Chapter e29: Evaluation of Cardiovascular Function

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KEY CONCEPTS

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1 Many cardiovascular disorders develop over years to decades. Evaluation of the patient with or at risk for cardiovascular disease (CVD) must therefore include a comprehensive patient (or caregiver) interview to identify traditional risk factors and risk-enhancing factors for CVD. Along with other key information (eg, vital signs, laboratory values), these data can be used to determine a patient's risk for future cardiovascular events.

2 Changes in the frequency, duration, and severity of cardiac-related symptoms (eg, ischemic chest pain, dyspnea) are essential to the assessment of CVD and often guide the urgency of intervention as well as the specific pharmacologic strategies selected. A comprehensive patient interview can also be useful for discerning CVD from noncardiac disorders that share similar symptomology.

3 Obtaining an accurate blood pressure measurement is paramount to the evaluation and treatment of several cardiovascular disorders. Guidelines for appropriate measurement techniques include recommendations on patient preparation and position, cuff size, and blood pressure documentation.

4 Several cardiovascular disorders, such as heart failure (HF) and peripheral arterial disease, warrant physical examination of areas that are more distal from the heart, including the neck (eg, carotid arteries, jugular venous pressure, abdominojugular reflux) and lower extremities (eg, peripheral pulses, edema). Abnormal findings can prompt further evaluation or alterations in pharmacologic therapy.

5 Auscultation of the chest provides key information on valvular structure and function. Abnormal heart sounds can be used to guide the need for further evaluation.

6 Two key cardiac-specific laboratory tests are cardiac troponin and brain natriuretic peptide (BNP). Elevations in cardiac troponin may indicate the presence of myocardial infarction and can be used to guide both pharmacologic and nonpharmacologic interventions. A normal BNP concentration in a patient with dyspnea excludes the presence of HF, whereas elevations are correlated with disease severity as well as long-term morbidity and mortality.

7 An electrocardiogram (ECG) records the pattern of electrical activity across the heart and each segment corresponds to an event in the cardiac cycle. The ECG provides an electrical map of the heart, which can be used to locate areas of ischemia or other pathology and identify arrhythmias. Alterations in the ECG such as QT-interval prolongation can be drug-related and may place patients at risk of potentially life-threatening arrhythmias.

8 Stress testing remains the most common initial strategy for evaluating chest pain suspicious for myocardial ischemia. The two main modalities for testing are inducing stress via exercise or the administration of a pharmacologic agent such as dobutamine or adenosine. The information provided by a stress test is often combined with echocardiography and radionuclide myocardial perfusion imaging.

9 Echocardiography uses sound waves to create an image of the heart, providing important information on the structure and function of heart valves and chambers. Although a transthoracic echocardiogram (TTE) is less invasive and provides the key information necessary for most clinical decisions, a transesophageal echocardiogram (TEE) may be required to visualize structures located in posterior areas of the heart

(eg, mitral valve, left atrial appendage) and to guide surgical planning.

10 Left heart catheterization (LHC) is an invasive procedure in which a catheter is inserted into a large artery and advanced to the left side of the heart. The most common indication for LHC is coronary angiography, in which radiocontrast dye is used to visualize the coronary anatomy, most often for evaluation of chest pain, concern for myocardial infarction, and abnormal stress testing, and to guide decision making regarding medical therapy, percutaneous coronary intervention, or coronary artery bypass grafting.

11 Right heart catheterization (RHC) involves advancing a catheter through a large vein and into the right side of the heart, where information on pulmonary and intracardiac hemodynamics can be obtained. Key parameters obtained during RHC include pulmonary artery pressures (including pulmonary capillary wedge pressure), cardiac output, and systemic and pulmonary vascular resistance, and these can be used to guide pharmacologic therapies in patients with HF or pulmonary hypertension.

12 Cardiac computed tomography (CCT) and cardiovascular magnetic resonance (CMR) imaging are noninvasive tests used to construct three-dimensional images of the heart. CCT can be used as an alternative to cardiac catheterization for performing coronary angiography, and CMR is commonly used to elucidate the etiology of HF.

BEYOND THE BOOK

BEYOND THE BOOK

The following activity will be useful for enhancing your understanding of the COLLECT and ASSESS steps of the patient care process. Tools you will need for this activity are a stethoscope and a pen and paper (or electronic device) for recording information. With a classmate, friend, or family member, conduct a focused interview to assess for traditional cardiovascular risk factors and risk-enhancing factors. If this information is not readily available, make note of how the data could be collected. Measure the heart rate using palpation and auscultation. When using the stethoscope, listen for S_1 and S_2 heart sounds and match them to the corresponding events in the cardiac cycle. If you have access to a blood pressure cuff, practice taking a blood pressure measurement according to the steps outlined in Table e29-4. Input the information you collected into an atherosclerotic cardiovascular disease (ASCVD) risk estimator such as this calculator (http://tools.acc.org/ASCVD-Risk-Estimator-Plus/) developed by the American College of Cardiology and American Heart Association. If your partner does not know their lipid profile, input normal and abnormal values (Table e29-6) to see how changes in serum cholesterol concentrations impact long-term ASCVD risk. To practice assessing for peripheral arterial disease, palpate the posterior tibial and dorsalis pedis and posterior tibial pulses (Fig. e29-3) and compare the strength of the pulses between both lower extremities. Finally, document all the data you collected as if it would be included in the medical record.

INTRODUCTION

Cardiovascular disease (CVD) remains the most common cause of death in the United States, and its incidence and prevalence continue to grow.[1] According to some estimates, the burden of treating CVD is expected to exceed $1 trillion by the year 2035.[2] Although some cardiovascular disorders emerge suddenly, most develop insidiously over the course of years and worsen with time. Additionally, many of the risk factors associated with CVD are either preventable or responsive to changes in lifestyle (eg, diet, physical activity). As a result of these and other factors, serial assessment of CVD is paramount to risk reduction and treatment.

Despite its deceptively simple role in circulating blood throughout the body, the cardiovascular system is quite complex. Each cardiac cycle represents a coordinated effort between the heart's electrical and mechanical systems, and a complex network of blood vessels provides the conduits through which oxygen and nutrients are delivered to tissues throughout the body and carbon dioxide and other waste products are transported away. Assessment of the cardiovascular system must therefore account for each of these physiological roles as well as how deficits in cardiac function may manifest elsewhere in the body, often necessitating a head-to-toe evaluation.

The purpose of this chapter is to introduce learners to the diagnostic and evaluative modalities used in the assessment of cardiovascular disorders. A

particular emphasis has been placed on those procedures that have important implications for pharmacotherapeutic decision making. Learners are encouraged to use this chapter in conjunction with each of the chapters in the "Cardiovascular Disorders" section to discern how signs and symptoms, physical examination findings, and the results of these procedures alter the treatment of CVD. An overview of commonly used assessments in CVD is provided in Table e29-1.

TABLE e29-1

Overview of Commonly Used Assessments in Cardiovascular Disease[a]

Diseases (relevant chapters for more details)	Signs and Symptoms	Physical Assessment	Laboratory Findings	Other Modalities
Arrhythmias (Chapter 40, "Arrhythmias")	• Dizziness/lightheadedness • Dyspnea • Palpitations • Syncope	Heart rate and rhythm	None	• ECG • Echocardiogram
Dyslipidemia (Chapter 32, "Dyslipidemia")	Xanthomas	None	Lipid profile	None
Heart failure (Chapter 36, "Chronic Heart Failure"; Chapter 37, "Acute Decompensated Heart Failure")	• Dyspnea • Orthopnea • Bendopnea • Paroxysmal nocturnal dyspnea • Weight gain	• Abdominojugular reflux • Blood pressure • Heart rate and rhythm • Heart sounds • Lung sounds • Jugular venous pressure • Point of maximal impulse • Lower extremity edema (bilateral) • Lower extremity color, temperature, and pulses	• Brain natriuretic peptide • Biomarkers of end-organ function	• Cardiac catheterization • Chest x-ray • CMR imaging • Echocardiogram • Nuclear imaging (MUGA, PET, SPECT)
Hypertension (Chapter 30, "Hypertension"; Chapter e31, "Acute Hypertensive Crisis")	• Target-organ damage during hypertensive crisis may cause: • Headache • Altered vision • Chest or back pain • Dyspnea	Blood pressure	None	None
Ischemic heart disease[b] (Chapter 33, "Stable Ischemic Heart	Chest pain (angina)	None	• High-sensitivity C-reactive protein	• ECG • Cardiac

Disease"; Chapter 34, "Acute Coronary Syndromes")			• Cardiac troponin • Creatine-kinase myocardial band • Lipid profile	catheterization • CCT angiography • CMR imaging • Coronary artery calcification score • Stress testing • Myocardial perfusion imaging (PET, SPECT)
Peripheral arterial disease (Chapter e35, "Peripheral Arterial Disease")	Lower extremity pain	• Ankle-brachial index • Lower extremity bruit • Lower extremity color and pulses	None	None
Pulmonary hypertension (Chapter 46, "Pulmonary Arterial Hypertension")	Dyspnea	• Lung sounds • Abdominojugular reflux (if right heart failure present)	Brain natriuretic peptide (if right ventricular dysfunction present)	• Cardiac catheterization • Echocardiography
Stroke (Chapter 39, "Stroke")	• One-sided muscle weakness or paralysis • Speech abnormalities • Sudden vision changes • Dizziness/loss of balance	• Blood pressure • Carotid bruit • Heart rate and rhythm (atrial fibrillation)	None	• Brain imaging (CT, MRI) • Carotid Doppler • See Chapter 38, "Venous Thromboembolism" for more details
Valvular heart disease	• Dyspnea • Palpitations • Syncope	Heart sounds	None	Echocardiogram
Venous thromboembolism (Chapter 38, "Venous Thromboembolism")	• Dyspnea (pulmonary embolism) • Lower extremity pain (deep vein thrombosis)	• Lower extremity temperature • Lower extremity edema (unilateral)	• D-dimer • See Chapter 38, "Venous Thromboembolism" for more details	• Pulmonary imaging (CT, V/Q scan) • Lower extremity ultrasonography • See Chapter 38, "Venous Thromboembolism" for more details

[a]This table provides an overview of commonly used modalities, with an emphasis on those discussed in this chapter, which are used to assess the disorders covered

in this textbook, and is not intended to be comprehensive.

[b]Includes acute coronary syndromes.

CCT, cardiac computed tomography; CMR, cardiovascular magnetic resonance; CT, contrast tomography; ECG, electrocardiogram; MRI, magnetic resonance imaging; MUGA, multiple gated blood pool imaging; PET, positron emission tomography; SPECT, simple photon emission computed tomography; V/Q, ventilation/perfusion.

Medical History

1 The interviewer should assess for the presence of traditional cardiovascular risk factors as well as risk-enhancing factors in all adult patients with or without established CVD (Table e29-2). Based on traditional risk factors and other patient-specific information, the 10-year risk for developing a first atherosclerotic cardiovascular disease (ASCVD) event can be determined in individuals aged 20 to 79 years by using the Pooled Cohort Equations Risk Calculator developed by the American College of Cardiology and American Heart Association (ACC/AHA) (http://tools.acc.org/ASCVD-Risk-Estimator-Plus/).[3] The 10-year risk of developing ASCVD may then be paired with an assessment of risk-enhancing factors to guide an individualized risk prevention strategy, such as determining the appropriate hypertension treatment, selecting lipid-lowering therapy, and identifying whether aspirin is indicated for primary prevention of CVD.[3-5] The identification of modifiable risk factors also provides clinicians with an opportunity to educate patients on therapeutic lifestyle changes that may also impact their risk of CVD.

TABLE e29-2

Major Cardiovascular Risk Factors and Risk-Enhancing Factors

Traditional Cardiovascular Risk Factors	Risk-Enhancing Factors
• Age • Sex • Race • High blood pressure • Elevated total cholesterol • Elevated LDL cholesterol • Low HDL cholesterol • Diabetes mellitus • Tobacco use • Overweight/obesity • Sedentary behavior • Diet (high saturated fats, low intake of fruit, vegetables, legumes, nuts, whole grains, and fish)	• Family history of premature cardiovascular disease in a first-degree relative (men <55 years of age; women <65 years of age) • Persistently elevated LDL cholesterol >160 mg/dL (4.14 mmol/L) • Chronic kidney disease (eGFR 15-59 mL/min/1.73/m^2 with or without albuminuria; not treated with dialysis or kidney transplantation) • Metabolic syndrome • Premature menopause (age <40 years) and pregnancy-associated conditions that increase the risk of ASCVD (eg, preeclampsia) • Chronic inflammatory diseases (eg, rheumatoid arthritis, HIV) • Ethnicity (eg, South Asian ancestry) • Persistently elevated triglycerides (>175 mg/dL [1.98 mmol/L]) • If measured, hs-CRP >2.0 mg/L, Lp(a) >50 mg/dL or >125 nmol/L, apoB >130 mg/dL [1.3 g/L], ankle-brachial index <0.9

apoB, apoprotein B; ASCVD, atherosclerotic cardiovascular disease; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Lp(a), lipoprotein (a).

Data from References 3 and 5.

The presence of clinical ASCVD, often defined as coronary artery disease (CAD), aortic aneurysm, cerebrovascular disease, or peripheral arterial disease (PAD), should also be determined, as this information will guide the assessment and treatment approach. Finally, a thorough medication history is also important for identifying allergies or adverse events that may impact clinical decision making as well as medications that may cause or exacerbate CVD.[3]

Risk Factor Assessment

Family History

Genetics play a role in the development of many cardiovascular conditions, including premature CAD, heart failure (HF), and cardiac arrhythmias. Clinicians should inquire about the health status of all first-degree relatives, and document the presence of premature CVD, defined as a cardiovascular event in male relatives under the age of 55 and female relatives under the age of 65.

Social History

Current and prior use of alcohol, tobacco, and illicit substances should be characterized at each encounter, including both the quantity (eg, drinks per day) and duration (eg, cigarette pack-years) of use. Clinicians should counsel patients on appropriate alcohol limits based on gender and other characteristics (eg, comorbid conditions). An assessment of tobacco use should be performed at each patient encounter (see Chapter 86, "Substance Use Disorders II: Alcohol, Nicotine, and Caffeine" for details).[3,6] Finally, obtaining a thorough social history is also important for identifying social determinants of health and other barriers to care (eg, education level, ability to afford medications).

Physical Activity

Patients should be questioned regarding the types and amounts of physical activity in which they engage on a daily and weekly basis.[3] Clinicians should assess factors that may limit or preclude a patient from engaging in physical activity, as these may indicate the presence or worsening of a cardiovascular condition (eg, HF, PAD).[7,8] An assessment of functional status in those with physical limitations can be performed by asking patients about their ability to complete activities of daily living (eg, bathing, dressing) and instrumental activities of daily living (eg, cleaning, cooking).

SIGNS AND SYMPTOMS OF ORGAN DYSFUNCTION

2 In addition to performing a past medical history (including prior cardiac tests and procedures) and identifying risk factors for CVD, a comprehensive patient history should also include an assessment of symptoms. When performed correctly, clinicians can often assess the severity and stability of disease without the use of expensive laboratory or diagnostic tests. The OPQRST (Onset, Provocation/Palliation, Quality, Region/Radiation, Severity, and Time) mnemonic can be a helpful guide to symptom assessment. The following sections provide an overview of common signs and symptoms in patients with CVD (as summarized in Table e29-1).

Chest Pain

Chest pain can occur for many reasons, requiring that the clinician distinguish cardiac and noncardiac etiologies (eg, pulmonary embolism [PE], gastroesophageal reflux disorder, costochondritis, panic attack) (Tables e29-2 and e29-3). Ischemic chest pain (ie, angina) typically begins in the retrosternal area and may radiate to the neck, jaw, and one or both arms. Ischemic chest pain may also be accompanied by nausea, dyspnea, diaphoresis, syncope, or abdominal pain. Atypical symptoms (eg, pleuritic chest pain, epigastric pain, unexplained acute or worsening dyspnea) may also be present, and these are more common in women and in patients with impaired renal function, diabetes, or dementia. Consequently, ischemia should not be ruled out in the absence of chest pain. The onset, duration, provocation, and palliation of symptoms must be ascertained to determine if the pain is stable or unstable. Pain that is new, occurring at rest, or worse compared to chronic pain is considered unstable. An electrocardiogram (ECG) should be performed in patients presenting with chest pain or other symptoms concerning for an acute coronary syndrome.[9]

TABLE e29-3

Characteristics of Ischemic Chest Pain

Characteristics	Not Characteristics
• Deep, poorly localized pain in chest and/or arm(s) • Reproducible with exertion or emotional stress, or develops at rest or with less exertion than the activity that previously precipitated the pain[a] • Begins in the retrosternal area • Relieved, in 5 minutes or less, with rest and/or short-acting nitroglycerin	• Pleuritic chest pain (provoked by respiration or cough and described as sharp or knifelike) • Localized to the middle or lower abdomen • Localized by the tip of one finger, specifically at the site of the left ventricular apex or costochondral junction • Reproduced with movement or palpation of chest or arms • Lasts less than a few seconds • Maximum intensity at onset • Radiates to the lower extremities

[a]Pain in those presenting with an acute coronary syndrome may have more severe and prolonged symptoms.

Data from Reference 9.

Nonischemic causes of chest pain include pericarditis, aortic dissection, and PE. Pericarditis, or inflammation of the pericardium, can cause sharp, pleuritic chest pain that can be partially or completely relieved by sitting up and leaning forward. Patients with a Type A aortic dissection (a tear beginning in the ascending aorta) most commonly present with chest pain in the anterior region, although some may present with posterior chest pain and/or abdominal pain. Those with a Type B dissection (a tear in the descending aorta) most commonly report back pain, although chest and abdominal pain are also frequently reported. Accordingly, an aortic dissection should not be ruled out in the absence of chest pain.[10]

Dyspnea

Dyspnea can occur with physical activity, termed “dyspnea on exertion,” or at rest. As with chest pain, clinicians must differentiate cardiac (eg, HF) and noncardiac etiologies (eg, chronic obstructive pulmonary disease, PE, pneumonia, and anemia). Patients should be asked about the activities they can perform before shortness of breath (SOB) occurs, such as the distance walked (eg, number of city blocks) or stairs climbed. An assessment of dyspnea also includes a characterization of the chronicity of symptoms, how they have changed over time, and their impact on the patient’s functional status, including activities of daily living.

Dyspnea that occurs when patients are in the recumbent position is known as orthopnea, a finding common in patients with HF due to changes in volume distribution and pulmonary pressures. The severity of orthopnea can be quantified by the number of pillows or the degree of elevation of the head needed to rest or sleep comfortably. In severe cases, patients may need to sleep in an upright position. Clinicians should explain the rationale for inquiring about the elevation of the head to differentiate it from other types of discomfort that may alter sleeping position (eg, neck or back pain). Alternatively, patients may be asked if they can sleep comfortably when lying flat and if not, the reason(s) why.

Paroxysmal nocturnal dyspnea (PND) refers to sudden episodes of dyspnea that present after the patient has been asleep for a few hours. The patient is often awakened from sleep and must sit or stand upright to relieve the SOB. Clinicians should document the number of PND episodes that occur per week or per night, as increasing frequency may indicate the presence of advanced disease.

Bendopnea is dyspnea that occurs when a person bends forward at the waist. Patients may experience bendopnea when bending over to put on socks or shoes and may purposefully wear slip-on footwear to avoid this symptom. Bendopnea is associated with a risk of HF hospitalization and clinical worsening in patients with pulmonary arterial hypertension (PAH).[11,12]

Various rating scales exist to grade the severity of dyspnea in patients with HF, and these can be used to track changes in symptoms over time. Although the Kansas City Cardiomyopathy Questionnaire and Minnesota Living with Heart Failure Questionnaire are used to characterize dyspnea in clinical

trials, the severity of dyspnea in HF is most commonly graded according to the New York Heart Association (NYHA) classification system.[13,14] The NYHA class is important for determining an appropriate treatment strategy in patients with chronic HF (see Chapter 36, "Chronic Heart Failure").[15] An analogous scale, the World Health Organization functional class, is imperative for designing a treatment plan for patients with pulmonary hypertension (see Chapter 46, "Pulmonary Arterial Hypertension").[16]

Patients with a PE may also present with dyspnea accompanied by chest pain, cough, and tachycardia. Therefore, dyspnea should be evaluated in context with other subjective and objective data to determine its underlying etiology.

Syncope

Syncope is an abrupt, transient, and complete loss of consciousness attributable to the loss of postural blood pressure (BP). Although loss of consciousness is followed by rapid and spontaneous recovery, patients are often unable to brace themselves for the fall, and trauma to the face often occurs. Syncope is the result of decreased cerebral perfusion, and cardiovascular etiologies include bradycardia, tachycardia, and hypotension due to valvular heart disease, vasodilation, or acute vascular dissection.

Patients presenting with syncope should be assessed for orthostatic hypotension, a condition in which shifts from a supine to an upright position are accompanied by a decrease in systolic blood pressure (SBP) of ≥20 mm Hg and/or a decrease in diastolic blood pressure (DBP) of ≥10 mm Hg. Orthostatic hypotension causes syncope when patients are in an upright position. The effect of positional changes on heart rate should also be evaluated, and electrophysiological testing should be performed when the suspected etiology is a brady- or tachyarrhythmia, as syncope may be a sign of a potentially life-threatening dysrhythmia. A pacemaker may be indicated for those with irreversible causes of bradycardia whereas medication therapy and/or cardiac ablation may be considered in patients who develop syncope secondary to a tachyarrhythmia. Syncope in the presence of severe aortic stenosis is associated with a poor prognosis and dictates the need for surgical or transcatheter valve replacement in suitable candidates. Noncardiac causes of syncope or loss of consciousness include dehydration, blood loss, alcohol or drug intoxication, and seizure.[17]

To determine the underlying etiology of loss of consciousness and an appropriate treatment approach, the relationship between the time of the event to meals, physical activity, and medication administration should be ascertained. Patients should also be asked if they experienced a prodrome (eg, nausea, vomiting, feeling warm), as this is uncommon in syncope of cardiovascular etiology. One exception is vasovagal syncope, a common form of reflex syncope, which may occur as a result of vasopressor-dependent hypotension and/or inappropriate bradycardia. Vasovagal syncope may occur when patients are upright or in any position when provoked by stress or pain. Patients will typically experience warmth, nausea, diaphoresis, and have a pale appearance; fatigue often follows. Triggers and/or a prodrome can often be identified, although less commonly in older patients.

A complete medication history is imperative in the assessment of syncope. When possible, a report of the event should be obtained from bystanders. Clinicians should also assess for the presence of any nonsyncopal conditions that may cause self-limited loss of consciousness, including seizures, hypoglycemia, and intoxication, among others. An electroencephalogram should be obtained when a concern for seizures exists, such as when prominent jerking muscle movements are observed.[17]

Palpitations

The term *palpitation* refers to the awareness of one's heartbeat. Patients may report feeling a pulsation or movement in the chest or adjacent areas and often describe it as being alarming and unpleasant or uncomfortable. The mechanism by which this sensation occurs is not well-defined. Cardiac awareness is normal if it occurs during activities that are typically associated with increases in the frequency and strength of cardiac contraction, such as physical activity or emotional stress. Palpitations of a cardiac origin include arrhythmias and structural heart disease (eg, severe mitral or aortic regurgitation and hypertrophic cardiomyopathy). An ECG can be performed to distinguish innocuous arrhythmias (eg, premature atrial contractions) from those requiring further evaluation. The absence of an arrhythmia should prompt an investigation of alternative causes, which may include medications (eg, anticholinergics, vasodilators), recreational drug abuse (eg, cocaine, amphetamines), caffeine, psychosomatic causes (eg, anxiety, panic attacks), and systemic diseases (eg, hyperthyroidism, anemia).[18] Patients may have more than one cause of palpitations.

Lower Extremities

Pain in the lower extremities may indicate the presence of PAD. If present, the location of the pain reflects the artery or arteries affected. To ascertain a cause of lower extremity pain, clinicians should assess its location; the effect of exercise, rest, and changes of position; and other associated

characteristics. Patients with PAD can present with “classic” intermittent claudication symptoms, which consist of localized pain, discomfort, or fatigue that occurs in one or both lower extremities with physical exertion and is relieved within 10 minutes of rest. Atypical symptoms include pain that lingers after rest. Patients should be questioned regarding the presence of nonhealing wounds and ulcers as well as an altered sensation or a dusky appearance in the toes. Pain at rest can be a sign of chronic limb-threatening ischemia. However, non-exertional pain is rarely of cardiovascular origin and may instead be due to arthritis or nerve root compression. Pain or discomfort associated with swelling may be the result of venous insufficiency or deep vein thrombosis.

The presence of PAD should not be excluded in patients who deny exertional leg pain, as a significant proportion are asymptomatic.[19] Additionally, the walking distance may be limited by reasons other than PAD and thus preclude the development of pain. As a result, physical examination of the lower extremities is of paramount importance in patients at risk for PAD, as the presence of the condition increases the risk of ASCVD events and should serve as a target for risk reduction strategies (see Chapter e35, “Peripheral Arterial Disease” for details).[8]

PHYSICAL ASSESSMENT

Vital Signs

Blood Pressure

3 Recommendations for obtaining a BP in the office are provided in Table e29-4. Inaccurate measurements may result from failing to place patients in the correct position, using the wrong cuff size, and/or using a device that has not been validated. Use of an oscillometric device is preferred whenever possible to avoid some of the limitations of auscultatory BP assessment (eg, inflating or deflating the cuff too rapidly). These devices detect oscillations in pulsatile blood volume during cuff inflation and deflation. The use of an automated cuff is preferred.

TABLE e29-4

Recommendations for the Measurement of Blood Pressure in Humans

Steps to Measure BP	Instructions
Step 1: Prepare the patient in the proper position.	• The patient should be relaxed, seated in a chair with the back upright, feet on the floor, and not moving for at least 3 to 5 minutes. • The patient and healthcare professional should not talk during this time period. • The patient should have an empty bladder. • Caffeine, exercise, and smoking should be avoided 30 minutes before the measurement. • Clothing covering the location of the cuff should be removed; sleeves should not be rolled up.
Step 2: Use the proper BP measurement technique.	• Use a calibrated and validated upper arm device. • Support the patient's arm. The patient should not hold their arm. • Determine and use the correct cuff size. The bladder length should encircle 75-100% of the arm; the bladder width should be 37%-50% of the arm circumference. • Measure the arm circumference at the acromion and olecranon midpoint. • If the auscultatory approach is used, use the bell or diaphragm of the stethoscope.

Step 3: Take the proper measurements.	• Record the BP in both arms at the first visit. The arm that gives the higher reading should be used for subsequent visits.
	• Repeated measures should be separated by 1-2 minutes.
	• If the auscultatory approach is used:
	  ○ Palpate the estimate of the radial pulse obliteration pressure to estimate the SBP.
	  ○ Inflate the cuff to 20-30 mm Hg above the obliteration point.
	  ○ Deflate the cuff pressure at 2 mm Hg per second and listen for the Korotkoff sounds.
	  ○ The SBP is the onset of the first two consecutive beats and the DBP is the last sound heard.

Step 4: Document the BP readings.	• Document the SBP and DBP. • Record the time at which any BP medications were taken prior the readings.
Step 5: Average the readings.	• Estimate the patient's BP using the average of two or more readings on two or more occasions to determine the patient's BP.
Step 6: Provide readings to the patient.	• Share the BP readings with the patient, both orally and in writing. • Results should be interpreted for the patient.

BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Data from Reference 25.

Blood pressure should be measured on two to three different occasions to determine an accurate estimate and minimize random error.[5,20] Although a "normal" adult BP is defined as an SBP <120 mm Hg and a DBP <80 mm Hg, readers are referred to Chapter 30, "Hypertension," for a full discussion of the thresholds at which hypertension is diagnosed as well as specific BP goals. Orthostatic hypotension should be routinely assessed for in older patients and those in whom postural changes result in dizziness, lightheadedness, blurry vision, or cognitive impairment. To assess for orthostatic

hypotension, BP should be measured in the seated or supine position and then again after 3 minutes of standing.[17,20]

The use of home blood pressure monitoring (HBPM) or ambulatory blood pressure monitoring (ABPM) is recommended to confirm the diagnosis of hypertension and to titrate blood pressure–lowering medications. Up to 30% of patients may have "white coat" hypertension, in which BP is higher in the office than at home.[20-23] Out-of-office BP assessment can also detect masked hypertension, a scenario in which BP is normal in the office but high at home. Finally, ABPM can be used to evaluate those with labile hypertension and postural hypotension and determine the extent of, if any, variations in BP throughout the day and night.[5,24] Further information on when to utilize HBPM and ABPM is discussed in Chapter 30, "Hypertension."

Patients should be trained before using HBPM or ABPM. With HBPM, patients should prepare for each measurement according to the recommendations outlined in the first step of Table e29-4. Clinicians should help patients determine the most appropriate device for their needs, including measuring and noting the patient's arm circumference should they need to purchase their own device. A device with the ability to store readings is preferred, although patients can also log their readings manually. Patients should measure their BP each day and are encouraged to obtain multiple readings daily, such as in the morning prior to taking medications and at suppertime. At a minimum, BP should be measured weekly, two weeks after a change in BP regimen, and the week of the next appointment.[5] Additional information for patients who self-monitor their BP is available on the American Heart Association website (https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings/monitoring-your-blood-pressure-at-home).

An ABPM device measures BP every 15 to 30 minutes during the day and every 15 to 60 minutes during the night and readings may be obtained over periods of 24 hours or more. Monitors are worn on a belt or carried in a pouch, allowing patients to engage in normal daily activities. However, patients should keep their arm still while the cuff is inflating.[24] A list of validated ABPM monitors is available at www.dableducational.org. Devices should be calibrated approximately every 1 to 2 years, according to the manufacturer's instructions.[25]

Pulses

The radial artery should be palpated to assess heart rate and rhythm. The tips of the index and middle fingers should be used (not the thumb). In patients with a regular rhythm, heart rate can be measured for 15 seconds and then multiplied by four to determine the number of beats per minute. In those with an irregular rhythm, the rate should be measured for 30 seconds to ensure that variations are accounted for; this rate should then be multiplied by two. The strength of the radial pulses should be compared on both sides. When a delayed arterial pulse is suspected, the heart should be auscultated while palpating the radial artery.

In adults, a normal resting pulse rate is 60 to 100 beats per minute (bpm). A rate of <60 bpm is referred to as bradycardia, whereas a rate of >100 bpm is referred to as tachycardia. Bradycardia may be physiologically normal in athletic individuals, or it may be the result of medications, hypothyroidism, or heart block. Any irregularities in heart rhythm should be documented. Examples of irregular rhythms include atrial flutter, in which intervals are similar and predictive (often termed "regularly irregular"), and atrial fibrillation, in which the intervals are not predictive or repetitive (termed an "irregularly irregular" rhythm). An ECG is necessary to confirm the presence of an arrhythmia, as the diagnosis cannot be made on physical examination findings alone.

Inspection

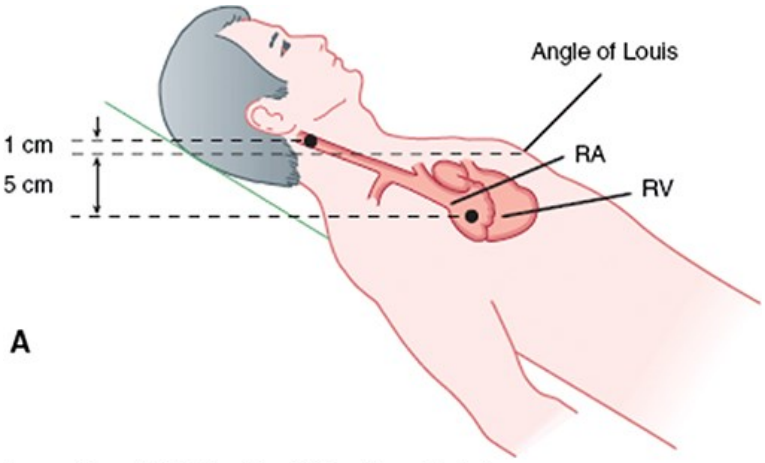
Jugular Venous Pressure

4 The jugular venous pressure (JVP) is an estimate of the central venous or right atrial (RA) pressure. The elevation of JVP, reported in cm, is determined as the distance between the sternal inflection point and the top of the jugular pulsation. The sternal inflection point or the angle of Louis is where the manubrium and the sternum intersect (Fig. e29-1). The internal jugular (IJ) is preferred over the external jugular (EJ) vein for inspecting JVP, as the IJ is directly in line with the superior vena cava and the RA. The presence of valves in the EJ and the potential for the vein to thrombose in older patients can also alter the interpretation of JVP.

FIGURE e29-1

Estimation of the jugular venous pressure. The distance between the base of the right atrium (RA) and the angle of Louis or sternal inflection point is 5 cm. In this figure, the top of the jugular venous pulse is 1 cm higher than that angle of Louis. The jugular venous pressure would be reported as 1 cm

above the sternal notch and thus a total of 6 cm above the RA. (RV, right ventricle.) *(Reproduced, with permission, from Hammer GG, McPhee SJ. Pathophysiology of Disease: An Introduction to Clinical Medicine. 8th ed. New York: McGraw Hill; 2019.)*



The JVP is determined by placing the patient at a 30 to 45-degree angle and reporting the number of centimeters above the sternal notch at which pulsation occurs (eg, "4 cm above the sternal notch"), or the observed distance plus 5 cm (eg, "a JVP of 9 cm"), which accounts for the estimated distance between the RA and the sternal notch. A JVP more than 4 cm above the sternal notch (more than 9 cm between the base of the RA and sternal notch) is considered elevated. The inability to detect a JVP on inspection should be reported as "not observed" (rather than "absent"), as any elevation between the top of the RA and the sternal inflection point cannot be observed.[26]

Extremities

Inspection of the skin on the lower extremities is useful for detecting the presence of PAD. Findings suggestive of severe limb ischemia include dependent rubor and elevated pallor. Dependent rubor refers to redness in the feet and toes when the legs are hanging from an elevated surface, whereas elevation pallor is a pale or ashen appearance in the lower extremities after they have been elevated at more than a 60-degree angle for greater than 60 seconds while the patient is in a supine position. Gangrene and nonhealing wounds or ulcers are signs of chronic limb ischemia and should prompt further evaluation. Wounds suggestive of PAD often occur distally, and cracked skin or fissures at the heel may also occur. The absence of leg hair is not diagnostic for PAD but should be considered when hair loss occurs unilaterally or when other features suggestive of the disease are present.[8,27]

Palpation

Carotid Pulses

To assess the carotid arteries, patients should be instructed to turn their head slightly and relax the neck muscles. The carotid pulse and rhythm should be evaluated on either side with gentle pressure using the index and middle fingers, but at separate times to prevent syncope. A normal carotid pulse is smooth and has a relatively quick upstroke and a more gradual downstroke. *Pulsus alternans* is a regular pulse at alternating strengths and is considered a sign of HF. A delayed upstroke and weak pulse (*pulsus parvus et tardus*) suggest aortic stenosis whereas aortic regurgitation may be observed as a Corrigan's or a water-hammer pulse, where the pulse is bounding with an abrupt expansion followed by a sudden collapse. Further evaluation is warranted in those with abnormal findings.[28,29]

Abdominojugular or Hepatojugular Reflux

Abdominojugular or hepatojugular reflux is often evaluated at the same time as JVP, while the patient is still positioned at a 45-degree angle. Pressure is applied to the middle or upper quadrant of the abdomen and held for at least 10 seconds and up to a minute. The test is considered positive if the JVP remains elevated while pressure is applied, indicating that the RA is unable to accommodate an increase in venous return, a finding suggestive of

right-sided HF, constrictive pericarditis, or cardiac tamponade.[26,30] In many patients, a brief rise and fall in JVP will occur when pressure is initially applied, but this is considered a negative finding.

Thrill

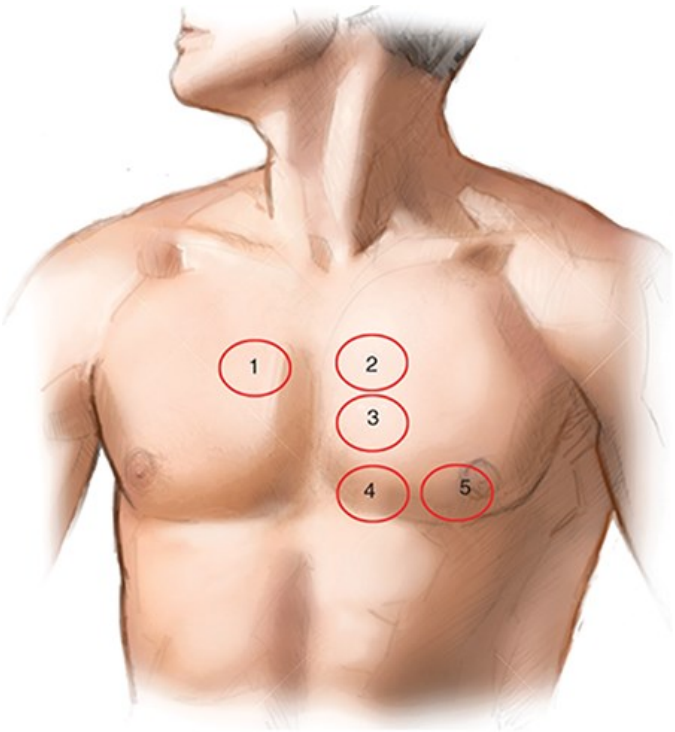
A thrill is a sensation that may be felt at the site where a bruit or murmur is heard and is indicative of significant turbulence in blood flow. A thrill is used in the definition of murmurs graded 4 or higher (discussed in detail in the section on auscultation).

Point of Maximal Impulse

The point of maximal impulse (PMI) refers to the area of the chest where the cardiac impulse is felt most strongly. A normal PMI is located at the fifth intercostal space at the mid-clavicular line (Fig. e29-2, in the area denoted "5"). When palpated, a single impulse should be felt with each cardiac cycle, and the PMI should be approximately 2 cm in diameter. The PMI may be challenging to palpate in patients who are obese or muscular. In patients with dilated cardiomyopathy, the PMI is shifted laterally to the left. A PMI larger than 2 cm may be indicative of a hypertrophic or dilated left ventricle. A forceful and hyperdynamic impulse may suggest the presence of a hypermetabolic state such as severe anemia or hyperthyroidism, or it may be evidence of mitral regurgitation.

FIGURE e29-2

The five typical areas for cardiac auscultation. 1, aortic valve; 2, pulmonic valve; 3, accessory aortic area; 4, tricuspid valve; 5, mitral valve (also where the point of maximal impulse is normally located). *(Reproduced, with permission, from Fuster V, Harrington RA, Narula J, Eapen ZJ, eds. Hurst's the Heart. 14th ed. New York, NY: McGraw Hill; 2017.)*



Extremities

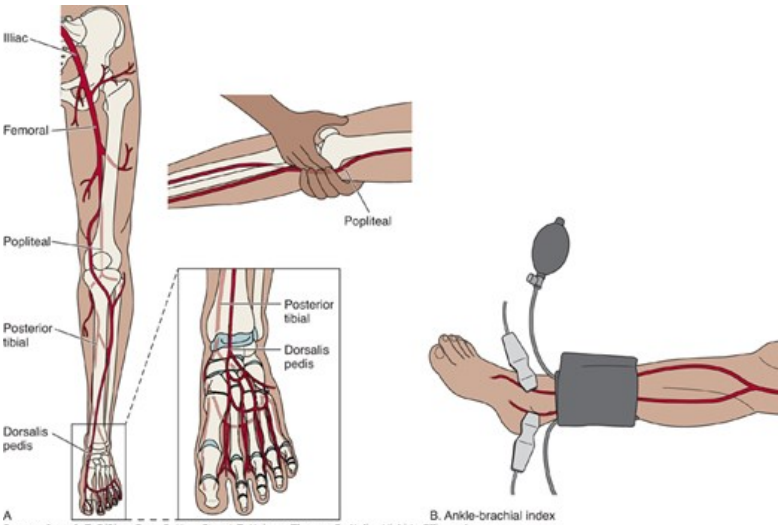
Temperature: Comparing temperatures at multiple points between the two legs can be useful in detecting abnormalities. Cool extremities may be a sign of low cardiac output in HF or arterial insufficiency, whereas localized warmth, swelling, and redness may indicate the presence of a deep vein

thrombosis.

Pulses: The femoral, popliteal, dorsalis pedis, and posterior tibial pulses are displayed in Fig. e29-3A. The strength of the pulses on both sides of the body should be directly compared. The popliteal artery should be palpated with the patient in the seated and supine positions as it can be difficult to find. The absence of pulses is not specific for PAD, as one or both dorsal pedis pulses may be absent in up to 17% of patients, and one or both posterior tibial pulses may be absent in up to 9%.[31] However, the absence of these pulses in combination with a femoral bruit is suggestive of PAD.[32]

FIGURE e29-3

Assessment of the lower extremity arteries. (*A*) Major arteries of the leg; (*B*) ankle-brachial index assessment.



Recommendations for grading the strength of pulses are as follows: 0, absent; 1, reduced; 2, normal; and 3, bounding. Clinicians are encouraged to document both the numeric grade and its definition, as various scales have been used for grading.[27] Findings suggestive of PAD should prompt additional testing to confirm the diagnosis.

The ankle- or toe-brachial index (ABI or TBI) is a simple, noninvasive test that can be used to diagnose PAD (Fig. e29-3B).[8] The ABI is the ratio of the SBP measured at the ankle to the SBP measured in the arm. The patient is placed in a supine position and pressures are obtained at the sites of the brachial, dorsalis pedis, and posterior tibial arteries using a Doppler ultrasound device. The ABI is calculated using measurements on both sides of the body, and the higher of the two ankle pulses is divided by the higher of the two brachial artery readings (Fig. e29-3B). An ABI ≤0.9 is generally considered abnormal.[8] Readers are referred to Chapter e35, "Peripheral Arterial Disease" for additional details.

Edema

Edema in the lower extremities can occur as a result of several different mechanisms. In some cases, the cause can be differentiated by the presence of pitting (ie, an indentation that remains after pressure is applied). In patients with HF, pitting edema occurs primarily as a consequence of increased hydrostatic pressure. Noncardiac etiologies of edema resulting from increased hydrostatic pressure include pregnancy, venous obstruction, and renal failure. Edema may also occur as a result of decreased oncotic pressure due to low plasma protein concentrations in conditions such as nephrotic syndrome, advanced liver disease, and malnutrition. Increased capillary permeability due to sepsis, burns, chemotherapeutic agents, or other factors can cause nonpitting edema, which tends to be more widespread rather than localized to the abdomen or lower extremities. Lipedema, or pathologic accumulation of fluid in adipose tissue, typically occurs in the upper torso and lower extremities, with the exception of the feet and ankles. Lymphedema, an accumulation of fluid that results from lymphatic obstruction, can appear in the upper or lower extremities and may be unilateral. Early stages have been described as being doughy in appearance, followed by thickened, fibrotic, hyperkeratotic skin later on. A variety of medications can cause edema as well.[33,34]

Clinicians should assess for the presence of edema in both legs starting in the ankle area. When present, the clinician should continue to palpate

progressively higher up the leg and note the area to which the edema extends. Male patients with edema extending to the thighs should be asked about the presence of scrotal edema. Sacral edema should be assessed in those with edema extending to the top of the leg.

The presence of ascites should also be determined even in the absence of lower extremity edema. Patients should be asked if they have observed changes in abdominal girth and the duration over which any changes have occurred. For example, patients can be asked if they have had to loosen their belt or experienced recent increases in pant size. Further questioning can enable one to determine if changes in abdominal girth are secondary to volume changes or an increase in weight due to caloric intake.

Lower extremity edema is a common finding in patients with HF, but volume overload should not be completely ruled out in patients with normal findings on palpation. When edema is present, it is typically bilateral and pitting in nature. Several systems exist for grading the severity of edema; most commonly, pitting edema is graded on a scale of 1+ to 4+. A score of 1+ indicates edema that is ≤2 mm in depth and rapidly disappears (sometimes referred to as “trace” edema); 2+ indicates edema that is 2 to 4 mm deep and disappears in 10 to 15 seconds; 3+ indicates edema that is 4 to 6 mm deep and lasts for a minute or more; and 4+ indicates edema >6 mm deep that lasts 2 minutes or more.

Unilateral edema is uncommon in HF and should prompt further evaluation. Potential etiologies include trauma, venous insufficiency, removal of veins (eg, coronary artery bypass graft [CABG] surgery), deep vein thrombosis, and infection.

Auscultation

Heart Sounds

5 Auscultation should occur over each valve area indicated in Fig. e29-3, using both the bell and diaphragm of the stethoscope. Heart sounds are designated S_1 through S_4; in adults, S_1 and S_2 are normal whereas S_3 and S_4 indicate the presence of pathologic conditions. Low-frequency sounds such as S_3 and S_4 are best heard using the bell of the stethoscope whereas high-frequency sounds, such as S_1 and S_2, are best heard using the diaphragm. The rate and rhythm of the heart should also be assessed during auscultation, as it may provide a more accurate assessment than palpation of the radial pulse alone.

S_1 – The first heart sound, S_1, is produced by the closure of the mitral and tricuspid valves. This sound occurs at the beginning of systole and is best heard at the left lower sternal border. The intensity of S_1 is diminished in those with severe mitral stenosis, as well as in patients who are mechanically ventilated or have obstructive lung disease, as the presence of air in the lungs limits the ability of sound to travel.[35]

S_2 – The second heart sound, S_2, is produced by the closure of the aortic and pulmonic valves. This sound indicates the beginning of diastole and is best heard at the second left intercostal space.[35]

S_3 – The S_3 heart sound or “ventricular gallop” is produced when blood strikes a compliant ventricle during passive filling. This sound is best heard at the apex and occurs in the mid-third of diastole. The presence of an S_3 is a sign of HF, as it occurs when the right or left ventricle is dilated and filling at high pressures.[35]

S_4 – The S_4 heart sound or “atrial gallop” occurs at the end of diastole, shortly before S_1, and is produced when the atria contract and blood strikes a non-compliant left ventricle. This sound may be heard in those with left ventricular hypertrophy secondary to hypertension, aortic stenosis, or hypertrophic cardiomyopathy.[35]

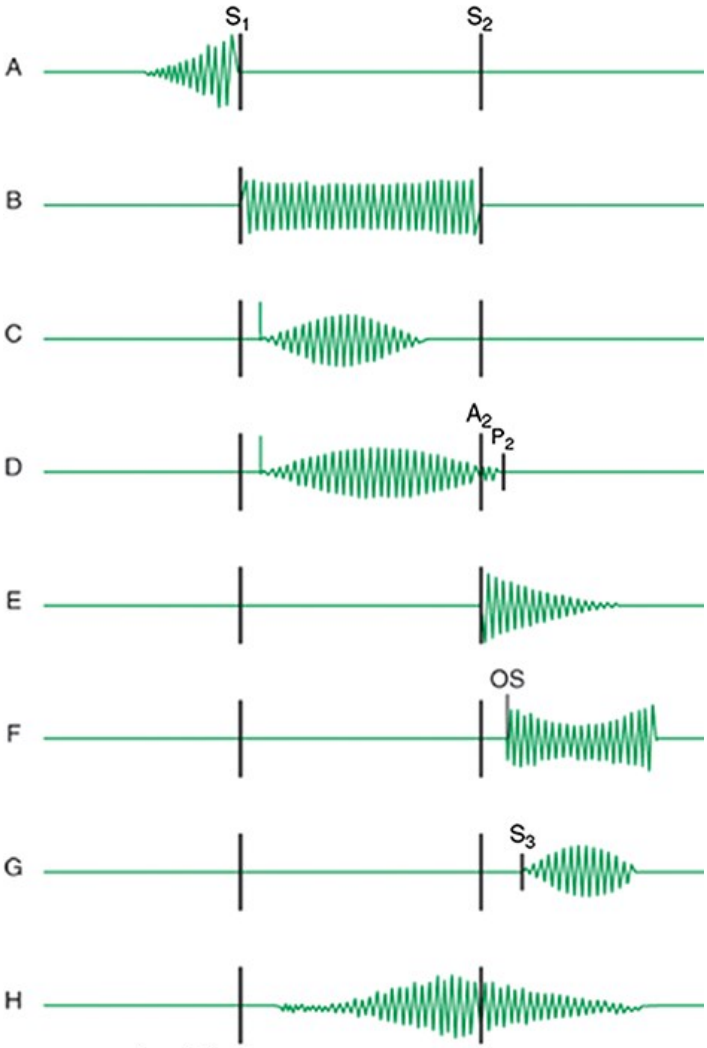
Murmurs – A murmur refers to the sound of blood as it passes through a heart valve. Some murmurs occur as the result of high flow across the valve or insignificant cardiac defects that are not pathologic in nature. Called innocent or flow murmurs, these sounds are usually soft and short in duration and have a “blowing” quality that may mimic the sound of ocean waves.

Murmurs may also be produced by turbulent blood flow through a heart valve and can indicate the presence and severity of valvular abnormalities. Murmurs are defined according to their timing within the cardiac cycle. Systolic murmurs are heard after the S_1 heart sound and before S_2, whereas diastolic murmurs are heard after S_2 but before S_1. Continuous murmurs extend across multiple phases of the cardiac cycle. A diagram of the principal

heart murmurs is shown in Fig. e29-4.

FIGURE e29-4

(*A*), tricuspid or mitral stenosis—late, crescendo diastolic murmur; (*B*), mitral or tricuspid regurgitation—holosystolic murmur; (*C*), aortic ejection murmur that begins with an ejection click—crescendo-decrescendo systolic ejection murmur; (*D*), pulmonic stenosis—crescendo-decrescendo systolic murmur with a delayed closure of the pulmonic valve; (*E*), aortic regurgitation—early, decrescendo diastolic murmur; (*F*), mitral stenosis—decrescendo-crescendo mid-diastolic murmur occurring after the opening snap (OS); (*G*), third heart sound (S3) followed by a decrescendo-crescendo mid-diastolic inflow; (*H*), patent ductus arteriosus—continuous murmur. *(Reproduced, with permission, from Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J, eds. Harrison's Principles of Internal Medicine. 19th ed. New York: McGraw Hill; 2015.)*



Murmurs are further described by several other features. The duration of the murmur can be characterized as occurring early, mid, or late in a phase of the cardiac cycle or *holo* (throughout). For instance, a murmur from mitral regurgitation (Fig. e29-4B) is a holosystolic murmur. The configuration of the murmur, or changes in sound due to alterations in pressure, may also be described as a crescendo, decrescendo, crescendo-decrescendo, or plateau. For example, an aortic ejection murmur (Fig. e29-4C) is a crescendo-decrescendo murmur, whereas a murmur from mitral regurgitation is a plateau. Additionally, the overall intensity of the sound of the murmur may be graded according to the criteria in Table e29-5. Finally, the location where the murmur originates and where it radiates should also be described. For instance, a murmur consistent with aortic insufficiency (or regurgitation) originates at the second intercostal space, right sternal border, and an aortic stenosis murmur will often radiate into the carotid arteries

as severity increases.

TABLE e29-5

Grade Scale for the Intensity of Murmurs

Grade	Criteria
I	Barely audible; no palpable thrill
II	Heard, not loud; no palpable thrill
III	Easily heard; no palpable thrill
IV	Easily heard; palpable thrill
V	Heard when the edge of the stethoscope touches the chest; a palpable thrill
VI	Heard with stethoscope off the chest; a palpable thrill

The presence of a new murmur warrant further evaluation by a cardiologist and potentially an echocardiogram to confirm the presence of a valvular abnormality. Prompt evaluation is also indicated when murmurs emerge or become more severe in the setting of worsening HF symptoms, new or worsening chest pain, or syncope, as valve replacement may be required.[35,36] A new murmur in the setting of infection, especially if accompanied by fevers and positive blood cultures, warrants immediate evaluation for endocarditis, as appropriate antibiotic treatment must be initiated quickly to prevent valve destruction and embolic complications.[37]

Pericardial Friction Rub

A pericardial friction rub is generated by friction between layers of inflamed pericardium and may be present in up to one-third of pericarditis cases.[38,39] To elicit the sound, patients should be asked to lean forward, increasing the area of contact between the visceral and parietal pericardium. A rub is present during both systole and diastole and is best heard over the left sternal border using the diaphragm of the stethoscope. The sound of a rub is harsh in nature and has been described as a "superficial scratchy or squeaking."[40]

Bruit

A bruit is the sound generated by turbulent blood flow through an artery due to abnormal narrowing (ie, stenosis), and is usually heard during systole. A bruit heard over the carotid artery is suggestive of carotid stenosis but may be difficult to discern from aortic stenosis. A bruit over the femoral artery may indicate the presence of PAD or a vascular complication resulting from a mechanical intervention such as cardiac catheterization. When present, further evaluation is warranted. A bruit may be present in the abdominal area in the setting of an abdominal aortic aneurysm, but this finding is nonspecific and should not be used as the sole criteria for diagnosis.[41]

Lung

The lungs should be auscultated with the patient in the seated position using the diaphragm of the stethoscope. Patients should be encouraged to breathe through their mouth and should cough once to clear their chest prior to auscultation. The bilateral posterior chest is auscultated first, followed by the anterior chest. In healthy lungs, the only sounds heard should be air traveling in and out of the airways as the patient breathes.

Crackles (also known as rales) are a nonspecific finding characteristic of several cardiovascular and pulmonary conditions. Crackles can be heard on both inspiration and expiration and have been described as the sound of hair being rubbed together or the slow peeling of two pieces of Velcro apart. Crackles may be present in acute decompensated heart failure (ADHF) when the lung alveoli are filled with fluid. However, as volume status improves,

crackles gradually disappear. Pulmonary causes of crackles include interstitial lung disease, pneumonia, and bronchitis.

Wheezing is a high-pitched whistling sound that typically occurs on expiration. Wheezing is a hallmark of asthma but may be heard in other lung conditions associated with airway obstruction, such as emphysema and bronchitis. Rhonchi are low-pitched, gurgling, or rattling sounds that can be heard both during inspiration and expiration. Rhonchi often suggest fluid or secretions in the large airways and may be heard in bronchitis or pneumonia.

Percussion of the lungs can assist in determining if a pleural effusion (a fluid collection between the lung and chest cavity) is present. A dull or thud-like sound can be heard over the area where the effusion is present, and it will gradually transition to a normal sound (like tapping a drum) at the meniscus of the effusion.[42,43]

LABORATORY FINDINGS

Biomarkers are measurements of biological function that can be used to diagnose certain conditions and assess the progress of a disorder or its response to pharmacologic therapy. In addition to cardiac-specific biomarkers, several noncardiac biomarkers are relevant to the assessment of CVD because they may influence risk or reflect alterations in heart function. Reference ranges for the laboratory values discussed in this section are displayed in Table e29-6.

TABLE e29-6

Common Laboratories Used in the Assessment of Cardiovascular Disease

Biomarker	Reference Range
Cardiac troponin[a]	
Troponin I	<0.01 ng/mL (mcg/L)
Troponin T	<0.04 ng/mL (mcg/L)
Creatine kinase–myocardial band (CK-MB)[a]	
Women	≤4 ng/mL (mcg/L)
Men	≤8 ng/mL (mcg/L)
Natriuretic peptides[b]	
Brain natriuretic peptide (BNP)	<100 pg/mL (ng/L; 29 pmol/L)
N-terminal proBNP (NT-proBNP)	<300 pg/mL (ng/L; 35 pmol/L)
High-sensitivity C-reactive protein (hs-CRP)	
Low risk	<1.0 mg/L
Intermediate risk	1.0-3.0 mg/L
High risk	>3.0 mg/L
Blood lipids[b]	
Total cholesterol	<200 mg/dL (5.17 mmol/L)
Triglycerides	<150 mg/dL (1.70 mmol/L)
Low-density lipoprotein (LDL)	<100 mg/dL (2.59 mmol/L)
High-density lipoprotein (HDL)	>40 mg/dL (1.03 mmol/L)

[a]May vary depending on individual clinical laboratory.

[b]Reference values provided; goals may differ in an individual patient.

Troponin

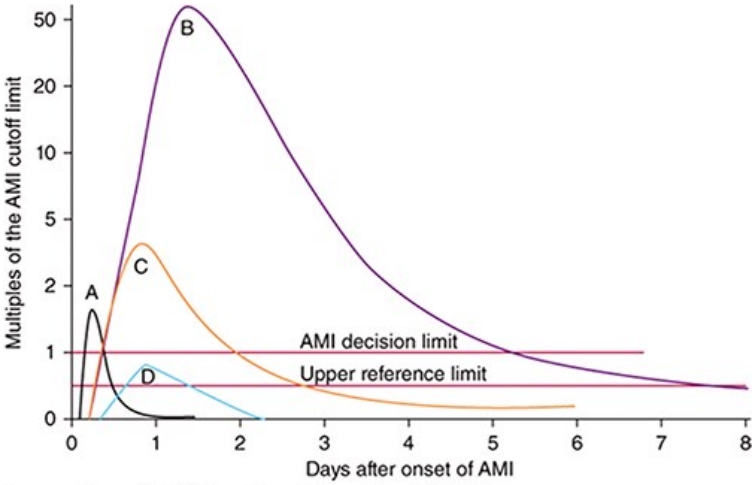
Cardiac troponin is an intracellular protein released into the bloodstream when myocardial necrosis occurs. Compared to troponin C, the troponin I and T subunits are more specific for cardiac tissue and are therefore useful indicators of myocardial injury. Since most assays are capable of

detecting circulating troponin in healthy individuals, the 99th percentile of the upper reference level is recommended as the threshold at which myocardial infarction (MI) should be suspected.[44]

An elevation in troponin can be detected within 2 to 4 hours of myocardial necrosis, making it the preferred biomarker for supporting the diagnosis of MI. The absence of cardiac troponin using most modern assays has a negative predictive value for MI approaching 100%.[9] However, given the delay in troponin release following an MI, patients with ischemic symptoms who have a normal troponin on initial presentation should have it measured again 3 to 6 hours later. If an elevation is detected, a series of troponin tests should be obtained to characterize a rising and/or falling pattern (Fig. e29-5).[9,44] The peak troponin concentration marks the point at which ongoing necrosis has ceased, and its magnitude can provide a crude estimate of infarct size. Following an MI, elevations in troponin may persist for up to 1 to 2 weeks, particularly in patients with renal dysfunction. Cardiac troponin also has prognostic value following an MI and can be used to risk-stratify patients as well as select an appropriate management approach.[45]

FIGURE e29-5

Serum-time profiles of cardiac biomarkers following myocardial injury. (*A*), myoglobin following acute myocardial infarction (AMI); (*B*), cardiac troponin following AMI; (*C*), creatine kinase–myocardial band (CK-MB) following AMI; (*D*), troponin following unstable angina. *(Reproduced, with permission, from Wu AH, Apple FS, Gibler WB, et al. National Academy of Clinical Biochemistry Standards of Laboratory Practice: Recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem. 1999;45(7):1104-1121.)*



Serum elevations of cardiac troponin may also occur in other cardiovascular disorders, such as tachyarrhythmias and ADHF, as well as several noncardiac conditions (eg, sepsis), although elevations are typically lower. Consequently, its use to establish an MI diagnosis must be placed in context with other findings suggestive of ischemia (eg, symptoms, ECG changes).

Creatine Kinase–Myocardial Band

Creatine kinase–myocardial band (CK-MB) is another biomarker released after myocardial cell death, but substantially greater injury is required to produce detectable concentrations compared to cardiac troponin.[9] Moreover, CK-MB is also present in skeletal muscle and can be released after other types of muscular injury (eg, rhabdomyolysis). For these reasons, it is not preferred in the diagnostic evaluation of MI, although it can be helpful for characterizing the extent of the injury and may be detectable prior to troponin in patients with recent-onset symptoms.[9] Given its short serum half-life, a new rise in CK-MB may be used to distinguish a new infarction in patients with persistently elevated cardiac troponin following an initial ischemic event.

B-Type Natriuretic Peptide

6 B-type natriuretic peptide (brain natriuretic peptide; BNP) and its biologically inactive precursor N-terminal pro-BNP (NT-proBNP) are released

from ventricular myocytes in response to stretch-related injury, most commonly due to volume overload. The natriuretic peptide system serves as a counter-regulatory response to the renin-angiotensin-aldosterone system, which is commonly activated in patients with HF. Natriuretic peptide concentrations are thus helpful tools in the diagnosis and evaluation of patients with both chronic and ADHF.

Serum BNP and NT-proBNP concentrations are primarily used to support the diagnosis of HF (ie, in concert with other clinical findings), or exclude HF in the differential diagnosis of patients presenting with dyspnea.[46-48] Elevations in serum BNP and NT-proBNP concentrations also portend HF severity as well as long-term morbidity and mortality.[48,49] Consequently, a measurement of baseline natriuretic peptides is recommended in patients admitted with ADHF.[46] An emerging indication for natriuretic peptide concentrations is to determine the prognosis in patients being discharged following ADHF.[46] Finally, an area of ongoing research is the use of serum BNP and NT-proBNP concentrations as a screening tool in patients at risk for developing HF.[50]

Either BNP or NT-proBNP concentrations may be used, but their thresholds are different (Table e29-6).[46] Several factors influence natriuretic peptide concentrations; thus clinical interpretation must account for age, gender, and body weight. Normal concentrations are higher in patients of advanced age and female gender and lower in patients who are overweight or obese. Because BNP and, especially, NT-proBNP undergo renal elimination, concentrations are also higher in patients with renal dysfunction. The use of neprilysin inhibitors (eg, sacubitril) must also be taken into consideration, as they may increase BNP but not NT-proBNP concentrations, and may reduce NT-proBNP concentrations over time.[46,51,52]

As with other biomarkers, elevations in BNP and NT-proBNP may also be present in related cardiovascular disorders, such as acute coronary syndromes, asymptomatic left ventricular dysfunction, and PE, as well as in several noncardiac conditions (eg, sepsis).

Inflammatory Mediators

Inflammation plays a pathologic role in several cardiovascular disorders, which has led to research involving the diagnostic and/or prognostic role of several inflammatory mediators. One of the biomarkers for which the most evidence exists is high-sensitivity C-reactive protein (hs-CRP), an acute phase reactant released by the liver in response to inflammation. At present, hs-CRP is regarded as a risk-enhancing factor and is, therefore, most useful for making decisions regarding treatment in patients without clinical ASCVD who are at uncertain risk for cardiovascular events in the future.[3,53]

Biomarkers of Related Metabolic Disorders

The risk of ASCVD increases with the presence and/or severity of certain chronic metabolic conditions, including dyslipidemia and diabetes mellitus. Consequently, biomarkers used in the management of these conditions are important for assessing the patient with or at risk for ASCVD. For patients without clinical ASCVD, screening for traditional risk factors such as dyslipidemia and diabetes mellitus should be performed every 4 to 6 years beginning at age 20; additionally, they should be used as part of the determination of estimated 10-year ASCVD risk every 4 to 6 years beginning at age 40.[54]

Elevations in total cholesterol, triglycerides, and low-density lipoprotein (LDL) concentrations, as well as low concentrations of high-density lipoprotein (HDL) all confer an increased risk of ASCVD. Total cholesterol, LDL, and HDL concentrations are used in the Pooled Cohort equations to determine 10-year ASCVD risk, and LDL concentrations are also used to assess response in patients who meet eligibility criteria for HMG-CoA reductase inhibitor (ie, statin) therapy.[3,53,54] Apoprotein B and lipoprotein (a) are risk-enhancing factors for ASCVD (Table e29-2) that can also be assessed to inform shared decision-making in patients with lower levels of ASCVD risk.[3] The use of specific LDL targets in ASCVD remains controversial, and readers are referred to Chapter 32, “Dyslipidemia,” for further discussion. Reference ranges for serum lipid concentrations are provided in Table e29-6.

The presence of diabetes mellitus also increases ASCVD risk, and cardiovascular events remain the most common cause of death in patients with the disorder. In general, a hemoglobin A1c <7% (0.07; 53 mmol/mol) is recommended in nonpregnant adults but different goals may be selected in individual patients based on risks and benefits (refer to Chapter 94, “Diabetes Mellitus,” for details).[55]

Miscellaneous Laboratory Tests

Several comorbid conditions can cause *de novo* cardiovascular disorders or worsen existing disease. As a result, screening patients for alterations in

biomarkers related to these conditions is often part of the routine evaluation of CVD. These may include measurements of thyroid hormones to evaluate for hypo- or hyperthyroidism; complete blood cell counts and markers of iron hemostasis to evaluate for anemia and/or iron regulation disorders, and tests for indicating the presence of human immunodeficiency virus (HIV).

Finally, since the heart is responsible for the circulation of blood to organs and tissues throughout the body, biomarkers of end-organ function may be used as surrogate measures of global cardiac function. Examples routinely used in practice include biomarkers of hepatic injury and function (eg, aspartate aminotransferase, alanine aminotransferase) and renal function (eg, serum creatinine, blood urea nitrogen).

ASSESSING ORGAN FUNCTION

Although considerable information regarding the health of the cardiovascular system can be gleaned from a comprehensive patient interview and targeted physical examination, these tools are occasionally inadequate for assessing the patient with or at risk for CVD. Further diagnostic testing is often required to establish a diagnosis, assess risk, and guide the selection of therapy. The following section provides an overview of some of the common diagnostic and evaluative modalities in cardiovascular medicine.

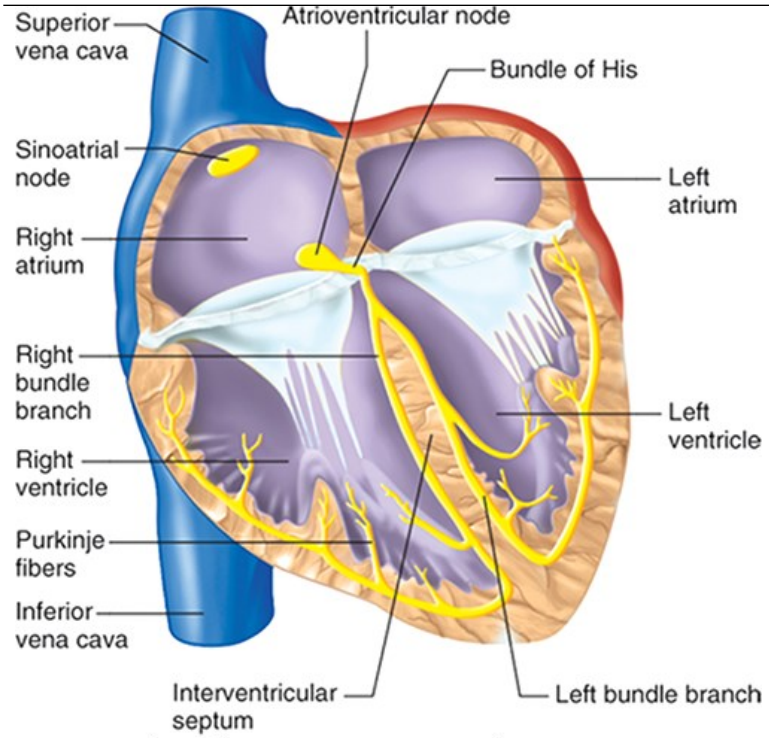
Electrocardiography

7 The ECG is the oldest diagnostic tool used in contemporary practice, and it remains a critical step in the evaluation of a wide range of clinical presentations, including chest pain or discomfort, palpitations, syncope, dizziness, and signs and symptoms of new-onset heart failure. The ECG provides a real-time map of electrical activity across the heart. As with other muscles in the body, the end result of these electrical impulses is a muscular contraction. Therefore, prior to learning the fundamentals of ECG interpretation, a basic framework of how electrical impulses in the heart trigger a muscular contraction is required.

Electrical activation in the heart begins within the right atrium, in the sinoatrial (SA) node (Fig. e29-6). The impulse generated by the SA node is then transmitted as a wave of depolarization across the atria and into the atrioventricular (AV) node. From the AV node, conduction flows through the right and left bundle branches, and finally into the His-Purkinje system, where it is transmitted to the ventricular myocardium. Electrical stimulation of cardiac myocytes triggers the entry of calcium into the cell, which leads to further release of calcium from within the cell, culminating in a muscle contraction. Following contraction, myocytes repolarize in preparation for the next impulse.

FIGURE e29-6

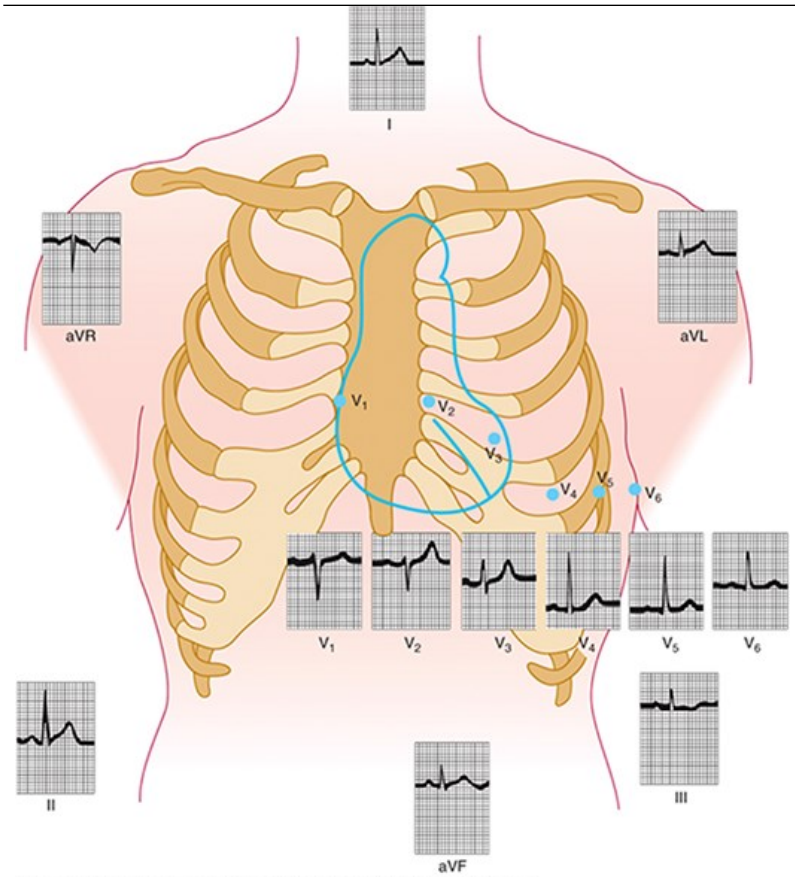
Electrical system of the heart. An electrical impulse begins at the sinoatrial node in the right atrium. Depolarization proceeds to the atrioventricular node. Finally, conduction proceeds down the left and right bundle branches, and then into the Purkinje fibers. *(Reproduced, with permission, from Barrett KE, Barman SM, Brooks HL, Yuan JJ, eds. Ganong's Review of Medical Physiology. 26th ed. New York, NY: McGraw Hill; 2019.)*



Since the heart is a three-dimensional structure, the wave of electrical depolarization does not travel in a straight line. By placing pairs of positively and negatively charged electrodes called leads at different locations across the chest, a comprehensive map of depolarization and repolarization can be produced. A standard ECG consists of 12 leads (Fig. e29-7). Six leads are placed across the chest wall and are named V_1 to V_6 (ie, the precordial or chest leads). The remaining six leads (ie, limb leads) are formed by pairs of electrodes on each arm and leg (or more commonly, on each shoulder and each side of the abdomen in the direction of the lower limbs), which monitor the signal on a frontal plane on the chest. Leads I, II, and III monitor the electrical vectors between the right arm and left arm, right arm and left leg, and left arm and left leg, respectively. Leads aVF, aVL, and aVR (ie, the augmented limb leads) monitor electrical vectors from an imaginary point in the middle of the abdomen to the left leg, left arm, and right arm, respectively.

FIGURE e29-7

Electrocardiogram lead placements. The positions of the unipolar lead placements (V_1-V_6) are shown. Bipolar leads are also placed on both arms and both legs to obtain tracings for leads I, II, and III, and aVL, aVF, and aVR. *(Reproduced, with permission, from Barrett KE, Barman SM, Brooks HL, Yuan JJ, eds. Ganong's Review of Medical Physiology. 26th ed. New York, NY: McGraw Hill; 2019.)*



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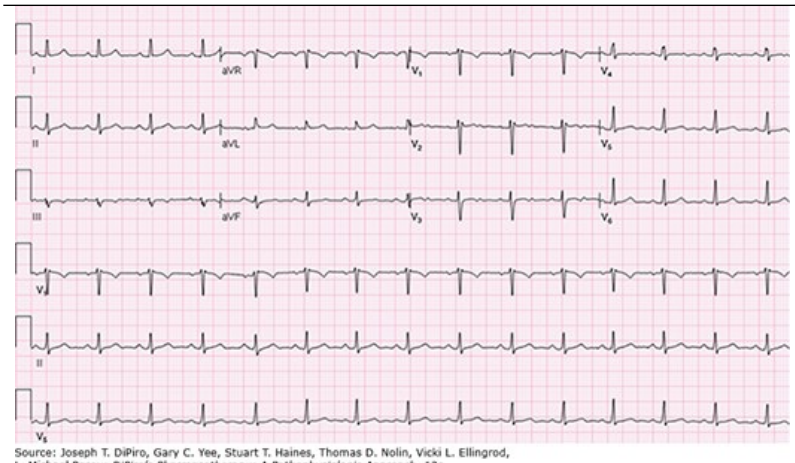
As electrical activity approaches the positive electrode of each lead (for bipolar leads) or the lead itself (for unipolar leads), a positive deflection is recorded. Current moving away from an electrode produces a negative deflection. Electrical signals are recorded from several leads simultaneously over the course of a few seconds, and these are displayed on an ECG (Fig. e29-8). The bottom three tracings of the ECG are often referred to as the *rhythm strip*, as they track the same leads over an entire tracing, facilitating rhythm interpretation. Because no two leads are in the same area, each displays a slightly different electrical signal. Combinations of leads can thus be used to detect a variety of disorders beyond arrhythmias, including the presence of myocardial ischemia and pathologic changes in heart structure, such as chamber enlargement or hypertrophy.

FIGURE e29-8

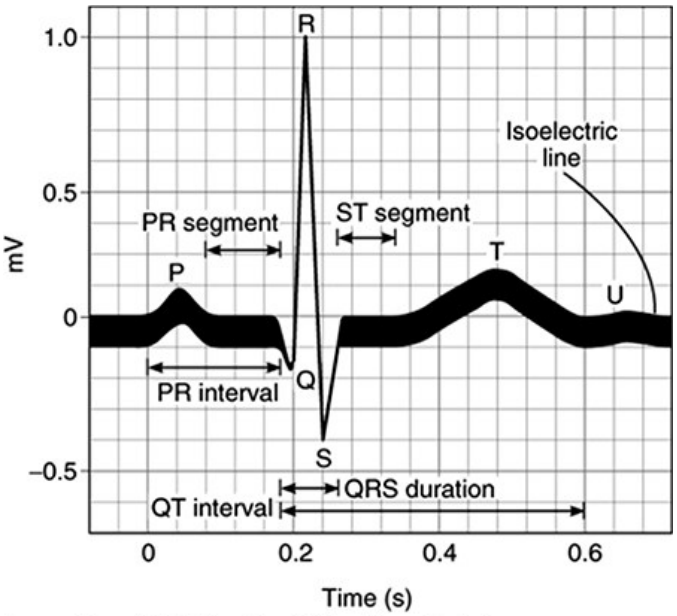
A normal 12-lead electrocardiogram (ECG). The ECG plots electrical activity on the Y-axis against time on the X-axis. Each lead records for a few seconds and then switches, with the exception of the bottom three, which do not change. These latter three leads constitute the *rhythm strip*, as they permit a more comprehensive assessment of cardiac rhythm.



The distinguishing features of a normal ECG are shown in Fig. e29-9. The X-axis of the ECG reflects time, and each large box on the ECG graph paper represents 0.2 seconds. The Y-axis reflects the magnitude of the electrical signal in each lead, described in terms of millimeters of deflection above or below the isoelectric baseline. The P wave represents atrial depolarization at the beginning of atrial systole. The PR interval is an isoelectric line from the end of the P wave to the onset of the QRS complex and reflects slowed conduction through the AV node and the delay between atrial and ventricular depolarization. The QRS complex reflects ventricular depolarization and the onset of ventricular systole. The QT interval reflects the delay in ventricular repolarization and the duration of the action potential. Finally, the ST segment and T wave occur during ventricular repolarization at the beginning of ventricular diastole. Normal ranges exist for the amplitude and timing of each wave and segment.

FIGURE e29-9

Terminology used to describe the distinguishing features of a normal ECG. *(Reproduced, with permission, from Barrett KE, Barman SM, Brooks HL, Yuan JX-Y. Ganong's Review of Medical Physiology Examination and Board Review. 26th ed. New York, NY: McGraw Hill; 2019.)*



Interpreting an ECG requires a systematic approach. No "one-size-fits-all" algorithm exists, and most individuals apply the technique of their mentors or training institution. Once a method is selected, clinicians are encouraged to use it consistently. A common approach to ECG interpretation is described in Table e29-7. Rhythm identification is often the most challenging aspect of electrocardiography, and complex arrhythmias may be difficult for even the most experienced cardiologists to interpret. The axis reflects the overall net depolarization vector in the frontal plane (gathered from the

limb leads), and certain conduction disorders or cardiovascular conditions may shift this axis. Following identification of the axis, the P wave and QRS amplitude are assessed, as prominent voltage may suggest chamber enlargement or hypertrophy. The QRS complex must be carefully inspected for Q waves (an initial downward deflection in the QRS complex), which may be a sign of prior MI. Next, the ST segments and T waves are inspected. In the appropriate context, ST segment depressions may reflect myocardial ischemia, and ST segment elevations may be seen with myocardial injury, although neither of these changes is specific and should therefore be evaluated in context with other clinical information (eg, symptoms). Finally, the intervals are assessed, as abnormalities may reflect electrolyte disorders.

TABLE e29-7

Approach to Electrocardiogram Interpretation

1. Identify atrial and ventricular rates.
2. Determine rhythm.
3. Determine axis.
4. Assess P and QRS amplitude/duration.
5. Review ST segment and T wave.
6. Calculate QT/QTc interval.

Another important aspect of ECG interpretation is determining the duration of the QT interval, as prolongation increases the risk of polymorphic ventricular tachycardia and sudden cardiac death.[56] The QT interval is measured from the beginning of the QRS complex to the end of the T wave and represents the time required for ventricular depolarization and repolarization. The QT interval varies based on heart rate and can be corrected according to Bazett's formula as follows:

$$\mathrm{QT}_{\mathrm{corrected}} = \frac{\mathrm{QT\ interval}}{\sqrt{\mathrm{RR\ interval}}}$$QTcorrected=QT intervalRR interval

A normal corrected QT (QTc) interval is <450 msec for men and <460 msec for women.[57] Electrolyte abnormalities (eg, hypokalemia) can affect the QT interval, along with ischemia, commonly prescribed medications (eg, atypical antipsychotics, azole antifungals, select antiarrhythmics), and inherited membrane channelopathies. Because the QT interval is comprised of the QRS complex, ST segment, and the T wave, conditions associated with a widened QRS (eg, bundle branch block, ventricular pacing) will also prolong the QT interval. In these scenarios, the standard QTc reference intervals do not apply.

One of the most common reasons for obtaining an ECG is in the evaluation of palpitations, which may occur intermittently and not at a time when they can be evaluated by a healthcare professional. If a determination of heart rhythm is all that is required, a 12-lead ECG may not be necessary, and instead, ambulatory monitoring may be performed using a portable ECG device known as a Holter monitor. Several ECG leads are placed on the patient's chest, and these are attached to a small recorder. All heartbeats are recorded over a period of time (typically 24-48 hours), and the patient keeps a record of any symptoms that emerge. If symptoms occur and correlate with the presence of an arrhythmia on the monitor, a diagnosis may be made. A Holter monitor will also provide information regarding the minimum, maximum, and average heart rates; the number of premature atrial and ventricular beats; and any ST segment changes.

For symptoms that occur very infrequently, an event monitor may be used. An event monitor is similar to a Holter monitor except that the device may be worn for 14 to 28 days. Unlike Holter monitors, event monitors do not record and store every heartbeat. Instead, when patients experience symptoms, they trigger the device with a button, prompting it to record and store several minutes of heart rate and rhythm data. For even less frequent episodes (ie, those occurring less than once a month) in patients with severe symptoms (eg, syncope), an implantable monitor may be surgically placed under the skin, and data can be recorded for many months and transmitted remotely. Portable and wearable devices, such as the Apple Watch (Apple Inc.; Cupertino, CA) have been developed with powerful rhythm monitoring capacities; these devices can detect infrequent arrhythmias, such as paroxysmal atrial fibrillation,[58] and can be paired with a mobile device to store and transmit rhythm strips.

Stress Testing

A resting ECG may be normal in patients with CAD, as blood flow may be adequate for meeting the heart's metabolic needs even in the face of

significant obstructive lesions.[59] However, physical exertion produces an increase in heart rate, myocardial contractility, and BP, leading to increased myocardial oxygen demand.[60] In the presence of a fixed coronary stenosis, oxygen delivery will be unable to keep up with demand, and myocardial ischemia may occur, manifesting as chest pain or abnormalities on ECG.

Based on these principles, stress testing is a common modality for detecting CAD in patients with anginal symptoms in the absence of an MI. If obstructive CAD is detected, patients may benefit from risk factor reduction, pharmacologic therapy, and potentially coronary angiography and revascularization. Although chest pain is the most common reason for stress testing, other established indications are listed in Table e29-8. Stress testing is not routinely recommended as a screening tool for CAD in asymptomatic patients.

TABLE e29-8

Common Indications for Stress Testing

- Chest pain suggestive of angina
- Risk assessment in patients with unstable angina or non-ST segment acute coronary syndrome
- Preoperative risk assessment in patients undergoing noncardiac surgery
- Assessment of severity in valvular heart disease
- Determining role for coronary revascularization in left ventricular dysfunction
- Clinical significance of arrhythmias or bradycardias

In the United States, most stress tests are performed on a treadmill rather than a bicycle. Although patients may be accustomed to walking or jogging on a treadmill, stress testing differs from a standard exercise regimen. The most common treadmill protocol is the Bruce protocol, which begins at a speed of 1.7 mph (2.7 km/h) and an incline of 10%. The speed then increases by 0.8 mph (1.3 km/h) and the grade increases by 2% every 3 minutes for a total of 21 minutes.[61] During the test, the ECG is monitored continuously, and BP is measured every 3 minutes. Patients are also routinely asked about chest pain symptoms. Most stress tests are symptom-limited; that is, patients exercise until they develop dyspnea that limits further activity. Other indications for early termination of the test include the development of arrhythmias or drastic changes in BP. In properly selected candidates under appropriate supervision, ECG stress testing is safe, with serious complications (eg, ventricular arrhythmias, MI) occurring at a rate of only one event per 10,000 studies.[62]

Patients must achieve 85% of the age-predicted maximum heart rate for a stress test to be diagnostic.[63] If patients cannot achieve this threshold despite maximal exercise, the study is considered “nondiagnostic,” even if no ECG abnormalities are observed. As a result, the presence of CAD cannot be definitively excluded, and alternative testing should be considered.

The development of chest pain, especially if accompanied by ECG abnormalities, is highly specific for CAD.[64] A positive stress test is defined as a change on the ECG of 1 mm of down-sloping or horizontal ST segment depressions in two contiguous leads persisting 80 msec after the QRS complex.[65] ST segment depressions can occur during exercise or in the recovery period after the test. If ST segment elevation occurs in a patient without baseline Q waves, profound myocardial ischemia is likely present, and the study should be terminated immediately so that urgent cardiac catheterization may be performed.

When certain ECG abnormalities are present at baseline, such as left ventricular hypertrophy with prominent repolarization abnormalities, the development of ST segment depression loses both sensitivity and specificity.[65] Additionally, the presence of a left bundle branch block renders the ST segments uninterpretable, and treadmill testing should not be performed; instead, pharmacologic vasodilator testing should be considered (discussed later).

Stress testing also suffers from the limitations common to all diagnostic studies, in that there may be both false positive and false negative results, and the likelihood of a positive test is dependent on the pretest probability of disease. Consequently, stress testing should not be the sole factor in determining whether further testing (eg, coronary angiography) should be performed. Instead, multiple data points should be considered, including traditional ASCVD risk factors and the nature of the patient’s symptoms.

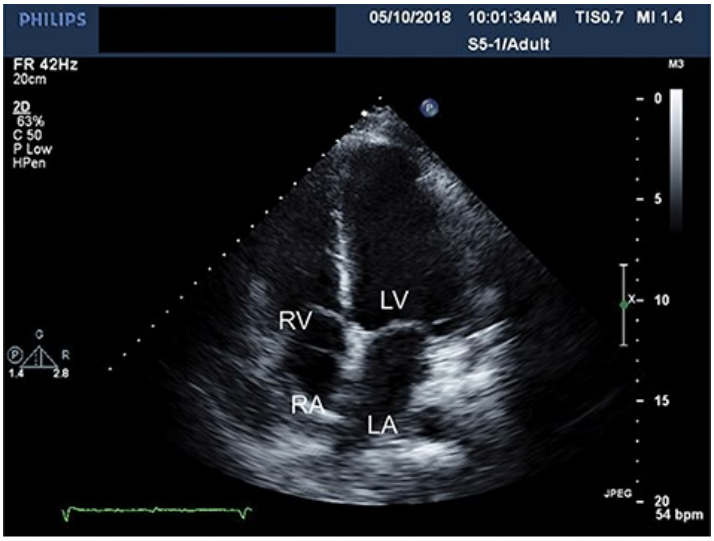
For patients who are unable to exercise (eg, orthopedic limitations, other factors that may limit ambulation) or who cannot achieve the target heart rate, pharmacologic stress testing may be performed instead. In a pharmacologic stress test, one of two mechanisms is employed: administration of an agent that increases myocardial oxygen demand and results in ischemia, or administration of an agent that dilates the coronary arteries, resulting in relative regional perfusion abnormalities. Since pharmacologic stress testing is always performed in conjunction with additional imaging studies such as echocardiography or radionuclide imaging, this modality will be discussed in further detail in the section on nuclear cardiology later in this chapter.

Echocardiography

9 Aside from the ECG, echocardiography is the most common modality for assessing cardiac function and the presence of CVD. Echocardiography is a noninvasive test involving the emission of ultrasound waves, which travel through tissue and are reflected back to a transducer probe, where they are processed to construct images of the heart and related structures. In early forms of echocardiography, only one-dimensional (m-mode) ultrasound was available. However, as probe technology improved, two-dimensional echocardiography was developed (Fig. e29-10). Although most devices are now capable of generating three-dimensional echocardiographs, two-dimensional imaging can be rapidly performed and is accurate and effective at answering most clinical questions.

FIGURE e29-10

Two-dimensional apical four-chamber view of the heart. The probe is placed at the left ventricular apex, usually in the fifth intercostal space at the mid-clavicular line. (LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.)



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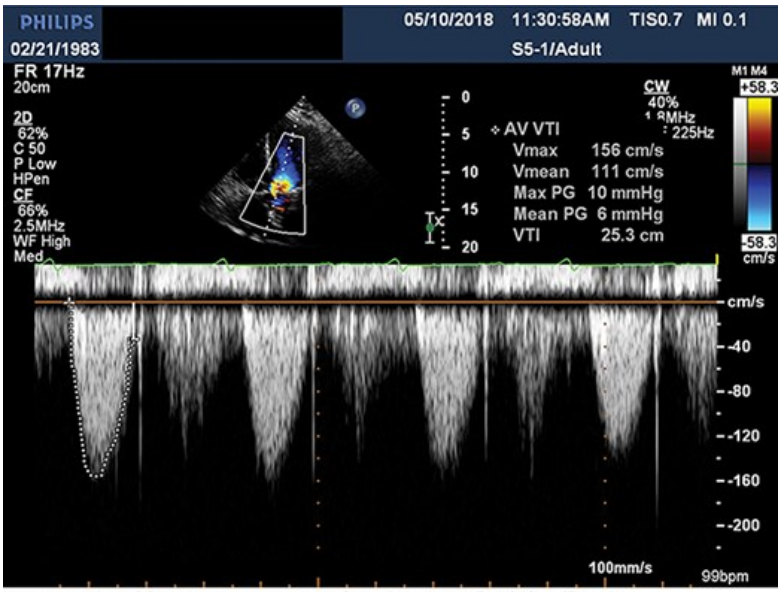
Echocardiographic images are broadly classified according to where the probe is placed during the procedure. During a transthoracic echocardiogram (TTE), the transducer probe is placed on several locations on the chest and upper abdomen. A TTE provides information on the chambers, valves, and contractile function of the heart. Consequently, TTE is the imaging modality of choice for the assessment of valvular heart disease, left and right ventricular function, and pericardial effusions. It is also a cornerstone in the evaluation of HF, as left ventricular ejection fraction (LVEF) is often critical in therapeutic decision-making.

An application of ultrasound is Doppler echocardiography, in which the directional flow and velocity of red blood cells can be visualized. Color Doppler images provide a qualitative assessment of turbulent blood flow through the heart valves, which can be subsequently classified as either regurgitation or stenosis. A continuous-wave Doppler provides a quantitative measurement of blood velocity (Fig. e29-11), which can then be used to calculate the pressure gradients across the valves and valve areas, and estimate pulmonary artery pressures. A more recent application of Doppler imaging is measuring myocardial tissue velocities, which can be useful in assessing diastolic function and determining prognosis in chronic HF.

FIGURE e29-11

Continuous-wave Doppler, measuring the velocity of blood (in centimeters/second) across the aortic valve.



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Echocardiography can also be used to detect intracardiac shunting. Color Doppler interrogation of the interatrial septum may detect left to right shunts, most commonly as a result of atrial septal defects. Additionally, in a procedure known as a bubble study, saline can be agitated to create microbubbles, which are then injected into an intravenous line. In a structurally normal heart, these bubbles will appear in the right ventricle but are subsequently absorbed in the lungs. However, bubbles that emerge on the left side of the heart suggest the presence of a right-to-left shunt, such as a patent foramen ovale (PFO).

The advantages of TTE are that it is highly portable, reproducible, and images can be obtained in even the most critically ill patients in the intensive care unit or operating room. Additionally, ultrasound waves do not use ionizing radiation, and intravenous access is not required for most procedures. However, occasionally a TTE is unable to provide satisfactory imaging. For example, in trauma or postoperative patients, the presence of lines and tubes as well as chest wall abnormalities may limit acoustic windows. Additionally, ultrasound waves are reflected by air and degrade as they travel through tissue, which may result in poorer image quality in obese patients. Contrast echocardiography, in which gas-filled microbubbles are injected intravenously, can improve the assessment of LV size and function in patients with poor imaging windows.[66] Finally, because of the orientation of the heart within the thoracic cavity, some structures located toward the posterior aspect of the heart are poorly visualized with a TTE. Similarly, TTE may not provide the image clarity necessary to evaluate subtle abnormalities, such as valvular vegetations. Fortunately, if information regarding these latter structures is needed, a transesophageal echocardiogram (TEE) may be performed.

During a TEE, the transducer probe is advanced through the mouth and into the patient's esophagus where ultrasound waves are transmitted through the posterior aspect of the heart. A TEE is commonly used to evaluate for the presence of aortic dissections, left atrial appendage thrombus prior to cardioversion, and valvular vegetations in patients with bacteremia or suspected endocarditis. Because of the close proximity of these structures to the esophagus (especially the mitral and aortic valves), TEE images are of higher quality than TTE. Consequently, TEE is used extensively in the operating room to ensure the proper functioning of newly implanted heart valves and overall heart function in patients undergoing CABG surgery.

Although a TEE is generally considered to be a safe procedure, it is invasive and therefore carries a small inherent risk.[67] Trauma to the esophagus and the vocal cords are rare but known complications of TEE. Contraindications include esophageal pathology that may limit the advancement of the probe, untreated esophageal varices, and oropharyngeal or cervical spine conditions that limit neck extension and flexion. Conscious sedation is used for procedural comfort and safety, and appropriate cardiac and respiratory monitoring by specialized personnel are required.

Echocardiography can also be used in conjunction with ECG stress testing to improve its sensitivity and specificity, as ischemia-related changes in systolic or diastolic function may be detected prior to ECG changes or ischemic symptoms. Stress echocardiography can be performed with exercise using a treadmill or bicycle, or pharmacologically, most commonly with dobutamine. Dobutamine is a beta-receptor agonist, which induces

physiologic changes similar to exercise (eg, increased myocardial contractility and heart rate), leading to increased myocardial oxygen demand. At peak exercise (or peak dobutamine infusion), echocardiogram images are obtained and compared to baseline images. Myocardium that is well-perfused will become hyperkinetic with stress, whereas ischemic segments may appear hypokinetic compared to baseline, and relatively hypokinetic compared to areas receiving adequate blood supply.

Cardiac Catheterization

Cardiac catheterization (or heart catheterization) is a procedure in which a catheter is inserted percutaneously into a large blood vessel and advanced to the heart, where it is used to obtain diagnostic or evaluative information. Therapeutic interventions may also be performed. Cardiac catheterization can be broadly classified as being left-sided (left heart catheterization or LHC) or right-sided (right heart catheterization or RHC), depending on whether the catheter is inserted into an artery (LHC) or vein (RHC). The selection of LHC versus RHC depends on the information desired. The common indications for each are listed in Table e29-9.[68]

TABLE e29-9

Common Indications for Cardiac Catheterization

Left Heart Catheterization	Right Heart Catheterization
• Acute coronary syndromes • Cardiogenic shock • Cardiomyopathy, with or without symptoms of heart failure • Coronary artery disease, especially if symptomatic and/or high-risk features are present (eg, new systolic dysfunction) • Pericardial tamponade • Valvular disease, as a preoperative evaluation prior to surgery or with indeterminate severity • Ventricular arrhythmias, including resuscitated cardiac arrest	• Acute decompensated heart failure, with indeterminate volume status, change in clinical condition, and/or to guide therapy (eg, inotropes) • Pulmonary hypertension • Surveillance endomyocardial biopsy after heart transplantation • Shock

Data from Reference 68.

Bleeding from the access site is the most common complication of cardiac catheterization, and thus coagulopathies and other bleeding diatheses should be corrected prior to the procedure. If radiocontrast dye is to be used as in the case of a LHC, the benefits of cardiac catheterization must be weighed against the risk of worsening preexisting renal dysfunction. Providing adequate hydration and limiting the volume of contrast dye used during the procedure may ameliorate the risk of renal injury.[9] Alternative strategies, such as the administration of oral N-acetylcysteine, are not effective and therefore not recommended.[69] With the exception of severe anaphylactic reactions, patients with allergies to contrast dye can often undergo cardiac catheterization safely if adequately premedicated prior to the procedure. Regimens for allergy prophylaxis generally consist of a corticosteroid and histamine-receptor blocker (eg, diphenhydramine). The need to provide prophylaxis in patients with shellfish or seafood allergies is a common misconception and is not recommended.[69]

Other relative contraindications to cardiac catheterization include hemodynamic instability, uncontrolled hypertension, intractable arrhythmias, severe electrolyte derangements, and systemic infections. Because of the invasive nature of the procedure and the risk of complications, cardiac catheterization is typically performed in a procedural unit by a specialized team and may not be available at smaller medical facilities.

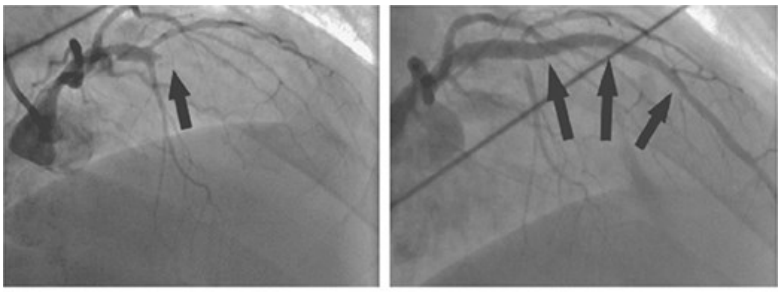
Left Heart Catheterization

10 During LHC, a catheter is inserted percutaneously through an incision in a large peripheral artery, such as the femoral or radial artery, and advanced in a retrograde fashion to the cardiac structure of interest. Access via the radial artery is becoming more common because of lower complication rates, faster recovery times, and improved patient satisfaction.[70]

The most common indication for LHC is coronary angiography, a procedure in which fluoroscopy (real-time x-ray) is used to diagnose or evaluate ASCVD. During the procedure, a catheter is advanced into the coronary arteries, where a contrast dye is injected to visualize the coronary anatomy and detect occlusion of blood flow (Fig. e29-12). Fluoroscopy produces two-dimensional images; given the three-dimensional nature of coronary anatomy and blood flow, multiple projections are required to accurately characterize and grade coronary lesions. Areas of stenosis are considered to be significant when the diameter of the arterial lumen has narrowed by ≥70% (≥50% for the left main artery).[69]

FIGURE e29-12

Coronary angiography showing complete occlusion of the left anterior descending artery in a patient presenting with ST segment acute coronary syndrome (*A*), and restoration of blood flow following angioplasty and coronary stenting (*B*). *(Reproduced, with permission, from Crawford MH, ed. Current Diagnosis & Treatment: Cardiology. 5th ed. New York, NY: McGraw Hill; 2017.)*



A B
Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

A limitation of angiography is that it does not provide information regarding the physiologic implications of a coronary lesion, such as whether the degree of stenosis present results in myocardial ischemia. In patients with stable coronary disease, revascularization of lesions because they appear stenotic to the operator does not improve outcomes.[71] For indeterminate lesions (50%-70% stenosis), fractional flow reserve (FFR) may indicate scenarios in which an intervention may be deferred. During FFR, a coronary vasodilator is administered, and the pressure difference across the area of stenosis is used to calculate flow. An FFR value of ≤0.80 (ie, ≥20% reduction in flow) is generally considered hemodynamically significant and thus warrants revascularization.[69]

Another limitation of angiography is that it does not provide information on the arterial wall, nor details regarding the morphology of a coronary lesion (eg, plaque volume, area, cross-sectional area). In cases where this information may alter treatment, a specialized catheter can be used to perform intravascular ultrasound (IVUS). Like FFR, IVUS may be used to guide decision-making in patients with indeterminate lesions, but it is less commonly used for this purpose due to the added complexity and expense of the procedure. Instead, IVUS is primarily reserved for the assessment of cardiac allograft vasculopathy (CAV), a special type of CAD found in heart transplant recipients, characterized by diffuse narrowing of the vessel lumen rather than the development of discrete lesions.[69]

If a significant coronary occlusion or severe stenosis is detected, a percutaneous coronary intervention (PCI) may be performed to restore blood flow (see Chapter 33, "Stable Ischemic Heart Disease" for more detailed explanation of PCI). Restoration of blood flow following PCI can be graded according to Thrombolysis in Myocardial Infarction (TIMI) Grade Flow on a scale of 0 to 3, where 0 represents no flow and 3 represents normal flow. Blood flow receiving a TIMI 1 score represents a partial restoration of flow but an incomplete filling of distal vessels, whereas a TIMI 2 score represents delayed flow but a complete filling of distal vessels. In instances where a patient would benefit from CABG surgery over PCI, LHC may be terminated once the anatomy has been characterized via angiography. The films obtained during LHC are then used by cardiac surgeons to determine the optimal grafting strategy for restoring blood flow.

Right Heart Catheterization

11 During RHC, a catheter is inserted percutaneously through an incision in a large vein, such as the IJ, femoral, or brachial vein, and advanced to the right side of the heart. Several diagnostic and therapeutic procedures can be performed with RHC, the most common of which is an assessment of cardiac hemodynamics. Reference ranges for common hemodynamic values are provided in Table e29-10. When hemodynamic values are needed in an urgent scenario, RHC can be performed at the bedside; otherwise, it is more commonly performed in the cardiac catheterization lab with

fluoroscopic guidance.

TABLE e29-10

Reference Ranges for Common Hemodynamic Values[a]

Hemodynamic Parameter	Reference Range
Heart rate (HR)	60-110 bpm
Cardiac output (CO)	4-6 L/min (0.07-0.1 L/s)
Cardiac index (CI)	2.8-4.2 L/min/m^2 (0.047-0.07 L/s/m^2)
Right atrial pressure (RAP)[b]	2-6 mm Hg
Right ventricular pressure (systolic/diastolic)	15-30 / 8-15 mm Hg
Mean pulmonary arterial pressure (mPAP)	10-20 mm Hg
Pulmonary arterial pressure (PAP, systolic/diastolic)	15-30 / 5-15 mm Hg
Pulmonary vascular resistance (PVR)	150-250 dynes·s/cm^5 (15-25 MPa·s/m^3)
Pulmonary capillary wedge pressure (PCWP)	6-12 mm Hg
Left atrial pressure (LAP)	4-12 mm Hg
Left ventricular pressure (systolic/diastolic)	100-140 / 4-12 mm Hg
Mean arterial pressure (MAP)	70-100 mm Hg
Systemic arterial pressure (systolic/diastolic)	100-120 / 60-80 mm Hg
Systemic vascular resistance (SVR)	800-1,200 dynes·s/cm^5 (80-120 MPa·s/m^3)

[a]The values presented in this table represent reference ranges, and may differ slightly from other resources; additionally, the "normal" value in an individual patient may vary according to clinical context (eg, a resting heart rate of 55 may be normal in a professional athlete).

[b]May be reported as central venous pressure (CVP).

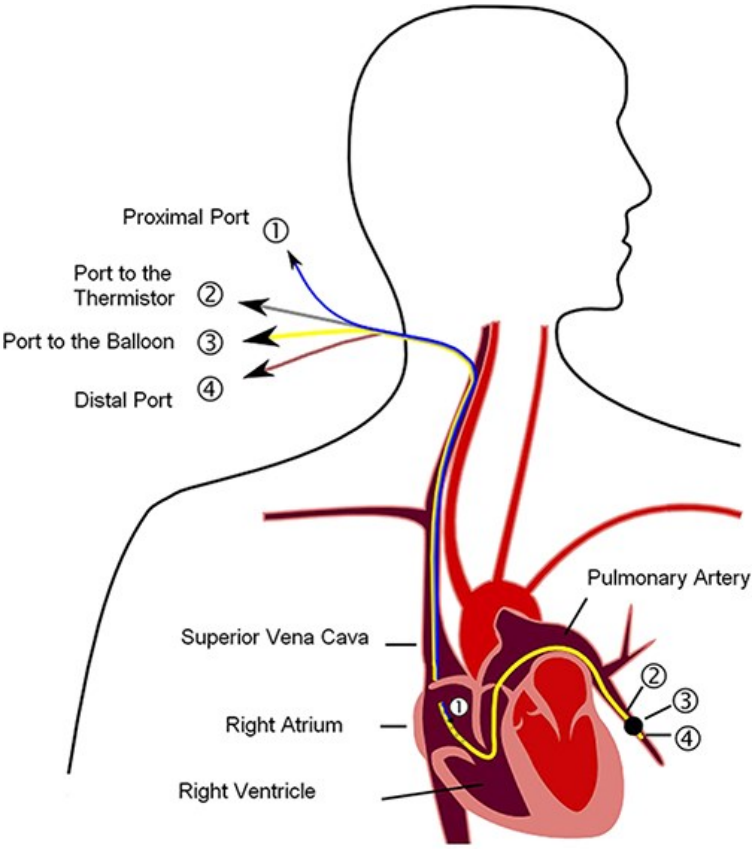
Although the routine use of invasive hemodynamic monitoring in patients with ADHF does not improve outcomes over clinical assessment alone, subsets of patients may still benefit from the information it provides, such as those patients whose volume or perfusion status remains unclear despite a thorough clinical evaluation or those whose status does not improve despite appropriate therapy (see Chapter 37, "Acute Decompensated Heart Failure").[15,68,72] An assessment of cardiac hemodynamics is also essential to determining patient eligibility for advanced therapies, such as mechanical circulatory support and cardiac transplantation, as well as in the diagnosis and evaluation of pulmonary hypertension.[68,73]

During an assessment of cardiac hemodynamics, a special balloon-tipped catheter known as a pulmonary artery (PA) catheter or Swan-Ganz catheter is advanced through the right atrium, right ventricle, and into a small branch of the PA, where pressures in each of these areas are measured (Fig. e29-13). The catheter can also be used to administer fluids and medications, and a thermistor near the distal end of the catheter measures changes in

temperature. The catheter may be inserted to obtain a single set of measurements and then removed, or it may be sutured in at the access site and left inside the patient to guide the titration of vasoactive medications.

FIGURE e29-13

During right heart catheterization, a pulmonary artery catheter is inserted into a large peripheral vein and advanced through the right atrium and right ventricle and into the pulmonary artery. *(Reproduced, with permission, from Boyle AJ. Acute myocardial infarction. In: Crawford MH, ed. Current Diagnosis & Treatment: Cardiology. 5th ed. New York: McGraw-Hill; 2017.)*



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After being advanced into a small branch of the PA, the balloon at the end of the catheter can be inflated to transiently occlude the artery, producing what is known as the pulmonary capillary wedge pressure (PCWP) or the pulmonary artery occlusion pressure. In the absence of significant pulmonary vein stenosis or mitral valve disease, the PCWP provides an estimate of left atrial pressure, which is approximately equal to the left ventricular end-diastolic pressure (LVEDP). The LVEDP is a surrogate measure of cardiac preload and can be used as an assessment of a patient's overall volume status.

Other key hemodynamic parameters that can be obtained during RHC are cardiac output (CO) and systemic vascular resistance (SVR). In practice, the CO is often normalized for body surface area and reported as the cardiac index (CI). Estimates of CO can be made using either the Fick or thermodilution method. According to the Fick principle, CO can be calculated by dividing total oxygen consumption within a unit of time by the arteriovenous oxygen difference. Although the Fick method has historically been considered the gold standard for determining CO, prior methods involved direct measurements of oxygen consumption requiring a metabolic cart. Since these are rarely used in contemporary practice in the cardiac catheterization lab, oxygen consumption is often assumed based on gender and body size, making it less reliable in some patients. For example, the Fick method is less accurate in patients with disorders that affect oxygen diffusion and transport, such as pulmonary disorders or anemia.

An alternative to the Fick equation is the thermodilution method, during which CO can be estimated by measuring a change in blood temperature as it flows between two points. During the thermodilution procedure, a small bolus of cold saline is infused from a proximal port on the PA catheter, and

the resulting change in blood temperature is measured at the thermistor on the distal end of the catheter. Greater changes in temperature between the two points are indicative of slower blood flow and thus reduced CO. As with the Fick method for determining CO, the thermodilution method is also subject to confounding by coexisting conditions, such as intracardiac shunts or regurgitant blood flow. The thermodilution CO is considered more reliable than the Fick method and should be calculated and reported when possible.

Once known, CO can be combined with the mean arterial pressure (MAP) and central venous pressure (CVP) to calculate SVR, an estimate of the resistance force imparted by the systemic vasculature. Because arterial impedance is often the greatest contributor of resistance against the ejection of blood out of the left ventricle, the SVR is commonly used as a surrogate for cardiac afterload. The use of CO, MAP, and CVP to calculate SVR is depicted in the following equation:

$$\text{SVR (dynes} \cdot \text{sec/cm}^5) = \left(\frac{\text{MAP} - \text{CVP}}{\text{CO}}\right) \times 80$$ SVR (dynes · sec/cm5)=(MAP−CVPCO)×80

Another common use of RHC is in the diagnosis and evaluation of pulmonary hypertension (PH), which is defined as a mean PA pressure >20 mm Hg. If elevated due to excess volume, PA pressures will improve and often normalize following reductions in PCWP. However, if PA pressures remain elevated despite a high-normal PCWP (≤15 mm Hg) and PVR is also elevated (>3 Wood units), a diagnosis of pre-capillary PH can be made.[73] Further evaluation is then required to distinguish among the various types of pre-capillary PH. In patients with PAH, a specific type of pre-capillary PH, RHC may be used to determine eligibility for high-dose calcium channel blocker therapy (termed vasoreactivity testing) as well as to guide the titration of disease-modifying therapies. Readers are referred to Chapter 46, "Pulmonary Artery Hypertension," for a more comprehensive discussion of these topics.

Patients being evaluated for cardiac transplantation must undergo RHC to determine the reversibility of elevated PA pressures. During a "vasodilator challenge," a vasodilating agent such as sodium nitroprusside is administered until PA systolic pressures are ≤50 mm Hg or PVR is ≤3 Wood units (≤240 dynes·s/cm^5 [24 MPa·s/m^3]). Patients unable to achieve these parameters without compromising SBP (<90 mm Hg) are deemed ineligible for cardiac transplantation and may require a left ventricular assist device or pharmacotherapy to treat pulmonary hypertension prior to listing.[74] Recipients of a heart transplant must also undergo routine RHC for the purposes of endomyocardial biopsy, a procedure in which samples of myocardial tissue are obtained from the septal wall of the right ventricle and evaluated for the presence of graft rejection.

Chest Radiography (x-ray)

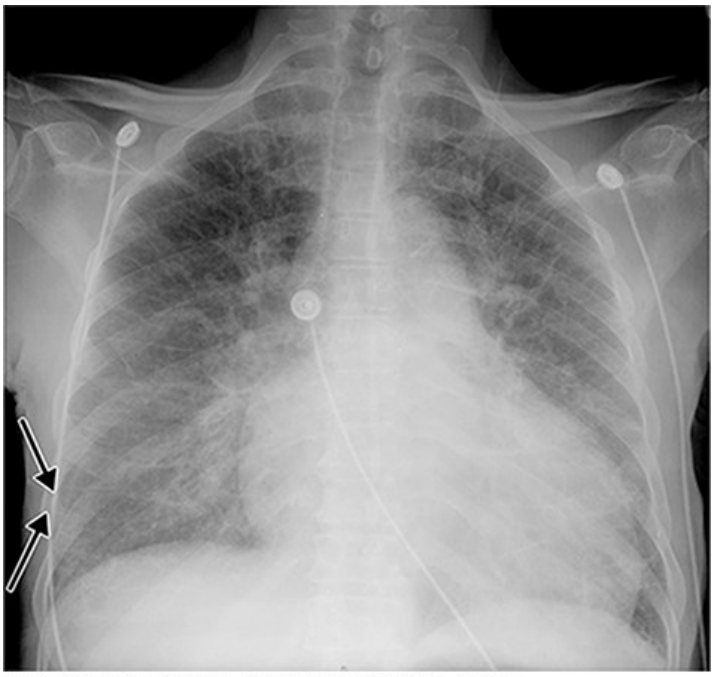
A chest radiograph or x-ray is a noninvasive imaging test that provides visual information about the heart, lungs, and related structures within the thoracic cavity. Chest x-rays are useful in differentiating acute dyspnea due to cardiogenic versus non-cardiogenic etiologies (eg, pneumonia, acute respiratory distress syndrome, effusion, pneumothorax). A chest x-ray is also recommended as part of the initial evaluation of patients suspected as having new or worsening HF even in the absence of dyspnea, as it can provide important information regarding the size and shape of the heart as well as other disorders that may contribute to HF.[15] The two standard views for a chest x-ray are the posteroanterior (front) and lateral (side) views.

Compared to an echocardiogram, a chest x-ray is not as helpful for visualizing structures within the heart and is therefore most often used to depict its overall size and shape. Relative heart size can be approximated in the posteroanterior view by the cardiothoracic ratio (CTR), which is the maximal horizontal diameter of the heart divided by the maximal horizontal diameter of the thorax. A CTR <0.5 is generally considered normal, whereas higher values indicate cardiac enlargement (ie, cardiomegaly). An elevated CTR may also be present in the setting of a pericardial effusion. Dilation of specific heart chambers can also be visualized with a chest x-ray. Left ventricular enlargement is visualized as inferior and lateral displacement of the cardiac apex on the posteroanterior view, whereas right ventricular enlargement is most optimally viewed as an intrusion into the retrosternal space.

Visualization of the lung fields is also important in the evaluation and management of pulmonary edema. Pulmonary edema due to an underlying cardiogenic etiology is commonly evidenced by bilateral opacities (sometimes referred to as a "bat wing" pattern) (Fig. e29-14). Bilateral pleural effusions are common and cause blunting of the costophrenic angles. Other findings characteristic of pulmonary edema include septal lines (also called Kerley B lines) seen at the bases of the lungs, thickening of the interlobar fissures, and peribronchial cuffing. Serial chest x-rays can be used to assess changes in pulmonary edema over time, complementing other information used in the management of dyspnea.

FIGURE e29-14

Chest radiograph (x-ray) in acute decompensated heart failure. Left ventricular enlargement can be visualized by displacement of the cardiac apex. Bilateral opacities provide evidence of diffuse intestinal pulmonary edema and Kerley B lines are annotated with black arrows. *(Reproduced, with permission, from Elsayes KM, Oldham SAA, eds. Introduction to Diagnostic Radiology. New York, NY: McGraw Hill; 2014.)*



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SPECIAL PROCEDURES

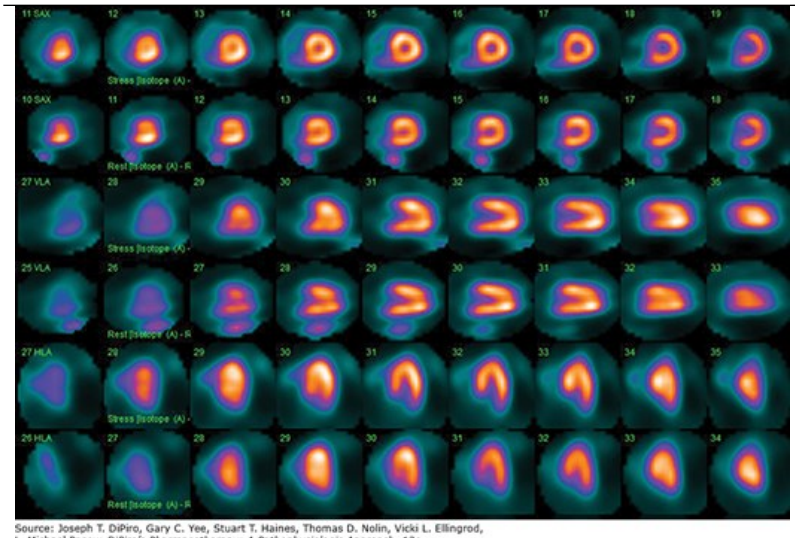
Nuclear Cardiology

For circumstances in which treadmill ECG testing is inappropriate or does not provide an adequate assessment of CAD, a technique known as radionuclide myocardial perfusion imaging (MPI) can be performed in conjunction with stress testing. In MPI, a cardiac-specific radionuclide tracer is administered intravenously, where it can be taken up by cardiac myocytes. The tracer will not be taken up by ischemic or scarred myocardium due to impaired blood flow, and the resulting pattern can be detected by gamma cameras, which rotate around the patient and construct a three-dimensional model of the heart. The two MPI techniques currently in use are simple photon emission computed tomography (SPECT) and positron emission tomography (PET).[75] In contrast with stress echocardiography, ionizing radiation is emitted with either MPI technique; although the risks conferred by an individual test are small, they accumulate with repeated studies and may result in significant radiation exposure over a lifetime.

In a standard nuclear stress protocol, patients receive an intravenous injection of the radionuclide tracer at rest. If defects are present at rest, this often suggests the presence of scar (ie, prior MI) or severely ischemic (hibernating) myocardium. Patients are then subjected to stress, which may be induced by exercise or the administration of a pharmacologic agent. Exercise protocols are similar to those used in standard treadmill testing. When patients achieve peak stress, the tracer is administered a second time. A computer processes the two sets of images, and by convention, the stress images are displayed above the resting images (Fig. e29-15).

FIGURE e29-15

A normal positron emission tomography scan. The images shown are cross-sections of the short axis (top two rows), vertical long axis (middle two rows), and horizontal long axis (bottom two rows) of the heart. Stress images are on the top, and resting images on the bottom of each pair of rows. The perfusion patterns are similar in both sets of images, consistent with a low likelihood of obstructive coronary artery disease. *(Reproduced, with permission, from Gupta N, Matta EJ, Oldham SA. Cardiothoracic imaging. In: Elsayes KM, Oldham SAA, eds. Introduction to Diagnostic Radiology. New York: McGraw Hill; 2014.)*



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

In contrast to SPECT imaging, PET scanning protocols can only be performed with a pharmacologic agent.[76,77] Consequently, if information such as functional capacity or exercise tolerance is required, PET should not be ordered. In either technique, pharmacologic stress is commonly induced using an intravenous coronary vasodilator rather than a beta-receptor agonist. Intravenous coronary vasodilators can increase blood flow by up to five times greater than that of resting blood flow. However, in patients with an obstructive coronary lesion, the degree of blood flow during stress will be significantly lower distal to the lesion when compared to healthy, nonobstructed arteries. The resulting differences in flow between ischemic and nonischemic tissue will emerge as different patterns of myocardial tracer uptake, producing perfusion defects on SPECT or PET imaging. Historically, pharmacologic MPI was performed primarily with adenosine. However, regadenoson, the selective adenosine A_{2A} receptor agonist, has been used more frequently over the past decade.[76] Due to their enhanced receptor specificity, adenosine A_{2A} receptor agonists produce fewer adverse effects, such as flushing, chest pain, and dyspnea.[77]

The decision to use PET versus SPECT is largely a function of institutional expertise and availability. Of the two MPI techniques, SPECT has been around for longer, and SPECT cameras are more widely available. However, the PET photon exhibits higher energy and is not degraded as readily by soft tissue, resulting in improved resolution and fewer artifacts in obese patients or in women with large breasts.[75] Additionally, although perfusion tracers (eg, rubidium 82) are used in stress testing, PET tracers capable of assessing myocardial metabolism (radiolabeled glucose) also exist.

An indication for which radiolabeled glucose may be used is to determine whether the cardiac function is likely to recover following coronary revascularization. As described above, a resting perfusion defect may represent either scar or hibernating myocardium. A viability study is used to distinguish between these two physiologic states. Fludeoxyglucose (FDG) is a radioactive glucose analog taken up by viable tissue, and patients with a perfusion/metabolism mismatch (ie, absent perfusion but active metabolism) on PET are considered to have viable, hibernating myocardium, which may recover function following revascularization.

Finally, while PET and SPECT can provide reliable, reproducible, and accurate measurements of LVEF, a more traditional approach to LVEF assessment using radionuclide tracers is ventriculography. The most common technique still used for this purpose is multiple-gated blood pool imaging (MUGA). With MUGA, red blood cells are radiolabeled, and changes in the tracer count in the right and left ventricles are measured throughout the cardiac cycle. Historically, MUGA was considered a reliable and reproducible method for producing a quantitative assessment of LVEF and was traditionally used to monitor patients receiving cardiotoxic chemotherapy. Although MUGA is still used, gated SPECT and PET scans are increasingly used for this purpose.

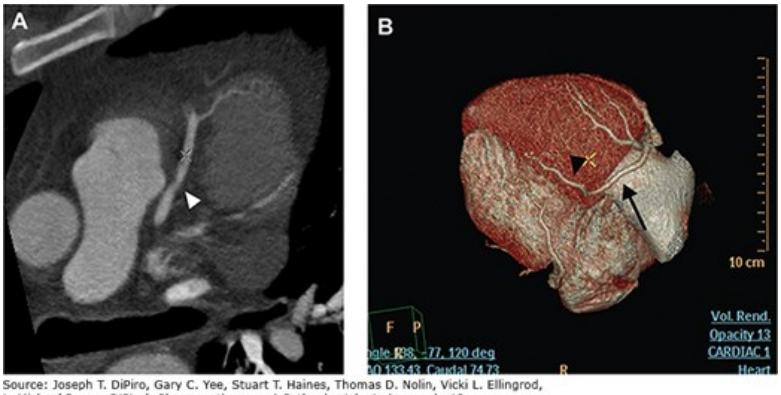
Computed Tomography

12 Cardiac computed tomography (CCT) is a noninvasive imaging modality in which a series of x-rays are used to construct a three-dimensional image of the heart (Fig. e29-16). Most modern CCT procedures are performed using multidetector-row computed tomography (MDCT), which permits visualization of the coronary arteries. Consequently, CCT angiography has emerged as a non-invasive alternative to cardiac catheterization for evaluating the presence and severity of CAD when there is no concern for active ischemia.[78] Other indications for CCT include assessments of

congenital coronary artery anomalies and mapping the pulmonary vein anatomy in preparation for atrial fibrillation ablation.

FIGURE e29-16

Two images generated from cardiac computed tomography angiography. In panel (*A*), mild stenosis of the left anterior descending artery is shown (as indicated by the white arrowhead), whereas a three-dimensional image has been constructed in panel (*B*) to show the left dominance of the patient's coronary vasculature, which is evidenced by the emergence of the posterior descending artery, noted by the black arrowhead, from the left circumflex artery, noted by the black arrow. *(Reproduced, with permission, from Elsayes KM, Oldham SAA, eds. Introduction to Diagnostic Radiology. New York, NY: McGraw Hill; 2014.)*



The use of CCT angiography over functional tests (eg, stress tests) in patients with suspected or stable CAD remains controversial. Functional tests can detect obstructive CAD but lack the sensitivity to detect atherosclerosis in its earlier stages when it may be more amenable to risk reduction strategies. Despite the long-term risks of nonobstructive disease, CCT angiography does not decrease morbidity and mortality compared to functional tests.[79] Although the noninvasive nature of CCT angiography confers several advantages over cardiac catheterization, it still requires the use of iodinated radiocontrast dye. Consequently, allergic reactions and acute kidney injury can occur with CCT angiography.

Another consideration during CCT is that imaging results can be confounded by motion artifacts. A heart rate of less than 60 to 70 bpm is needed for optimal imaging, and the presence of tachyarrhythmias may preclude CCT in some patients. Agents that slow AV node conduction, such as beta-blockers or nondihydropyridine calcium channel blockers, may be administered to slow heart rate. Patients must also be able to hold their breath for up to 20 seconds during the procedure.

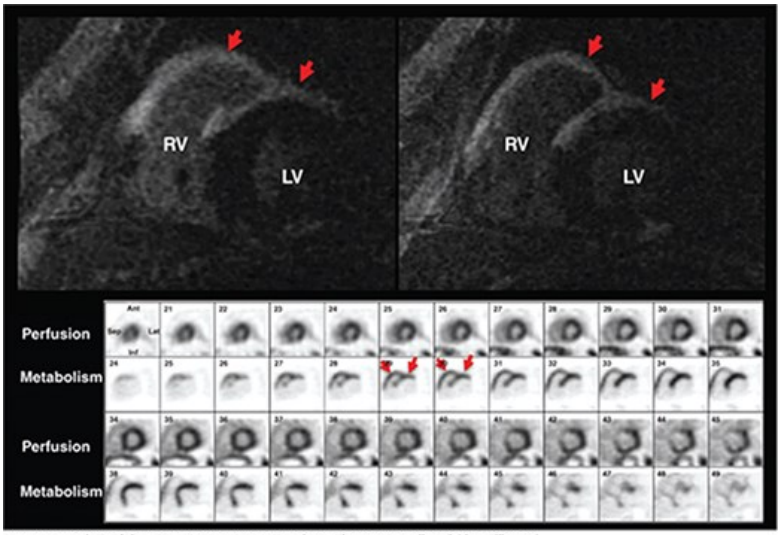
A common use of CCT, especially in patients without established CAD, is to detect the presence of coronary artery calcification (CAC), a finding associated with ASCVD events.[80] Because CAC provides limited incremental value over traditional cardiovascular risk factors, its use is primarily reserved for patients whose risk remains uncertain.[53] CAC is expressed as a score that ranges from 1 to 99 (mild disease) to ≥400 (severe disease). Scores are highly sensitive for the presence of CAD but only moderately specific. Most patients over 50 to 60 years will have some degree of coronary calcification.[81] As a result, CAC results are provided both as a score and an age-adjusted percentile. An advantage of using a CAC score over other risk evaluation modalities is that it can be obtained without radiocontrast dye and requires minimal radiation.

Cardiovascular Magnetic Resonance Imaging

Cardiovascular magnetic resonance imaging (CMR) is a noninvasive imaging test that permits an evaluation of the structure and function of the heart in three dimensions (Fig. e29-17). A major advantage of CMR is that images with high spatial and temporal resolution can be constructed without the use of ionizing radiation or iodinated contrast media.[82] The most common indication for CMR is determining the etiology of HF when an underlying cause remains unclear after initial evaluation (eg, echocardiography, angiography in patients with ischemic symptoms). The use of CMR is particularly useful in the diagnosis of less common causes of nonischemic cardiomyopathy, including inflammation (eg, myocarditis) and infiltrative disorders (eg, cardiac amyloid or sarcoid). In patients with ischemic disease, CMR may identify viable myocardium amenable to revascularization and may be used in combination with pharmacologic stress testing. Late gadolinium enhancement (LGE) is a technique used in many CMR cases to differentiate diseased from normal myocardium, and the pattern of enhancement observed via LGE can indicate the type of injury present (eg, ischemic, infiltrative).

FIGURE e29-17

In the top two panels, cardiac magnetic resonance (CMR) imaging showing late gadolinium enhancement in the walls of both the left and right ventricle (indicated by red arrows). Below, a series of images from a positron emission tomography scan show extensive metabolic function. Together these findings are suggestive of active inflammation consistent with a diagnosis of cardiac sarcoidosis. *(Reproduced, with permission, from Gupta N, Matta EJ, Oldham SA. Cardiothoracic imaging. In: Elsayes KM, Oldham SAA, eds. Introduction to Diagnostic Radiology. New York: McGraw Hill; 2014.)*



Historically, CMR has been contraindicated in patients with cardiac implantable electronic devices. However, an increasing number of devices have been deemed magnetic resonance (MR) conditional, meaning they are not known to be hazardous during CMR. Recommendations regarding CMR in patients with MR-conditional devices were recently published, and many types of non-MR-conditional devices may safely undergo CMR at institutions with sufficient expertise.[83,84] All patients should be screened for the presence of devices with ferromagnetic components prior to CMR and some devices remain contraindicated with CMR (eg, ventricular assist devices). Mechanical heart valves and intracardiac stents can be safely imaged with CMR.

Most of the remaining risks of CMR relate to the use of LGE. As with other types of imaging media, a subset of patients may experience allergic reactions to gadolinium, which range from mild-to-moderate symptoms (eg, itching) to anaphylaxis in rare cases.[82] Another rare complication of gadolinium administration is nephrogenic systemic fibrosis, which may lead to renal failure in patients with preexisting moderate-to-severe kidney disease.

CONCLUSION

Although the technologies available to evaluate patients with or at risk for CVD have grown considerably over the last several decades, patient interview and physical examination continue to play a critical role in its initial detection and assessment. Significant insight into the development and progression of CVD can also be provided by noninvasive tests, such as ECG, echocardiography, and stress testing. More advanced or invasive testing may be required in those with indeterminate findings. Many of these tests are not without risks, and this must be carefully weighed against the potential benefits. Moreover, unnecessary testing is one of the major drivers of healthcare costs in the United States and has prompted calls for greater stewardship of healthcare resources.[85] The need for each test should be considered in the context of the patient's overall condition and, most importantly, whether the findings of the test would change patient management or treatment.

ABBREVIATIONS

ABI	ankle-brachial index
ABPM	ambulatory blood pressure monitoring

ADHF	acute decompensated heart failure
ASCVD	atherosclerotic cardiovascular disease
AV	atrioventricular
BNP	brain natriuretic peptide
BP	blood pressure
CABG	coronary artery bypass graft
CAC	coronary artery calcification
CAD	coronary artery disease
CCT	cardiac computed tomography
CMR	cardiovascular magnetic resonance imaging
CVP	central venous pressure
CI	cardiac index
CK-MB	creatine kinase–myocardial band
CO	cardiac output
CVD	cardiovascular disease
CTR	cardiothoracic ratio
DBP	diastolic blood pressure
ECG	electrocardiogram
EP	electrophysiology
FFR	fractional flow reserve
HBPM	home blood pressure monitoring
HDL	high-density lipoprotein
hs-CRP	high-sensitivity C-reactive protein
HF	heart failure
IVUS	intravascular ultrasound
JVP	jugular venous pressure

LGE	late gadolinium enhancement
LHC	left heart catheterization
LDL	low-density lipoprotein
LVEDP	left ventricular end-diastolic pressure
LVEF	left ventricular ejection fraction
MAP	mean arterial pressure
MDCT	multidetector-row computed tomography
MI	myocardial infarction
MPI	myocardial perfusion imaging
MR	magnetic resonance
NT-proBNP	N-terminal pro-brain natriuretic peptide
PA	pulmonary artery
PAD	peripheral arterial disease
PAH	pulmonary arterial hypertension
PCI	percutaneous coronary intervention
PCWP	pulmonary capillary wedge pressure
PET	positron emission tomography
PH	pulmonary hypertension
PMI	point of maximal impulse
PND	paroxysmal nocturnal dyspnea
PVR	pulmonary vascular resistance
RHC	right heart catheterization
SA	sinoatrial
SBP	systolic blood pressure
SOB	shortness of breath
SPECT	simple photo emission computed tomography

SVR	systemic vascular resistance
TBI	toe-brachial index
TEE	transesophageal echocardiogram
TIMI	Thrombolysis in Myocardial Infarction
TTE	transthoracic echocardiogram

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SELF-ASSESSMENT QUESTIONS

1. All of the following are traditional risk factors for cardiovascular disease, except:

   A. Hypertension

B. Physical activity

C. Total cholesterol

D. Chronic kidney disease

2. Which of the following characteristics can be used to differentiate nonischemic from ischemic chest pain?

A. Concomitant nausea or epigastric pain

B. Relief when sitting up and leaning forward

C. Radiation to the neck, jaw, or shoulder

D. Improvement with rest

3. All of the following are important steps for obtaining an accurate blood pressure measurement, except:

A. Using the arm that gives the lower reading at each visit

B. Removing clothing that covers the location of the cuff

C. Being seated for at least 5 minutes prior to the reading

D. Using a cuff that encircles at least 75% of the arm

The next two questions (Questions 4 and 5) relate to the following vignette:

A 64-year-old man with a history of nonischemic cardiomyopathy presents to clinic with gradually worsening shortness of breath over the past several weeks.

4. When interviewing the patient about his symptoms, which of the following can be used to characterize orthopnea?

A. The number of city blocks he can walk before dyspnea occurs

B. Whether he is awakened at night by sudden episodes of dyspnea

C. Whether dyspnea occurs when he walks up a flight of stairs

D. The number of pillows he requires to sleep comfortably

5. Which of the following physical examination findings would suggest that volume overload is the cause of his symptoms?

A. An S_2 heart sound on auscultation of the chest

B. A jugular venous pressure of 8 cm above the sternal notch

C. Wheezes on auscultation of the lungs

D. A negative abdominojugular reflux test

6. In the absence of a history of vascular complications, which of the following physical examination findings in isolation is suggestive of peripheral arterial disease warranting further evaluation?

A. Bilateral lower extremity edema

B. An ankle-brachial index of 1.2

C. Presence of a femoral artery bruit

D. Absence of leg hair bilaterally

7. The following laboratory values were obtained from a patient who was diagnosed with a myocardial infarction (MI) after presenting to the emergency department with chest pain and shortness of breath: cardiac troponin T 3.0 ng/mL (mcg/L), creatinine kinase-myocardial band (CK-MB) 24 ng/mL (mcg/L), and brain natriuretic peptide (BNP) 40 pg/mL (ng/L; 12 pmol/L). Based on these results, which of the following is true?

   A. The CK-MB value is sufficient for making an MI diagnosis.

   B. Obtaining a high-sensitivity C-reactive protein would be helpful for further risk stratification.

   C. It is unlikely that the patient has coexisting heart failure based on the BNP value.

   D. Compared to cardiac troponin T, it will take longer for the CK-MB to return to normal.

8. First-degree atrioventricular (AV) block refers to slowed AV nodal conduction, which can occur with excess doses of beta-blocker therapy. Which of the following components of an electrocardiogram would be most useful for detecting this phenomenon?

   A. PR interval

   B. QRS complex

   C. QT interval

   D. ST segment

9. For which of the following scenarios would a transesophageal echocardiogram (TEE) be preferred over a transthoracic echocardiogram (TTE)?

   A. Assessment of left ventricular function in a patient with heart failure symptoms

   B. Detection of a pericardial effusion in a patient with nonischemic chest pain

   C. Assessment of tricuspid regurgitation in a patient with a holosystolic heart murmur

   D. Detection of left atrial appendage thrombus prior to cardioversion

The next three questions (Questions 10-12) relate to the following vignette:

A 56-year-old woman presents to her primary care physician (PCP) with complaints of nausea and diaphoresis that occur with physical exertion but are relieved by rest. Her physical activity has been limited by osteoarthritis but she recently started swimming at the local community center, where she first noticed her symptoms. She is a former smoker but quit 5 years ago when she was diagnosed with high blood pressure. Since her symptoms are not characteristic of typical angina, her PCP considers her to be at low-to-intermediate risk of coronary artery disease (CAD) and refers her to a cardiologist for further evaluation.

10. Which of the following would be an appropriate initial test for ischemia in a patient at low-to-intermediate risk of CAD?

    A. Echocardiogram

    B. Left heart catheterization

    C. Cardiac stress test

    D. Cardiovascular magnetic resonance imaging

11. Which of the following procedures for assessing CAD is noninvasive but requires the use of radiocontrast dye?

A. Left heart catheterization

B. Cardiac computed tomography

C. Electrocardiogram

D. Exercise stress test

12. If the patient is referred for cardiac catheterization, which of the following tests may be performed during the procedure if initial findings on angiography are indeterminate?

A. Fractional-flow reserve

B. Myocardial perfusion imaging

C. Multiple gated blood pool imaging

D. Coronary artery calcium score

13. Which of the following conditions is not assessed via right heart catheterization?

A. Heart transplant rejection

B. Pulmonary arterial hypertension

C. Acute decompensated heart failure

D. Acute coronary syndrome

The next two questions (Questions 14 and 15) relate to the following vignette:

A 48-year-old man with a history of hypertension is transferred to your facility after presenting to an outside hospital with acute decompensated heart failure (ADHF). His left ventricular ejection fraction (LVEF) on echocardiogram is 15% (0.15). Shortly after arrival, a left heart catheterization is performed, which reveals only nonobstructive coronary artery disease. Despite aggressive diuretic therapy, the patient's symptoms improve only minimally, prompting the placement of a pulmonary artery (PA) catheter. Initial readings are significant for a pulmonary capillary wedge pressure (PCWP) of 24 mmHg, cardiac index (CI) of 1.8 L/min/m^2 (0.03 L/s/m^2), and a systematic vascular resistance (SVR) of 1150 dynes·sec/cm^5 (115 MPa·s/m^3).

14. Which of the following is true based on the patient's PA catheter readings?

A. The PCWP is elevated, suggesting the patient is volume overloaded.

B. The SVR is low, suggesting the patient has vasodilatory shock.

C. The CI is normal, suggesting the patient does not have low output ADHF.

D. The PA catheter readings cannot be interpreted because the patient's LVEF is 15% (0.15).

15. The patient's condition improves and the team would like to investigate for potential causes of his nonischemic cardiomyopathy. Which of the following tests would be preferred for determining if the patient has an infiltrative etiology (eg, sarcoidosis)?

A. Cardiac magnetic resonance imaging

B. Pharmacologic stress test

C. Chest radiography

D. Intravascular ultrasound

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** Traditional risk factors for cardiovascular disease (CVD) include age, sex, and race/ethnicity. Guidelines now recognize a list of "risk-enhancing factors" that can be used to further individualize risk, especially when traditional risk calculators produce an indeterminate result. Example risk-enhancing factors include a family history of premature CVD in a first-degree relative, chronic kidney disease, metabolic syndrome, and premature menopause. See Table e29-2 for a comparison of traditional risk factors and risk-enhancing factors for CVD TABLE e29-2.

2. **B.** Pain relief with a change in position is more likely to occur with pericarditis or other inflammatory conditions and not with ischemic chest pain. Ischemic chest pain is more likely to be relieved by rest. See the section on chest pain for more information.

3. **A.** The blood pressure should be measured in both arms at the first visit and the arm that gives the *higher* reading should be used for subsequent visits. Recommendations for obtaining an accurate blood pressure reading can be found in Table e29-4.

4. **D.** Orthopnea refers to dyspnea symptoms that occur when lying down, and it can be quantified by asking patients how many pillows are required to sleep comfortably. Patients should also be asked why such elevation is necessary, as multiple pillows may be used for reasons other than relief of dyspnea. See the "Dyspnea" section for more information.

5. **B.** A normal jugular venous pressure is less than 5 cm, which accounts for the distance between the right atrium and the sternal notch. Numbers in excess of 5 cm are indicative of volume overload. An S_2 heart sound and negative abdominojugular reflux are normal findings and wheezes are often characteristic of noncardiac disease. See the "Inspection" and "Auscultation" sections for more information.

6. **C.** The presence of a femoral artery bruit, especially in the absence of lower extremity pulses, is strongly suggestive of peripheral artery disease and should warrant further evaluation. See the "Auscultation" and "Inspection" sections for more information.

7. **C.** Brain natriuretic peptide (BNP) is released following stretch-related injury to myocardial tissue and is strongly suggestive of heart failure; consequently, the absence of an elevated BNP makes heart failure an unlikely cause of dyspnea. See the "B-Type Natriuretic Peptide" section for further discussion.

8. **A.** The PR interval represents the heart's electrical impulse as it moves across the atrioventricular (AV) node. First-degree AV block can be detected as a prolonged PR interval. See the "Electrocardiography" section for more information.

9. **D.** Although a transesophageal echocardiogram (TEE) is more invasive than a transthoracic echocardiogram (TTE), it may be required to visualize posterior aspects of the heart, such as the left atrial appendage. Since a thrombus may be dislodged from the left atrial appendage during cardioversion, a TEE is often indicated prior to the procedure. See the "Echocardiography" section for more information.

10. **C.** Since the patient is asymptomatic and low-to-moderate risk for coronary artery disease (CAD), a noninvasive test such as a stress test is preferred as the initial modality for assessing ischemia. A pharmacologic stress test would be preferred for this patient since her ability to exercise may be limited by osteoarthritis. See the "Stress Testing" section for more information.

11. **B.** Although cardiac computed tomography (CCT) angiography is less invasive than cardiac catheterization, visualization of the coronary arteries via CCT still requires the use of radiocontrast dye. As a result, CCT angiography is not advantageous in a patient with contrast dye-related contraindications to cardiac catheterization (eg, acute kidney injury). See the section on CCT for more information.

12. **A.** In patients with indeterminate findings on angiography via cardiac catheterization, fractional-flow reserve or intravascular ultrasound may be useful for determining whether the patient may benefit from revascularization. See the "Left Heart Catheterization" section for more information.

13. **D.** Patients presenting with an acute coronary syndrome should be evaluated for revascularization using coronary artery angiography, which cannot be performed with a right heart catheterization. Instead, a left heart catheterization should be performed. See the "Left Heart Catheterization" and "Right Heart Catheterization" sections for a discussion of the indications for each.

14. **A.** Of the readings provided by the pulmonary artery catheter, the abnormal values include an elevated pulmonary capillary wedge pressure (PCWP, normal 6-12 mmHg) and low cardiac index (normal 2.8-4.2 L/min/m^2 [0.047-0.07 L/s/m^2]). An elevated PCWP is suggestive of elevated left ventricular end-diastolic pressure, which indicates volume overload. See the "Right Heart Catheterization" section and Table e29-10 for more information.

15. **A.** Cardiovascular magnetic resonance (CMR) imaging is the modality of choice for diagnosing an infiltrative etiology of nonischemic cardiomyopathy, as it can characterize pathologic changes in myocardial tissue. See the "Cardiovascular Magnetic Resonance Imaging" section for more information.