Echocardiographic evaluation of coronary artery disease

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Although the availability and utilization of other noninvasive imaging modalities for the evaluation of coronary artery disease have expanded over the last decade, echocardiography remains the most accessible, cost-effective, and lowest risk imaging choice for many indications. The clinical utility of mature echocardiographic methods (i.e. two-dimensional echocardiography, stress echocardiography, contrast echocardiography) across the spectrum of coronary artery disease has been well established by numerous clinical studies. With continuing advancements in ultrasound technology, emerging ultrasound technologies such as three-dimensional echocardiography, tissue Doppler imaging, and speckle tracking methods hold significant promise to further widen the scope of clinical applications and improve diagnostic accuracy. In this review, we provide an update on the role of echocardiography in the diagnosis, management, and prognosis of coronary artery disease and introduce emerging technologies that are anticipated to further increase the clinical utility of echocardiography in the evaluation of patients with coronary artery disease. ***Coron Artery Dis*** **24:613–623 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Despite numerous advances over the past several decades, the diagnosis and management of coronary artery disease remains challenging. Noninvasive imaging methods have been utilized to surmount the limitations of nonimaging techniques, such as the poor sensitivity and specificity of exercise testing and the difficulty in evaluation of ischemia in patients with impaired mobility or left bundle branch block [1–3]. In these patients, imaging is generally required to evaluate for the presence, extent, and severity of coronary artery disease. Because of its broad availability, lack of radiation, and relatively low cost, echocardiography is an increasingly widely used examination. The clinical utility of echocardiography across the spectrum of coronary artery disease has been well established by a large number of studies (Table 1). With continuing advancements in ultrasound technology, emerging ultrasound methods such as three-dimensional echocardiography, ultrasound contrast agents, tissue Doppler imaging, and speckle tracking methods hold significant promise to further widen the scope of clinical applications and improve diagnostic accuracy.

The purpose of this review is (i) to provide an update on the role of echocardiography in the diagnosis, management, and prognosis of coronary artery disease and (ii) to introduce emerging technologies that are anticipated to further increase the clinical utility of echocardio-graphy in the evaluation of patients with coronary artery disease.

Chronic myocardial ischemia

Myocardial ischemia is the result of a regional transient imbalance between myocardial oxygen supply and demand, most often because of inadequate myocardial perfusion as a result of atherosclerotic coronary artery disease. Hypoperfusion initiates an ischemic cascade of intracellular changes that results in a shift in cellular metabolism from glucose to fatty acids [2,4]. Decreased ATP production because of decreased oxygen supply required for aerobic metabolism results in failure

Table 1 Role of echocardiography in the spectrum of coronary artery disease

Coronary artery disease manifestation	Echocardiography method
Chronic myocardial ischemia	Stress echocardiography Contrast-enhanced stress echocardiography Myocardial contrast echocardiography Three-dimensional echocardiography Doppler tissue imaging Speckle tracking imaging
Acute coronary syndrome	Two-dimensional resting echocardiography Stress echocardiography Myocardial contrast echocardiography Speckle tracking imaging
Complications of myocardial infarction	Two-dimensional resting echocardiography Contrast-enhanced two-dimensional echocardiography
Risk stratification	Two-dimensional resting echocardiography Stress echocardiography
Myocardial viability	Dobutamine stress echocardiography Myocardial contrast echocardiography Strain imaging
Ischemic cardiomyopathy	Two-dimensional resting echocardiography

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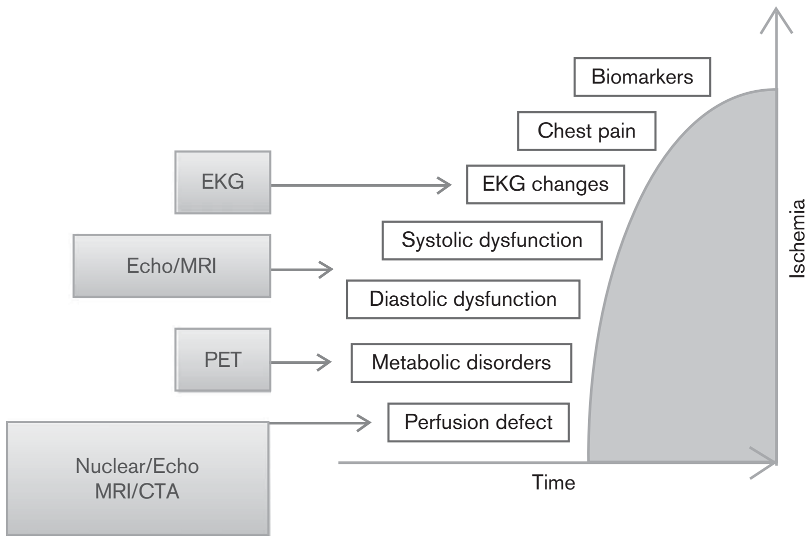
Fig. 1



Ischemic cascade and the role of standard imaging modalities in the assessment of each element of the cascade. CTA, computed tomography angiography; EKG, electrocardiography; PET, positron emission tomography.

of calcium reuptake into the sarcoplasmic reticulum. As a result, diastolic dysfunction is the initial manifestation, later followed by systolic dysfunction and repolarization abnormalities seen as ST-segment changes on the surface ECG. Chest pain is a late manifestation of this cascade. The severity of left ventricular dysfunction, ECG changes, and clinical presentation are dependent on the extent and severity of hypoperfusion. Figure 1 presents the ischemic cascade and the role of standard noninvasive imaging modalities in assessing each element of this cascade. Standard echocardiography methods can provide important information when the hypoperfusion results in ischemia and systolic dysfunction before the onset of ECG changes, or clinical symptoms. The appropriate use criteria of echocardiography in chronic myocardial ischemia are summarized in Table 2 and Fig. 2 [5].

Stress echocardiography

In severe cases of chronic myocardial hypoperfusion, myocardial ischemia may result in decreased regional or global systolic function [6]. More commonly, wall motion and wall thickening abnormalities are observed only when ischemia is induced by exercise or pharmacologic stress.

Stress echocardiography techniques

Stress echocardiography can be performed with exercise or pharmacologic agents, most commonly dobutamine [3,7]. Common exercise protocols include treadmill and upright or supine bicycle exercise. With treadmill exercise, stress echocardiography images are obtained at baseline before the initiation of exercise and after exercise within the first minute after the conclusion of exercise. Rapid acquisition of high-quality images requires careful planning and high technical skill levels on the part of the sonographer. Ultrasound contrast may be administered to improve visualization of wall motion abnormalities. Hemodynamic monitoring (heart rate and blood pressure) is also performed. Figure 3a presents the protocol used for treadmill stress echocardiography. Upright or supine bicycle exercise enables imaging at peak exercise, thereby increasing the sensitivity of the method by reducing the possibility of resolution of ischemia between the end of exercise and the start of imaging.

For patients who are not able to exercise or for the assessment of myocardial viability, pharmacological stress echocardiography with sympathomimetics (i.e. dobutamine) or vasodilators (i.e. dypiradamole, adenosine) is preferred. Most commonly, increasing rates of dobutamine infusion to a peak dose of 40 mcg/kg/min may be supplemented by atropine in divided doses up to 2 mg to achieve the target heart rate (i.e. 85% of the age-predicted maximum heart rate). Dobutamine stimulates adrenoreceptors in the myocardium, inducing positive inotropic and chronotropic effects, thereby increasing myocardial oxygen demand and resulting in ischemia and myocardial systolic dysfunction in regions subtended by coronary branches downstream of flow-limiting lesions. Figure 3b presents the commonly used protocol for dobutamine stress echocardiography.

Vasodilator agents are less commonly used for pharmacologic stress echo. These agents stimulate adenosine receptors, which causes coronary vasodilation. In the presence of severe or extensive coronary disease, this may result in coronary steal and subsequent systolic dysfunction. In some cases, the secondary effect of

Table 2 Echocardiography appropriate use criteria in coronary artery disease [5]

Chronic myocardial ischemia	Stress echocardiography	Low pretest probability of CAD ECG uninterpretable or unable to exercise Intermediate pretest probability of CAD ECG interpretable and able to exercise Intermediate pretest probability of CAD ECG uninterpretable or unable to exercise High pretest probability of CAD Irrespective of ECG interpretability and ability to exercise
	Myocardial contrast echocardiography	No current guidelines
Acute coronary syndrome	Two-dimensional echocardiography	Acute chest pain with suspected myocardial infarction and nondiagnostic ECG when a resting echocardiogram can be performed during pain Evaluation of a patient without chest pain but with other features of an ischemic equivalent or laboratory markers indicative of ongoing myocardial infarction
	Stress echocardiography	Possible acute coronary syndrome ECG: no ischemic changes or with LBBB or electronically paced ventricular rhythm Low-risk TIMI score Peak troponin: borderline, equivocal, minimally elevated Possible acute coronary syndrome ECG: no ischemic changes or with LBBB or electronically paced ventricular rhythm High-risk TIMI score Negative troponin levels Possible acute coronary syndrome ECG: no ischemic changes or with LBBB or electronically paced ventricular rhythm High-risk TIMI score Peak troponin: borderline, equivocal, minimally elevated Possible acute coronary syndrome ECG: no ischemic changes or with LBBB or electronically paced ventricular rhythm Low-risk TIMI score Negative troponin levels
	Myocardial contrast echocardiography	No current guidelines
Complications of myocardial infarction	Two-dimensional echocardiography	Suspected complication of myocardial ischemia/infarction, including but not limited to acute mitral regurgitation, ventricular septal defect, free-wall rupture/tamponade, shock, right ventricular involvement, heart failure or thrombus
Risk stratification	Two-dimensional echocardiography	Initial evaluation of ventricular function following acute coronary syndrome Re-evaluation of ventricular function following acute coronary syndrome during recovery phase when results will guide therapy
	Stress echocardiography	STEMI/non-ST acute coronary syndrome Hemodynamically stable, no recurrent chest pain symptoms, or no signs of heart failure To evaluate for inducible ischemia No previous coronary angiography since the index event Post-PCI or bypass Incomplete revascularization Additional revascularization feasible
Myocardial viability	Dobutamine stress echocardiography	Known moderate or severe LV dysfunction Patient eligible for revascularization Use of dobutamine stress only
	Myocardial contrast echocardiography	No current guidelines
Ischemic cardiomyopathy	Two-dimensional echocardiography	Initial evaluation of known or suspected ischemic cardiomyopathy Re-evaluation of known ischemic cardiomyopathy with a change in clinical status or cardiac examination or to guide therapy

CAD, coronary artery disease; LBBB, left bundle branch block; LV, left ventricular; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.

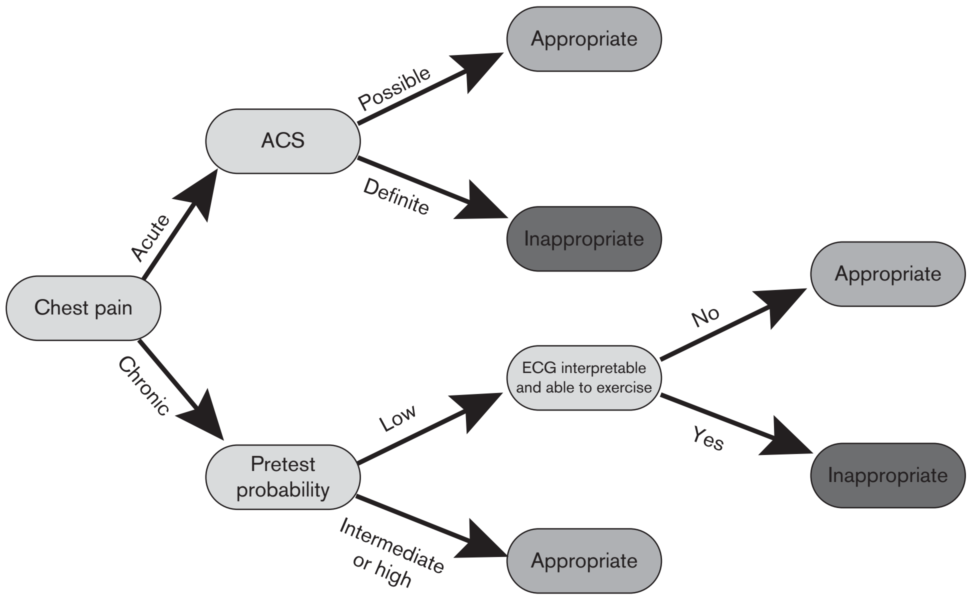
increased heart rate in response to systemic vasodilation may also cause ischemia. When coupled with perfusion imaging methods, vasodilator agents can provide excellent sensitivity for the diagnosis of coronary artery disease. As such, they are best suited for use with myocardial contrast perfusion echocardiography, nuclear perfusion imaging methods, or cardiac MRI.

Interpretation of stress echocardiograms

Generally, multiple views of each segment of the myocardium are obtained at rest and stress to maximize diagnostic certainty. Standard protocols include short axis imaging at three levels: basal, mid-ventricular (usually at the level of papillary muscles), and apex. Long-axis views from either the apical and/or the parasternal windows, as well as apical two-chamber and four-chamber views are obtained when possible. Depending on the clinical questions, additional imaging may be obtained to assess valvular function or pulmonary pressures.

The interpretation of stress echo is primarily qualitative, on the basis of the visual comparison of systolic wall motion and thickening prestress, during stress and peak stress or immediately after stress in case of treadmill exercise stress echocardiography. Utilization of contrast to improve endocardial delineation improves diagnostic accuracy while decreasing the frequency of nondiagnostic studies [8,9].

Fig. 2



Role of stress echocardiography in the management of acute and chronic chest pain [5]. ACS, acute coronary syndrome.

Rest and stress images are reviewed side by side over several successive cardiac cycles and compared for the development of: (i) new regional wall motion abnormalities, (ii) worsening of existing baseline wall motion abnormalities, (iii) global systolic left ventricular dysfunction, or (iv) left ventricular dilatation. A normal response to stress involves increased systolic wall thickening and systolic function (hyperkinesis) and decreased left ventricular size compared with rest. Ischemic response is characterized by new or worsening regional wall motion abnormalities (hypokinesis, akinesis, or dyskinesis) usually in at least two adjacent wall segments. The severity of stress-induced ischemia is proportional to the site, extent, and severity of wall motion abnormalities. Stress-induced global systolic left ventricular dysfunction or left ventricular dilatation is indicative of severe coronary artery disease, including left main or multivessel disease. Table 3 summarizes the major response patterns in stress echocardiography.

Diagnostic role of stress echocardiography

Meta-analyses of many clinical studies have shown that both exercise and pharmacologic stress echo have excellent sensitivity and specificity for the detection of coronary artery disease. Overall, the sensitivity of stress echocardiography ranges from 80 to 86% and the specificity ranges from 84 to 92% [3,7,10–12]. Of note, the sensitivity of stress echocardiography is lower in patients with one-vessel disease (66–83%), especially left circumflex or right coronary artery disease, and increases considerably with multivessel disease (86–90%) [7]. The major causes of false-positive or false-negative results with stress echocardiography are presented in Table 4.

Safety and contraindications of stress echocardiography

Both exercise and pharmacological stress echocardiography are considered to be safe and well-tolerated tests [3]. Major complications such as myocardial infarction, death, severe hypotension, high-grade atrioventricular block, malignant ventricular arrhythmias, and bronchospasm occur in $\sim 1:1000$ procedures. Minor but limiting side effects occur in less than 10% of patients with dobutamine and less than 5% of patients with dipyridamole stress. Dobutamine stress echo should be avoided in patients with current atrial or ventricular arrhythmia and severe hypertension. Adenosine or dipyridamole stress echo is not indicated in patients with high-grade heart block, hypotension, active bronchospasm, and those receiving caffeine or theophylline. Antianginal medications (β-blockers in particular) significantly reduce the diagnostic accuracy of stress echocardiography; therefore, it is recommended whenever possible to withhold such medications before the test to avoid false-negative results [3].

Strengths and weaknesses of stress echocardiography

Stress echocardiography is a safe, nonionizing, versatile, and inexpensive imaging technique with adequate diagnostic and prognostic value in coronary artery disease. However, it has several weaknesses including dependence on image quality, level of achieved stress, use of antianginal medication, relatively high interobserver variability in image interpretation, and reduced sensitivity for the assessment of ischemia in patients with resting wall motion abnormalities or multivessel disease [7].

Myocardial contrast in stress echocardiography

In addition to facilitating improved endocardial delination, advances in ultrasound contrast agents and technology have enabled the detection of myocardial hypoperfusion, which may exist before the development of overt regional or global systolic dysfunction [9,13]. The evaluation of myocardial perfusion with echocardiography involves the intravascular injection of contrast agents that scatter ultrasound waves [13]. Ultrasound contrast agents generally consist of microbubbles with a diameter of less than 8 μm made of surfactant, human albumin, or natural lipids containing a high-molecular-weight gas (e.g. sulfur hexafluoride, perfluoropropane). Because of their small size, comparable with a red blood cell, these microbubbles can pass through the pulmonary microcirculation and concentrate in the myocardium proportionate to the relative myocardial blood volume within the corresponding

Table 4 Causes of false-positive and false-negative stress echocardiograms

False negatives	False positives
Inadequate stress	Overinterpretation, interpretation bias
Antianginal treatment (β-blockers)	Localized basal inferior wall abnormalities
Mild stenoses	Abnormal septal motion (e.g. left bundle branch block, right ventricular pacing)
Left circumflex disease	Cardiomyopathies
Poor image quality	Hypertensive responses to stress
Delayed images after stress	

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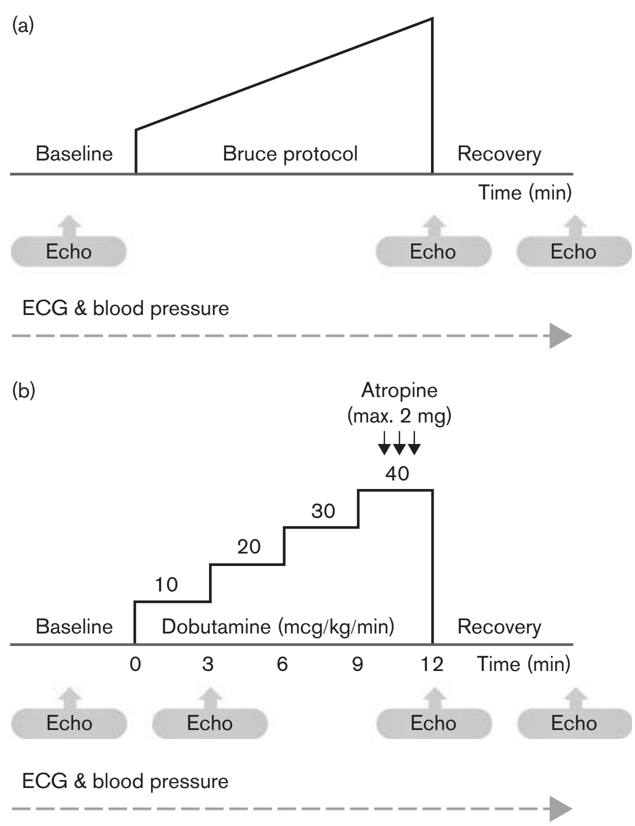
Fig. 3



Stress echocardiography protocols with exercise (a) and dobutamine (b).

Table 3 Response patterns in stress echocardiography

Rest	Peak stress	Diagnosis
Normokinesis	Hyperkinesis	Normal myocardium
Normokinesis	Hypokinesis, akinesis, dyskinesis, global hypokinesis[a], LV dilatation[a]	Ischemic myocardium
Akinesis	Hypokinesis, normokinesis	Viable stunned myocardium
Akinesis	Biphasic response[b]	Viable hibernating myocardium
Akinesis, dyskinesis	Akinesis, dyskinesis	Necrotic (nonviable) myocardium

LV, left ventricular.
[a]Global hypokinesis or LV dilatation with stress indicate left main or three-vessel disease.
[b]Biphasic response involves initial improvement with low-dose dobutamine and subsequent worsening with increased doses of dobutamine.

regional myocardial microvasculature. Harmonic imaging techniques enable longer persistence of microbubble contrast and improved signal/noise ratios [14].

Studies have proved the ability of stress myocardial contrast echocardiography to evaluate the presence and the extent of coronary artery disease during exercise or infusion of inotropic or vasodilator agents [13,15]. Because microbubbles remain entirely intravascular, when the infusion of a contrast agent is continuous, echocardiographic signal intensity reflects myocardial microcirculatory blood volume. During stress, the capillary blood volume decreases distal to flow-limiting stenoses, resulting in reduction of myocardial signal intensity and contractility in segments subtended by the diseased coronary branch (Fig. 4) [16].

Diastolic stress testing

Ischemia-induced diastolic dysfunction can also be assessed by a stress test (i.e. 'diastolic stress testing'). Normally, both E wave velocity in transmitral Doppler and Ea wave velocity in tissue Doppler, which reflects the diastolic relaxation of mitral annulus, increase with exercise, thereby resulting in a stable E/Ea ratio between rest and exercise. Induced diastolic dysfunction in ischemic myocardium leads to decreased mitral annulus recoil and therefore reduced Ea wave velocities. As a result, the E/Ea ratio may increase with exercise compared with rest [17–19]. The utility of diastolic stress testing in the diagnosis of myocardial ischemia warrants further clinical investigation.

Emerging methods

Three-dimensional echocardiography

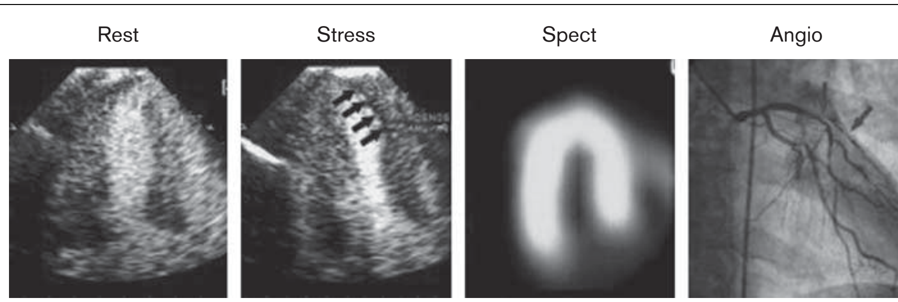
Although researchers have been developing methods for three-dimensional echocardiography since the early 1970s [20], recent advances have enabled real-time volumetric acquisitions [21]. Initial methods required manual rotation of the transducer to sequentially collect images in multiple planes, which were then reconstructed offline. Although mechanized transducers eliminated the need for manual probe rotation, three-dimensional datasets continued to be reconstructed from two-dimensional data acquired across multiple cardiac cycles. Advances in material science, parallel processing electronics, and software have enabled the development of phased array transducers that can image large pyramidal volumes in real time [22]. Corresponding improvements in software have enabled both online and offline visualization of volumetric datasets. As a result, three-dimensional imaging is now a routine part of both transthoracic and transesophageal echocardiography protocols in many laboratories.

For the evaluation of coronary artery disease, there are several important advantages for three-dimensional volumetric imaging over two-dimensional echocardiography. All of the standard two-dimensional views can be reconstructed from a small number of three-dimensional acquisitions [23]. Volumetric datasets also allow more reliable and accurate quantification of chamber volume and mass (Fig. 5) [24,25]. The ability to rapidly and simultaneous acquire multiple views may simplify stress echocardiography [26] and may improve diagnostic accuracy [27].

Tissue Doppler imaging and speckle tracking methods

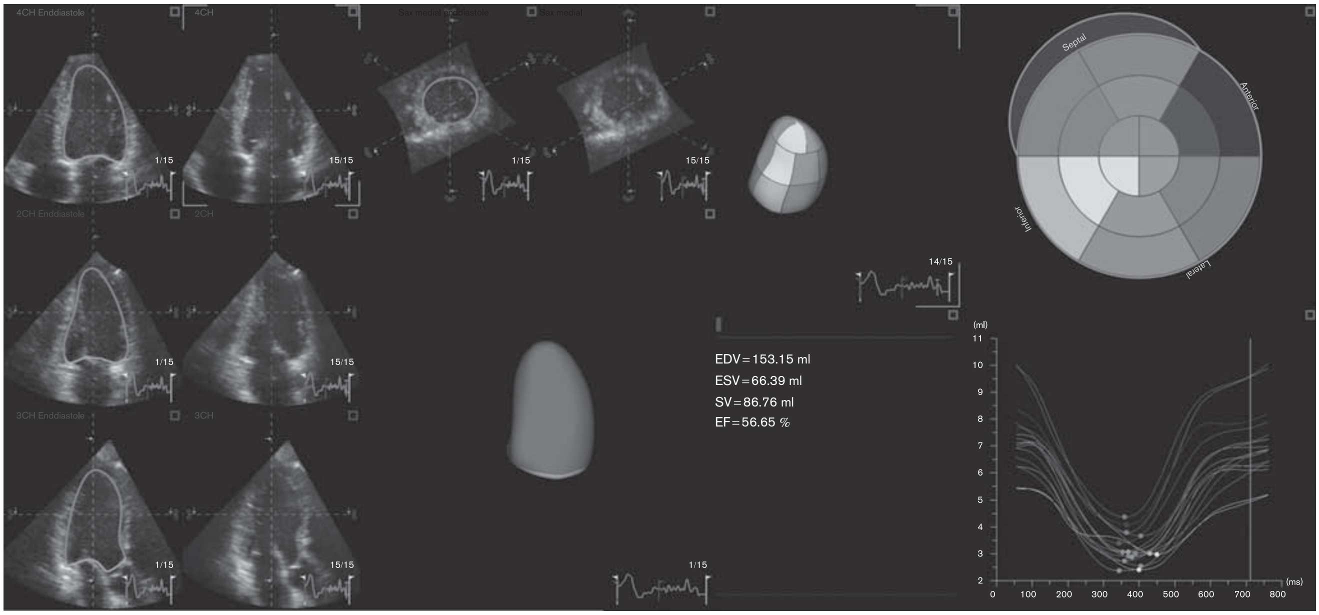
Qualitative and quantitative evaluations of systolic function with traditional measures, such as left ventricular ejection fraction, may be insensitive for the identification of subclinical decreases in systolic function, which may be signs of incipient coronary disease. Furthermore, traditional measures of systolic function do not reflect abnormalities in diastolic function, which may be important markers of disease. Two methods hold promise in this area: tissue Doppler imaging and speckle tracking. As in traditional pulse Doppler imaging, tissue Doppler imaging measures the velocities in a region of interest. However, in contrast to traditional pulse Doppler imaging, a low-pass filter is applied to exclude high-velocity signals from moving blood, enabling measurement of myocardial tissue velocities [28,29]. From the myocardial tissue velocities, strain and strain rates can be computed. Speckle tracking methods use computer algorithms to evaluate changes in distance

Fig. 4



Representative myocardial contrast echocardiogram showing a myocardial perfusion defect in the anteroseptal and apical segments of the left ventricle (black arrows) during adenosine stress imaging. The corresponding coronary angiogram shows the presence of significant coronary artery disease in the left anterior descending artery (grey arrows). Reprinted with permission from Xie *et al.* [16].

Fig. 5



Three-dimensional echocardiography. The two-dimensional image data can be contoured semiautomatically to generate three-dimensional representations of the left ventricle and allow precise estimates of chamber volumes and ejection fraction. EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; EF, ejection fraction.

between 'speckles' observed in normal myocardium to compute the strain and the strain rate [30] (Fig. 6).

Both tissue Doppler imaging and speckle tracking methods have been used for assessment of systolic and diastolic dysfunction in the setting of coronary artery disease [28,31]. Tissue Doppler imaging is routinely used to quantify early and late mitral annual relaxation velocity, an important measure of diastolic function. Although used less often, mitral annual systolic velocity may be a sensitive measure for early abnormalities in systolic function [32]. Tissue Doppler imaging and speckle tracking can be used to quantify myocardial strain and strain rate, which may be abnormal even in the setting of the overall normal ejection fraction. Both these methods have been applied to stress testing to improve diagnostic performance in coronary artery disease [33].

Currently, most echocardiography systems include capabilities for acquiring and analyzing tissue Doppler imaging images. Software for speckle tracking is available from multiple vendors both for offline and for real-time analysis. However, because speckle tracking analysis is time consuming, few laboratories have integrated it into routine workflows.

Acute myocardial ischemia

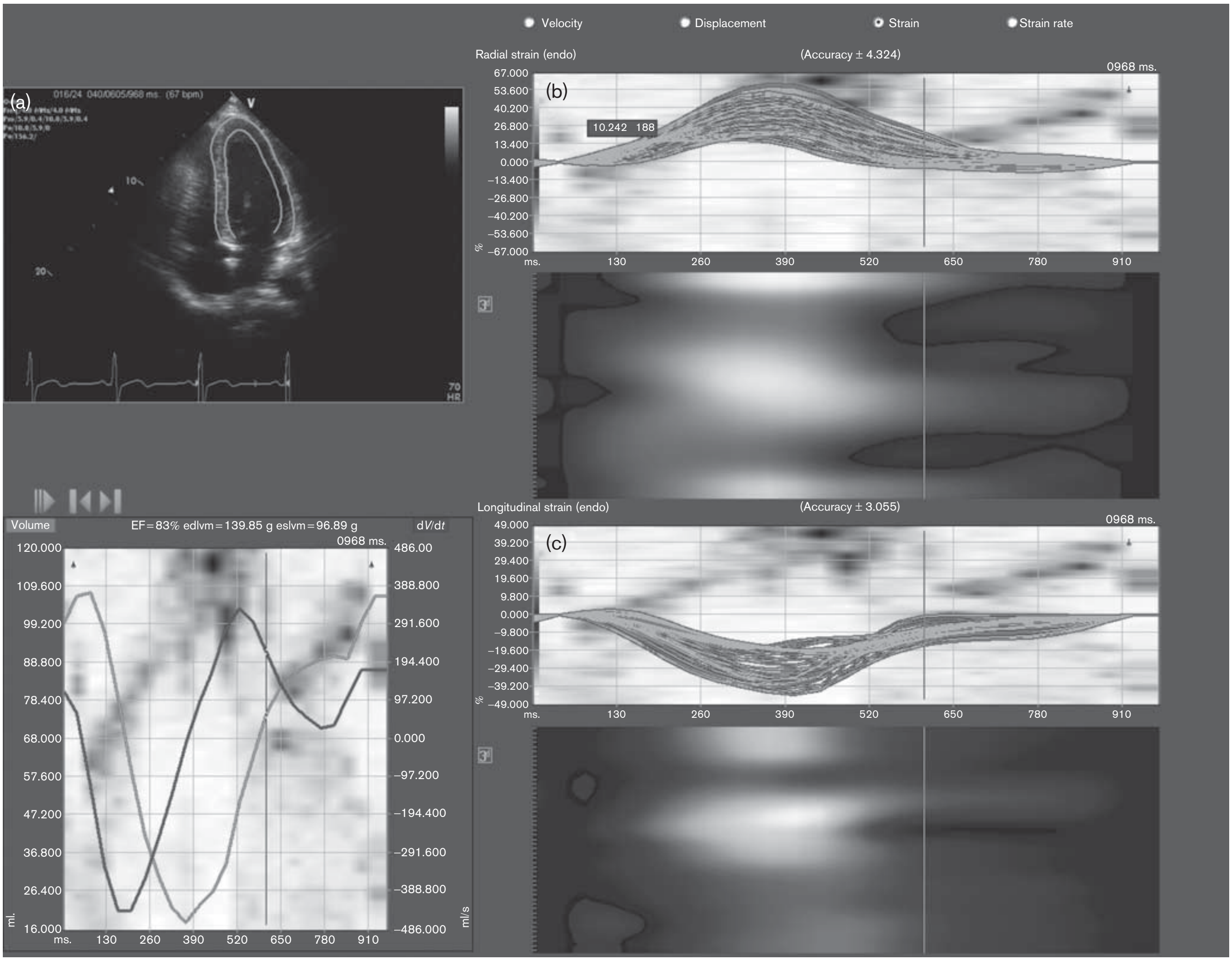
Resting two-dimensional echocardiography

Table 2 and Fig. 2 summarize the appropriate use criteria of echocardiography in acute coronary syndromes [5]. Resting two-dimensional echocardiography is a useful and inexpensive tool for the assessment of acute chest pain. Normal overall left ventricular systolic contractile function without regional wall motion abnormalities during acute chest pain excludes large regions of myocardial ischemia or infarction, whereas the development of new regional wall motion abnormalities in the setting of acute chest pain is of major concern for ongoing myocardial ischemia or infarction. Contrast-enhanced imaging appears to further aid the assessment of regional wall motion abnormalities [9]. Because of limitations in spatial resolution, inadequate acoustic windows in many patients, and the fact that early or mild hypoperfusion may exist without overt systolic dysfunction, resting two-dimensional echocardiography is generally considered inadequate to rule out the presence of functionally significant coronary artery disease, especially in the absence of ongoing chest pain or ECG signs of ischemia [17,34]. Nonetheless, this method can be very helpful in the acute setting to rule out alternative cardiac and noncardiac causes of acute chest pain, including pericardial effusion, pulmonary embolism, or aortic dissection.

Stress echocardiography

Stress echocardiography provides invaluable diagnostic information in acute chest pain patients with no ischemic changes or with left bundle branch lock or paced ventricular rhythm and negative or minimally elevated troponin levels (Table 2 and Fig. 2) [5].

Fig. 6



Speckle tracking imaging. After tracing the myocardium in the apical four-chamber view (a), radial (b) and longitudinal (c) strain measures for each segment can be plotted as a function of time across the cardiac cycle and presented as a maps.

Myocardial contrast echocardiography

Myocardial contrast echocardiography can assess directly both the myocardial tissue perfusion and wall motion at the bedside, playing a unique role in the diagnosis and prognosis of acute coronary syndromes [35,36]. Of note, because the use of ultrasound contrast for this application has not received regulatory approval in the USA, although many laboratories have gained considerable experience with research and clinical examinations, it has yet to garner widespread clinical acceptance.

Emerging methods

Speckle tracking imaging and diastolic relaxation of ischemic regions have also been used for the diagnosis of acute myocardial ischemia mostly in research applications [25]. Although these methods hold promise for improved diagnostic accuracy and decreased inter-reader variability, they are not yet widely applicable and further investigation of their clinical utility is required.

Complications of acute myocardial infarction

Resting two-dimensional echocardiography with Doppler imaging is the first-line imaging method for the diagnosis and prompt treatment of complications of acute myocardial infarction, including infarct expansion, left ventricular thrombus formation, right ventricular infarction, ventricular septal rupture, left ventricular free-wall rupture with subsequent pericardial effusion, tamponade or psedoaneurysm formation, and papillary muscle rupture or ischemia with subsequent acute mitral regurgitation [17,34]. Contrast-enhanced echocardiography has added value in identifying the presence of thombus in regions of severe hypokinesis or akinesis. In situations where transthoracic echocardiography is technically difficult, such as in patients who may be intubated or have recently undergone cardiac surgery, transesophageal echocardiography may be used. The appropriate use criteria of echocardiography in complications of myocardial infarction are summarized in Table 2 [5].

Role of echocardiography in risk stratification

Two-dimensional echocardiography is an easy and effective initial approach for baseline and follow-up evaluation of ventricular function and prognosis following an acute coronary syndrome [5]. Stress echocardiography techniques offer valuable prognostic information in the risk evaluation of stable chronic coronary ischemia and after acute ischemic episodes; that is, unstable angina or myocardial infarction [37]. A normal stress echocardiogram yields a low risk (< 1% year) for major events [3], comparable with a low-risk nuclear perfusion scan. In contrast, an abnormal stress echocardiogram carries a considerably high annual risk for major adverse events. Patients with positive stress echocardiograms can be further stratified into intermediate (1–3% year) or high risk (> 3% year) for major events on the basis of a composite of the extent and severity of ischemia with the hemodynamic response to exercise, stress-induced ECG findings, exercise capacity, patient's symptoms with stress, baseline echo parameters, anti-ischemic therapy, and clinical risk factors (Table 5) [3]. Coronary angiography and revascularization should be considered in patients with a positive stress echocardiogram, especially if high-risk clinical or imaging characteristics are present. The appropriate use criteria of echocardiography in risk stratification are summarized in Table 2 [5].

Table 5 Risk stratification on the basis of positive stress echocardiography

1-year risk (hard events)	Intermediate (1–3% year)	High (>10% year)
Dose/workload	High	Low
Resting ejection fraction (%)	>50	<40
Antianginal medications	Off	On
Coronary territory	LCX/RCA	LAD
Peak wall motion stress index	Low	High
Recovery	Fast	Slow
Coronary flow reserve	>2.0	<2.0

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LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Myocardial viability

Multiple large studies have shown that the presence of unrevascularized, viable or hibernating myocardium increases the risk of adverse outcomes. Although the STITCH study raised questions of whether revascularization improves outcomes in these patients [38], other studies have come to conflicting conclusions [39]. Echocardiographically, normal viable myocardium is usually thicker than 0.6 mm during diastole, whereas a thin myocardium (< 0.6 mm) with increased echodensity because of fibrosis is usually nonviable (scarred). Nevertheless, in most of the cases, the wall thickness and echodensity criteria are not adequate to distinguish viable from nonviable myocardium [17]. More advanced echocardiography imaging techniques, such as dobutamine stress echo, myocardial contrast echo, and strain imaging, may be used to distinguish viable versus nonviable myocardium. The appropriate use criteria of echocardiography in the assessment of myocardial viability are summarized in Table 2 [5].

Dobutamine stress echocardiography

Low-dose dobutamine stress echocardiography is the most widely used method for assessment of myocardial viability with echocardiography [3]. For this protocol, dobutamine infusion is increased in a stepwise manner, starting with 5 mcg/kg/min and increasing to 10, 20, 30, and 40 mcg/kg/min in 3-min intervals. Normally, the systolic function of the myocardium monotonically increases with increasing dobutamine dose. Nonviable (scarred) myocardium, which is akinetic or dyskinetic before stress, generally does not improve at all with dobutamine infusion (necrotic response), whereas viable myocardium has either a normal or a biphasic response (Table 3). Segments with a normal response pattern show sustained improvement in myocardial contractility with increasing dobutamine infusion, consistent with nonjeopardized (stunned) myocardium. Segments with a biphasic response pattern show increased contractility during infusion of low-dose dobutamine because of increased coronary blood flow. However, as the dobutamine infusion increases further than 30 mg/kg/min, the coronary blood flow does not increase and myocardial ischemia occurs because of increased myocardial oxygen demand as a result of the inotropic effects of dobutamine combined with the underlying coronary stenosis. This results in deterioration in segmental or global systolic function at higher doses of dobutamine. The biphasic response indicates a jeopardized chronically ischemic (hibernating) myocardium, which may have improved function following revascularization. Table 3 summarizes the responses to low-dose dobutamine infusion. When dobutamine infusion is contraindicated or not well tolerated, low-level exercise, adenosine, dipyridamole, or enoximone can also be used [3].

Myocardial contrast echocardiography

Myocardial contrast echocardiography has also been used to assess viability [9]. Myocardial viability can be expressed quantitatively as (i) contrast intensity and (ii) myocardial replenishment assessed 10–15 cardiac cycles after a destructive pulse is applied to destroy microbubbles already in the region of interest. Increased contrast enhancement and normal wall motion are observed in normally perfused myocardial segments because of contrast enhancement, whereas scarred areas show the absence of contrast enhancement and akinesis [15].

Strain imaging

Postsystolic shortening reflects actively contracting and therefore viable myocardium. Myocardial strain can be quantified using several echocardiographic techniques and appears to be effective for assessment of myocardial viability; however, further clinical investigation is warranted before mainstream application [17,31,40].

Ischemic cardiomyopathy

Ischemic cardiomyopathy is the major source of systolic heart failure. Resting echocardiography with Doppler imaging is pivotal in studying patients with ischemic left ventricular systolic dysfunction by providing information on the left ventricular size, remodeling and volume, resting regional wall motion abnormalities, myocardial viability, left ventricular filling pressures, functional status of the mitral valve, and pulmonary artery systolic pressure. Contrast-enhanced echocardiography also has incremental value in assessing the left ventricular volume and ejection fraction. Advances in three-dimensional echocardiography are also anticipated to facilitate the assessment of left ventricular shape, volume, and size in patients with ischemic cardiomyopathy. These measures may have important therapeutic and prognostic implications. The appropriate use criteria of echocardiography in ischemic cardiomyopathy are summarized in Table 2 [5].

Comparison of echocardiography with other imaging modalities

In contrast to other cardiac imaging modalities, including cardiac computed tomography, cardiac MRI, and nuclear methods, echocardiography offers the opportunity for rapid, bedside evaluation of suspected coronary disease, such as during acute chest pain, which are unlikely to be as practical or readily available for clinically unstable patients. Echocardiography remains the standard choice for follow-up after myocardial infarction for serial evaluation of ejection fraction, chamber remodeling, wall motion abnormalities, and acute or subacute mechanical complications.

For the evaluation of stable patients for coronary artery disease, stress echocardiography with exercise or pharmacologic stress is a broadly available and effective test with diagnostic performance comparable to competing modalities. Compared with nuclear myocardial perfusion imaging, stress echocardiography has slightly lower sensitivity (80 vs. 82%) and higher specificity (84 vs. 75%) for the diagnosis of coronary artery disease [41]. It also has greater versatility, lower cost, and no radiation exposure. Stress echocardiography is also superior in terms of specificity compared with nuclear imaging in women, as well as in patients with left ventricular hypertrophy and left bundle branch block. Single-vessel disease, especially involving the left circumflex, is better identified with nuclear myocardial perfusion imaging as opposed to stress echocardiography.

For the assessment of viability, low-dose dobutamine stress echocardiography generally has lower sensitivity but higher specificity than myocardial perfusion imaging. Dobutamine stress MRI has comparable accuracy to stress echocardiography but requires costly specialized equipment as well as high-level expertise.

Overall, the most important factor in the decision on which test to select is dictated by local availability and expertise. Stress echocardiography should be the first choice for the assessment of coronary artery disease because of its lower cost, wider availability, and radiation-free nature compared with nuclear imaging and cardiac MRI.

Conclusion

Echocardiography is central in the diagnosis, management, and prognosis of the entire spectrum of coronary artery disease from chronic myocardial ischemia to acute ischemic pain, complications of myocardial infarction, and ischemic cardiomyopathy. Although the noninvasive imaging modalities for the evaluation of coronary artery disease have expanded over the last decade, echocardiography remains the most cost-effective and risk-effective imaging choice in most settings. Improvement of existing well-established echocardiographic methods (i.e. two-dimensional echocardiography, stress echocardiography, contrast echocardiography) in conjunction with the development of new emerging echocardiography methods (i.e. three-dimensional echocardiography, tissue Doppler imaging, speckle tracking imaging) is anticipated to increase the clinical utility of echocardiography in coronary artery disease.

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Conflicts of interest

V.L.M. owns minor equity in General Electric. For the remaining authors there are no conflicts of interest.

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