Methods for Assessment of Left Ventricular Systolic Function in Technically Difficult Patients with Poor Imaging Quality

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The assessment of left ventricular (LV) systolic function is often the most important information obtained during clinical echocardiography. Although LV systolic function may be visually estimated in many patients with or without contrast opacification, technically difficult patients may require alternative methods for evaluating LV systolic function. In this review, the authors describe several surrogate echocardiographic methods that might be helpful for the evaluation of LV systolic function in patients with poor image quality, including endocardial border delineation by contrast agents, mitral annular plane systolic excursion, mitral annular velocity derived from tissue Doppler, systolic time intervals, mitral regurgitation–derived LV dP/dt, and estimation of cardiac output by Doppler echocardiography. After a short introduction to the various issues involved, the authors propose a method for suitable measurement. In addition, indications and clinical implications, as well as limitations, of the different methods are discussed. (J Am Soc Echocardiogr 2013;26:105-13.)

Keywords: Poor image quality, Contrast echocardiography, Mitral annular plane systolic excursion, Doppler echocardiography, Tei index

As one of the most widely used diagnostic examinations in cardiology, echocardiography has been routinely used for diagnosing and monitoring patients with suspected or known cardiovascular disease. In daily clinical echocardiography, left ventricular (LV) systolic function can be correctly assessed using various echocardiographic imaging methods in the majority of patients. However, the assessment of LV systolic function remains a challenge in a small proportion of patients with poor image quality, caused mainly by obesity, lung disease, tachycardia, or cardiac translocation. The quantitative assessment of ventricular function in these patients is still difficult despite the use of transducers with variable frequencies and harmonic imaging as well as the application of various advanced echocardiographic techniques, such as strain rate imaging, speckle-tracking imaging, and three-dimensional echocardiography. Besides poor image quality, there are other situations that make the determination of LV systolic function difficult, such as in patients with atrial fibrillation, LV hypertrophy, or mitral regurgitation. The purpose of this review is to summarize the clinical applications and limitations of several echocardiographic methods that can be used to evaluate LV systolic function in patients with poor image quality.

CONTRAST ECHOCARDIOGRAPHY

Contrast echocardiography using ultrasound contrast agents plays an essential role in clinical diagnosis in patients with technically suboptimal echocardiographic images.

Contrast Agents

Contrast echocardiography involves the interaction of microscopic gas bubbles with ultrasonic waves to enhance the recognition of the blood pool and/or the blood-tissue interface. The first agents capable of left-heart contrast after intravenous injection (first-generation agents) were air bubbles stabilized by encapsulation (Albunex; Molecular Biosystems, Inc., San Diego, CA) or by adherence to microparticles (Leovist; Bayer Schering Pharma AG, Berlin, Germany). In second-generation agents, replacing air with a low-solubility fluorocarbon gas stabilized the bubbles (Optison, GE Healthcare, Waukesha, WI; Definity, Lantheus Medical Imaging, North Billerica, MA; SonoVue, Bracco Diagnostics Inc., Princeton, NJ), further increasing the duration of the contrast effect. The aforementioned agents are untargeted microbubbles, and targeted microbubbles are presently in preclinical development.

Implementation of Contrast Agents

Details of the implementation of contrast agent, including joint training of physicians, sonographers, and nurses, have been introduced in recent guidelines. Briefly, contrast enhancement is indicated in difficult-to-image patients at rest when echocardiographic image
Optimization and Clinical Applications

The mechanical index reflects the output acoustic power. Standard clinical echocardiography imaging uses a mechanical index of about 1.0, but a lower setting (<0.6) is usually optimal for LV opacification during contrast echocardiography to avoid bubble destruction. Common causes of setting artifacts include inadequate focus position, inadequate ultrasound transmit frequency, and excessivereceive gain. Tissue signals in the left ventricle may not be distinguishable from the contrast signals, because of inadequate contrast dose (the so-called anticontrast effect) and can be avoided by injecting a slightly larger contrast dose. Attenuation is particularly problematic in parasternal windows, in which dense opacification of the right ventricle may obviate visualization of the left ventricle, and can be prevented by using apical views, in which attenuation is lowest and usually subsides by waiting for contrast washout. Attenuation can also be caused by rapid infusion or high-concentration contrast agent. Instead of a bolus, continuous slow infusion and slow flush are recommended. Swirling artifacts may result from high mechanical index, high frame rate, insufficient contrast agent, or LV dysfunction with low flow at the apex. Moving the focus position toward the base may help avoid attenuation and swirling. Adjusting the transducer position along the rib space or holding respiration during image acquisition can help reduce chest wall artifacts and wall motion artifacts.

Contrast agent use is particularly valuable for the evaluation of LV structure and function in difficult-to-image patients with reduced image quality for rest or stress echocardiography. It can improve endocardial visualization and the assessment of LV structure and function and quality does not permit the adequate assessment of cardiac structure and function. Specifically, contrast enhancement for stress echocardiography is not recommended for all patients but should be considered on a case-by-case basis, depending on image quality. To ensure quality control and maximize benefit to patients, the American Society of Echocardiography recommends that contrast echocardiography be performed by appropriately trained cardiac sonographers and physicians with level 2 or level 3 training in laboratories that have been successful in establishing contrast agent use.

Safety and Limitations

A large number of studies have proved that contrast echocardiography is safe in clinical practice. A large retrospective analysis of 18,000 patients showed that there was no significant difference in mortality between patients who received contrast and those who did not in the acute setting. However, serious allergic reactions have been observed at a very low incidence (1 in 12,000 to 1 in 15,000). As shown in the updated guidelines on the safety of echocardiographic contrast agents of the US Food and Drug Administration in June 2008, contraindications to perflutren-containing ultrasound contrast agents (Definity and Optison) include (1) right-to-left, bidirectional, or transient right-to-left cardiac shunts; (2) hypersensitivity to perflutren; and (3) hypersensitivity to blood, blood products, or albumin (Optison only). Additional contraindications include acute myocardial infarction, worsening or unstable heart failure, serious ventricular arrhythmias or high risk for arrhythmia, respiratory failure, severe emphysema, pulmonary emboli, or other conditions that cause pulmonary hypertension.

MITRAL ANNULAR PLANE SYSTOLIC EXCURSION

LV longitudinal shortening is a sensitive parameter reflecting cardiac pump function and can be evaluated by measuring long-axis mitral annular plane systolic excursion (MAPSE). The measurement of M-mode-derived MAPSE does not require high imaging quality, because of the high echogenicity in the ativoventricular annulus.

Measurement

MAPSE can be measured from four sites of the ativoventricular plane corresponding to the septal, lateral, anterior, and posterior walls using the apical four-chamber and two-chamber views on M-mode echocardiography. In healthy hearts, the values of lateral MAPSE are usually somewhat higher than those of septal MAPSE. Mondillo et al also demonstrated that MAPSE was lower at the septum and anterior wall in comparison with the lateral and inferior levels in healthy middle-aged individuals. The M-mode cursor should be aligned parallel to the LV walls. The systolic excursion of the mitral annulus should be measured from the lowest point at end-diastole to aortic valve closure (the end of the T wave on the electrocardiogram; Figure 2).

Clinical Implications

The average normal value of MAPSE derived from previous studies for the four annular regions (septal, anterior, lateral, and posterior) ranges from 12 to 15 mm. MAPSE < 8 mm was associated with a depressed LV EF (<50%), with specificity of 82% and sensitivity of 98%. Mean MAPSE ≥ 10 mm was linked with preserved EF (=55%), with sensitivity of 90% to 92% and specificity of 87%. In addition, mean MAPSE < 7 mm could detect an EF < 30% with sensitivity of 92% and specificity of 67% in patients with dilated cardiomyopathy with severe congestive heart failure. A recent study by Matos et al showed that MAPSE measurement by an untrained observer was a highly accurate predictor of EF determined by an expert echocardiographer.

Limitations

The association between MAPSE and EF is valid only in normal or dilated left ventricles, whereas the correlation is rather poor in patients with LV hypertrophy. Another limitation of this parameter is that small localized abnormalities (i.e., small areas of fibrosis) cannot be detected, because MAPSE can evaluate only the longitudinal function of the entire LV wall and is unable to evaluate segmental function.
Doppler tissue imaging (DTI) has become an established component of the diagnostic ultrasound examination. This technique detects low-velocity frequency shifts of ultrasound waves to calculate myocardial velocity. DTI offers the promise of an objective measure to quantify regional and global LV function through the assessment of myocardial velocity data. The velocity traces can be extracted from the basal segments of the left ventricle in most patients, even when the overall image quality is bad. The decrease in systolic velocity on pulsed DTI correlated significantly with both

**Figure 1** Noncontrast (A) and contrast (B–D) images of a giant left ventricular aneurysm at the posterior wall as a complication of prior myocardial infarction. The vague left ventricular apex and anteroseptum (A) became clear after contrast administration (D). The contrast agent entered the left atrium (LA) (B), left ventricle (LV) (C), and then the left ventricular aneurysm cavity (D).

**Figure 2** MAPSE measurement. (A) MAPSE is measured by M-mode echocardiography in the apical four-chamber view. (B) Pulsed Doppler recording of mitral inflow. (C) MAPSE. (D) Pulsed Doppler recording of aortic outflow. (E) Electrocardiogram. MAPSE should be measured from the lowest point to the highest point during systole.

**MITRAL ANNULAR VELOCITY DERIVED FROM TISSUE DOPPLER**

Doppler tissue imaging (DTI) has become an established component of the diagnostic ultrasound examination. This technique detects low-velocity frequency shifts of ultrasound waves to calculate myocardial velocity. DTI offers the promise of an objective measure to quantify regional and global LV function through the assessment of myocardial velocity data. The velocity traces can be extracted from the basal segments of the left ventricle in most patients, even when the overall image quality is bad. The decrease in systolic velocity on pulsed DTI correlated significantly with both
systolic shortening \((r = 0.90)\) and regional myocardial blood flow \((r = 0.96)\) in patients with reduced coronary blood flow.\(^{31,32}\)

**Measurement**

The measurements of systolic mitral annular velocity \((Sm)\) should be taken at the peak of myocardial systolic velocity, in accordance with recent guidelines.\(^{33}\) In the apical four-chamber view, the DTI cursor should be placed at the septal side of the mitral annulus in such a way that the mitral annulus at the septum moved along the sample volume line. In normal myocardium, a Doppler velocity range of \(-20\) to \(20\) \(\text{cm/sec}\) is recommended to avoid aliasing. As shown in Figure 3, three major velocities can be recorded: the positive systolic velocity when the mitral ring moves toward the apex \((Sm)\) and two negative diastolic velocities when the mitral annulus moves away from the apex (one during the early phase of diastole \([Em]\) and another in the late phase of diastole \([Am]\)). By moving the sample volume to the lateral site of the mitral annulus, systolic and diastolic velocities of the LV lateral wall can be recorded. These velocities can be extracted by pulsed-wave tissue Doppler and in addition also by color tissue Doppler. It is important to note that color tissue Doppler data are mean data, and extracted velocities are approximately \(20\%\) lower than the pulsed-wave tissue Doppler velocities. Pulsed tissue Doppler–derived \(Sm\) measurement is more often used in daily practice. Pulsed tissue Doppler–derived \(Sm\) was significantly lower at the septum \((8.3 \pm 1.7 \text{ cm/sec})\) than at the inferior \((9.5 \pm 1.9 \text{ cm/sec})\) and lateral \((9.9 \pm 2.4 \text{ cm/sec})\) levels in healthy middle-aged individuals.\(^{23}\)

**Clinical Implications**

Tissue Doppler data can be rapidly acquired in almost all patients for the estimation of global LV function.\(^{32}\) Mitral annular velocity is also a quite sensitive indicator for inotropic stimulation–induced alterations in LV contractility.\(^{34}\) LV function assessment by mitral annular velocity on DTI is valuable especially when endocardial delineation is suboptimal.\(^{35}\) Ruan and Nagueh\(^{36}\) showed that \(Sm\) had the best correlation with LV EF \((r = 0.65, P < 0.03)\), and \(Sm < 7 \text{ cm/sec}\) was the most accurate parameter in identifying patients with LV EFs < \(45\%\) (sensitivity, \(93\%;\) specificity, \(87\%\)).\(^{36}\) \(Sm\) was also a strong predictor of cardiac mortality or rehospitalization for worsening of chronic heart failure in patients with LV dysfunction.\(^{37}\) Nikitin et al.\(^{38}\) found that DTI-derived \(Sm < 2.8 \text{ cm/sec}\) was associated with worse survival in patients with chronic heart failure and LV EFs < \(45\%\).

**Limitations**

DTI only quantifies myocardial motion. It cannot differentiate whether velocities are caused by active or passive movement, so global cardiac motion and tethering effects of adjacent myocardium may result in “false” velocity increases of dysfunctional segments.

**SYSTOLIC TIME INTERVALS**

Systolic time intervals can provide useful information concerning the performance of the left ventricle.\(^{39-41}\) Thus, isovolumetric contraction time, pre-ejection period (PEP), LV ejection time (ET), and the PEP/LV ET index have been studied extensively as measures of cardiac systolic function.\(^{42}\) More recently, a combined myocardial performance index (termed the Tei index, the sum of isovolumic contraction time and isovolumetric relaxation time divided by LV ET) was introduced and serves as a clinically useful parameter for analyzing global cardiac function. The longer the isovolumetric phases, the higher the Tei index and the worse the ventricular perfor-

![Figure 3](image_url) Mitral annular velocity derived from TDI. In the apical four-chamber view, the DTI cursor is placed at the septal side of the mitral annulus in such a way that the mitral annulus at the septum moves along the sample volume line. Three major peak velocities can be recorded: the positive systolic velocity \((Sm)\) when the mitral ring moves toward the apex and two negative diastolic velocities when the mitral annulus moves away from the apex (one during the early phase of diastole \([Em]\) and another in the late phase of diastole \([Am]\)).

**Clinical Implications**

The Tei index appears to have close correlation with the widely accepted systolic and diastolic hemodynamic parameters\(^{51,52}\) as well as
potential for clinical application in the assessment of overall cardiac performance. The index has been proposed as a useful method for the evaluation of global LV performance in congestive heart failure, congenital heart diseases, and valvular heart disease and for monitoring interventional therapies. Furthermore, the Tei index has been shown to have strong prognostic value in severe cardiac diseases, such as dilated cardiomyopathy, cardiac amyloidosis, and myocardial infarction. Patients with cardiac amyloidosis with higher Tei indexes (>0.77) have a higher overall and cardiac-related mortality risk than patients with lower values (<0.77). A prognostic study by Saso et al. suggested that a Tei index > 0.70 was the only significant explanatory factor for cardiac death or developing congestive heart failure in patients with acute myocardial infarction after successful primary angioplasty. Møller et al. investigated 799 patients with acute myocardial infarctions and followed them for a median of 34 months, finding that patients with Tei indexes > 0.68 had a fourfold increase in mortality compared with those with Tei indexes < 0.46.

Limitations
Data from large-scale epidemiologic studies regarding the application and the clinical impact of the Tei index are lacking. One major limitation of the pulsed Doppler Tei index is that both relaxation and contraction velocities cannot be measured simultaneously within one cardiac cycle, whereas DTI enables the measurement of both relaxation and contraction velocities simultaneously. Pulsed Doppler Tei index is therefore not feasible in patients with variable beat-to-beat duration, as in atrial fibrillation, frequent supraventricular and ventricular extrasystole, atrioventricular conduction abnormalities, and significant atrial tachycardia. In addition, the Tei index should not be used in patients with ventricular pacing and in those with intraventricular dyssynchrony.

Estimation of Left Ventricular dP/dt
The rate of pressure rise in the ventricles (dP/dt) is a good index of ventricular performance that is sensitive to changes in contractility and insensitive to changes in afterload but can be mildly affected by changes in preload. The clinical utility of dP/dt has been limited, however, by the fact that its measurement conventionally requires the insertion of an intraventricular catheter. The estimated mean rate of pressure change (dP/dt) in pre-ejection systole from the mitral regurgitation continuous-wave Doppler tracing has been used as a non-geometric index of LV systolic function. A number of studies have confirmed a good correlation between Doppler-derived non-invasive LV dP/dt and catheter-derived invasive dP/dt.

Measurement
Continuous-wave Doppler tracings of mitral regurgitation velocity curves are needed for the measurement of LV dP/dt. The flow direction of the mitral regurgitation must be detected by color Doppler imaging using an apical window in which the sample volume should be positioned correctly with minimal angulation at the level of the annulus. It is important to note that in eccentric significant mitral regurgitation, it may be difficult to record the full envelope of the jet because of its eccentricity. Mean LV dP/dt is commonly calculated by measuring the time required for the mitral regurgitation jet to increase in velocity from 1 to 3 m/sec during the isovolumetric contraction time, which reflects a 32 mm Hg change during this time period between the left ventricle and the left atrium, derived from the modified Bernoulli equation (Figure 5). The average normal value of mean LV dP/dt from the Doppler regurgitant velocity spectrum is >1,200 mm Hg/sec (≈32 msec). A value < 1,000 mm Hg/sec was associated with reduced LV function.

Clinical Implications
LV dP/dt is less influenced by afterload, wall motion abnormalities, or the variations in ventricular anatomy and morphology commonly encountered in patients with congenital heart disease. It is more
related to myocardial contractility than chamber performance. LV dP/dt can be used to determine alterations in myocardial contractility in patients with congestive heart failure, and mitral regurgitation can be detected in the majority of patients with congestive heart failure.

The major advantage of this Doppler method is that it provides a non-invasive estimation of LV dP/dt on a beat-by-beat basis, which makes it ideal for serial measurements in patients with congestive heart failure with mitral regurgitation. Kolias et al. found in patients with chronic congestive heart failure with reduced LV EFs that LV Doppler-derived dP/dt < 600 mm Hg/sec was associated with lower event-free survival compared with dP/dt \( \geq 600 \) mm Hg/sec.

**Limitations**

A complete, well-delineated velocity spectral envelope from mitral regurgitation is mandatory for accurate measurements of instantaneous pressure gradients. As with any Doppler velocity measurement, the ultrasound beam should be aligned parallel to the velocity vectors of the mitral regurgitation flow to prevent underestimation of the pressure gradients. Careful scanning is necessary to obtain maximal velocity spectra. Additionally, the full envelope of the mitral regurgitation jet is sometimes difficult to obtain in eccentric significant mitral regurgitation, which may limit the use of measuring LV dP/dt in patients with eccentric mitral regurgitation.

**ESTIMATION OF CARDIAC OUTPUT BY DOPPLER ECHOCARDIOGRAPHY**

The Doppler technique enables the noninvasive determination of LV stroke volume (SV) and cardiac output (CO), which might be useful in identifying and projecting trends for cardiac function. Doppler-estimated CO correlates well with invasive estimation using a thermodilution pulmonary artery catheter.

**Measurement**

SV and CO are calculated as follows (Figure 6): CO (L/min) = SV (mL) \times \text{heart rate (beats/min)} / C^2 \times \text{velocity-time integral (cm)}.

The velocity-time integral is obtained by tracing the envelope of the peak velocity detected throughout systole. The cross-sectional area of the region of the heart from which the blood flow velocity was extracted is calculated from its diameter (area = \( \pi r^2 \)). The preferred site for determining SV and CO is the LVOT. LVOT diameter is measured in the parasternal long-axis view in midsystole from the white-black interface of the septal endocardium to the anterior mitral leaflet, parallel to the aortic valve plane and within 0.5 to 1.0 cm of the valve orifice. LVOT velocity is recorded with pulsed Doppler, because the blood flow velocity in the LVOT needs to be extracted to obtain the velocity-time integral, whereas accurate estimates of the location of the source of a Doppler shift in a patient are difficult to achieve with continuous-wave Doppler. The largest of three to five measurements should be taken, because the inherent error of the tomographic plane is to underestimate the LVOT diameter. The normal range of CO is 4.0 to 8.0 L/min. It is important to note that the correct measurement of LVOT is essential for correct CO determination. In some cases, variations in cardiac anatomy and orientation may not permit parallel alignment of the Doppler beam with the LVOT in the proposed plane, which can result in underestimation of the true CO.

**Clinical Implications**

For patients in the intensive care unit, the ultrasonic determination of CO is likely to be supplementary rather than a replacement for invasive methods. It may be used to screen potential candidates for invasive monitoring. Because the technique is noninvasive, measurements can be repeated as often as necessary, making it suitable for studying serial CO changes in individual subjects. Other areas of possible application include early hemodynamic monitoring in patients after myocardial infarction or with decompensated heart failure and intraoperative hemodynamic monitoring in noncardiac operations.
overestimation of CO. Additionally, it should be noted that SV at rest may be normal or even increased in dilated hearts with impaired systolic function. Thus, SV may not accurately reflect overall systolic LV function in patients with dilated hearts.

CONCLUSIONS

In general, most of the methods described here are either dependent on movement of the mitral annulus from the base toward the apex of the left ventricle (MAPSE and Sm) or based on Doppler methods that rely on ultrasound scattering rather than specular reflection from targets that are (optimally) oriented perpendicular to the direction of the ultrasound beam. These methods take advantage of recording motion relative to the apex (along the axis of the ultrasound beam), which is still feasible even when B-mode image quality is not good. Contrast echocardiography is not only based on the scattering of incident ultrasound at a gas-liquid interface to increase the strength of returning signal but also takes advantage of microbubble oscillations that can be detected using harmonic imaging.

The methods described here are useful for evaluating LV systolic function in patients with unsatisfactory image quality. Contrast echocardiography is certainly the best method for defining LV systolic function, but this method requires appropriately trained cardiac sonographers and physicians in laboratories that have been successful in establishing contrast agent use. MAPSE is a simple method and can assess longitudinal function of the complete LV walls, but it cannot detect small localized myocardial abnormalities. Other methods (Tei index, pulsed-wave Doppler-derived CO, dP/dt, DTI) are based on Doppler techniques and can be used to assess LV systolic function even in case of poor endocardial delineation. It is essential for echocardiographers to be aware of the merits and limitations of individual methods when choosing practical techniques for individual patients to achieve the optimal measurement of LV systolic function in daily practice.

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