Techniques for comprehensive two dimensional echocardiographic assessment of left ventricular systolic function

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The quantitation of left ventricle (LV) volumes and ejection fraction is an important aspect of cardiac evaluation in all cardiac disorders. Prognosis in many types of heart disease is closely related to global left ventricular ejection fraction (LVEF), falling off rapidly as the ejection fraction falls below 40% (fig 1). However, although ejection fraction has the advantage of being a simple numerical parameter that reflects LV function, it is strongly influenced by loading conditions and does not correlate well with symptom status. Perhaps more importantly, although two dimensional (2D) ejection fraction is meaningful when applied across populations or to stratify risk in individuals, its value as a sequential test within individuals is constrained by limited test−retest reliability.

GLOBAL FUNCTION ASSESSMENT BY 2D ECHOCARDIOGRAPHY

Subjective assessment

Whatever the limitations of subjective assessment, the reality is that echocardiographic assessment of global left ventricular systolic function is usually performed subjectively. Moreover, the eye of an experienced observer is comparable to trackball measurements.[1] The situations where this approach can be misleading are when the rhythm is irregular (when examining a long tape run rather than individual cine loops is essential), the LV size is very large or very small, and at the extremes of heart rate.

Measurement of ventricular volumes and ejection fraction

Two dimensional echocardiography approaches for calculation of LV volumes have largely superseded M mode echocardiography techniques that used geometric assumptions based on the minor dimension of the ventricle. A number of 2D approaches have been described (table 1),[2–4] some using more sophisticated geometric assumptions. With each of these methods, once volumes have been measured, ejection fraction is simply measured as (LVEDV − LVESV)*100/LVEDV.

Modified Simpson's rule

This method is based on disc summation, analogous to examining a stack of coins.[5] Provided a sufficient number of discs are measured, this method will overcome non-geometric bulges in the longitudinal axis, although the technique is not truly ''non-geometric'', as each disc is expected to be circular, ignoring the dimension in other than the measured plane. The definition and calculation of each disc is automatically performed by the ultrasound machine software after the sonographer defines the central axis of the LV cavity and traces the borders. Biplane data acquisition (apical four and two chamber views) is desirable in order to overcome this, although this is sometimes not possible because of inadequate endocardial resolution of the anterior wall or foreshortening in the apical two chamber view. The usual rule is that views should not be combined if the chamber length calculations are different by > 20%.

Area−length method

This method is appropriate in symmetrical LV cavities and is usually applied using the apical four chamber view. The volume is derived from the area of the LV squared, divided by length and multiplied by 0.85, to reflect the non-cylindrical shape of the apex. This has a number of shortcomings related to non-geometric LV shapes and remodelling (which may change the LV shape from a cylinder to a sphere).

Geometric methods

These involve some combination between the shape in the short axis view and ventricular length, or combined geometric figures including combinations of cylinders, truncated cones, and cones. These have been superseded by the high feasibility of the Simpson's method.

Volumetric approaches

Although the results with 2D echo have been useful for categorising risk within populations, the limited test−retest reproducibility of 2D imaging poses problems for the application of this test on a sequential basis within an individual. The topic of 3D imaging is outside the ambit of this review, but it should be recognised that more accurate and reproducible measurements have been obtained using three dimensional (3D) techniques.[6] Previously, 3D echocardiography was constrained by the need to reconstruct a 3D dataset from a number of 2D images, identified in direction and position relative to a fixed frame of reference. Recently, real time 3D imaging has become available, and in conjunction with offline edge detection programs (fig 2) it is likely that this approach will become the standard for LV volume and ejection fraction measurement with echocardiography.[7 8]

Exercise ejection fraction

While also out of the remit of this review, exercise 2D echocardiography may be useful for the identification of subclinical LV dysfunction—for example, in valvar heart disease. In this situation, standard measurements (including Simpson's rule) have been used to measure the LV contractile reserve.[9]

Abbreviations: BNP, type B natriuretic peptide; CAD, coronary artery disease; EBCT, electron beam computed tomography LV, left ventricle; LVEF, left ventricular ejection fraction; SPECT, single photon emission computed tomography

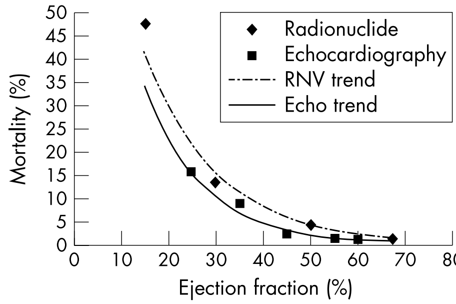

Figure 1 Mortality after measurement of ejection fraction by radionuclide ventriculography (one year follow up, Multicentre Post-infarction Research Group, 1983) and after 2D echo measurement of ejection fraction (six month follow up, GISSI study 1993). Note the close correlation of the curves, allowing for the difference in follow up between the two cohorts.

Table 1 Normal values of LV volumes by 2D echocardiography. Variation of ejection fraction is 7–10%[2–4]

	Men	Women	95% CI
Biplane Simpson's			
EDV	111 (22)	80 (12)	11%
ESV	34 (12)	29 (10)	15%
Area length (A4C)			
EDV	112 (27)	89 (20)	15%
ESV	35 (16)	25 (12)	25%
Area length (A2C)			
EDV	130 (27)	92 (19)	
ESV	40 (14)	31 (11)	

Values are mean (SD)
CI, confidence interval; EDV, end diastolic volume, ESV, end systolic volume.

Load independent techniques

Assessment of LV systolic function is usually performed in order to gather insight about the contractile state of the left ventricle. The problem is that performance is dependent on not only contractile state but also load. Thus, while image quality and geometric assumptions pose important practical limitations on the use of 2D echo ejection fraction as a clinical tool, the major limitation is the dependence of ejection fraction on loading conditions and heart rate (fig 3). There are two ways of addressing this: to measure afterload and preload in order to correct the ejection fraction, or to try to measure contractility independent of loading.

Measurement of load

Load determines wall stress (σ), which is defined by force over each unit of cross sectional area; this force being determined by pressure (P). Afterload is reflected by systolic wall stress. Cuff systolic pressure may overestimate LV systolic pressure (due to wave reflection), so some authors have used mean arterial pressure, which is usually equivalent centrally and peripherally. As LV diastolic pressure cannot be accurately determined non-invasively, wall stress parameters cannot be used to measure preload, the closest analogue of which is diastolic volume.

Meridional stress relates to the load posed by long axis shortening (that is, base−apex), and is calculated as $\sigma m = P \times LVID/[4 \times Th(1 - LVID/Th)]$, where P (pressure) is approximated to systolic blood pressure, LVID (cavity dimension) is end systolic dimension, and Th is average wall thickness.[10] Circumferential stress reflects stress in the minor axis; $\sigma c = P \times a^2[1 + (b^2/r^2)]/(b^2 - a^2)$, where a is the internal radius, b is the epicardial radius, and r is the midwall radius.[11] Both stress measurements can be measured with dimensions acquired with 2D echo, or using areas from 2D echo.

Load corrected parameters

All clinical parameters of LV function are load dependent. The problem with trying to isolate contractility is that alterations of loading result in length dependent changes in contractility, independent of the Frank-Starling mechanism.

LV midwall shortening expresses the stress shortening relation of the ventricle. The use of midwall shortening is less dependent on LV geometry than are endocardial measurements.

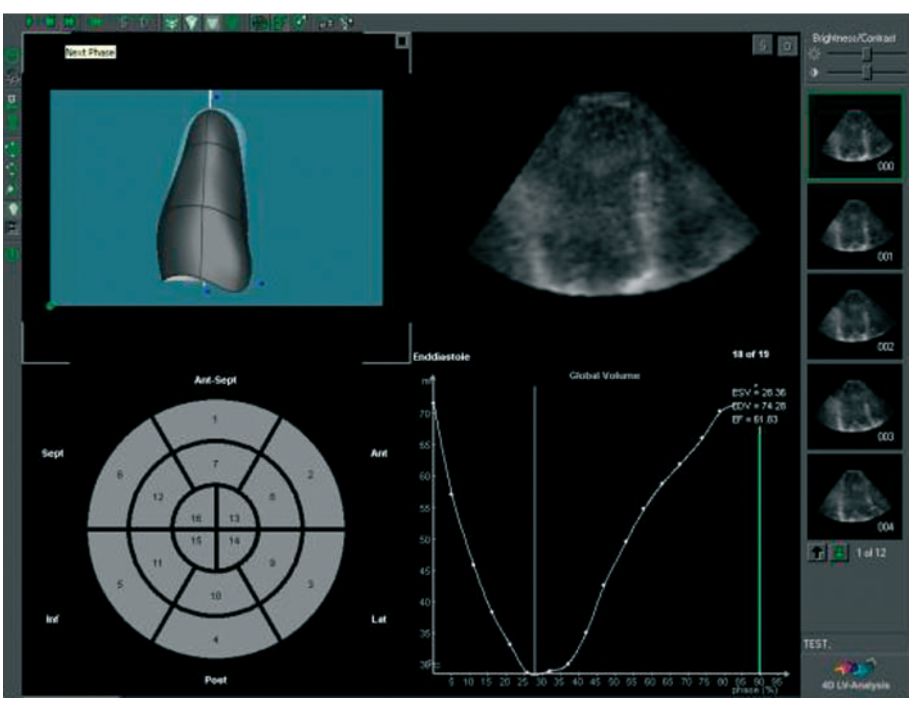

Figure 2 Three dimensional (3D) echocardiographic evaluation of left ventricular (LV) volumes and ejection fraction. Images from a volumetric dataset are reconstructed (upper centre and right column) and semi-automated edge detection is used to trace the endocardial border and construct a 3D model in systole and diastole (upper left). Expression of volumes in each image yields a time−volume curve (lower left) from which ejection fraction is calculated.

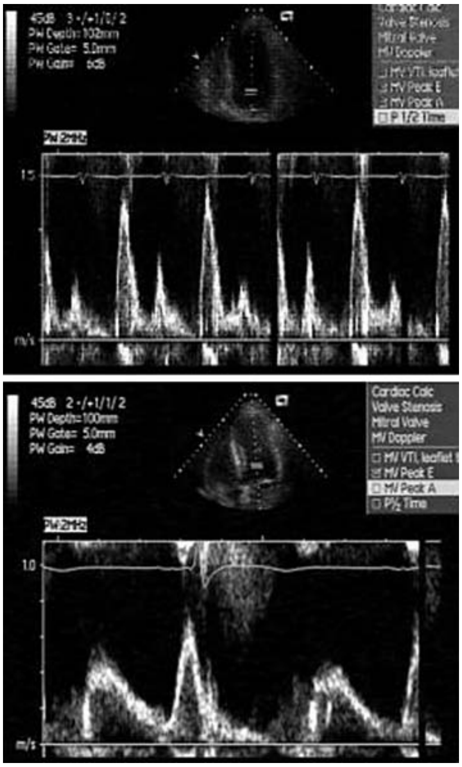

Figure 3 Dependence of LV volumes and standard Doppler indices of diastolic function on loading conditions. This patient with renal failure was studied before (above) and after dialysis (below). LV size and LV filling patterns are altered by loading.

Pressure–volume loops are the standard approach to expressing the association between loading and inotropic state. The end systolic pressure–volume relation is drawn in a sequence of these curves under different inotropic states, to generate end systolic elastance. Other authors have charted LV wall stress against LV dimension.[12] An increase in the slope of this curve reflects increasing contractile state, and a decrease corresponds to depressed contractility. The development of automated LV volume measurement techniques has been used to apply this approach non-invasively,[13] but the AQ technique has some limitations related to image quality and beat-to-beat variations of LV volume may be large, reflecting the impact of different cut planes with respiration, for example. This approach has therefore not been widely applied for clinical research.

Preload recruitable stroke work has been used in animal models for over 15 years.[14] These investigators found that the relation between stroke work and end diastolic segment length or chamber volume (termed the preload recruitable stroke work relation) was highly linear. This contrasts with the use of filling pressure as the marker of preload, when a curvilinear function is obtained that plateaus at higher filling pressures.[14] The problems of using this clinically are in accurately measuring stroke work (which requires accurate knowledge of central aortic pressure) and LV volume (the limitations of 2D echo for which are discussed above), and for altering loading without altering inotropy—in experimental settings, these steps have included balloon occlusion of the vena cava. For practical reasons, this technique has not attained everyday use.

Alternative and less load dependent measures include the peak systolic pressure–end systolic volume ratio[15] and cardiac power.[16]

Cardiac power correlates with Vo_2max and predicts prognosis, but has previously been measured invasively. Mean power is calculated from the product of stroke volume, mean arterial pressure, and heart rate, and peak instantaneous power is the peak instantaneous product of left ventricular outflow and pressure during systole.[16 17] Either parameter may be derived using Doppler echocardiography to measure stroke volume, and 2D echocardiography is used to calculate ''preload adjusted'' power (corrected for end diastolic volume).[18] Nonetheless, this is not strictly a 2D echocardiography technique.

Complementary techniques

Doppler may be used to measure LV ejection. However, the measurement of stroke volume is dependent on the accuracy of LV outflow tract measurement, errors of which are squared in the course of volume calculations. The measurement of LV dP/dt is a relatively load independent marker of LV contractility, which is especially valuable in mitral regurgitation, when contractility may be overestimated by the ejection fraction. The myocardial performance index is derived from the sum of the isovolumic contraction time and isovolumic relaxation time, divided by the ejection time. This measurement is reproducible, easily obtainable, and correlated closely with invasive measures of both systolic and diastolic function.[19] It appears to be independent of geometry, although it remains somewhat load dependent. Finally, tissue Doppler techniques have the benefit of being less dependent on image quality than 2D imaging, and do not require tracing; both annular displacement[20] and average velocity[21] have been correlated with ejection fraction.

REGIONAL FUNCTION ASSESSMENT BY 2D ECHOCARDIOGRAPHY

Subjective assessment

The qualitative evaluation of LV systolic function is based on the division of the LV into a number of segments, after which each segment is scored as normal, hypokinetic, akinetic, or dyskinetic. The main problems pertain to the distinction of hypokinesia from akinesia. We judge akinesia to be present when endocardial excursion is < 2 mm, and hypokinesia with endocardial excursion < 5 mm. However, movement may be passive, and thickening is the more reliable marker of contractility.

The standard 16 segment model of the American Society of Echocardiography (septal, lateral, anterior, and inferior at the apex, with these segments as well as anteroseptal and posterior segments at the base and mid papillary muscle level) (fig 4) is likely to remain in widespread use because the suggested 17 segment model (which includes a true apical segment) ignores the small but important detail that most echocardiograms fail to identify the true apex of the heart. Our laboratory uses a modification of the American Society of Echocardiography segmentation.[22] With this, a score of 1 is given for normal regions, with scores of 2, 3, and 4 for hypokinesis, akinesis, and dyskinesis, 5 for aneurysm, and 6 and 7 for akinesis or dyskinesis with thinning, respectively. The wall motion ''score index'' (obtained by averaging the scores of individual segments), gives a semi-quantitative index of global systolic function, analogous to the ejection fraction and with similar prognostic significance.[23]

Regional wall motion scoring is highly reproducible within individual sites,[24] reflecting common reading styles. However, reproducibility of wall motion assessment between centres may be quite limited, especially during stress 2D echo.[25] Concordance may be improved with the use of standard reading criteria[26] and harmonic imaging.[27] While it is unlikely that echocardiographers will stop visually assessing the LV, an objective measure that supplemented this assessment

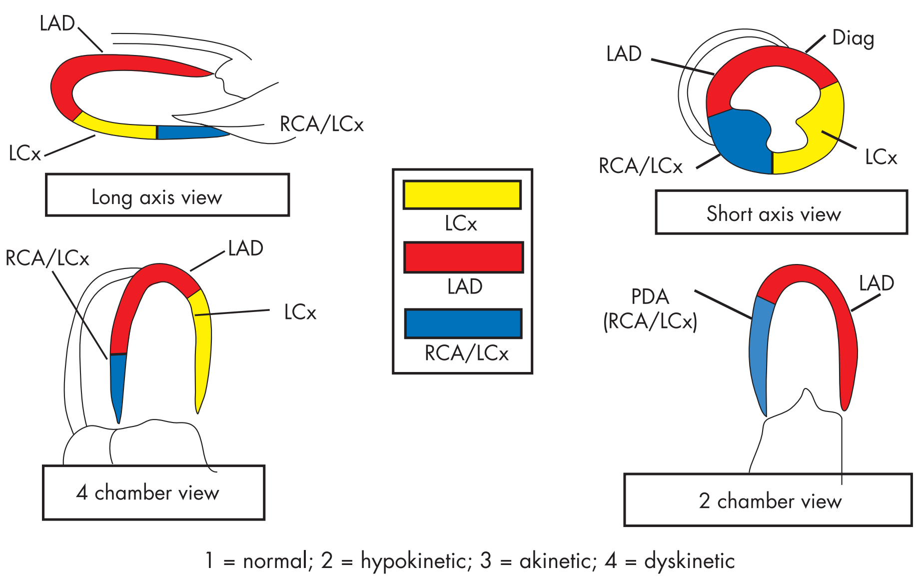

Figure 4 The 16 segment American Society of Echocardiography model for characterisation of regional LV function, and usual coronary artery distribution of the segments. Reproduced from: Marwick TH. Stress echocardiography – its role in the diagnosis and evaluation of coronary artery disease. Boston: Kluwer Academic Publishers, 2003, with permission of the publisher.

with objective criteria could act as a "common language" to reduce variation between readers.

Objective assessment

A number of echo and Doppler modalities are able to offer quantitation of regional function,[28] and most are outside the remit of this review (table 2). The 2D echo based techniques include techniques for assessing radial displacement (using the centre line method or colour kinesis) or thickening (anatomical M mode).

Centre line method

This method is based upon three steps: tracing the LV end diastolic and end systolic borders; superimposition of the traces with interpolation of the centre line; and measurement of the excursion from this line in a series of chords perpendicular to the centre line, which can be compared to a normal range of displacement. Each step poses potential pitfalls.

Tracing of contours, preferably in two orthogonal planes (usually apical four and two chamber views) is dependent on good quality border definition, and the reliance on apical views may compromise edge detection because of the parallel orientation of the echocardiographic beam with the endocardium. Although good border definition has become more available with the development of harmonic and contrast imaging, tracing the edge may still need an element of guesswork. More than a single frame may need to be traced at both systole and diastole, making the procedure time consuming, although automated and semi-automated methods of tracking the wall have been developed (fig 5).

The superimposition of systole and diastole may have a critical effect on the measurement of excursion from the centre line. Either fixed or floating frames of reference can be used to compensate for rotational or translational movement of the heart.[29] Failure to correct for such movements may cause false positives, but the use of correction may hinder the detection of milder abnormalities. Finally, different variations of the technique measure the chords relative to the centre line or relative to the centre of LV mass.

Table 2 Alternative techniques for the quantification of regional LV function[28]

	Radial	Longitudinal
Displacement	Centre line (from 2D echo) Colour kinesis	Annular M mode Tissue tracking
Thickening	Anatomical M mode Integrated backscatter	
Velocity	Velocity from displacement Longitudinal velocity Tissue Doppler gradient	Tissue Doppler velocity Strain
Timing	Time to peak systole Time to onset of diastole	Time to peak systole Time to onset of diastole

Colour kinesis method

The colour kinesis method uses acoustic quantification to define the border, based on the difference in backscatter between the LV wall and cavity. This has the benefit of avoiding the onerous process of tracing the border in every frame, although the frame rate is somewhat limited, compared to standard 2D imaging. The excursion of the myocardium from each frame to the next is filled with a different colour, and the resulting display overlaid on the 2D image ("colour kinesis").[30] The displacement is portrayed as segmental area shrinkage,[31] and arranged in stacked histograms (fig 6), which can be compared to normal ranges. This approach has been particularly applied during stress echo, where it correlates with expert wall motion analysis and may be of value to less expert readers.[32]

This technique is heavily dependent on image quality, and appears to be more feasible with the use of myocardial contrast for LV opacification.[33] Measurements show a variation of 10–20%. As with any technique that measures endocardial motion, this is sensitive to extrinsic cardiac movement.

Anatomic M mode

Myocardial thickening is the optimal parameter for measurement, because unlike excursion, it is independent of cardiac rotation or translation. However, the measurement of thickening requires definition of both the endocardium and the epicardium—and the latter can pose a problem in the apical views. M mode ultrasound has conventionally been used for gathering wall thickening data, but has been constrained by the angle dependence of standard M mode imaging. Two dimensional images at high temporal and spatial resolution have been used to reconstruct M mode

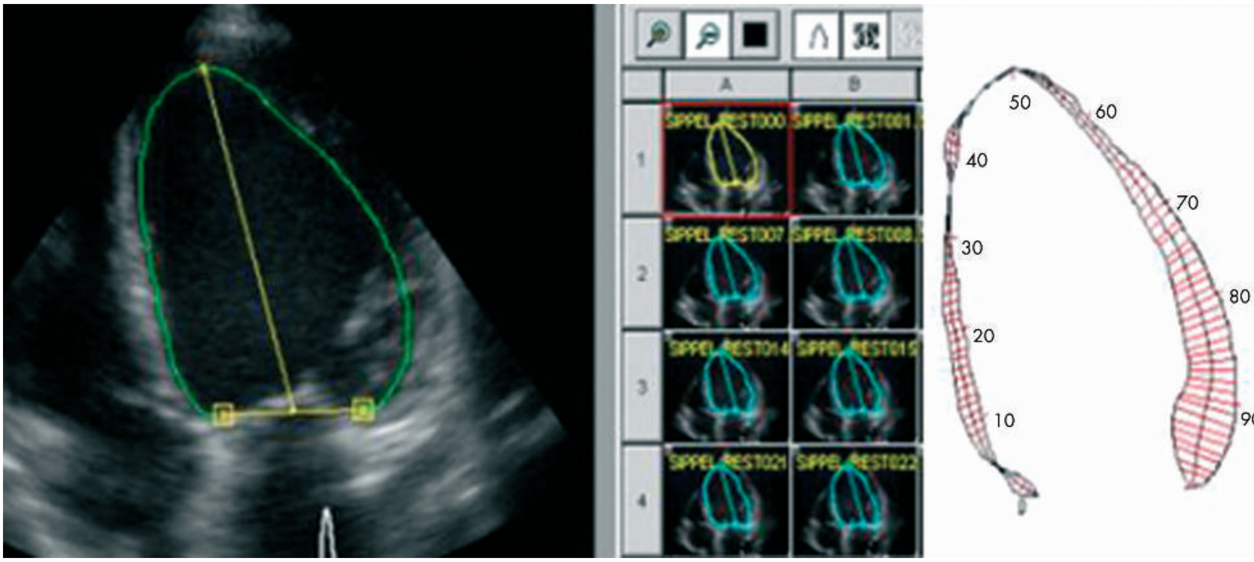

Figure 5 Centre line approach to quantification of regional LV function. Automated detection of the endocardial border is applied in each view (left), repeated in each frame (thumbprint images, centre), and regional excursion between end diastole and end systole is measured using the centre line method. Reproduced from: Marwick TH. Stress echocardiography – its role in the diagnosis and evaluation of coronary artery disease. Boston: Kluwer Academic Publishers, 2003, with permission of the publisher.

images in any plane ''anatomic M-mode'',[34] although caution has to be applied with angle corrections of > 60–70°.[35] The results correlate well with visual assessment but it has been difficult to designate a normal range, because of variations of baseline thickening,[34] and the clinical benefit of this approach is not well defined.

ALTERNATIVE APPROACHES

Two dimensional echocardiography remains the most widely accepted technique for assessment of LV systolic function, reflecting its versatility and ability to identify complications (for example, thrombi) and associated problems (for example, mitral regurgitation). Nonetheless, other modalities may represent alternatives or may even be used to select patients for 2D echo.

Clinical evaluation

The clinical signs of LV dysfunction are insensitive—for example, in 14 507 patients in the CASS registry, a third heart sound or crackles had a respective sensitivity of 9% and 5% for the detection of significant LV dysfunction on contrast ventriculography.[36] Part of this low sensitivity is caused by

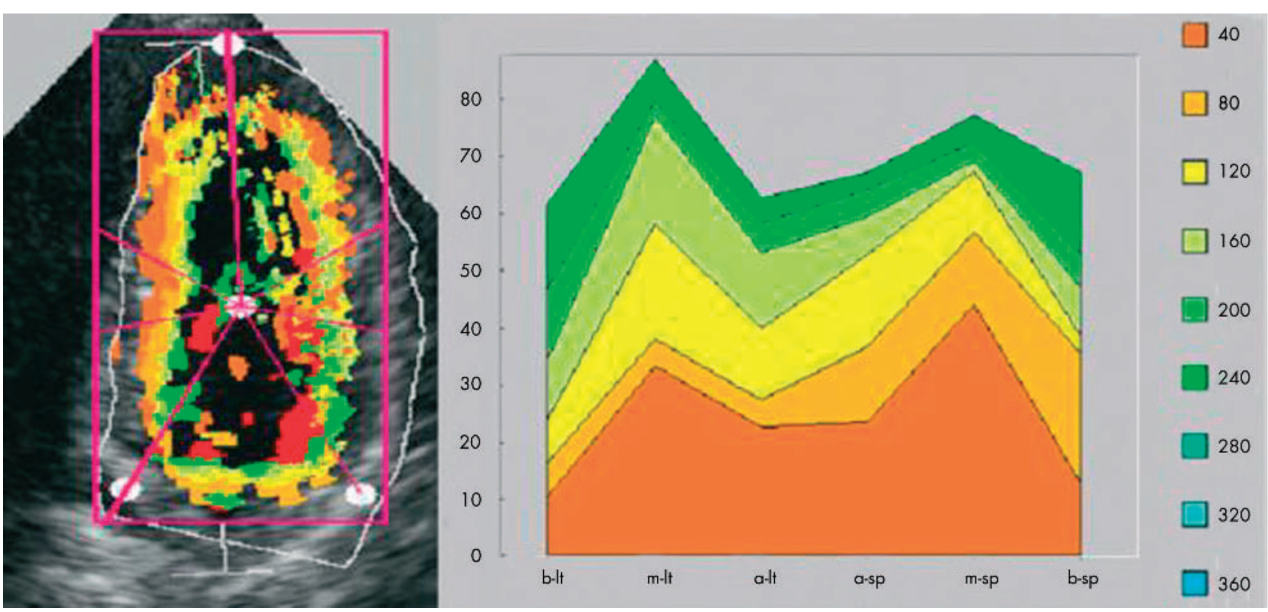

Figure 6 Quantitation of radial function using colour kinesis. Each successive ultrasound frame on the image (left) is coded with a different colour. The histogram (right) shows the fractional area change within each segment (x axis). Reproduced from: Marwick TH . Stress echocardiography – its role in the diagnosis and evaluation of coronary artery disease. Boston: Kluwer Academic Publishers, 2003, with permission of the publisher.

masking of the clinical signs by treatment. Moreover, the signs and symptoms of LV systolic and predominantly diastolic dysfunction are indistinguishable.

The limitations of the clinical exam are concerning from a health economy standpoint. Fortunately, the standard 12 lead ECG may be used to identify patients with possible LV dysfunction.[37 38] A completely normal ECG, or even narrow QRS complexes, has a high negative predictive value for excluding significant LV dysfunction.[39] Thus, a normal ECG could assist triage of patients referred for echocardiography.[40] Indeed, a normal cardiothoracic ratio measured in the posteroanterior chest *x* ray does not add significantly to the value of a normal ECG in predicting normal systolic function.[36]

Type B natriuretic peptide (BNP)

The clinical signs of LV dysfunction are insensitive, and the detection of LV dysfunction by echocardiography in all ''at risk'' patients is prohibited by cost and availability. Although BNP has been shown to be a useful marker of systolic dysfunction in symptomatic patients,[41] the ability of this test to act as a screening tool for subclinical disease appears limited.[42]

Nuclear ventriculography

Nuclear techniques include first pass ventriculography, equilibrium RNV (gated blood pool scanning), and gated single photon emission computed tomography (SPECT), during myocardial perfusion scanning with thallium-201 or Tc^{99m}-sestamibi.[43 44] After myocardial infarction, LVEF measured by these tests has been correlated with prognosis, in both the pre-thrombolytic[45] and thrombolytic eras,[46] and is incremental to clinical indicators of prognosis.[47] Reduction of exercise LVEF is an indicator of severe coronary artery disease (CAD),[48 49] but not a specific marker of CAD.[50] Nonetheless, peak exercise LVEF by gated SPECT provides incremental prognostic value to SPECT perfusion imaging.[51]

Computed *x* ray tomography

Electron beam computed tomography (EBCT) permits precision measurement of cardiac structure and function, from images acquired during a single cardiac cycle. EBCT has been validated against contrast ventriculography[52] and radionuclide ventriculography.[53] There are limited data using EBCT derived LV function to predict cardiac risk in clinical practice. Conventional CT has previously lacked the spatial or temporal resolution to permit measurement of LV volumes and function, but ECG gating and other developments have made this more feasible.

Cardiac magnetic resonance imaging (MRI)

Cine MRI has excellent temporal and spatial resolution, and image plan reproduction is much higher than with 2D echo because it can image in any plane. Cardiac MRI has become the in vivo ''gold standard'' for LV volumes and function assessment, and has been validated against contrast ventriculography,[54] radionuclide ventriculography[55] and echocardiography.[56] The excellent test–retest reliability of this technique has enabled much smaller sample sizes for research studies with MRI than 2D echo,[57] but its use as a routine clinical tool is constrained by cost, availability, and expertise.

CONCLUSION

Despite its limitations, 2D echocardiography remains the most widely used non-invasive technique for clinical assessment of LV systolic function, and is likely to remain so because it is non-invasive, inexpensive, and widely available. LV systolic measurements are dependent on loading conditions, and assessment of loading should be considered in the interpretation of ejection fraction. Problems with accuracy and reproducibility of volumes and ejection fraction pertain largely to the geometric challenges of 2D imaging, and are likely to be solved by 3D approaches.

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