, and atrioventricular conduction blocks. Hypocalcemia causes a long QT interval and some broadening of the T wave. A number of drugs cause characteristic changes in the ECG that may mask interpretation of other findings. Table 13–2 lists commonly used drugs that may alter the ECG. Pericardial effusion, obesity, and large breasts limit the amount of voltage that is measured on the skin surface and reduce the QRS voltage. In the presence of large pericardial effusions, rapid changes in the positive to negative deflection of the QRS complex or electrical alternans may occur because the heart is swinging on a beat-to-beat basis.

Signal-averaged ECG may be used to help elucidate the presence of low-amplitude bioelectrical potentials.[23] Derangements of ventricular activation and late potentials can be detected on the ECG after the QRS and ST segments and are thought to be associated with increased risk of ventricular arrhythmias. Traditional ECGs are unable to detect these potentials because they are "lost" in the noise of the ECG recording. Signal-averaged ECG improves the signal-to-noise ratio, enabling the low-amplitude potentials to be interpreted. Signal-averaged ECG can be used to identify patients at risk for developing sustained ventricular tachycardia after myocardial infarction. Patients with IHD and unexplained syncope who are at risk for sustained ventricular tachycardia also may be candidates for signal-averaged ECG. Other potential uses of signal-averaged ECG include patients with nonischemic cardiomyopathy with sustained ventricular tachycardia, detection of acute rejection of heart transplant, and assessment of the proarrhythmia potential of antiarrhythmic drug therapy.

AMBULATORY ELECTROCARDIOGRAM MONITORING

Ambulatory ECG monitoring (AECG), or Holter monitoring, named for its inventor, is an aid to detect, document, characterize, and evaluate arrhythmias and other ECG abnormalities over extended periods of time.[24,25] AECG provides information regarding random abnormal cardiac electrical activity during daily activity and helps relate altered electrical activity to precipitating factors and patient symptomatology. algorithms. AECG also helps in the discovery and investigation of arrhythmias and ST-segment deviation along with more sophisticated analyses of R-R intervals, QRS-T morphology including late potentials, Q-T dispersion, and T-wave alternans. Additionally, some findings on AECG have been used to determine prognostic implications. Different types of recording systems are discussed later in this chapter in the Echocardiogram section: one version is noninvasive, which can be patient activated and varies in duration of recording from hours to days, and the other version is invasive, which can be implanted like a pacemaker and removed later and can record for years. Most of the current new recording systems are digital (recommended guidelines by AHA/ACC) and have a diagnostic frequency response range for more accurate investigation of ST-segment deviations.

Although controversial, AECG is used as a diagnostic and screening tool for asymptomatic ischemia. It is difficult to interpret

changes in the ST segment recorded during AECG owing to amplitude, and definitions of significant changes recorded with AECG are still in evolution. As a prognostic tool, it is used primarily to evaluate patients with known CVD who have symptoms that may be associated with an arrhythmia. It is also used in clinical trials to evaluate the efficacy of drug therapy.[26]

Guidelines as to the recommended uses of AECG are available from AHA/ACC. The major class I indications for AECG include diagnosis in patients with symptoms suggestive of arrhythmias, prognostic delineation in patients with cardiac disease considered at risk for arrhythmia-related events, and measurement of efficacy of interventions in patients with known and characterized arrhythmias. Examples of indications and clinical rhythm disturbances are listed in Tables 13–3, 13–4, and 13–5.

A major limitation of AECG is the amount of data collected with ECG abnormalities that are of unknown clinical significance. High day-to-day variability of frequency and type of arrhythmias means that repeat AECG may demonstrate as much as a 90% difference in the number of premature ventricular contractions. Little correlation of arrhythmia suppression and clinical outcomes is available. No AECG study has shown a mortality advantage when used in conjunction with antiarrhythmic drugs or devices. Following an intervention (drugs or device), at least a 63% to 95% reduction in arrhythmia frequency is required for AECG to be considered a valuable arrhythmia detection and evaluation tool. Compared with electrophysiology testing in the Electrophysiologic Study Versus Electrocardiographic Monitoring (ESVEM) study, AECG was equivalent but not superior to electrophysiology testing in the ability to select initial drug therapy.[22] The Asymptomatic Cardiac Ischemia Pilot (ACIP) study found that 75% of patients with asymptomatic evidence of ischemia on AECG had multivessel coronary artery disease on angiography.[26]

During AECG, the patient wears a portable ECG recorder that weighs about 8 to 16 oz. The recorder uses two to four chest leads (V_5 and V_3 most commonly). Additional leads do not improve the sensitivity of AECG significantly. If ST-segment changes are known to occur in certain leads, these can be used during AECG. Most AECG recordings are for 24 to 48 hours, but they can extend to weeks or months where the frequency of events related to ECG abnormalities is low. Implantable devices are used when long periods of monitoring are necessary. Currently used equipment is able to detect and analyze arrhythmias, ST-segment deviations, QRS complexes, RR intervals, and late potentials.

Three types of monitors are available: (a) continuous monitors, which record an ECG strip over the duration of the test, (b) event or intermittent recorders, which continuously monitor the ECG but only record preprogrammed abnormal ECG events or are patient-activated based on occurrence of symptoms, and (c) real-time analytical recorders, which record throughout the monitoring period and analyze each beat as it occurs. Monitors digitize, encode, and store the information in a solid-state memory or on magnetic tape. Event monitors are preprogrammed to record parameters such as the number of premature ventricular contractions and heart rate. During monitoring, the patient maintains a diary, in which the occurrence, duration, and severity of symptoms (e.g., light-headedness, chest pain) are recorded, plus any specific activities undertaken, development of symptoms with the activity, and any interventions such as the taking of medication. A clocking device in the recorder allows later correlation of the patient's diary with the recorded ECG.

Evaluation and analysis of the ECG record are complex. Computer-assisted interpretation is used to scan the ECG and identify irregular rhythms, rates, and specific preprogrammed changes. The main advantage of computer analysis is to reduce interpretation of artifact recordings. Each beat recorded during AECG is evaluated for its arrhythmia potential and classified as normal or abnormal. The morphology of each QRS-T section is examined for ischemia potential, although, as indicated previously, baseline ST-segment abnormalities and adjustments in amplitude of the recording may preclude interpretation of these segments. The ACC/AHA guidelines provide detail as to the suitability of using ST segments for analysis of ischemia.[27] Various drugs, such as digoxin and the tricyclic antidepressants that cause baseline ECG abnormalities, may preclude patients from being evaluated with AECG.

Sections identified by the computer as abnormal or those correlating with patient symptoms are then evaluated and characterized

TABLE 13-3 Indications for Ambulatory Electrocardiogram Monitoring to Assess Symptoms Possibly Related to Rhythm Disturbances

Class I
Patients with unexplained syncope, near syncope, or episodic dizziness in whom the cause is not obvious
Patients with unexplained recurrent palpitation
Class IIb
Patients with episodic shortness of breath, chest pain, or fatigue that is not otherwise explained
Patients with neurologic events when transient atrial fibrillation or flutter is suspected
Patients with symptoms such as syncope, near syncope, episodic dizziness, or palpitation in whom a probable cause other than an arrhythmia has been identified but in whom symptoms persist despite treatment of this other cause
Class III
Patients with symptoms such as syncope, near syncope, episodic dizziness, or palpitation in whom other causes have been identified by history, physical examination, or laboratory tests
Patients with cerebrovascular accidents, without other evidence of arrhythmia

TABLE 13-4 Indications for Ambulatory Electrocardiogram Arrhythmia Detection to Assess Risk for Future Cardiac Events in Patients without Symptoms from Arrhythmia

Class I
None
Class IIb
1. Post-myocardial infarction patients with left ventricular dysfunction (ejection fraction <40%)
2. Patients with congestive heart failure
3. Patients with idiopathic hypertrophic cardiomyopathy
Class III
1. Patients who have sustained myocardial contusion
2. Systemic hypertensive patients with left ventricular hypertrophy
3. Post-myocardial infarction patients with normal left ventricular function
4. Preoperative arrhythmia evaluation of patients for noncardiac surgery
5. Patients with sleep apnea
6. Patients with valvular heart disease

Adapted from AHA/ACC guidelines.

TABLE 13-5 Indication for Ambulatory Electrocardiogram Monitoring for Ischemia

Class I
None
Class IIa
1. Patients with suspected variant angina
Class IIb
1. Evaluation of patients with chest pain who cannot exercise
2. Preoperative evaluation for vascular surgery of patients who cannot exercise
3. Patients with known coronary artery disease and atypical chest pain syndrome
Class III
1. Initial evaluation of patients with chest pain who are able to exercise
2. Routine screening of asymptomatic subjects

Adapted from AHA/ACC guidelines.

TABLE 13-6 Confounding Factors in Ambulatory Electrocardiogram Monitoring

Patient Factors	Equipment Factors
Electrolyte abnormalities	Battery failure
Hyperventilation	Loose lead
Lead interference by patient	Mechanical failure of recorder
Medications	Motor failure
Physiologic variations in waveforms	Overrecording
Medications	Computer inability to detect arrhythmia
Patient activities (e.g., sudden exercise)	
Presence of atrial fibrillation	

further (e.g., potentially pathologic rhythms) by technical personnel and physicians. Confounding factors when using AECG can arise from the patient and the device (Table 13–6). AECG is evolving rapidly, primarily related to improved technology with respect to data interpretation, signal quality, and improved understanding of the implications of ECG changes.

EXERCISE STRESS TESTING

5 Exercise stress (tolerance) testing (ETT) is a noninvasive test used to evaluate clinical and cardiovascular responses to exercise.[27–29] ETT is used frequently as an initial test, in conjunction with physical examination and patient symptoms, to aid in the selection of additional testing modalities. It is a simple test that can be conducted in a physician's office and is about 20 times less expensive than an angiogram and almost three times less expensive than stress echocardiography. Almost two-thirds of ETTs billed to Medicare in 1996 were conducted in physicians' offices, and one-third was conducted by noncardiologists.[27]

Central facts to remember about ETT is that its value to diagnose CAD is largely dependent on the risk of the population studied. For example, it is not very helpful in identifying CAD if one does ETT on patients who are young and without risk factors because their risk is extremely low; but if one tests a population of people that has multiple risk factors and is older, it is more useful (Table 13–7). Even though one uses these considerations, randomized trial data on the clinical value of screening exercise testing are absent and it is not known whether a strategy of routine screening exercise testing in selected subjects reduces the risk for premature mortality or major cardiac morbidity. A recent report from the U.S. Preventive Services Task Force[26] recommended against the use of exercise testing as a screening tool, in a large part because most studies were completed in asymptomatic patients, and because of the well-established Bayesian argument.

One of most important parts of exercising testing is functional capacity, even though it is rarely measured directly. Functional capacity can be obtained by directly measuring the oxygen consumption but this is not routinely available because of complexity and cost of equipment. If one uses functional capacity to exercise capacity, prediction of cardiovascular risk can be assessed.[30] It is also essential to evaluate the inability of the heart rate to increase appropriately during exercise (chronotropic incompetence) testing. Peak heart rate, age related predicted maximum heart rate have important prognostic importance. Heart rate during exercise is an expression of decreased parasympathetic tone and increased sympathetic tone. In disease states affecting electrical conduction or possibly heart failure this becomes important. The second important area is heart rate recovery after exercise testing. Normal individuals and especially athletes have a rapid fall in heart rate during the first 30 seconds after exercise vs a patient with heart disease who has slow fall in heart rate. This heart rate response is markedly influenced by parasympathetic tone.

The ETT provides diagnostic information in patients with known or suspected IHD and prognostic information in patients after myocardial infarction or revascularization. However, there are no data that support its use as a screening tool for CAD or for detection of early CAD in asymptomatic subjects.

The principle behind ETT is to increase myocardial oxygen demand above myocardial oxygen supply and coronary reserve, thereby provoking ischemia (inadequate myocardial perfusion), using exercise as a stressor. Ischemia is detected by patient symptoms, ECG changes, and/or hemodynamic changes. The type of ECG changes, leads affected, and patient performance are used as an index of severity and location of disease. ETT is a very practical test in that it can assess patients' functional capacity.[30]

Some examples of classes I, II, and III indications from the ACC/AHA guidelines for ETT are presented here.[31] The major class I indications are evaluation of males older than age 40 years who have symptoms suggestive of CAD and risk factors for CAD or atypical symptoms suggestive of CAD. Another class I indication is to help assess prognosis and functional capacity in patients with confirmed CAD.[32] Frequently, the ETT is performed following an acute myocardial infarction for this purpose (Table 13–8). Class II indications

TABLE 13-7 Comparing Pretest Likelihoods of Coronary Artery Disease in Low-Risk Symptomatic Patients with High-Risk Symptomatic Patients–Duke Database

Age (Years)	Nonanginal Chest Pain		Atypical Angina		Typical Angina	
	Men	*Women*	*Men*	*Women*	*Men*	*Women*
35	3–35	1–19	8–59	2–39	30–88	10–78
45	9–47	2–22	21–70	5–43	51–92	20–79
55	23–59	4–25	45–79	10–47	80–95	38–82
65	49–69	9–29	71–86	20–51	93–97	56–84

Each value represents the percent with significant coronary artery disease (CAD). The first is the percentage for a low-risk, mid-decade patient without diabetes, smoking, or hyperlipidemia. The second is that of the same age patient with diabetes, smoking, and hyperlipidemia. Both high- and low-risk patients have normal resting electrocardiograms. If ST-T–wave changes or Q waves had been present, the likelihood of CAD would be higher in each entry of the table.

TABLE 13-8 Exercise Stress Testing after Myocardial Infarction

Class I

1. Before discharge for prognostic assessment, activity prescription, evaluation of medical therapy (submaximal at about 4 to 76 days).
2. Early after discharge for prognostic assessment, activity prescription, evaluation of medical therapy, and cardiac rehabilitation if the predischarge exercise test was not done (symptom limited; about 14–21 days).
3. Late after discharge for prognostic assessment, activity prescription, evaluation of medical therapy, and cardiac rehabilitation if the early exercise test was submaximal (symptom limited; about 3 to 6 weeks).

Class IIa

After discharge for activity counseling and/or exercise training as part of cardiac rehabilitation in patients who have undergone coronary revascularization.

Class IIb

Periodic monitoring in patients who continue to participate in exercise training or cardiac rehabilitation.

Class III

1. Severe comorbidity likely to limit life expectancy and/or candidacy for revascularization.
2. At any time to evaluate patients with acute myocardial infarction who have uncompensated congestive heart failure, cardiac arrhythmia, or noncardiac conditions that severely limit their ability to exercise. (*Level of Evidence: C*)
3. Before discharge to evaluate patients who have already been selected for, or have undergone, cardiac catheterization. Although a stress test may be useful before or after catheterization to evaluate or identify ischemia in the distribution of a coronary lesion of borderline severity, stress imaging tests are recommended. (*Level of Evidence: C*)

Adapted from AHA/ACC guidelines.

TABLE 13-9 2002 Exercise Testing Guideline Recommendations

Class I

1. Patients undergoing initial evaluation with suspected or known CAD, including those with complete right bundle-branch block or less than 1 mm of resting ST depression.
2. Patients with suspected or known CAD, previously evaluated, now presenting with significant change in clinical status.
3. Low-risk unstable angina patients 8 to 12 hours after presentation who have been free of active ischemic or heart failure symptoms.
4. Intermediate-risk unstable angina patients 2 to 3 days after presentation who have been free of active ischemic or heart failure symptoms.

Class IIa

1. Intermediate-risk unstable angina patients who have initial cardiac markers that are normal, a repeat ECG without significant change, and cardiac markers 6 to 12 hours after the onset of symptoms that are normal and no other evidence of ischemia during observation. (*Level of Evidence: B*)

Class IIb

1. Patients with the following resting ECG abnormalities:
   Preexcitation (Wolff-Parkinson-White) syndrome.
   Electronically paced ventricular rhythm.
   1 mm or more of resting ST depression.
   Complete left bundle-branch block or any interventricular conduction defect with a QRS duration greater than 120 ms.
2. Patients with a stable clinical course who undergo periodic monitoring to guide treatment.

Class III

1. Patients with severe comorbidity likely to limit life expectancy and/or candidacy for revascularization.
2. High-risk unstable angina patients.

CAD, coronary artery disease; ECG, electrocardiogram.
Adapted from AHA/ACC guidelines.

are patients with variant angina or women with a history of typical or atypical chest pain (Table 13–9). Examples of class III indications are patients with simple premature ventricular contractions on a resting ECG with no other signs or symptoms of CAD. Additionally, ETT is used to assess symptoms such as chest pain or breathlessness. ETT should be used only if the results are able to alter patient management or to assess patient function.

Guidelines for conducting and interpreting the tests and details of testing equipment and environment are outlined in the 2002 ACC/AHA guidelines on ETT standards.[33] ETT is conducted on a treadmill or bicycle ergometer or by means of a handgrip. These dynamic methods are used to assess exercise tolerance because they induce both a volume and pressure load on the heart. Both modalities also allow the degree of stress to be delivered in a graded and calibrated manner. Treadmill walking is preferred over the ergometer because it involves more muscle mass and the maximal oxygen consumption (VO_2max) achieved with cycle ergometer is 10% to 15% lower than with the treadmill.

Many protocols have been designed and validated for use with ETT, but the two used most commonly are the Bruce and Naughton protocols. Protocols help to decrease inter- and intrapatient variability and allow for standardization in the interpretation of the tests. Protocols may be customized for individual patients to ensure an exercise time of 6 to 12 minutes and a heart rate of 85% to 90% of maximum predicted (adjusted for age and gender). Protocols detail gradient, speed, and rates of change of these parameters during the test.

In preparation for ETT, patients fast prior to the test for a minimum of 3 hours, may not exercise 12 hours prior to the test, and must dress suitably for exercise. Baseline evaluation consists of history and physical examination, blood pressure, heart rate, and ECG. The test begins with a 1-minute warmup period to orient the patient to the equipment. Each stage of the test is maintained for at least 3 minutes. Continuous blood pressure, heart rate, and ECG recordings are obtained, with definitive readings 2 minutes into each stage. Patients are questioned 2 to 3 minutes into each stage of the test about symptoms such as headache, dizziness, and chest pain. Clinical symptoms assessed include color of skin, level of perspiration, and evidence of peripheral cyanosis and light-headedness. Patients are encouraged to exercise as vigorously as they can to ensure an optimal test result. Onset, nature, and duration of all changes in symptoms, hemodynamics, and ECG are noted. Following the test there is a cool-down period during which the patient is seated or lying and is observed for changes as described earlier.

ETT requires considerable effort, with many patients requiring encouragement to perform to the best of their ability. Some patients use the test as a personal challenge and perform better on repeated attempts. This is referred to as a *training effect* and may be a confounding factor in using ETT to assess the effect of drug therapy or after interventions for IHD in clinical trials.

Interpretation of the test requires correlation of clinical, ECG, and other parameters measured during the test with the patient's history (e.g., age, gender, concurrent risk factors, and medical history) and concomitant therapy. Results of ETT can be used as a guide to future patient management, including suitability for interventional cardiology and selection of pharmacotherapy. A positive test is defined as 1 mm of horizontal or downsloping depression or elevation of the ST segment for 60 to 80 milliseconds after the QRS complex. For patients with baseline ST-segment depression, combinations of abnormal responses (e.g., 2 mm of ST-segment depression with hemodynamic abnormalities) would be necessary to call a test positive. ST-segment depression of 2 mm or more, especially in conjunction with heart rates of less than 120 beats per minute, low levels of stress, or depression persisting for up to 6 minutes after the cessation of the test, is associated with a poor prognosis. Depression of the ST segment in multiple leads is also significant. Other ECG changes include development of U waves and increased complexity and/or frequency of premature ventricular contractions or beats, especially if associated with bigeminy or periods of ventricular tachycardia.

Although ECG changes and heart rate responses are used as objective end points of ETT, patient and clinical end points are actually preferred. The use of the 85% to 90% maximally predicted heart rate is highly variable among patients and often is not achieved because of concomitant drug therapy and different levels of fitness. Symptom-limited or patient-directed tests are continued to the predetermined end point(s) unless the patient tires or certain characteristics are noted. Clinical symptoms, exhaustion, chest pain, and changes in blood pressure, heart rate, and the ECG (rhythm, configuration, and rate) are used as end points for such *open-ended tests.* Also, patient performance, measured as exercise duration, time until symptoms, stress at which symptoms occur, and hemodynamic parameters, is a better indicator of an adequate test than is heart rate response. *Close-ended testing* is the use of fixed end points such as time on the treadmill or maximal heart rate.

The product of blood pressure and heart rate (*double product*) is a measure of myocardial oxygen demand. In patients with stable angina, the double product is reproducible on repeat ETTs; consequently, it is used as an objective parameter to follow an individual patient's disease. Inappropriate or inadequate responses in blood pressure and/or heart rate to exercise suggest heart disease. A reduction in heart rate or a flat response (failure to increase heart rate above 120 beats per minute) with increasing levels of stress has a poor prognosis. Likewise, failure to increase the systolic blood pressure or the finding of a sustained decrease of more than 10 mm Hg is also associated with a worse prognosis. Such responses indicate that the heart has an inadequate reserve to respond to stress. Patients who are unable to progress beyond stage II of the Bruce protocol have a poor prognosis and more severe IHD. Other rating scales (e.g., Borg, which measures perceived exertion) may be

TABLE 13-10 MET Relationship to Activity and Function

METS	Level of Activity	ET Result
1	Resting	<6 METS
2	Level walking at 2 miles/h	Symptom-limited lifestyle
4	Level walking at 4 miles/h	Sedentary lifestyle tolerated
13	Cycling 9–10 miles/h	Little or no activity-limited lifestyle
20	Shoveling heavy snow	No limitations on lifestyle

ET, exercise testing; METS, metabolic equivalents of task.

used in conjunction with the objective results from the ETT to classify patients into high- and low-risk groups. Silent ischemia may confound the interpretation of ETT because blood pressure and ECG changes may occur in the absence of symptoms.

To provide standardized comparability between tests and patients, metabolic equivalents (METS) are used as a measure of VO_2max. A MET is a measure of resting oxygen uptake. Activity energy demands then can be calculated in terms of METS. For example, 4 METS is equivalent to walking at 4 miles per hour. The number of METS a patient can undertake without symptoms of ischemia correlates with prognosis and helps to guide appropriate management strategies. Table 13–10 has examples of METS and activity correlations. Exercise capacities of less than 5 METS are associated with a poor prognosis; those greater than 13 METS have a good prognosis despite the presence of disease.

Meta-analysis of more than 24,000 patients in 147 studies showed a mean sensitivity of 68% and specificity of 77% for ETT as a diagnostic test. The specificity of ETT to detect the presence of CAD, compared with angiography, is 84%. Sensitivity ranges from 40% to 90%, depending on the number of vessels affected, with a mean of 66%.

As a prognostic test, ETT is very popular after myocardial infarction and can be conducted within 3 days of an acute event. It can be used to determine functional capacity, assess the degree of rehabilitation, and identify patients at risk for further cardiovascular events. Immediately after myocardial infarction, a modified protocol is used; the test is terminated when a heart rate of 70% to 75% of age- and gender-predicted maximum is reached (e.g., 140 beats per minute for those younger than age 40 years and 130 beats per minute for those older than age 40 years) or a METS level of 5 for patients older than age 40 years or of 7 for those younger than age 40 years. Tests usually are done prior to discharge or within 6 weeks of infarction. In the periinfarction period, mortality and reinfarction rates caused by ETT are 0.02% and 0.09%, respectively. Patients may be stratified into low-, intermediate-, and high-risk categories, depending on the evidence for ischemia and the level of exercise tolerance.[33]

TABLE 13-11 Exercise Testing before and after Revascularization

Class I
1. Demonstration of ischemia before revascularization.
2. Evaluation of patients with recurrent symptoms that suggest ischemia after revascularization.

Class IIa
After discharge for activity counseling and/or exercise training as part of cardiac rehabilitation in patients who have undergone coronary revascularization.

Class IIb
1. Detection of restenosis in selected, high-risk asymptomatic patients within the first 12 months after percutaneous coronary intervention.
2. Periodic monitoring of selected, high-risk asymptomatic patients for restenosis, graft occlusion, incomplete coronary revascularization, or disease progression.

Class III
1. Localization of ischemia for determining the site of intervention.
2. Routine, periodic monitoring of asymptomatic patients after percutaneous coronary intervention or coronary artery bypass grafting without specific indications.

Adapted from AHA/ACC guidelines.

TABLE 13-12 Contraindications to Exercise Testing

Absolute
- Acute myocardial infarction (within 2 days)
- High-risk unstable angina
- Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
- Symptomatic severe aortic stenosis
- Uncontrolled symptomatic heart failure
- Acute pulmonary embolus or pulmonary infarction
- Acute myocarditis or pericarditis
- Acute aortic dissection

Relative
- Left main coronary stenosis
- Moderate stenotic valvular heart disease
- Electrolyte abnormalities
- Severe arterial hypertension
- Tachyarrhythmias or bradyarrhythmias
- Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
- Mental or physical impairment leading to inability to exercise adequately
- High-degree atrioventricular block

Adapted from AHA/ACC guidelines.

ETT is relatively safe, with an estimated risk of acute myocardial infarction or death of 10 per 10,000 tests overall. Most adverse effects are cardiac in nature, including arrhythmias (primarily bradyarrhythmias), sudden death, hypotension, and myocardial infarction. Patients in whom ETT is contraindicated are those who are unable or who should not exercise because of physiologic or psychological limitations and indications for termination (Tables 13–11, 13–12, and 13–13). Unstable angina is usually a contraindication to ETT because of the instability of the patient's disease state and because patients cannot exercise to a satisfactory level for the test to be considered adequate. However, once such a patient is stable, ETT is excellent for prognostic evaluation. In patients with untreated life-threatening arrhythmias or congestive heart failure, ETT is also contraindicated. Patients with comorbid diseases such as chronic obstructive pulmonary disease or peripheral vascular disease may be limited in their exercise capacity, whereas lower-limb amputees are unable to perform the standard treadmill test. For patients with disabilities or other medical conditions that limit their exercise capacity independent of heart disease, pharmacologic stress testing with dipyridamole, adenosine, or dobutamine is an alternative (see Pharmacologic Stress Testing below).

Drug therapy rarely is discontinued for the test primarily because few data exist to support better test results off drug therapy. Patients on β-blockers or calcium channel blockers may not achieve maximal heart rates, but ETT helps to demonstrate patients' exercise capacity on drug therapy. Nitrates do not alter exercise capacity directly and theoretically may improve patient response because they relieve or prevent symptoms of ischemia. Digoxin interferes with interpretation of ST-segment changes, and patients rarely achieve ST-segment changes greater than 1 mm even in the face of significant ischemia.

TABLE 13-13 Indications for Terminating Exercise Testing

Absolute indications
- Drop in systolic blood pressure of >10 mm Hg from baseline blood pressure despite an increase in workload, when accompanied by other evidence of ischemia
- Moderate to severe angina
- Increasing nervous system symptoms (e.g., ataxia, dizziness, or near syncope)
- Signs of poor perfusion (cyanosis or pallor)
- Technical difficulties in monitoring electrocardiogram or systolic blood pressure
- Subject's desire to stop
- Sustained ventricular tachycardia
- ST elevation (>1.0 mm) in leads without diagnostic Q-waves (other than V1 or aVR)

Adapted from AHA/ACC guidelines.

Because of its long half-life, digoxin does not need to be discontinued prior to the test (see Table 13–2).

ECHOCARDIOGRAM

7 The echocardiogram (ECHO) is the use of ultrasound to visualize anatomic structures, such as the valves, within the heart and to describe wall motion.[34,35] Clinically, the ECHO is the most frequently used noninvasive cardiovascular test, aside from the ECG. It competes well with invasive techniques, such as cardiac catheterization with angiography, for the evaluation of ischemia and valvular abnormalities. ECHO is relatively cheap to perform and can be done at the bedside, in the operating room, or in the physician's office. The major disadvantages of the ECHO relate to technical limitations of operator-dependent images and competition from other noninvasive technologies such as MRI and CT scanning that provide similar information with superior tissue-type resolution. The ECHO is often used as an initial evaluative tool following auscultation detection of an abnormality, thus providing a baseline visual characterization. Serial determinations in a given patient, especially following a change in clinical condition or a procedure, allow evaluation of progression of disease over time.

The ECHO remains the procedure of choice in the diagnosis and evaluation of a number of conditions such as valvular dysfunction (aortic and mitral stenosis and regurgitation and endocarditis), wall motion abnormalities associated with ischemia, and congenital abnormalities, such as ventricular or atrial septal defects. Images obtained from ECHO are used to estimate chamber wall thickness and left ventricle ejection fraction, assess ventricular function, and detect abnormalities of the pericardium such as effusions or thickening.

Echocardiography is based on the principle of differential acoustic impedance (or tissue density) and the laws of reflection and refraction. Sound waves directed across tissues from a transducer will reflect back sound waves of different frequencies. The ability of the ultrasonic beam to penetrate chest wall structures is inversely proportional to the frequency of the signal. With transthoracic echocardiography, frequencies of 2.0 to 5.0 MHz are commonly used in adults, and frequencies of 3.5 to 10.0 MHz are used in children. Serial determinations in a given patient using the same conditions and ECHO images (windows) provide the best form of internal control to allow comparisons of test results. In clinical trials, echocardiograms are read and interpreted independently by two or three clinicians to provide a means of control.

Two primary approaches to ECHO are used in clinical practice. Transthoracic echocardiography (TTE) is conducted with the transducer on the chest wall, whereas transesophageal echocardiography (TEE) is conducted with the transducer in the esophagus. In TTE, several modes of operation are possible, the most common being M-mode (motion) and two-dimensional (2D) imaging. Both M-mode and 2D echocardiography provide visualization of heart structures and can indicate numerous structural abnormalities such as aneurysms, wall thickness abnormalities, chamber collapse (e.g., tamponade), and valvular stenosis. TEE is used primarily for assessment of valvular anatomy and function or to image intracardiac masses such as tumors or thrombi and valvular vegetations.[36]

In M-mode echocardiography, the transducer is placed at a single site on the chest (usually along the sternal border), and the ultrasound is directed posteriorly. M-mode echocardiography records only static objects in one plane, producing a single picture of a small region of the heart, or an "ice pick view." Results depend on the exact placement of the transducer with respect to the underlying structures. Conventional M-mode echocardiography provides visualization of the right ventricle, left ventricle, and posterior left ventricular wall and pericardium. If the transducer is swept in an arc from the apex to the base of the heart, virtually the whole heart can be visualized, including the valves and left atrium. Images are displayed as "windows."

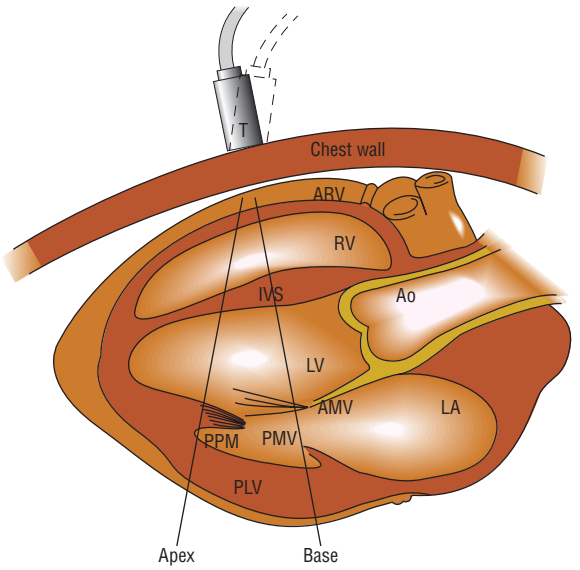

FIGURE 13-8. Schematic of two-dimensional echocardiography to illustrate location of cardiac structures as "seen" by the transducer. The transducer is swept in an arc so that several pictures of the heart are obtained to generate the final electrocardiogram. (Ao, aorta; AMV, anterior mitral valve; ARV, anterior right ventricle; IVS, interventricular septum; LA, left atrium; LV, left ventricle; PLV, posterior left ventricle; PMV, posterior mitral valve; PPM, posterior papillary muscle; RV, right ventricle.) *(Redrawn from Coryu BC, et al. Application of electrocardiography in acute myocardial infarction. Cardiovasc Clin 1995;2:113, with permission.)*

Two-dimensional echocardiography employs multiple windows of the heart, and each view provides a wedge-shaped image. Windows most commonly used include parasternal long- and short-axis and apical two- and four-chamber views (Fig. 13–8). These views are processed onto a videotape to produce a motion picture of the heart. Two-dimensional echocardiography renders increased accuracy in calculating ventricular volumes, wall thickness, and degree of valvular stenosis compared with M-mode echocardiography. Patient-specific calculated parameters such as ejection fraction and wall thickness are compared with standardized values (population-based) or with previously obtained values from the patient. Although ejection fraction is still commonly obtained with echocardiography, it is a derived number, so it is considered subjective. Other tests to determine ejection fraction provide different numbers and highlight the difficulty of comparing results between tests. Ejection fraction from echocardiography is also limited by the diminished views of total ventricular volume able to be visualized, especially in persons with distorted ventricles. Despite these limitations, echocardiography remains the most common modality for ejection fraction determination.

The ECHO can be used for diagnosis and prognosis and as a serial evaluation tool to assess acute and chronic ischemic heart disease and regional left ventricular function. Areas of ischemic myocardium are seen on the ECHO as aberrations in wall motion. Wall motion abnormalities are seen as altered thicknesses of various segments of the heart. Wall motion abnormalities are graded using descriptive terms such as *akinetic, hypokinetic, dyskinetic,* and *hyperkinetic.* It is possible to visualize the complete ventricle (in segments), allowing both global and regional left ventricular function to be assessed. Studies show that the locations of segmental ventricular wall motion abnormalities correspond with areas of CAD. Echocardiography can be linked with the various stress tests (ETT, dipyridamole or dobutamine) to assess stress-induced structural or functional abnormalities (e.g., changes in wall motion). As a serial

monitoring test, echocardiography is comparable with angiography as a prognostic tool and can be used as a treatment planning tool. After myocardial infarction, echocardiography is a useful noninvasive diagnostic tool for detection of ventricular aneurysms, thrombi, and pericardial effusions and can be used serially for diagnostic and prognostic information.

In TEE, the transducer is advanced into the esophagus and rests just behind the heart.[37] The transducer also can be passed into the fundus of the stomach to obtain better images of the ventricles. Images are obtained in either the horizontal or vertical plane.[38] This is a low-risk invasive procedure and does not require routine antibiotic prophylaxis for patients at risk of developing endocarditis. Complications such as esophageal tears or perforation, esophageal burns, transient ventricular tachycardia, minor throat irritation, and transient vocal cord paralysis have been reported rarely. In one series of 10,218 studies, only 1 death (0.0098%) was reported, comparable with that with esophageal gastroduodenoscopy (0.004%). TEE is contraindicated in patients with esophageal abnormalities, in whom passage of the transducer might be limited (e.g., esophageal strictures or varices).

TEE yields higher resolution and improved visualization of structures, especially pulmonary veins and valves, compared with TTE. Interference of ribs, lungs, and subcutaneous tissues is reduced, enabling TEE to be more useful in patients in whom TTE is limited because of pulmonary disease, mechanical ventilation, or obesity. A high-frequency transducer (5 MHz for adults) is used, thus producing better image resolution. TEE is used for the same indications as TTE. Visualization of the heart valves—in particular, the mitral valve—is superior, allowing more accurate evaluation of both native and prosthetic valves. Clinical studies show that it is possible to visualize valvular vegetations as small as 5 mm with TEE. The ACC/AHA guidelines recommend TEE if the TTE is equivocal and the patient has staphylococcal bacteremia. In a study comparing vegetation visualization, TEE detected vegetations in 90% of patients, compared to TTE detecting vegetations in 58%. It also can help to define complications of endocarditis such as thrombosis or valve leakage. In aortic dissection, TEE is able to identify the initial flap and origin of dissection and has an overall sensitivity and specificity of 97% and 100%, respectively. CT remains the diagnostic method of choice for aortic dissection, but TEE offers a sensitive and fast test that can be conducted in the emergency room.

Other uses of TEE include identification of cardiac thrombus, especially thrombi in the left atrium, and assessment of atrial dilation. After transient ischemic attacks or cerebrovascular accidents, TEE may enable identification of the site of cardiac emboli by providing excellent images of likely sources, namely, ventricular or atrial thrombus, valvular vegetation, cardiac shunts, cardiac tumors, or atrial and ventricular septal defects. In a study of almost 1,500 patients with cerebral ischemia or nonvalvular atrial fibrillation, atrial thrombi were seen in 183 patients when evaluated by TEE versus only in 2 patients when evaluated by TTE. TEE can be used for intraoperative cardiac imaging to ascertain development of ischemia.

Another advance with echocardiography has been the addition of Doppler and color-flow Doppler technology. The Doppler principle involves reflecting sound off a moving object—in the case of echocardiography, the red blood cell. As the red cell moves in relation to the transducer, a frequency shift occurs in the reflected wave. Assessment with Doppler echocardiography combines structural images and hemodynamic monitoring. Thus it is possible to evaluate the impact of structural disease on cardiac function and quantify the associated hemodynamics. Color enhancement allows flow direction to be visualized; different colors are used for antegrade and retrograde flow. These improve resolution of structures, identify patterns of blood flow, and allow calculation of flow gradients.

Doppler echocardiography is used primarily in conjunction with traditional echocardiography for analysis of valvular function or blood flow patterns. It allows measurement of transvalvular pressure gradients, valve area, and pressure changes on either side of the valve. Doppler echocardiography is either continuous or pulsed; the former is used to assess pressure changes, whereas the latter is used to localize points of origin and creation of turbulent and high blood flow. Color Doppler is used to visualize blood flow (e.g., regurgitation). Turbulence associated with valvular and wall motion abnormalities can be visualized and quantified clearly. In aortic regurgitation, Doppler echocardiography is one of the best noninvasive technique to assess the pressure and severity of regurgitation. Color-flow mapping allows tracing of the jet direction and an indication of its volume, point of wall contact, and width. Because Doppler echocardiography distinguishes different types of turbulence, it can simultaneously identify more than one type of valvular abnormality (e.g., aortic regurgitation and mitral stenosis) and the source of concomitant heart murmur.

The ACC/AHA 2003 task force has published clinical guidelines for application of echocardiography. In recent years, the use of intraoperative TEE has significantly increased and standard for valvular heart surgery and other types of cardiovascular surgery (Table 13–14).

NUCLEAR CARDIOLOGY[39,40]

Nuclear cardiology continues to be a major advance as a noninvasive testing method. Radionuclides with short half-lives, which can be

TABLE 13-14 Recommendations for Intraoperative Echocardiography

Class I
1. Evaluation of acute, persistent, and life-threatening hemodynamic disturbances in which ventricular function and its determinants are uncertain and have not responded to treatment.
2. Surgical repair of valvular lesions, hypertrophic obstructive cardiomyopathy, and aortic dissection with possible aortic valve involvement.
3. Evaluation of complex valve replacements requiring homografts or coronary reimplantation, such as the Ross prodecure.
4. Surgical repair of most congenital heart lesions that require cardiopulmonary bypass.
5. Surgical intervention for endocarditis when preoperative testing was inadequate or extension to perivalvular tissue is suspected.
6. Placement of intracardiac devices and monitoring of their position during port-access and other cardiac surgical interventions.
7. Evaluation of pericardial window procedures in patients with posterior or loculated pericardial effusions.

Class IIa
1. Surgical procedures in patients at increased risk of myocardial ischemia, myocardial infarction, or hemodynamic disturbances.
2. Evaluation of valve replacement, aortic atheromatous disease, the Maze procedure, cardiac aneurysm repair, removal of cardiac tumors, intracardiac thrombectomy, and pulmonary embolectomy.
3. Detection of air emboli during cardiotomy, heart transplant operations, and upright neurosurgical procedures.

Class IIb
1. Evaluation of suspected cardiac trauma, repair of acute thoracic aortic dissection without valvular involvement, and anastomotic sites during heart and/or lung transplantation.
2. Evaluation of regional myocardial function during and after off-pump coronary artery bypass graft procedures.
3. Evaluation of pericardiectomy, pericardial effusions, and pericardial surgery.
4. Evaluation of myocardial perfusion, coronary anatomy, or graft patency.
5. Dobutamine stress testing to detect inducible demand ischemia or to predict functional changes after myocardial revascularization.
6. Assessment of residual duct flow after interruption of patent ductus arteriosus.

Class III
1. Surgical repair of uncomplicated secundum atrial septal defect.

Cheitlin MD, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography–summary article. J Am Coll Cardiol 2003;42(5):954-970. Full text at http://content.onlinejacc.org/.[41]

used either alone or combined with other substances to form agents with particular properties, such as technetium-99m pyrophosphate, have expanded the role for nuclear imaging in cardiology.

Nuclear imaging techniques have demonstrated equal sensitivity and specificity to many of the invasive "gold standard" testing modalities. The major limitations of nuclear cardiology are the availability of suitable radionuclides and correlation of nuclear images with cardiovascular function.

Despite the availability of new radionuclides, technetium-99m (^{99m}Tc) and thallium-201 (^{201}Tl) remain the two most commonly used radionuclides. ^{99m}Tc is ideal for clinical imaging because it has a half-life of about 6 hours, a single 140-keV photon peak suitable for available imaging systems, primarily gamma ray emission, and the ability to be combined with multiple pharmaceuticals. It is generated in-house by a benchtop generator that reduces transportation costs and provides immediate availability. The short half-life means high doses and repeat injections can be given to evaluate efficacy of interventional therapy over a relatively short period of time. ^{201}Tl has a much longer half-life of 73 hours, which prevents the use of multiple doses close together but does mean that delayed imaging is possible following administration of the agent. Uptake into cells depends on blood flow. The energy from ^{201}Tl is x-ray, with an energy level of 69 to 83 keV. Production of ^{201}Tl requires a cyclotron. Images are obtained with a conventional gamma camera.

Technetium Scanning

Technetium scanning is used for the evaluation of blood pool and myocardial perfusion and as an infarct-avid agent to identify damaged myocardium. Analysis of the blood pool, as in multigated angiography, uses technetium either alone or as a red blood cell complex. The former obtains images following a bolus of technetium and traces its passage from the venous system through the heart to the aorta and is known as *first-pass angiography*. Equilibrium tests where technetium is bound to red blood cells provide an imaging time of several hours, which allows serial images to be obtained. These tests are used to determine right and left ventricular ejection fractions, detect cardiac shunts, estimate ventricular volumes, and view wall motion.[42]

Infarct-avid radionuclides such as technetium-pyrophosphate (^{99m}Tc-PYP) are used to describe the presence and extent of damaged myocardium after myocardial infarction, in suspected myocardial contusion, and following chest wall injuries. Imaging with ^{99m}Tc-PYP is applicable when myocardial infarction is suspected clinically, but patient history, ECG changes, and laboratory evidence are not definitive. Uptake of ^{99m}Tc-PYP into infarcted tissue depends on regional blood flow, myocardial calcium concentration, the degree of irreversible myocardial injury, and time after infarction. ^{99m}Tc-PYP attaches to calcium deposited in the infarcted area, so the approach is known as *hot-spot scanning*. False hot spots may occur where there is necrotic myocardial tissue, as in myocarditis, myocardial abscesses, old infarctions, and myocardial trauma. Additionally, uptake has been seen during unstable angina and ventricular dyskinesia and at sites of ventricular aneurysms, suggesting that these are associated with transient low blood flow. In infarcted tissue, ^{99m}Tc-PYP levels can be as high as 18 to 20 times that of normal myocardium, which gives rise to very distinct borders between the infarcted and normal myocardium. Uptake of ^{99m}Tc-PYP into necrotic myocardium is delayed and not measurable until after about 4 hours of coronary occlusion. Scans prior to this time are usually negative and become positive about 12 hours after occlusion. Peak intensity of ^{99m}Tc-PYP is reached at 48 hours. Washout occurs over 5 to 7 days, so ^{99m}Tc-PYP is a useful late marker of infarction, especially in patients who present late or with a silent infarction. Images are viewed by comparing sternum and rib uptake with that seen in the myocardium. This type of imaging also can be used to assess graft patency after coronary artery bypass. Certain characteristics of the images obtained have been linked with various prognostic values but await confirmation in comparative and long-term prognostic trials.

Other technetium-labeled agents used include technetium-*t*-butyl isonitrile (^{99m}Tc-TIBI); technetium-carboxy isopropyl isonitrile (^{99m}Tc-CPI); technetium-sestamibi, also known as methoxy-isobutyl isonitrile (Tc-MIBI); and technetium-teboroxime. Technetium-sestamibi has a similar myocardial uptake pattern to thallium and produces similar results but with improved image quality because it generates a much higher photon yield. This is now popular as an alternative perfusion imaging agent to thallium. Technetium-teboroxime is still primarily an investigational agent. The main advantage of the newer technetium compounds is the lack of redistribution perfusion, allowing for delayed imaging. This is particularly useful in acute clinical settings; the radiopharmaceutical can be injected during the acute event and imaging undertaken when the patient is more stable.

Thallium Scanning

Thallium is a potassium analog taken up into normal myocardium by passive diffusion and possibly by active transport via the Na^+-K^+-adenosine triphosphatase (ATPase) pump. Uptake depends on regional blood flow and in a linear fashion up to very high blood flow rates. It is used primarily for the analysis of coronary and myocardial perfusion. High thallium uptake occurs in perfused myocardium; in ischemic myocardium, uptake is reduced significantly. Scans taken during acute ischemia or following infarction show areas of poor or nil distribution of thallium corresponding to the site of ischemia. A scan repeated 4 to 6 hours after the initial scan may show a redistribution of the thallium into areas that previously had little to no thallium uptake. These defects are referred to as *partial defects,* demonstrating areas hypoperfused during "stress" but viable myocardium at rest. Redistribution occurs because there is delayed washout of thallium from poorly perfused myocardium, resulting in less contrast between the density of thallium in different areas of the heart. This gives the appearance of "redistribution" of the radionuclide into the previously ischemic area. To enhance evaluation of potential partial defects, a second injection of thallium can be used. Areas of nil distribution are called *cold spots* or *fixed defects* and reflect infarcted myocardium.

Thallium scanning with the aid of computer analysis segregates the images into anatomic regions and specifically localizes areas of dead or necrotic myocardial tissue. In conjunction with echocardiography or single-photon emission computed tomography (SPECT), thallium scans can correlate areas of abnormal wall motion with areas of poor perfusion. Sensitivity and specificity of thallium scanning to detect IHD disease are comparable with those of ETT (75% and 80%, respectively). When used in conjunction with exercise ECG, sensitivity increases to approximately 80%. Thallium scanning also can be used in conjunction with ETT to allow detection of lower levels of ischemia than may be determined from ECG abnormalities or patient symptoms. Thallium is injected at the peak of the ETT, and exercise continues for another 30 to 60 seconds, when the initial images are taken. Repeat images are taken at 3 to 4 hours.

Thallium scanning is useful in patients with atypical chest pain and ambiguous or false-positive ETT to determine if IHD is the cause of symptoms and the ETT abnormalities. Thallium scanning is also used for postoperative evaluation of revascularization or angioplasty procedures and for preoperative evaluation for prognostic stratification for persons with IHD. A normal thallium scan heralds a benign outcome, even in patients who have angiographically evident CAD. The finding of redistribution is a marker of jeopardized but viable myocardium that has important prognostic value. Major cardiac events such as myocardial infarction in patients with normal ^{201}Tl studies average less than 1% per year. The

best predictor of coronary events, which correlates thallium scans with clinical significance, is the number of myocardial segments with transient (redistribution) defects.

A number of other radiopharmaceuticals have found some use in cardiovascular testing, such as labeled antimyosin antibodies. Theoretically, these antibodies should be more specific markers of myocyte necrosis. The currently used antibodies are a murine Fab fragment. Phase I, II, and III trials suggest that these are highly specific for irreversibly injured myocytes, but they have limitations in terms of pharmacokinetic properties. Uptake into myocardial tissues is very slow, with a prolonged blood pool activity seen for at least 24 hours. In clinical use, the antibody is given within 24 hours of the infarction, and planar or SPECT imaging is undertaken 24 to 48 hours later. Despite the supposed specificity of the antibody to myosin, localization is more dependent on blood flow than on myosin concentration, so measurement of infarction size is not as accurate as expected. Another investigational agent, [^{123}I]phenylpentadecanoic acid, is able to assess both myocardial perfusion and metabolism by virtue of its affinity for fatty acid metabolism.

Pharmacologic Stress Testing

9 Pharmacologic stress testing is an alternative to ETT and ETT with thallium in patients who are unable or unwilling to undergo ETT.[43,44] Additionally, pharmacologic stress testing is now used more than 50% of the time to assess coronary perfusion. The pharmacologic agent produces stress by a hyperemic (vasodilator) response or by increasing myocardial oxygen demand (heart rate and myocardial contractility). Agents currently used include dipyridamole and adenosine (hyperemic stress) and dobutamine (myocardial stress). Pharmacologic stress tests can be linked to various imaging techniques such as thallium planar scanning, SPECT, MRI, and echocardiography. Dobutamine is linked most frequently to echocardiography, allowing quantification of wall motion abnormalities, which correlate well with areas of ischemia.

The principle of dipyridamole and adenosine thallium imaging is related to their coronary arteriolar vasodilator properties. Dipyridamole inhibits adenosine cellular reuptake, resulting in increased concentrations of adenosine in the blood and tissues. Adenosine is a potent coronary artery vasodilator and can increase perfusion four to five times over baseline. Areas distal to a coronary artery obstruction will show a relative hypoperfusion compared with normal coronary arteries because there is reduced perfusion pressure as a consequence of preferential perfusion of normal segments over stenotic segments. Acutely, these areas will appear as cold spots, but on the redistribution scans, the defects will fill, indicating viable but jeopardized myocardium.

Dipyridamole is given intravenously in a dose of 0.142 mg/kg per minute over 4 minutes. This dose has been shown to increase baseline coronary blood flow in the normal tissues up to four to five times over control. Some studies have used doses up to 0.84 mg/kg to enhance the vasodilator response. At the higher dose, acute adverse effects such as chest pain are more common. Adenosine for stress testing is an unlabeled use of this drug. Adenosine is given over 6 minutes at a dose of 0.140 mcg/kg per minute. At the end of infusion (dipyridamole) or after 3 minutes (adenosine), a 2.5- to 4-mCi dose of thallium is given. The maximum effect of dipyridamole occurs at 5 to 7 minutes and adenosine at approximately 30 seconds after the end of infusion. Imaging follows immediately and can be repeated at 24 hours (thallium scanning) to heighten the redistribution defects from fixed or partial defects.

Like exercise thallium scanning, dipyridamole and adenosine scanning or echocardiography is used to detect IHD, evaluate the prognosis of patients with known disease, assess patients after myocardial infarction, and as a risk-stratification method prior to vascular, cardiac, and noncardiac surgery. Pharmacologic stress testing evaluates wall motion abnormalities and perfusion defects under stress and has been shown in numerous studies to have comparable sensitivity and specificity with the traditional ETT. Using planar scanning and dipyridamole, sensitivity to detect IHD ranges from 67% to 95% with a 67% to 100% specificity. A summary of 13 studies in almost 900 patients gave a pooled sensitivity of 85% and specificity of 87%. SPECT scanning has at least comparable sensitivity and slightly lower specificity to planar imaging but produces higher-quality imaging, which may enhance quantitative interpretation.

Dipyridamole testing is safe and effective in the elderly and in those with unstable angina immediately after myocardial infarction (within days). It also may be used to assess the status of revascularization procedures.[43] As a prognostic test, dipyridamole testing is very useful. In several studies, abnormal scans have shown about a 10-fold increase in event rates over 1 to 2 years of followup. Abnormal scans also have been shown to be an independent risk factor for myocardial infarction and death with a relative risk ratio of 3.1. Reversible defects correlate best with events, with one study demonstrating a 4.41 relative risk ratio for cardiac events.

Adverse effects with dipyridamole thallium testing are minimal, the main adverse effects being chest pain (with or without ischemic changes on the ECG), headache, dizziness, and nausea. Adverse effects are related to the increased adenosine activity and can be ameliorated by xanthine compounds because they are direct competitive antagonists of adenosine. Caffeine products must be avoided for about 24 hours prior to the test. Adenosine is associated with a higher incidence of adverse effects (80% versus 50%), but these are very transient, and some studies have shown that patients prefer it over dipyridamole. Both agents are relatively contraindicated in patients with a history of bronchospasm.

Dobutamine, a synthetic catecholamine, raises heart rate and cardiac output, which increases myocardial oxygen demand. Ischemia develops in areas where stenosis prevents the increase in oxygen demand from being met with increased blood flow. Ischemia is detected by the ECHO as regional wall motion abnormalities or with thallium scanning.

Dobutamine, when used as a stress test, is given in doses of 10 to 40 mcg/kg per minute.[44] The dose is titrated at 3-minute intervals in increments of 10 mcg/kg per minute. If thallium is used, it is given 2 to 3 minutes before the end of infusion. Atropine 0.5 to 1 mg may be given to augment the heart rate response to 85% of the patient's calculated maximum. ECG and blood pressure are recorded continuously throughout the test, and ECHO recordings are made during the last minute of each dose level and during recovery.

β-Blocker and calcium channel blocker therapy may interfere with the heart rate response to dobutamine stress tests and is recommended to be discontinued prior to the test. Dobutamine stress testing is relatively well tolerated. Reasons to discontinue the test include development of severe chest pain, extensive new wall motion abnormalities, ST-segment elevation and depression suggestive of significant ischemia, tachyarrhythmias, and symptomatic reductions in blood pressure.[45] β-Blockers can be used to reverse most adverse effects if they persist. Dobutamine stress tests are contraindicated in patients with aortic stenosis, uncontrolled hypertension, and severe ventricular arrhythmias. Ventricular fibrillation and myocardial infarction occur at a rate of approximately 0.05%.

Dobutamine stress testing has been studied as a diagnostic, prognostic, and therapy assessment tool after myocardial infarction and for unstable and chronic angina. One study compared dobutamine, dipyridamole, and ETT with coronary angiography for diagnostic accuracy in patients with IHD and showed an overall accuracy of 87% for ETT, 82% for dobutamine, and 77% for dipyridamole. A recent review of 14 studies of 942 patients for the detection of IHD with dobutamine stress testing calculated the sensitivity to be

approximately 80% (70% to 100%) with a 75% (64% to 100%) specificity. Sensitivity is highest for detection of three-vessel disease (92%). Dobutamine-sestamibi stress testing seems to be less sensitive than thallium even for multivessel disease. Comparative studies with ETT and dipyridamole echocardiography show dobutamine to be more sensitive. After myocardial infarction, dobutamine stress testing identifies patients at high risk of subsequent cardiac events. For patients with suspected or known IHD, a positive dobutamine stress test is an independent predictor of cardiac events, and a negative test affords protection from cardiac death.[46]

The current 2006 guidelines on the use of these tests in clinical practice are rather brief, only to say that cardiac imaging is currently undergoing rapid evolution. The use of these types of test in intermediate to high risk patients are markedly increasing. The identification of asymptomatic intermediate-risk patients (10% to 20% risk of cardiovascular death/myocardial infarction in 10 years) is still undergoing considerable debate. The clinical treatment of these patients with atherosclerosis *must* include appropriate risk factor treatment according to existing AHA guidelines. Patients with high-risk findings of cardiovascular disease may require more invasive testing but global risk reduction will still be required before and after there testing or invasive treatment if essential.[47]

COMPUTED TOMOGRAPHY

CT scanning is becoming more popular as a primary screening procedure in the evaluation of CVD and function because it provides similar information as other diagnostic procedures (e.g., catheterization, echocardiography) and is less expensive and less invasive than a routine heart catheterization. In recent years, advancement in technology has considerably enhanced definition and spatial resolution of all cardiac structures that are useful in evaluation of many specific areas, such as coronary arteries, aortic and pericardial disease, and paracardiac and cardiac masses. Very accurate determination of chamber volume and size and mass calculations of myocardial wall thickness can be obtained from CT scanning than with other methods such as echocardiography or angiography. Additionally, CT scanning acquires three-dimensional images.[48] New techniques such as ultrafast CT (cine-CT) scanning have significantly improved problems with cardiac motion that distorted conventional CT images. In cine-CT scanning, complete tomograms are assembled within one cardiac cycle (50 msec), thus providing real-time images. For ultrafast CT scanners, a set event within the cardiac cycle (determined by ECG) usually is used as initiator for imaging to ensure standardization. Conventional CT scanning requires that images be correlated with the cardiac cycle by gating the CT to the ECG. Cine-CT scans examine the heart at 10 to 14 tomographic levels in <10-mm slices. The resolution has improved considerably in the last few years as a result of advances in many areas of computer science and now 64-section multidetector CT scans are significantly better.

Although still in its infancy, cine-CT scanning has matured significantly and is now being used as a screening tool for evaluating the risk of significant obstructive CAD and as a diagnostic tool for CAD in limited centers. Recent AHA/ACC guidelines address the current state of practice with this methodology. The CT scan will show localized areas of infarction and abnormal perfusion and allows quantification of the extent and density of coronary artery calcification.[49] Cine-CT scanning is more sensitive and specific than fluoroscopy in identifying the extent and density of coronary artery calcification. The calcium score (calcium density and volume of calcium) in patients older than 30 to 70 years with known CAD is significantly higher than in subjects with no CAD and appears to correlate well with the degree of coronary artery occlusion (Table 13–15).[50]

New CT scanning may be more definitive and accurate in the diagnosis of aortic dissection and evaluation of the pericardium than TTE but in many expert centers, TEE maybe as good. Currently 3D echocardiography can add other important information to a critical patient's case, for example, valvular leaks and wall motion changes. Diagnostic accuracy of aortic dissections with CT scanning is >90%. CT scanning affords definition of the

TABLE 13-15 ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring By Computed Tomography—Conclusions

1. What is the role of coronary calcium measurement by coronary CT scanning in asymptomatic patients with intermediate CHD risk (between 10% and 20% 10-year risk of estimated coronary events)?

The Committee judged that it may be reasonable to consider use of CAC measurement in such patients based on available evidence that demonstrates incremental risk prediction information in this selected (intermediate-risk) patient group. This conclusion is based on the possibility that such patients might be reclassified to a higher risk status based on high CAC score, and subsequent patient management may be modified.

2. What is the role of coronary calcium measurement by CT scan in patients with low CHD risk (below 10% 10-year risk of estimated CHD events)?

The Committee does not recommend use of CAC measurement in this selected patient group. This patient group is similar to the "population screening" scenario, and the Committee does not recommend screening of the general population using CAC measurement.

3. What is the role of coronary calcium measurement by fast CT scan in asymptomatic patients with high CHD risk (greater than 20% estimated 10-year risk of estimated CHD events, or established coronary disease, or other high-risk diagnoses)?

The Committee does not advise CAC measurement in this selected patient stratum as they are already judged to be candidates for intensive risk-reducing therapies based on current NCEP guidelines.

4. Is the evidence strong enough to reduce the treatment intensity in patients with calcium score = 0 in patients who are considered intermediate risk before coronary calcium score?

No evidence is available that allows the Committee to make a consensus judgment on this question. Accordingly, the Committee felt that current standard recommendations for treatment of intermediate risk patients should apply in this setting.

5. Is there evidence that coronary calcium measurement is better than other potentially competing tests in intermediate risk patients for modifying cardiovascular disease risk estimate?

In general, CAC measurement has not been compared to alternative approaches to risk assessment in head-to-head studies. The question cannot be adequately answered from available data.

6. Should there be additional cardiac testing when a patient is found to have high coronary calcium score (e.g., CAC is greater than 400)?

Current clinical practice guidelines indicate that patients classified as high risk based on high-risk factor burden or existence of known high-risk disease states (e.g., diabetes) are regarded as candidates for intensive preventive therapies (medical treatments). There is no clear evidence that additional noninvasive testing in this clear patient population will result in more appropriate selection of treatments.

7. Is there a role for CAC testing in patients with atypical cardiac symptoms?

Evidence indicates that patients considered to be at low risk of coronary disease by virtue of atypical cardiac symptoms may benefit from CAC testing to help in ruling out the presence of obstructive coronary disease. Other competing approaches are available, and most of these competing modalities have not been compared head-to-head with CAC.

8. Can coronary calcium data collected to date be generalized to specific patient populations (women, African American men)?

CAC data are strongest for Caucasian, non-Hispanic men. The Committee recommends caution in extrapolating CAC data derived from studies in white men to women and to ethnic minorities.

9. What is the appropriate followup when an incidental finding in the lungs or other noncardiac tissues is found on a fast coronary CT study?

Current radiology guidelines should be considered when determining need for followup of incidental findings on a fast CT study, such as that which was recently published to guide followup of small pulmonary nodules.

CAC, coronary artery calcium; CHD, coronary heart disease; CT, computed tomography; NCEP, National Cholesterol Education Program.

Greenland, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain. J AM Coll Cardiol 2007;49:378–402.

edges of the intimal flap of the dissection, and true and false channels can be seen. It also demarcates the components of the myocardial wall from the inner endocardial wall through to the epicardial surface and pericardium, allowing visualization of abnormalities, such as aneurysms and thrombin. Detection of the presence of a thrombus on a CT scan is comparable in accuracy with 2D echocardiography. The pericardium appears as a distinct entity and can be evaluated for thickening and calcification. CT scanning is the most sensitive technique to differentiate types of pericarditis and estimate pericardial fluid volume. Compared with echocardiography, CT scanning is equivocal to define loculated and hemorrhagic effusions. Important advances in 3D echocardiography is currently making significant advancement as we have seen with new CT scanners.

In the evaluation of cardiac masses, CT scanning shows the mass as a distinct space-occupying entity. Tissue density differentiation as seen on a CT scan allows characterization of density, aiding in determination of the nature of masses. Masses as small as 0.5 to 1 cm can be identified on CT scans.

Like radionuclide assessment, contrast angiography, and echocardiography, CT scanning can be used to calculate ejection fraction, left ventricular volume, and stroke volume. The blood pool is defined with intravenous iodinated contrast material. Ventricular volumes, ejection fraction, and stroke volume are determined directly from the blood pool on each image. Values obtained with CT scanning are more accurate and reproducible than those obtained on angiography and ECHO. The three-dimensional image of a CT scan also allows determination of the extent and distribution of LVH in patients with hypertrophic or congestive cardiomyopathy.

CT scanning has proven to be an effective noninvasive method to visualize congenital heart disease, but its role is challenged by the higher-resolution capacity of MRI.[50] For measuring parameters in some congenital disorders, such as evaluation of ventricular function and estimation of the volume of cardiac shunts, CT scanning still remains an important choice. As patients have more procedures related to implanted metallic devices, CT scanning is a very important option and newer CT scanners are making major strides in many areas of congenital heart disease.

A few practical considerations when one considers CT for evaluating the coronary arteries. Diagnostic quality imaging may require in most cases the patient to have normal sinus rhythm, and a targeted heart rate of less than 65 beats per minute during image acquisition. The patient's heart rate should be measured during a breath-holding test to determine whether the administration of a β-blocker is necessary. If the heart rate drops after inspiration breath holding by 10 beats per minute, the study should be of good quality. However, sometimes short-acting β-blockers are needed to reduce heart rates to below 65 beats per minute.[51]

Recently published guidelines from the AHA[52] on the assessment of coronary artery disease by cardiac computed tomography have an excellent review of the topic with a wonderful reference section. Table 13–16 is an overview of current considerations for scanning. Most expert panels generally agree that patients with a prior probability of a coronary event in the intermediate range (>6% in 10 years but <20% in 10 years), a calcium score of >100 would yield a posttest probability >2% per year in the majority of patients. This would place the patient in the range of a coronary heart disease risk equivalent population and within a level requiring secondary prevention strategies. Table 13–17 describes the American College of Cardiology Foundation (ACCF) results of appropriate use of cardiac computed tomography in cardiovascular disease from the Appropriateness Criteria Working Group.[53]

In summary, CT scanning, especially cine-CT scanning, is a rapidly evolving technique for evaluation of CVD. It remains an expensive alternative to other methodologies in many instances, but the high resolution and spatial capabilities mean that CT scanning offers unique properties. It is important to remember that CT scanning radiation dosage on average is three times more than a routine heart catheterization. Current coronary angiography has a mean effective radiation dosage of approximately 5 mSv (millisievert) and cardiac CT varies between 6.9 and 20 mSv depending on the configuration.[54,55]

TABLE 13-16 Criteria for Cardiac Computed Tomography (CCT) and Cardiac Magnetic Resonance (CMR) ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 Appropriateness

Appropriate test for specific indication (Score 7–9)
Detection of CAD: Symptomatic
Intermediate pretest probability of CAD
ECG uninterpretable *or* unable to exercise
Evaluation of Intracardiac Structures (Use of CT Angiogram)
Evaluation of suspected coronary anomalies
Acute Chest Pain (Use of CT Angiogram)
Intermediate pretest probability of CAD
No ECG changes and serial enzymes negative
Morphology (Use of CT Angiogram)
Assessment of complex congenital heart disease including anomalies of coronary circulation, great vessels, and cardiac chambers and valves
Evaluation of coronary arteries in patients with new onset heart failure to assess etiology.
Evaluation of Intra- and Extracardiac Structures (Use of Cardiac CT)
Evaluation of cardiac mass (suspected tumor or thrombus)
Patients with technically limited images from echocardiogram, MRI, or TEE
Evaluation of pericardial conditions (pericardial mass, constrictive pericarditis, or complications of cardiac surgery)
Patients with technically limited images from echocardiogram, MRI, or TEE
Evaluation of pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation
Noninvasive coronary vein mapping prior to placement of biventricular pacemaker
Noninvasive coronary arterial mapping, including internal mammary artery prior to repeat cardiac surgical revascularization
Evaluation of Aortic and Pulmonary Disease (Use of CT Angiogram[a])
Evaluation of suspected aortic dissection or thoracic aortic aneurysm
Evaluation of suspected pulmonary embolism
Uncertain for specific indication (Score 4–6)
Inappropriate test for that indication (Score 1-3)

CAD, coronary artery disease; ECG, electrocardiogram; MRI, magnetic resonance imaging; TEE, transesophageal echocardiography.
[a]Nongated, CT angiogram which has a sufficiently large field of view for these specific indications.
Hendel (Guidelines). JACC 2007;48:1475. Summary of Table 11–20.

POSITRON EMISSION TOMOGRAPHY

PET is a relatively new modality for diagnostic imaging in CVD medicine.[56,57] PET has found a niche to characterize myocardial physiologic and metabolic activity, perfusion, and viability. PET can measure regional myocardial uptake of exogenous glucose and fatty acids, quantitate free fatty acid metabolism, define perfused myocardium energy source(s), and evaluate myocardial chemoreceptor sites.[61] Although many other techniques can be used similarly to evaluate myocardial function, PET images are superior in definition. The primary advantages of PET are its noninvasive nature, the ability to do repeat scans within a short period of time, such as before and after percutaneous transluminal coronary angioplasty (PTCA), and the reproducibility of images over time. PET is very expensive because of the need for onsite cyclotrons for many of the radiotracers, and there is limited availability of sites that offer the technique. Cheaper forms of PET-like scanning are in development, but image resolution is lower.

PET uses positron-emitting isotopes such as oxygen-15, nitrogen-13, carbon-11, and fluoride-18. These are incorporated into sub-

TABLE 13-17 Interpretation and Recommendations for CT Heart Scanning and CACP Scoring

Negative test result
A negative test (score = 0) makes the presence of atherosclerotic plaque, including unstable or vulnerable plaque, highly unlikely.
A negative test (score = 0) makes the presence of significant luminal obstructive disease highly unlikely (negative predictive power by EBCT on the order of 95% to 99%).
A negative test is consistent with a low risk (0.1% per year) of a cardiovascular event in the next 2 to 5 years.
Positive test result
A positive test (CAC 0) confirms the presence of a coronary atherosclerotic plaque.
The greater the amount of coronary calcium, the greater the atherosclerotic burden in men and women, irrespective of age.
The total amount of coronary calcium correlates best with the total amount of atherosclerotic plaque, although the true atherosclerotic burden is underestimated.
High score
A high calcium score (an Agatston score >100) is consistent with a high risk of a cardiac event within the next 2 to 5 years (2% annual risk).
Risk prediction
Coronary artery calcium measurement can improve risk prediction in conventional intermediate-risk patients, and CACP scanning should be considered in individuals at intermediate risk for a coronary event (1.0% per year to 2.0% per year) for clinical decision making with regard to refinement of risk assessment.
Decisions for further testing (such as stress testing or cardiac catheterization) beyond assistance in risk stratification in patients with a positive CACP score cannot be made on the basis of coronary calcium scores alone, as calcium score correlates poorly with stenosis severity in a given individual and should be based upon clinical history and other conventional clinical criteria.

CACP, coronary artery calcified plaque; CAC, coronary artery calcium; CT, computed tomography; EBCT, electron-beam computed tomography.

stances such as water, glucose analogs, or fatty acids, the metabolic substrates for myocardial tissue. For myocardial perfusion studies, rubidium-82 (^{82}Rb), nitrogen-13 ammonia ([^{13}N]H_3), and $^{15}O_2$-labeled water are used. For myocardial substrate metabolism studies, [^{11}C]palmitate, [^{11}C]acetate, and [^{18}F]2-deoxyglucose (FDG) are used. All these substances have very short half-lives (<10 minutes). In the fasting state, perfused myocardium primarily uses fatty acids as energy source. Postprandially, glucose is the preferred substrate. Ischemic myocardium primarily metabolizes glucose because mitochondrial fatty acid oxidation is impaired. Hence, with PET using either a fatty acid or glucose substrate, ischemic versus nonischemic areas can be defined. Frequently, PET is used in conjunction with pharmacologic stress testing to provoke ischemia, with images obtained before and after stress application.

Uptake of ^{82}Rb occurs via the Na^+-K^+-ATPase pump and occurs preferentially in viable tissue. Net uptake into tissue resolving from an ischemic insult and infarcted tissue is reduced. With a half-life of 1.26 minutes, serial images of myocardial perfusion can be taken as frequently as every 5 minutes, and a dobutamine stress test is completed within 45 minutes. Comparative studies with ETT, SPECT, and stress echocardiography show PET to be more accurate in the detection of IHD. The substrate [^{13}N]H_3 rapidly crosses capillary membranes and is trapped in the myocardium by glutamate–glutamine reactions. This product produces high-contrast images with a sensitivity of 88% to 97% and a specificity of 90% to 100% to detect IHD. $^{15}O_2$-labeled water has a high extraction ratio into myocardial tissue, which appears to be independent of blood flow or the metabolic state of the myocardium. $^{15}O_2$-labeled water studies are done in conjunction with [^{15}O]carbon monoxide (labels red blood cells in the vascular space) studies to help eliminate some of the background activity that occurs as a result of the high extraction ratio.[58]

Tracers used for assessment of myocardial metabolism are selected based on the type of metabolism of interest: FDG traces glucose metabolism, [^{11}C]palmitate traces mitochondrial fatty acid metabolism, and [^{11}C]acetate is an indirect marker for myocardial oxygen consumption, allowing assessment of ventricular performance. [^{11}C]Palmitate is a useful marker for normal myocardial oxygen consumption because baseline energy needs of the myocardium are met through fatty acid oxidation. Clearance of [^{11}C]palmitate is biexponential, and studies in animals and in healthy men show clearance to be proportional to cardiac workload and myocardial oxygen consumption. In acute ischemia, the first component of clearance is reduced and the second is increased. The use of [^{11}C]palmitate to assess myocardial metabolism in ischemic tissue is limited because there is altered transport and storage of the compound and significant back diffusion of the agent into the vascular space.

FDG accumulates in the heart proportional to glucose use by the myocardial cell and so is a marker of cell viability. FDG studies help to identify the affected vascular bed and allow evaluation as to whether angioplasty or surgery might be used. Detection of hibernating myocardium is possible because it predominantly uses glucose and can be seen readily on PET scans. Patients with a significant degree of jeopardized or hibernating myocardium identified on PET scanning then could be candidates for revascularization procedures. In contrast, a perfusion study would not show as good differentiation of infarcted versus hibernating tissue, and revascularization may not be considered. In studies of recovery of left ventricular function following revascularization, PET has a positive predictive value of 72% and a negative predictive value of 83%. PET with FDG has been used in the assessment of cardiomyopathies. In ischemic cardiomyopathy, discrete regional ischemia is seen as a patchy, nonhomogeneous uptake of the tracers; dilated cardiomyopathies show global decreased uptake of tracers.

In CAD, PET is used to assess and follow the physiologic significance of stenotic lesions. After infarction, PET myocardial substrate metabolism studies are used to evaluate the amount and activity of viable tissue around the infarcted area and the site and extent of infarction. Myocardial perfusion studies with PET identify more accurately the viable and nonviable myocardium compared with technetium and thallium. PET also quantifies regional myocardial perfusion more accurately than other modalities. When linked with physiologic or pharmacologic stress tests, PET enables evaluation of the myocardium under stress conditions. Studies in patients with more than 50% stenosis on angiography suggest that dipyridamole stress SPECT and [^{13}N]ammonia PET are comparable tests to assess coronary artery perfusion, with respective sensitivities of 98% and 96% and specificities of 88% and 81%. SPECT analysis using FDG compared with PET with FDG shows comparable accuracy for the detection of CAD. Comparative studies with SPECT thallium in conjunction with bicycle ergometer or dipyridamole versus PET perfusion scanning showed comparative sensitivities (76% to 79%) but improved specificity (90% versus 82%, p <0.005).[58]

The future of PET appears promising. Improved tomographic scanners, development of new radiopharmaceuticals, and improved understanding of substrate metabolism and its relationship to myocardial tissue viability will provide new dimensions to assess and evaluate myocardial function. Research enterprises are developing agents to label receptors as a tool to determine cardiovascular physiology and how altered receptor function, biochemical abnormalities, substrate metabolism, or other as yet unrecognized abnormalities impair cardiac function. It continues to be used mostly to answer research questions than in clinical practice settings. A few specialized, large centers do offer PET scanning.

CARDIAC CATHETERIZATION AND ANGIOGRAPHY[59]

4 Development of the cardiac catheterization technique was a major milestone in the diagnosis and management of CVD because

it provided a physiologic and anatomic approach to assess patency of coronary vessels and hemodynamic parameters of cardiac function. Cardiac catheterization is the technique used to gain vascular access to the coronary arteries by intravascular catheters and heart chambers. Once cardiac catheterization is complete, other diagnostic and therapeutic procedures, such as angiography, ventriculography, and PTCA, and drug administration (e.g., thrombolytics) may be undertaken. Following interventional procedures such as PTCA, catheterization with angiography can be used to evaluate efficacy of the intervention. In recurrent clinical syndromes, following a procedure, catheterization is used to help delineate a new management strategy. Catheterization is also now used commonly with PTCA and/or drug therapy in the management of acute coronary syndromes.

Additionally, catheterization allows assessment of valvular function and computation of various cardiac performance parameters such as cardiac output, stroke volume, systemic vascular resistance, cardiac chamber pressures, and blood flow. It also allows for placement of cardiac pacemakers. Drug administration during cardiac catheterization is used primarily for assessment of end points in clinical trials (e.g., thrombolytics to assess coronary artery patency), for management of events (e.g., chest pain) during catheterization, or for diagnostic purposes (e.g., ergonovine to evaluate coronary spasm). Further applications of cardiac catheterization include aortic root angiography, pulmonary angiography, retrieval of foreign bodies, and atherectomy.[60]

More than 1 million cardiac catheterizations are performed in the United States each year, making it the second most frequent in-hospital procedure. Images obtained during catheterization are stored on 35-mm cineradiographic film or are digitized, allowing comparison of studies at a later date. The ACC/AHA guidelines on angiography and PTCA describe the classes I, II, and III indications for each of these procedures; examples are given in Tables 13–18 and 13–19.[63] The guidelines for angiography, PTCA, and catheterization also include recommendations regarding technique, procedures, facilities, personnel, and training.

The cardiac catheterization procedure requires vascular access, usually obtained percutaneously at brachial or femoral arteries or veins. Left-sided catheterization provides access to the aorta, left ventricle, and left atrium. Right-sided catheterization enables the right side of the heart, coronary sinus, pulmonary arteries, and pulmonary wedge position to be reached. Left-sided catheterization is used for coronary angiography and ventriculography, whereas right-sided catheterization is used for determination of cardiac performance parameters.

Prior to an elective procedure, the patient is given nothing by mouth (after midnight) except for oral medications. It is not necessary to stop any medications except warfarin prior to catheterization. Patients receiving warfarin may be transitioned to low-molecular-weight or unfractionated heparin or anticoagulation may be discontinued depending on the clinical scenario about 3 days prior to the procedure. Heparin products are stopped about 6 hours before the procedure to allow normalization of coagulation. There are no data to support low-molecular-weight heparin during catheterization procedures because its longer half-life may increase the risk of intra- and postprocedural bleeding. Patients who require anticoagulation prior to angiography (e.g., those with acute coronary syndromes) usually are treated with unfractionated heparin or low-molecular-weight heparin.

Patients frequently develop chest pain and/or vasospasm during introduction and manipulation of catheters and injection of angiographic dyes. Nitroglycerin/nitroprusside and/or morphine may be given for chest pain. Nitroglycerin also is used to prevent vasospasm and is given sublingually or by intravenous infusion. The use of nitroprusside has increased in recent years because it is a direct smooth muscle vasodilator. Sedatives, such as midazolam and other short-acting benzodiazepines, frequently are given to ensure patient comfort and safety, but the patient is awake and aware of the procedure. Patient cooperation is necessary to obtain the angiographic views and assess symptoms. The patient is required to remain still for about 6 to 8 hours to reduce the risk of bleeding from the catheter entry site(s). Depending on the procedure, patients may be discharged the same day or within 24 hours, if stable.

Heparin products are used during procedures such as angiography, left-sided heart catheterization, and PTCA to prevent thrombotic complications. Depending on the procedure undertaken,

TABLE 13-18 Recommendations for Coronary Angiography in Patients with Known or Suspected Coronary Artery Disease Who Are Currently Asymptomatic or Have Stable Angina

Class I
1. Canadian Cardiovascular Society (CCS) class III and class IV angina on medical treatment. (*Level of Evidence: B*)
2. High-risk criteria on noninvasive testing regardless of anginal severity. (*Level of Evidence: A*)
3. Patients who have been successfully resuscitated from sudden cardiac death or have sustained (>30 seconds) monomorphic ventricular tachycardia or nonsustained (<30 seconds) polymorphic ventricular tachycardia. (*Level of Evidence: B*)

Class IIa
1. CCS class III or IV angina, which improves to class I or II with medical therapy. (*Level of Evidence: C*)
2. Serial noninvasive testing with identical testing protocols, at the same level of medical therapy, showing progressively worsening abnormalities. (*Level of Evidence: C*)
3. Patients with angina and suspected coronary disease who, because of disability, illness, or physical challenge, cannot be adequately risk stratified by other means. (*Level of Evidence: C*)
4. CCS class I or II angina with intolerance to adequate medical therapy or with failure to respond, or patients who have recurrence of symptoms during adequate medical therapy as defined above. (*Level of Evidence: C*)
5. Individuals whose occupation involves the safety of others (e.g., pilots, bus drivers, etc.) who have abnormal but not high-risk stress test results or multiple clinical features that suggest high risk. (*Level of Evidence: C*)

Class III
1. Angina in patients who prefer to avoid revascularization even though it might be appropriate. (*Level of Evidence: C*)
2. Angina in patients who are not candidates for coronary revascularization or in whom revascularization is not likely to improve quality or duration of life. (*Level of Evidence: C*)
3. As a screening test for coronary artery disease in asymptomatic patients. (*Level of Evidence: C*)
4. After coronary artery bypass grafting or angioplasty when there is no evidence of ischemia on noninvasive testing, unless there is informed consent for research purposes. (*Level of Evidence: C*)
5. Coronary calcification on fluoroscopy, electron-beam computed tomography, or other screening tests without criteria listed above. (*Level of Evidence: C*)

Scanlon PJ, Faxon DP, Audet A-M, et al. ACC/AHA Guidelines for Coronary Angiography: Executive Summary and Recommendations. Circulation 1999;99:2345–2357. ©American Heart Association, Inc.

TABLE 13-19 Recommendations for Coronary Angiography in Patients with Nonspecific Chest Pain

Class I
High-risk findings on noninvasive testing. (*Level of Evidence: B*)

Class IIa
None.

Class IIb
Patients with recurrent hospitalizations for chest pain who have abnormal (but not high-risk) or equivocal findings on noninvasive testing. (*Level of Evidence: B*)

Class III
All other patients with nonspecific chest pain. (*Level of Evidence: C*)

Scanlon PJ, Faxon DP, Audet A-M, et al. ACC/AHA Guidelines for Coronary Angiography: Executive Summary and Recommendations. Circulation 1999;99:2345–2357. ©American Heart Association, Inc.

heparin is either discontinued almost immediately following the procedure or continued for 12 to 24 hours. Heparin administration during the procedure is measured with the activated clotting time, not the partial thromboplastin time. For patients undergoing percutaneous coronary intervention, aspirin, and clopidogrel are used prior to and following the procedure. Despite the invasive nature of the procedure, there are no data to support the need for prophylactic antibiotics in patients at risk for bacterial endocarditis because of valvular prostheses or a prior history of rheumatic fever. At present, the infectious risk of this procedure is extremely low. With the advent of classes IIb/IIIa receptor antagonists such as tirofiban, eptifibatide, and abciximab, which improve short- and long-term coronary artery patency rates with high-risk percutaneous coronary intervention, patients who receive a stent also will receive one of these agents prior to, during, and/or after the procedure. Abciximab is usually preferred.

During the procedure, hemodynamic parameters, blood pressure, and heart rate are monitored continuously. ECG monitoring and intermittent 12-lead ECGs are also maintained. Measurements taken during catheterization are obtained only after hemodynamic stabilization: at baseline, following catheter movement, or during pharmacologic intervention. Information obtained during catheterization is in real time and is assumed to reflect the ongoing status of the coronary circulation. Procedurally related vasospasm may be misleading because the catheter itself is a powerful stimulus for spasm.

Complications associated with cardiac catheterization procedures and attending angiographic or interventional activities are related to the expertise and experience of the operator, with case load being a good indicator of the latter. The incidence of significant complications related to catheterization with angiography is reported to be less than 2%, with mortality approximately 0.11%. Patient factors such as hemodynamic stability and renal function increase risk. There are no absolute contraindications to coronary angiography, and the relative contraindications are not well substantiated (Table 13–20). In essence, clinical stability of the patient and potential benefit of the procedure in terms of future patient management predicate the importance of relative contraindications. Complication rates, especially those of a thrombotic nature, increase with the dwell time of the catheters, duration of catheterization, catheter type, and operator technique. Bleeding complications can be reduced by ensuring that patients have normal coagulation studies prior to the procedure and remain at bedrest for several hours after the procedure, and that the nursing staff undertakes good care of the catheter entry and exit sites. In the event of bleeding complications, direct pressure is required with sandbags, followed by emergency surgery if there is no resolution, to prevent further complications. Heart perforation is an uncommon but potentially lethal complication requiring emergency surgical intervention. Other complications, such as a vagal reflex with hypotension, bradycardia, and nausea, can occur. These occur most frequently in conjunction with patient anxiety and can be prevented or treated with atropine. An increased predisposition to myocardial infarction during and after the procedure is seen in patients with unstable angina, recent subendocardial infarction, and type 1 diabetes mellitus. After catheterization, patients may have elevated creatine phosphokinase and troponins as a consequence of tissue damage during the procedure. There is some controversy as to how to interpret these values with respect to what they indicate regarding myocardial damage. Acute closure of a coronary vessel or myocardial ischemia is managed by return to the catheterization laboratory or cardiac surgery. All facilities should be in close liaison with a cardiothoracic surgery unit.

TABLE 13-20 Contraindications of Cardiac Catheterization and Other Procedures[a]

Recent stroke	Patient noncompliance[b]
Advanced physiologic age	Digoxin intoxication
Severe anemia	Anaphylaxis to radiographic dyes
Severe hypertension	Active infection
Active gastrointestinal bleed	Severe electrolyte imbalances
Fever	Unstable condition
Other comorbid illnesses, e.g., COPD[c,d]	

COPD, chronic obstructive pulmonary disease; PTCA, percutaneous transluminal coronary angioplasty.

[a]Primarily contraindications to procedures such as arteriography and PTCA.

[b]Patient not willing to undergo further treatment (e.g., surgery based on results of catheterization).

[c]Disease states that may prohibit or increase risk of other interventions (e.g., surgery).

[d]Patients in whom emergency cardiac surgery would pose a high risk (e.g., during acute asthma or acute exacerbation of COPD).

Angiography, which accompanies most cardiac catheterization procedures, is defined as the "radiographic visualization of coronary vessels after injection of radiopaque contrast medium." Despite the expanding role of cardiac catheterization, angiography is used most frequently to describe the presence and extent of CAD and to allow planning for medical or surgical intervention. Cardiac catheterization with angiography is the "gold standard" in the diagnosis and assessment of CAD, against which all new invasive and noninvasive tests are measured. Unlike most other procedures, angiography determines the morphology of a stenotic lesion and the degree of luminal obstruction. However, this does not relate well to physiologic or functional significance of the lesion.[59] For example, a 50% luminal occlusion not considered significant by radiologic standards may still be the lesion producing symptomatic chest pain, and a diabetic patient with significant microvascular CAD may appear to have unaffected larger arteries at angiography and yet still be at risk of a cardiac event. Angiography also assesses the presence of collateral circulation and dynamic abnormalities such as vasospasm.

The extent of disease by angiography is defined as the number of vessels, and the vessels affected are named. Angiography is able to detect lesions that occlude the vessel by as little as 20%. Occlusions of 75% or more are almost always seen on angiography. Significant narrowing is usually assumed to be 50% or more, although some studies use 70% narrowing as the cutoff point. The lesion can be measured in several ways. Considerable controversy exists as to the best methodology. During angiography, the lesion is compared visually with surrounding vessels. Inherent difficulties include individual evaluator variability and also the assumption that surrounding vessels are normal. Calipers can be used to document physical size, but generally, the degree of stenosis is reported as a percentage of narrowing. Various grading scales, such as the coronary artery score and myocardial jeopardy scores, are used, and these scores predict long-term outcomes. Coronary artery lesions most prone to rupture and thrombosis are those with 40% to 60% narrowing, so lesions with less than 50% narrowing are not benign.

Multiple views are required to obtain a good image of the vessel; the right anterior oblique planes are used most commonly (two views at 90° to each other). Lesions may be described as concentric and smooth (simple lesions) or eccentric and broad with a rough surface (complicated lesions). The number of lesions is also considered of importance to the severity and prognosis of IHD, although there is considerable variation in the accuracy of such predictions because angiographic and pathologic correlation of lesions is imperfect. The occurrence of spasm, variants in anatomy, and collateral filling also complicate interpretation of the angiogram.

Angiographic films are used to plan interventions, in particular coronary artery bypass grafting and percutaneous coronary intervention. They are also used during both surgery and percutaneous coronary intervention to guide the procedure. Ventriculographic studies may be performed during cardiac catheterization to obtain information about the contours of the heart and to assess global and segmental function. Regional wall motion, filling defects, and the

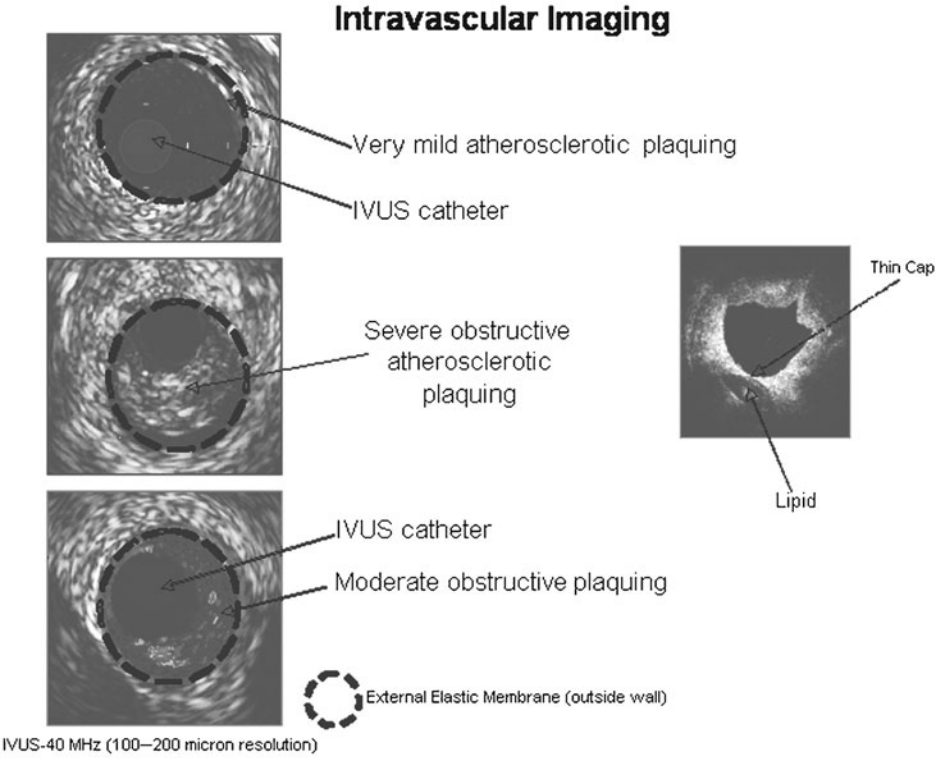

FIGURE 13-9. Intravascular ultrasound (IVUS) imaging demonstrating mild to severe atherosclerosis. Optical coherence tomography demonstrating a lipid pool inside of a plaque.

presence of mural thrombi also may be visualized. During this procedure, radiopaque dye is injected into the heart chambers, and serial films are taken to follow the dye passage. Left ventricular ventriculography is a routine part of left-sided catheterization unless ventricular function information is already available from other noninvasive studies or there are specific contraindications to the procedure.

Cardiac performance is also best assessed during catheterization procedures as direct visualization of performance along with calculated parameters that can be obtained simultaneously and represent real-time values. Measured and observed parameters obtained during catheterization are used to determine cardiac performance. Contractility, as judged by wall motion and ejection fraction, can be used to assess global cardiac performance and to plan and evaluate or assess therapy.

Invasive cardiology is growing rapidly not only in terms of the numbers of patients undergoing such procedures but also in terms of the diversity of procedures. The development of electrophysiologic studies for the assessment and treatment of arrhythmias was made possible because of catheterization. The diversity of techniques is "limited only by the imagination of the physician and inventiveness of the microtechnologist."

INTRAVASCULAR ULTRASOUND

Intravascular ultrasound (IVUS) is a procedure that uses a very small ultrasound transducer on the tip of a coronary catheter to construct detailed images of the inner wall of a coronary artery. It combines braided polyethylene catheter technology with miniaturized ultrasound transducers that can be inserted into a variety of vascular beds within the body, including the coronary artery vasculature.[60–63] Catheter configurations vary and may include over-the-wire, monorail, and fixed-guidewire tip configurations, resulting in different torqueability, steerability, and pushability characteristics for each type of catheter. There are two basic types of transducers: the solid-state phased array and a rotating mechanical transducer. In general, the phased-array transducers are smaller and may be mounted on more flexible catheters so that smaller vessels (such as coronary arteries) can be visualized, but they require a more complex system for image reconstruction and show more artifacts in imaging. Recently, new software packages have allowed detailed images identifying calcium, fibrofatty, and lipid plaques. This could be a major advance in IVUS clinical use (Fig. 13–9).

In contrast to angiography, IVUS provides quantitative information from within the vessel on diameter, circumference, luminal diameter, plaque volume, and percent stenosis. Qualitative information regarding the amount of plaque stenosis, plaque composition (e.g., calcific, fibrous, or fatty plaque), and the presence of plaque versus thrombus, thrombus versus tumor, and aneurysm and hematoma can be provided by IVUS. IVUS is also used as a therapeutic adjunct with PTCA, atherectomy, stent or graft placement, and fibrinolysis, although routine use may not be justified. These combination procedures may be monitored in real time as the procedure (e.g., atherectomy) is being performed. In current trials, IVUS has been very helpful in evaluation of disease progression or regression. Many current trials are underway to test medication for atherosclerosis regression, plaque morphology changes and other.[66]

Another new development in imaging the inner wall of the coronary is the recently developed, intravascular optical coherence tomography providing high-resolution, cross-sectional images of tissue with an axial resolution of 10 microns and a lateral resolution of 20 microns.[63] Optical coherence tomography images of human coronary atherosclerotic plaques are much more structurally detailed than IVUS.[63] Clinically, the detection of thin fibrous caps (vulnerable atheromas) (<65 microns) is below the resolution of the current 40-MHz IVUS (100 to 200 microns).[60] A summary of tests used in cardiovascular medicine is provided in Appendices 13–1 and 13–2.

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