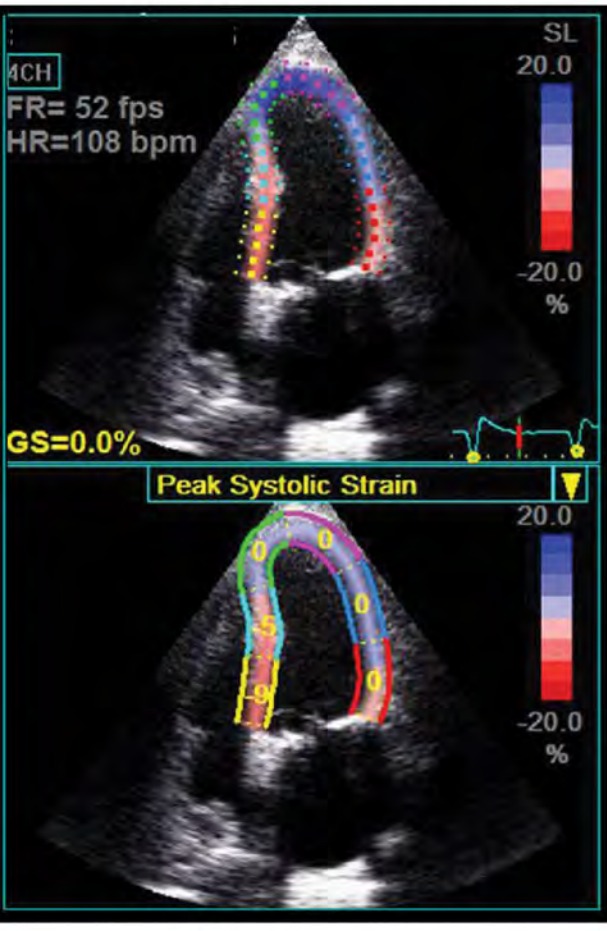
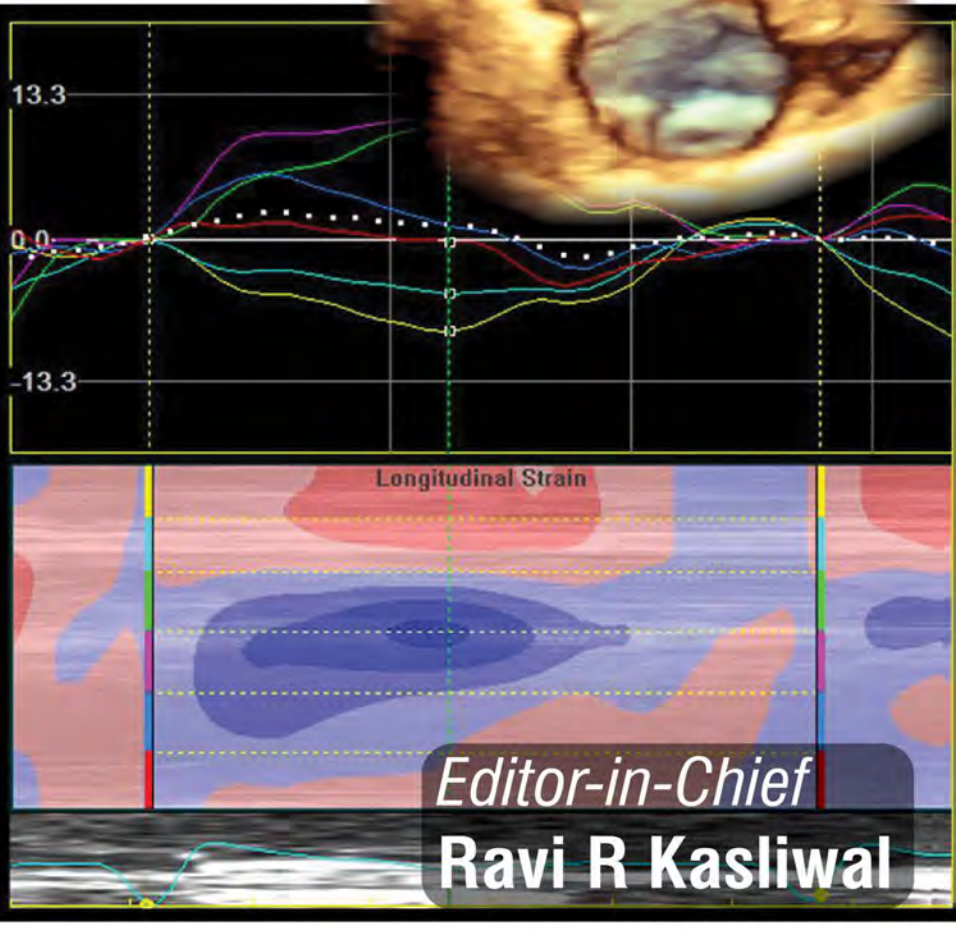
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# Applied Echocardiography *in* Coronary Artery Disease




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# Pharmacologic Stress Echocardiography

4 CHAPTER

*Srikanth Sola*

## INTRODUCTION

Stress echocardiography is a well-validated, versatile non-invasive imaging modality that has proven utility in the detection of myocardial ischemia, viability, determining prognosis, and evaluating therapy.[1] Compared to other imaging modalities, stress echocardiography is less costly, avoids the use of ionizing radiation or iodinated contrast agents, is widely available and is easy to perform. We discuss common clinical indications for pharmacologic stress testing, review protocols for the different pharmacologic stress agents available, and discuss pitfalls in image acquisition which can impact the test's accuracy.

## CLINICAL INDICATIONS AND CHOICE OF MODALITIES

The most common clinical indications for pharmacologic stress testing include evaluation for ischemia, typically in a patient with baseline ECG abnormalities who is unable to exercise, a previous nondiagnostic exercise treadmill test, or cardiac chest pain in patients with prior surgical or percutaneous revascularization. Other important but less frequent indications for pharmacologic stress testing include assessment of myocardial viability, and finally, low gradient low flow aortic stenosis. In most patients, exercise testing is the preferred test for ischemia over pharmacologic stress testing, as exercise capacity measured in metabolic equivalents (METs) provides important prognostic information. In addition, exercise results in a higher rate-pressure product (>25,000) vs. dobutamine (average 20,000) or pacing (<20,000).[2,3] However, pharmacologic stress testing is preferred when the patient is unable to exercise, most commonly due to neurologic, orthopedic, or other impairments that limit the ability to exercise. Many echocardiography laboratories also prefer pharmacologic stress testing, particularly, dobutamine stress echocardiography (DSE) in patients with baseline left ventricular (LV) systolic dysfunction. In such patients, the typical biphasic response to dobutamine in ischemic segments or lack of improved contractile response in nonviable segments is more easily assessed with DSE than with exercise or vasodilator stress echocardiography.

In some patients, pharmacologic stress testing is preferred as the hyperventilation and excessive chest wall movement after exercise can limit the echocardiographic examination of the heart. This degrades image quality, increases inter-reader variability, and reduces the diagnostic accuracy of exercise stress echocardiography. Some indications for stress testing, however, are better evaluated by symptom-limited exercise stress echocardiography. These include aortic regurgitation, aortic stenosis (asymptomatic, with normal systolic function), mitral regurgitation, mitral stenosis, hypertrophic cardiomyopathy to assess for provocable LV outflow tract (LVOT) gradients, pulmonary hypertension and the diastolic stress test. Important contraindications to pharmacologic stress echocardiography are listed in **Table 4.1**.

The decision regarding which stress echocardiography protocol (exercise, dobutamine, or vasodilator) to use depends on both the clinical indication and the experience of the echo lab. However, it is advisable that labs develop expertise with all 3 protocols, as no single protocol is suitable

**Table 4.1:** Contraindications to pharmacologic stress echocardiography

- Ongoing chest pain in patients with acute coronary syndromes
- Acute decompensated heart failure
- Unstable brady- or tachyarrhythmia
- Severe hypertension
- Hypotension
- Acute myocarditis
- Acute aortic syndromes (aortic dissection, intramural hematoma, or penetrating ulcer)
- Acute pulmonary embolism
- Mobile intracardiac thrombus
- High degree atrioventricular block
- Additional contraindications for vasodilator stress:
  - Active bronchospasm or significant asthma (usually requiring home $O_2$, oral steroids, prior history of intubation, or ongoing exacerbation)

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for all patients. For example, a DSE test that is stopped early due to a hypertensive response to dobutamine will yield a nondiagnostic result, whereas in a lab with proficiency in vasodilator stress, the patient can then be rescheduled to complete a vasodilator stress test comfortably.

## DOBUTAMINE STRESS ECHOCARDIOGRAPHY PROTOCOL

### Pharmacology of Dobutamine

Dobutamine is a synthetic catecholamine agent which has a very short plasma half-life (<2 minutes), requiring that it should be given as a continuous intravenous infusion. The effects of dobutamine vary depending on the dose at which it is given. At *lose dose dobutamine* (<10 μg/kg/min), it has a predominant inotropic effect (without tachycardia) via its effect on $\beta_1$-adrenergic receptors in the heart. In addition, it has a relatively lesser effect on the $\beta_2$-adrenergic receptors and $\alpha_1$-adrenergic receptors in the peripheral vasculature, which at low doses, balance any changes in systemic vascular resistance and lead to a neutral effect on blood pressure.[4]

At higher doses, however, the inotropic and chronotropic effects of dobutamine increase, leading to progressive increases in heart rate (average increase 40–50 beats/min) and contractility of the heart, thus increasing cardiac output, blood pressure, and myocardial oxygen demand. However, there is also a greater effect on the $\beta_2$-adrenergic receptors at higher dobutamine doses, which can lead to peripheral vasodilation and, in some patients, a decrease in blood pressure and even hypotension. Bradycardia with high dose dobutamine is less common and is due to a reflex response to increased blood pressure, activation of mechanoreceptors due to increased myocardial contractility, or both.[5]

### Dobutamine Protocols

The 2007 guidelines from the American Society of Echocardiography and the 2008 guidelines of the European Association of Echocardiography recommend dobutamine as the first-line agent for the performance of pharmacologic stress echocardiography.[6,7] The specific dobutamine protocol used depends on the clinical indication and whether the patient has a pacemaker. *For ischemia testing,* dobutamine infusion is started at 5 μg/kg/min for three minutes, followed sequentially by 10 μg/kg/min, 20 μg/kg/min, 30 μg/kg/min, and 40 μg/kg/min for 3 minute stages each or until 85% of the age predicted maximum heart rate is achieved. Some echo labs forgo the 5 μg/kg/min stage and start dobutamine at 10 μg/kg/min, particularly, in patients with a normal resting ejection fraction. For patients who fail to achieve 85% age predicted maximum heart rate at the dose of 40 μg/kg/min stage; adjunctive agents, such as atropine and hand grip exercise can be used (see section on Hand-grip Exercise further).

*For viability testing,* protocols vary widely but dobutamine infusion is typically started at 2.5–5 μg/kg/min, followed by 10 μg/kg/min and ending at 20 μg/kg/min. These low doses of dobutamine provide a predominant inotropic effect with minimal chronotropy. Therefore, no target heart rate is required for viability testing when this protocol is used. In patients with LV systolic dysfunction and suspected ischemia, the complete DSE protocol, starting with the 2.5–5 μg/kg/min stage and extending until indication for termination of the test is reached, allows for the assessment of both viability and ischemia (i.e. the classic biphasic response). The latter protocol is more frequently used, as this also has a higher positive predictive value for the assessment of myocardial viability than a low dose protocol.[8] In patients with low gradient low-flow aortic stenosis, only the low-dose dobutamine protocol is used (up to 20 μg/kg/min), along with measurements of aortic valve gradients and cardiac output at each stage.

*For patients with permanent pacemakers,* the dobutamine protocol is combined with changes in the patient's paced rate to achieve an adequate stress. Typically, dobutamine is started at 5 μg/kg/min for 3 minutes, then 10 μg/kg/min for 3 minutes, and 20 μg/kg/min. At the end of the 20 μg/kg/min stage, the pacemaker is adjusted as follows: If the patient's heart is already paced, then pacing is adjusted to 70% of age predicted maximal heart rate while dobutamine is continued at 20 μg/kg/min for 3 minutes. If the patient's heart is not paced, the heart is paced at just above resting heart rate for 3 minutes, then increased to 70% of age predicted maximal heart rate while dobutamine is continued at 20 μg/kg/min for 3 minutes. Finally, the pacing rate is increased to 85% of the age-predicted maximum heart rate for 3 minutes (in all patients) while dobutamine is continued at 20 μg/kg/min for 3 minutes. For recovery, dobutamine is discontinued and the pacemaker returned to its normal baseline settings.

Atrial pacing is preferred to ventricular pacing as the latter results in asynchronous ventricular pacing that can cause difficulties in interpretation, particularly, in the interventricular septum. An alternate protocol to dobutamine plus pacing is to use pacing alone, usually to a target rate of 160 beats/min. Unlike dobutamine, the resulting tachycardia with pacing alone is accompanied by unchanged loading conditions and stable blood pressure, resulting in better hemodynamic control than with dobutamine.[9] The disadvantage of pacing alone protocols is that the absence of an increased blood pressure response leads to at best only a modest increment in the rate-pressure product.

For all dobutamine protocols, the test is terminated when the patient (i) reaches target heart rate (and completes imaging at that stage), (ii) develops new regional wall motion abnormalities in at least 2 contiguous segments, (iii) completes the study protocol (40 μg/kg/min for ischemia or 20 μg/kg/min for viability alone), or (iv) experiences an

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adverse event that necessitates discontinuation of the infusion and supportive or emergent care. Adverse events that would necessitate stopping the study include hypotension (systolic blood pressure <90 mm Hg or decrease in systolic blood pressure >20 mm Hg from baseline), severe hypertension (>220 mm Hg systolic or >120 mm Hg diastolic), anginal chest pain, ST depression >2 mm on ECG, or sustained ventricular tachycardia. Isolated nonsustained ventricular tachycardia can be a side effect of dobutamine administration and does not necessarily require termination of the test if the patient is hemodynamically stable and asymptomatic.

After completion of the dobutamine infusion and when recovery images are obtained, patients are typically monitored in either the stress echo room or recovery area until the heart rate returns to within 20 minutes of baseline, all new wall motion abnormalities have returned to baseline, and the patient is asymptomatic.

## OTHER ADJUNCTIVE AGENTS

### Atropine

Atropine is an anticholinergic drug that, among other effects, increases the heart rate. Atropine can be used in doses of 0.25–0.3 mg (depending on how it is supplied) every minute up to a maximum of 2 mg. Many echo laboratories have moved toward early administration of atropine to improve time to target heart rate. A common atropine protocol would be to give one dose of atropine under the following conditions: (i) if heart rate is less than 90 beats/min at the end of the 20 μg/kg/min stage, or (ii) if the heart rate is less than 70% of the age predicted maximum heart rate at the end of the 30 μg/kg/min stage. Additional doses of atropine (up to 2 mg maximum) can be given if the heart rate is less than 85% of the age predicted maximum heart rate at the end of the 40 μg/kg/min stage.

Atropine has additional benefits in DSE beyond reaching target heart rate. Patients taking β blockers can experience blunting of the effects of dobutamine, reducing the double-product to 14,000. This can be prevented by the administration of atropine.[10] In addition, the combined use of dobutamine and atropine can prevent vagal activation, and the depression of heart rate occurs due to a hypertensive reaction or stimulation of the cardiac mechanoreceptors.

Atropine has a half-life of 3.5 hours, which means that the tachycardia effect of this agent can continue even after the cessation of dobutamine administration. Intravenous β blockers are commonly used to return heart rate to within 20 beats/min of baseline in patients with adequate blood pressure. Patients should be warned that atropine dilates the pupil which can lead to visual disturbance and intolerance to light. Sensations of thirst and dry mouth are frequent. Some patients may experience giddiness and staggering, and therefore, they should avoid driving a vehicle or operating machinery for 6 hours after receiving atropine. Atropine is contraindicated in patients with acute-angle glaucoma, paralytic ileus, and severe benign prostatic hypertrophy with urinary retention, although these patients are infrequently seen in the stress echo laboratory.

### Hand-grip Exercise

Hand grip increases afterload, causing a small incremental increase in heart rate and blood pressure, leading to a modest increase in myocardial $O_2$ demand.[11] Hand grip is usually performed at the end of the 40 μg/kg/min stage of a DSE test or the last stage of exercise stress echo test, typically when the patient fails to reach target heart rate. At some centers, a tennis or soft cricket ball is used as an aid to the hand grip, and the patient is asked to squeeze the ball with 30% of his or her maximum strength for 30 seconds. Specially designed devices for isometric hand grip exercises are popular in some European echo labs, as they require a calibrated amount of hand pressure leading to a more reliable increase in afterload. In patients with extensive coronary artery disease (CAD), hand-grip exercise alone can cause regional wall motion abnormalities, although it is rarely used for diagnostic purposes in this manner.

### Nitroglycerin-Dobutamine Stress-Echocardiography for Viability

A small body of literature exists to support the use of nitroglycerin enhanced DSE testing for viability. Ling et al. have shown that nitroglycerin can be used in addition to dobutamine and can enhance the accuracy of detecting hibernating myocardium.[12] Nitroglycerin was given as a 0.4 mg sublingual spray, followed 5 minutes later by rest images, and the standard DSE protocol. Nitroglycerin alone increases regional thickening in approximately 20% of akinetic but viable segments, whereas the combination of nitroglycerin plus dobutamine had the best specificity for viability compared with intracoronary myocardial contrast echo and rest-redistribution thallium-201 single photon emission computed tomography (SPECT). Although infrequently used for DSE viability testing, nitroglycerin has been used to increase contractility of akinetic but viable segments on ventriculography,[13] enhance radionuclide uptake in 18F-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) and SPECT,[14] and augment wall thickening in dobutamine stress magnetic resonance imaging.[15] The mechanism of nitroglycerin in viability assessment by DSE is not clear, but it may be related to effects of vasodilation leading to recruitment of collateral circulation or improvement of loading conditions.[16,17]

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## VASODILATOR STRESS ECHOCARDIOGRAPHY PROTOCOL

Vasodilator stress echocardiography is an alternative to DSE and is more commonly used at some European centers. Three vasodilators are approved for use in vasodilator stress protocols: dipyridamole, adenosine, and regadenoson. Dipyridamole acts by increasing endogenous adenosine levels, whereas both adenosine and regadenoson (an $A_{2A}$ adenosine receptor agonist) act directly on adenosine receptors in the vasculature to cause vasodilation. All of these agents produce a modest tachycardia, a small decrease in blood pressure, and a minor increase in ventricular systolic function. Of these three agents, only adenosine is available commercially in South Asia.

Adenosine is most commonly given as a continuous infusion at a dose of 140 μg/kg/min for 6 minutes. For patients who fail to respond to adenosine, as determined by an increase in heart rate by at least 10 beats/min above baseline, the dose of adenosine is increased to 180, then finally 210 μg/kg/min over 3 minute stages until the expected increase in heart rate is achieved. Atropine may be given during vasodilator administration to increase heart rate and myocardial oxygen demand, resulting in improved diagnostic sensitivity.[18] Patients must be counseled to avoid caffeinated beverages, including tea, coffee, colas, and energy drinks, as well as chocolate and xanthine derivative medications, such as deriphylline for 24–48 hours prior to the study, as these interfere with the effects of adenosine and lead to a false-negative test.

## IMAGING ACQUISITION PROTOCOLS

The diagnostic accuracy of stress echocardiography is dependent on the quality of image acquisition and optimal image display. Guidelines from the American Society of Echocardiography provide details on image acquisition and display in stress echocardiography.[6] The physio setting on the echo machine should be adjusted so that ECG triggering is used for imagine acquisition. Tissue harmonic imaging should be employed routinely, as this enhances the definition of the endocardial to LV cavity interface and reduces near field noise. Gain and time gain compensation settings, focus, transducer frequency, and sector width should be optimized for imaging the left ventricle. Active collaboration between the patient and sonographer, including brief breath holds at mid inspiration or mid expiration, can help maintain the echocardiographic window and avoid respiratory motion artifacts. Common mistakes made by less experienced operators include using too high a depth, too narrow a sector, foreshortening of the LV apex on apical windows, and opening up the LVOT or aortic valve on the apical 4-chamber view **(Figure 4.1A to E)**.

For patients who have not undergone a recent echo study, baseline images should screen for pathology beyond the left ventricle which may be related to the patient's symptoms. These include assessment for valvular stenosis and regurgitation, diastolic function, pulmonary hypertension, the ascending aorta (for dissection or dilation), and pericardial effusion. If asymmetric hypertrophy or systolic anterior motion of the mitral valve is present, then assessment of LVOT gradients using continuous wave Doppler at rest and with amyl nitrate should be performed to exclude unrecognized hypertrophic cardiomyopathy. Findings on pre-stress screening which may lead to cancelation of the test include hypertrophic cardiomyopathy with a resting or provocable gradient of more than 50 mm Hg, aortic stenosis which is moderate or greater in severity, thoracic aortic aneurysm or dissection, severe LV systolic dysfunction (except when DSE is being done for viability), large pericardial effusion, and LV or left atrial thrombus.

Transthoracic echocardiography images are acquired at rest, at each stage of dobutamine infusion, and during recovery. At each stage, images should include the parasternal long-axis, parasternal short-axis at mid-papillary level, apical 4-chamber, apical 2-chamber, and apical long-axis views. To ensure accurate comparison between the rest images and subsequent dobutamine and recovery stages, care should be taken to ensure that all images are in the same imaging planes and depth as the baseline images. Anatomic landmarks, such as the papillary muscle heads in the parasternal mid short-axis levels or thickened valve chordae on the parasternal long-axis view, can facilitate this. For the parasternal long-axis view, moving the probe laterally 3–4 cm away from the sternum will allow the mid segments of the left ventricle to be seen. The apical windows allow imaging of the LV apex, but care must be taken to avoid foreshadowing on the apical 4-chamber and 2-chamber views. The anterior and anteroseptal walls can be difficult to visualize on the apical windows. Breath holding by the patient, steep lateral decubitus positioning (facilitated by an examination bed with a cut out for apical windows), and steep angulation of the transducer can facilitate this. When two or more contiguous segments cannot be visualized, then contrast can be used (see section on Echo Contrast further).

In some echocardiography laboratories, additional views include the basal and apical parasternal short-axis views. Since display software for multistage acquisition typically allows for only one parasternal short-axis view (usually the mid-papillary level is chosen since all three coronary territories are seen), the additional short-axis views are archived for later review if more detailed analysis is required. The subcostal short-axis views can be substituted for the parasternal window when views are limited, but this requires patient repositioning when moving from apical to subcostal windows, and obtaining the subcostal short-axis view at

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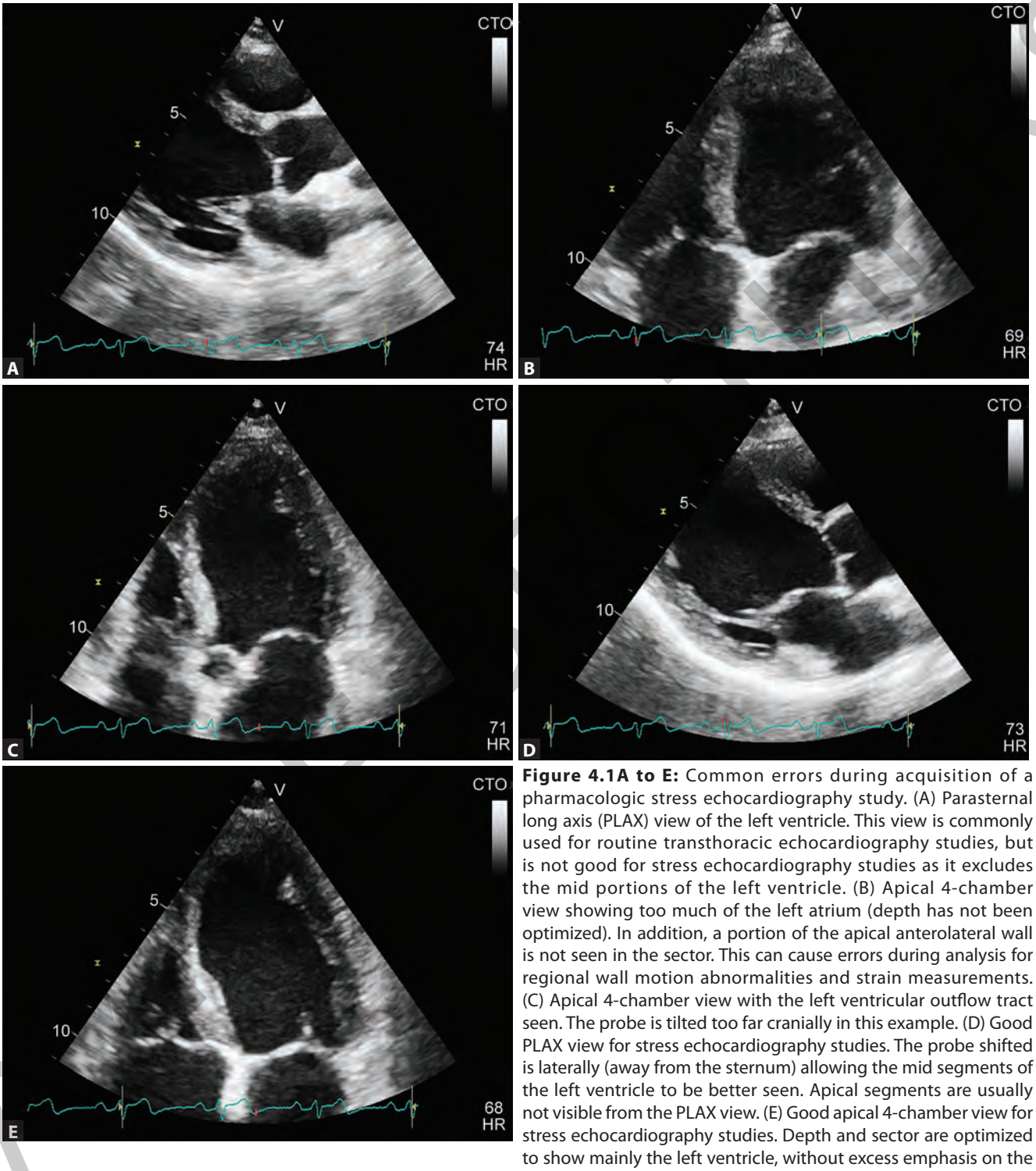



**Figure 4.1A to E:** Common errors during acquisition of a pharmacologic stress echocardiography study. (A) Parasternal long axis (PLAX) view of the left ventricle. This view is commonly used for routine transthoracic echocardiography studies, but is not good for stress echocardiography studies as it excludes the mid portions of the left ventricle. (B) Apical 4-chamber view showing too much of the left atrium (depth has not been optimized). In addition, a portion of the apical anterolateral wall is not seen in the sector. This can cause errors during analysis for regional wall motion abnormalities and strain measurements. (C) Apical 4-chamber view with the left ventricular outflow tract seen. The probe is tilted too far cranially in this example. (D) Good PLAX view for stress echocardiography studies. The probe shifted is laterally (away from the sternum) allowing the mid segments of the left ventricle to be better seen. Apical segments are usually not visible from the PLAX view. (E) Good apical 4-chamber view for stress echocardiography studies. Depth and sector are optimized to show mainly the left ventricle, without excess emphasis on the right ventricle or left atrium.

the same level for each stage of the study can sometimes be challenging.

Additional information, which may be required depending on the clinical scenario, include transmitral inflow and TDI of the mitral annulus (for diastolic stress testing), estimated right ventricular systolic pressure (in suspected pulmonary hypertension, mitral stenosis), vena contracta and effective regurgitant orifice area for patients with mitral or tricuspid regurgitation, and pulse waved Doppler/continuous wave Doppler of the LVOT and aortic valve, respectively, plus cardiac output for patients with paradoxical low-flow low-gradient aortic stenosis. Except for the latter indication, however, most of these additional views are more common with exercise-stress echocardiography.

## DISPLAY PROTOCOLS

Upon completion of the study, the sonographer should select the best images for each view, ensuring that all images are labeled with the correct window name and include the ECG tracing. Images acquired during ventricular ectopic beats should be excluded, as these can cause difficulty in interpretation.

Images are displayed in either a standard quad-screen format (DSE) or split screen (vasodilator stress) on the echocardiography machine or the workstation. For DSE studies, rest, low-dose, pre-peak, and peak images are displayed simultaneously. Recovery images are viewed separately and are used to assess for post-stress (late) ischemia. Newer echocardiography machines provide additional display options. However, the image size in these other display formats must be adequate for image interpretation.

## ADJUNCTIVE MODALITIES

### Strain DSE

Longitudinal, circumferential, and radial strain as assessed by either two-dimensional (2D) or three-dimensional (3D) speckle tracking echocardiography quantitatively analyzes global and regional myocardial function. It presents an objective, semiautomatic, and angle-independent analysis of myocardial deformation based on speckle tracking and provides a single bull's-eye summary of the LV segmental wall strain.

Recent studies have shown that strain analysis, when added to standard diagnostic criteria for ischemia (e.g. new or worsening wall motion abnormalities), improves the diagnostic accuracy of DSE testing compared with standard diagnostic criteria alone. Arnold et al. conducted a multicentered study of 102 patients who underwent concurrent DSE and invasive coronary angiography.[19] While global longitudinal strain (GLS) alone was as accurate as wall motion score index (WMSI) for the diagnosis of ischemia, the result from the combination of GLS and WMSI highest sensitivity, specificity, and accuracy was 100%, 87.5%, and 96.3%, respectively.

In our laboratory, analysis of global longitudinal strain and peak segmental strain is routinely done for DSE studies with adequate image quality. Training of the sonographer and/or physician performing the study and analyzing the image data is needed to ensure high quality images and avoid artifacts that would affect interpretation. In addition, care is needed to avoid loss of image data in the anterior and anteroseptal walls on the apical windows. We do not use strain analysis in exercise stress echocardiography studies (due to respiratory motion artifact) or when contrast is used. However, measurement of longitudinal segmental strain 5 minutes after cessation of exercise (i.e. during the recovery phase) can be a useful adjunct for detection of ischemia during exercise stress echocardiography.

## 3D ECHOCARDIOGRAPHY

Advances in hardware and postprocessing for 3D echocardiography have led to impressive improvements in temporal and spatial resolution in the past 2–3 years. Two approaches are currently in use for 3D echocardiography based DSE. The first and simpler technique is to utilize the multiplanar capability of the 3D transthoracic probe to acquire the required apical and parasternal views using a single acquisition from each of these windows (e.g. the probe is positioned once on the apex and the apical 4-chamber, apical 2-chamber, and apical long-axis views are acquired simultaneously using a 3D triplane acquisition). This has the theoretical advantage of improving acquisition time and workflow, although there is a steep but short learning curve for sonographers or physicians new to 3D echocardiography particularly as very high quality images are typically required for DSE.

The second, a more comprehensive approach, utilizes the full volume capability of 3D echocardiography to acquire the entire left ventricle from the apical window. The resulting volume can then be sliced into multiple short axis, 4-chamber, 2-chamber, and apical long-axis views, allowing a more detailed analysis of wall motion compared with the limited views available from current 2D DSE imaging planes. Foreshortening of the LV apex is avoided using the volumetric approach, imaging planes can be easily standardized across stages, and imaging time is reduced since only a single apical acquisition is required at each stage. Commercially available 3D DSE viewing systems are now available which simplify workflow and interpretation.

Limitations of full volume 3D DSE include lower temporal resolution compared to 2D echocardiography, which can potentially reduce the ability to detect subtle wall motion abnormalities, including tardokinesis. In addition, multibeat

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acquisitions, if used to improve temporal resolutions, can lead to stitch artifacts due to patient respiration. This is an obvious limitation of 3D echocardiography during exercise stress echocardiography, but is not so problematic for DSE where breath holds of 3–7 heartbeats are feasible for most patients. As 3D echocardiography continues to advance, it is likely that the majority of DSE studies in the future will be performed using this modality.

## ECHO CONTRAST AND MYOCARDIAL CONTRAST ECHOCARDIOGRAPHY

Ultrasound contrast agents for LV opacification are indicated when two contiguous segments cannot be adequately visualized. At some centers, however, contrast is used when only one segment cannot be adequately visualized at rest, since high-quality stress images are typically more difficult to obtain than are rest images (particularly with exercise).

Myocardial contrast echocardiography (MCE) can be used to assess coronary perfusion and microvascular integrity, making it a potential adjunct in the assessment of ischemia and viability.[20] An MCE can be performed with either dobutamine or vasodilators, and adds incremental predictive value to traditional wall motion assessment.[21] However, MCE has still not received widespread adoption at most echocardiography laboratories, despite more than two decades of research.

## SAFETY CONCERNS

Pharmacologic stress echocardiography using dobutamine or vasodilator stress is widely regarded as a safe, noninvasive imaging modality for the heart. The American Society of Echocardiography guidelines note that DSE has been demonstrated to be safe in patients with severe LV dysfunction,[22] abdominal aortic aneurysms,[23] cerebral aneurysms,[24] and implantable cardioverter defibrillators.[25]

For dobutamine, significant side effects, which cause termination of the study, occur in a minority of patients (5%) and most commonly include severe hypertension (2%), symptomatic hypotension (0.5%), severe chest pain (1%), nausea (0.5%), and cardiac arrhythmias (1%).[26] In most cases these side effects are self-limiting and cease after termination of drug infusion. Even clinically important side effects, such as cardiac arrhythmias and systolic hypotension, are usually well-tolerated and are not associated with myocardial ischemia or LV dysfunction.[27] However, due to the potential adverse effects of dobutamine, the patient's heart rate and ECG must be continuously monitored, and blood pressure measured at rest, at each stage of dobutamine, and during recovery.

Hypotension during dobutamine infusion is easily managed by discontinuing the infusion and, in some cases, administering intravenous fluids. Hypertension and tachyarrhythmias are most frequently treated by intravenous esmolol or metoprolol. Esmolol is a short-acting β blocker that can be given in doses of 0.5 mg/kg. Metoprolol has a longer half-life and slower onset of action and is typically given in doses of 5 mg as a slow IV push. Up to 3 doses of IV metoprolol can be given, each dose 5 minutes apart (15 mg IV metoprolol is equivalent to 50 mg oral metoprolol). Chest pain can be treated by a sublingual nitroglycerin spray or tablet, plus IV β blocker as needed. Vomiting can often be prevented by giving metoclopramide 5 mg injection as soon as nausea occurs. Metoclopramide should not be used in patients with Parkinson's disease. A kidney basin or emesis tray must be kept near the patient's head during the study, or can be quickly provided as soon as nausea or vomiting occurs.

Adenosine is a short-acting agent that can occasionally cause chest pain, headache, nausea, and hypotension. Patients should be counseled prior to starting the test that these symptoms can occur as a result of medication administration and that they should avoid excessive movement if possible during that time, as this would interfere with the quality of the echo images. These adverse effects typically resolve within 15–30 seconds of discontinuing the infusion. Unlike adenosine, regandenason has a longer half-life (2–3 minutes) but a very favorable side effect profile. When side effects do occur, they can be treated by a slow injection of IV aminophylline (required in approximately 3% of patients).

Regardless of which pharmacologic agent is used, the cardiac rhythm must be monitored continuously during the study. A 12-lead electrocardiogram and noninvasive blood pressure measurements are obtained at baseline, at each stage of stress, and during the recovery phase. An emergency resuscitation cart, defibrillator, intubation equipment, including suction catheters, portable oxygen, patient trolley, and other emergency equipment are mandatory for any stress echo lab and must be maintained in good working order. At our lab, we routinely conduct emergency drills in the stress echo lab to ensure that all of our medical and administrative staff are proficient with code blue (cardiac arrest) procedures.

### Quality Assurance

Pharmacologic stress echocardiography requires a higher level of expertise, both in terms of acquisition as well as interpretation, than routine transthoracic echocardiography. For each sonographer or physician who routinely performs stress echocardiography, peer review of 5–10 studies should be performed annually to assess image quality and adherence to protocols for image acquisition.[28]

## SUMMARY

Pharmacologic stress echocardiography is a valuable noninvasive modality to assess patients with suspected myocardial

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ischemia, determine viability, and evaluate patients with low-flow low-gradient aortic stenosis. Knowledge of the pharmacologic stressors and adjunctive agents used, as well as imaging protocols and pitfalls in acquisition can improve image quality and enhance diagnostic accuracy.

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