Echocardiographic evaluation of systolic heart failure

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Abstract Echocardiography is the most commonly used modality for evaluating left ventricular size and function in the context of systolic heart failure. Traditional techniques, though extensively used, have their limitations and more recently several newer technologies have emerged that are more reproducible, provide prognostic information, guide therapies and have an important role in monitoring progress. This review will evaluate the traditional and more novel techniques used and briefly provide an overview of the role of echocardiography in guiding and monitoring therapies in patients with systolic heart failure.

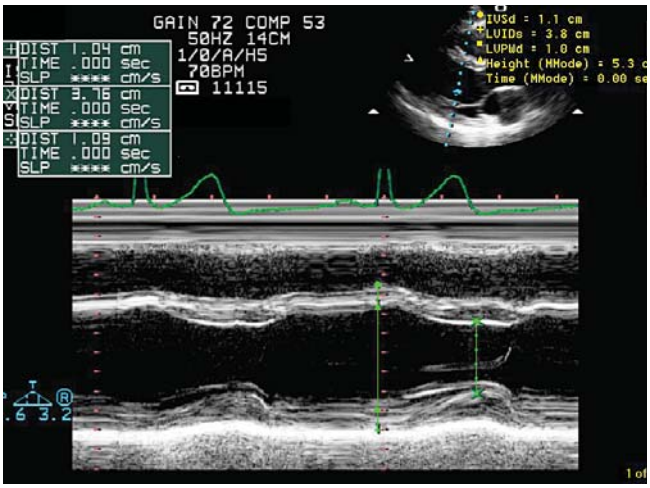

Fig. 1: M-mode echocardiogram of the left ventricle showing septal and posterior wall thickness as well as LV end diastolic and LV end systolic diameters.

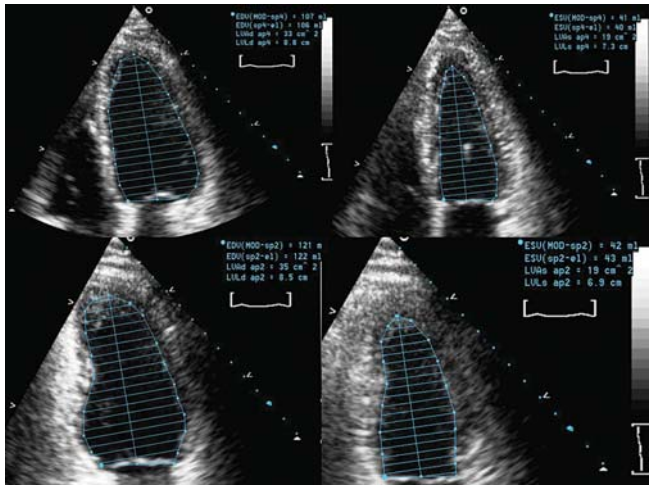

Fig. 2: Apical 4 chamber (top panel) and 2 chamber (bottom panel) modified biplane method of discs measuring LV end diastolic and end systolic volumes.

Introduction

Heart failure (HF) is a global health problem, with an estimated 15 million symptomatic patients worldwide[1]. In 2001, 300,000 Australians had chronic HF with 30,000 new cases diagnosed yearly [2]. HF was the third largest cause of death in 2002[3] while deaths associated with HF accounted for 8.3% of circulatory deaths[4]. Current guidelines emphasise the importance of early identification of HF patients for initiation of therapy, thereby containing health care costs[5]. Echocardiography, according to ACC/AHA guidelines is "the single most useful diagnostic test in the evaluation of patients with HF" [6]. This article addresses the utility of echocardiography in systolic HF, with discussion of traditional and newer techniques of assessment.

Traditional measurements

M mode

Left ventricular (LV) volumes, ejection fraction (EF) and fractional shortening can be measured by M-mode (Fig. 1) but are only applicable to a symmetrical heart without regional abnormality. Current American Society of Echocardiography (ASE) guidelines recommend two-dimensional (2D) LV volume and EF quantification discouraging M-mode measurements that rely on geometric assumptions to convert linear measurements to volumes[7].

2-dimensional LV volumes

2D LV end systolic (LVESV) and end diastolic volumes (LVEDV), indexed LVESV (LVESVI) are important predictors of outcome. Current ASE guidelines recommend the modified biplane method of discs for LV volume and EF quantification from apical 4 and 2 chamber views [7] (Fig. 2), but measurements rely on image quality and inherently underestimate LV volume. However, the V-HeFT [8], SOLVD [9]and Val-HEFT [10,11] trials have shown the close association of these parameters with morbidity and mortality.

White, *et al*.[12] showed that LVESVI was an independent predictor of survival and hospitalisation after acute myocardial infarction (AMI), while from the Heart and Soul study, LVESVI was an independent predictor of hospitalisation in patients with stable coronary heart disease (CHD)[13]. From the multicentre BEST study[14], LVEDVI was a predictor of adverse outcome in advanced HF. Reproducibility of 2D measurements is a problem with a test-retest variability of 11%, inter-observer and intra-observer variability of 5% and 3% respectively[15].

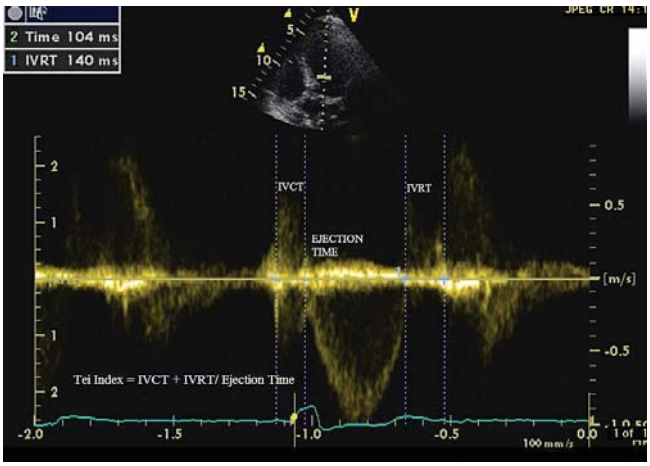

Fig. 3: Tei index calculated as IVCT + IVRT/Ejection time use Doppler.

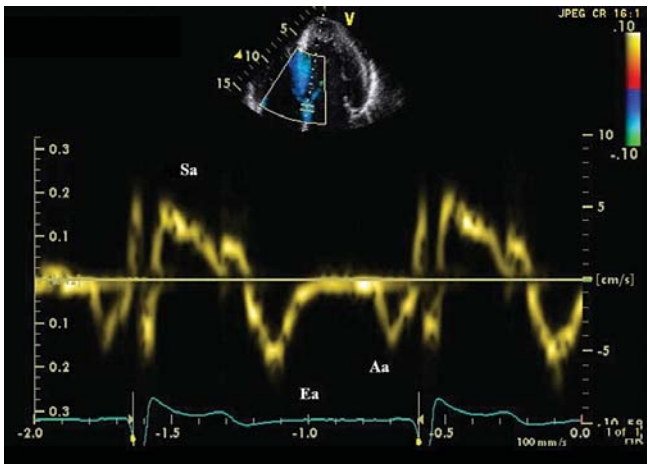

Fig. 4a: Pulse wave tissue Doppler imaging from the septal mitral annulus demonstrating the systolic Sa and diastolic Ea and Aa velocities.

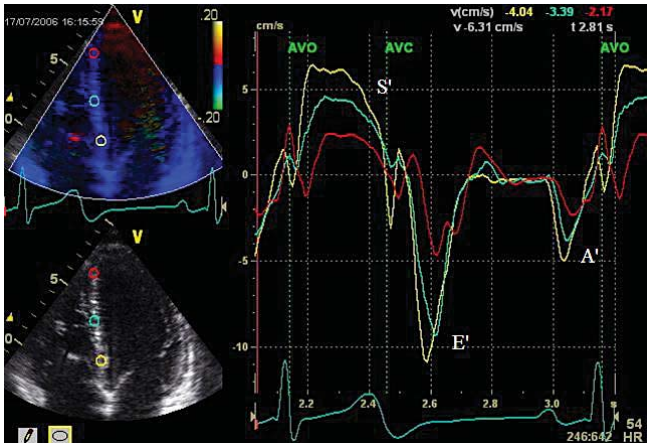

Fig. 4b: Colour tissue Doppler imaging with the offline curves obtained demonstrating the systolic S′ and diastolic E′ and A′ velocities.

LV ejection fraction

LVEF is a parameter of global systolic function that provides a numeric interpretation for the diagnosis and therapeutic guidance in HF management and for device implantation. Despite the fact that LVEF does not correlate with HF symptoms, exercise capacity or myocardial oxygen consumption[16], it remains a powerful prognostic marker for future cardiac events, especially post AMI[17]. Curtis, *et al*. examined the relationship of LVEF to clinical outcomes in 7,788 stable HF patients[18] and a higher LVEF was associated with a linear decrease in mortality. Additionally, an LVEF < 35% was the bench mark for intra-cardiac defibrillator (ICD) implantation based on the MADIT I trial[19].

Wall motion abnormality

The ASE advocates the use of a 17 segment model, dividing the LV into three levels (basal, mid and apical) with further subdivision into six segments at the basal and mid level and 4 segments at the apical level and a single segment at the apex to produce 17 segments. A wall motion score index (WMSI) can be derived by grading segmental dysfunction severity (normal = 1, hypokinesis = 2, akinesis = 3, dyskinesis = 4)[20]. WMSI and LVEF for risk stratification after an AMI[21] demonstrated that both were powerful predictors of all-cause mortality, with WMSI being an independent predictor of death and HF hospitalisation.

Ischaemic mitral regurgitation

Ischaemic mitral regurgitation (MR) is functional regurgitation consequent to infarction with structurally normal leaflets and subvalvar apparatus. Leaflet motion is restricted with apical displacement of the coaptation zone, causing incomplete systolic closure of the mitral valve or "systolic tenting"[22]. Ischaemic MR results from complex alterations of spatial relationships between the LV and mitral apparatus[23] and a recent study confirmed that MR severity is related to systolic tenting and not LV dysfunction[24]. Ischaemic MR occurring early or late after AMI is associated with increased mortality[25,26], and severe MR portends poor prognosis[27,28]. Transthoracic echocardiography (TTE) enables analysis of the mechanism and severity of MR, and transoesophageal echocardiogram (TOE) is only occasionally necessary. The quantification of ischaemic MR differs from organic MR[26] with thresholds for severe ischaemic MR being 30 mL for regurgitant volume and 20 mm^2 for ERO, compared with 60 ml and 40 mm^2 respectively, in organic MR[26,29].

Tei Index

The myocardial performance index, or Tei index, reflects global performance incorporating both systolic and diastolic function. The Tei index is the ratio of the sum of isovolumic contraction and relaxation times to the ejection time, with these parameters obtained from Doppler assessment (Fig. 3). The Tei Index is independent of heart rate, blood pressure, does not rely on geometric assumptions, is highly reproducible[30] and correlates with invasively measured LV dP/dt[31]. The Tei Index has prognostic value in various patient cohorts[32] and an index > 0.77 proved superior to LVEF in predicting death[33]. Other studies have shown its value in prediction of HF in an elderly cohort[34] as well as predicting lack of treatment response in patients with HF[35].

Newer parameters and application

Newer echocardiographic techniques utilising tissue Doppler imaging (TDI) and strain (S) and strain rate (SR) imaging are more robust and reproducible, providing quantitative assessment of global and regional function.

Tissue Doppler imaging

TDI uses low-velocity, high amplitude myocardial velocity signals[36] and is obtained by pulsed Doppler (Fig. 4a) or colour Doppler (CTDI) (Fig. 4b) function[37]. CTDI acquires tissue velocity information from the entire sector and thus multiple sites can be interrogated simultaneously and analysed offline. Pulsed Doppler measures peak velocity and

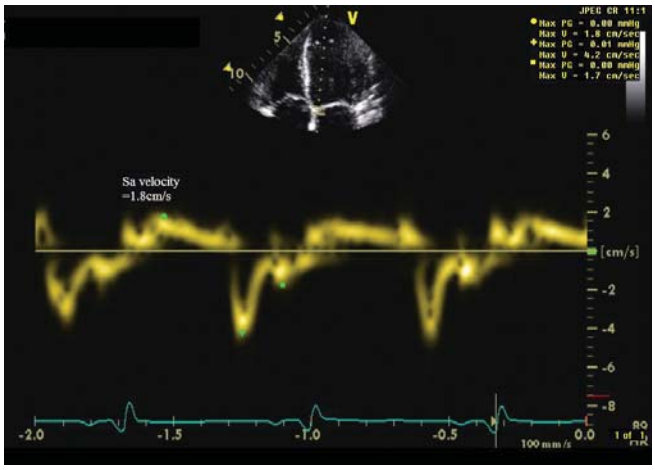

Fig. 5: Pulse tissue Doppler imaging from the septal mitral annulus in a patient with ischaemic cardiomyopathy. Note the significant decrease in Sa velocity correlating with the systolic dysfunction.

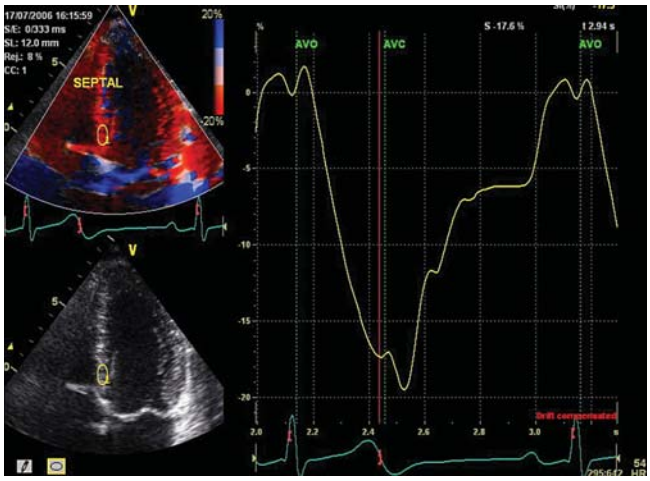

Fig. 6a: Ventricular strain trace obtained with sample volume placed in the basal ventricular septum.

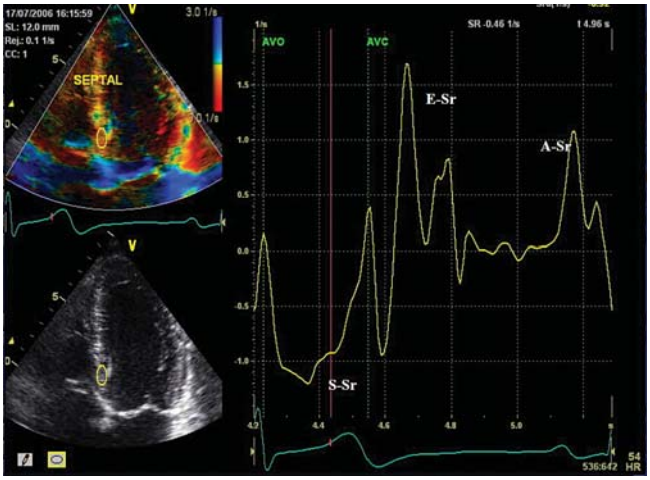

Fig. 6b: Ventricular strain rate trace obtained with sample volume placed in the basal ventricular septum demonstrating systolic S-Sr and diastolic E-Sr and A-Sr.

is ~20–30% higher than the mean velocity measured by CTDI[38].

TDI has been validated extensively in a variety of cardiac pathologies including HF[39], AMI[40], hypertension[41], diabetes[42] and in stress echocardiography[43] where TDI systolic velocities are used as an adjunct to WMSI[44]. The peak systolic septal annular (Sa) or basal septal segmental velocity (Sm)

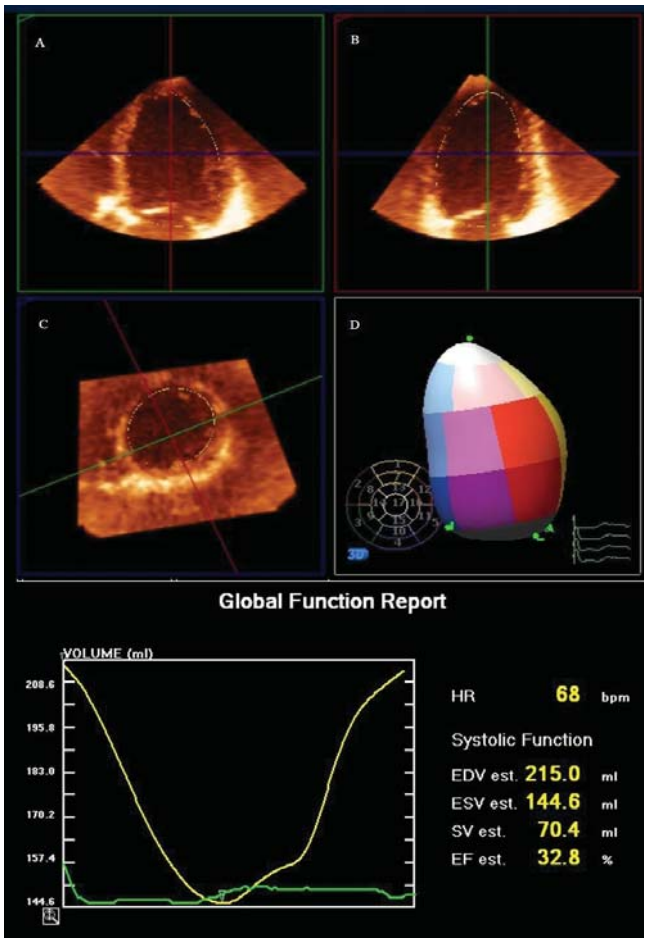

Fig. 7: Real time 3-dimensional echocardiography demonstrating LV contour tracing in the two apical and parasternal short axis views (panels A-C). Panel D demonstrates the 3D LV volume and the bottom panel demonstrates graphically, LV volume change over the cardiac cycle.

is a sensitive marker of impaired LV systolic function, even in those with a normal LVEF[45]. Sm velocity is a predictor of outcomes and in patients with cardiac disease, mortality was higher when Sm was < 3 cm/s[46]. In HF patients, CTDI Sm velocity and diastolic arterial pressure were independent predictors of outcome[47].

Strain and strain rate

Strain (S) is a measure of tissue deformation, defined as the change in length normalised to the original length, whilst strain rate (SR) measures the rate of deformation[48] (Figs. 5a, 5b). Strain imaging is derived from TDI[49] and more recently from 2D myocardial speckle-tracking[50]. Unlike TDI measurements, S and SR are not subjected to cardiac tethering[51,52]. Normal ranges for S and SR have been described[53], and while S is influenced by increasing age, pre-load and after-load, SR is less load dependent. S and SR can detect subclinical disease in hypertension[54] and diabetes[55] as well as infiltrative myocardial disease[56], correlates with myocardial fibrosis[57] and has been used to evaluate therapeutic response[58]. S and SR have been used in stress echocardiography[56]. SR correlates with myocardial perfusion during dobutamine stress[59] and is superior to TDI in detecting CAD[60]. S and SR are reduced in ischaemia/infarction with augmentation in viable segments[61].

Diastolic parameters

Several diastolic parameters such as deceleration time and

Table 1: Strengths and weaknesses of various echocardiographic techniques.

Parameter	Utility	Strengths	Limitations
M-Mode	• Part of standard TTE assessment • Available on all U/S systems	• Easy to perform	• Relies on geometrical assumptions • Off axis imaging • Dependent on image quality
2D volume (biplane modified Simpsons method)	• Assess global LV function • Used to monitor therapy	• Powerful prognostic marker of outcomes in HF and CAD	• Underestimates volume due to inherent foreshortening • Dependent on image quality • Lacks reproducibility
Ejection fraction (biplane modified Simpsons method)	• Estimates global systolic function • Widely used • Guides medical, device therapy	• Powerful prognostic marker for future cardiac events in HF and post AMI	• Poor correlation with HF symptoms or ex capacity • Load dependent • Dependent on image quality
Wall motion score index	• Semiquantitative score of segmental dysfunction	• Easy to perform • Predictor of death and hospitalisation post AMI	• Requires adequate visualisation of all segments • Visualisation of lateral segments problematic
Tei Index	• Reflects global performance • Incorporates systolic and diastolic function	• Independent of HR, BP • Highly reproducible • Prognostic value in HF	• Less accurate in atrial fibrillation and pacing • Partial preload dependence
TDI	• Estimates myocardial velocity signals	• Independent of 2D quality • Prognostic in cardiac disease • Detects subclinical LV dysfunction	• Subject to cardiac tethering • Less accurate in AF, pacing • Requires TDI soft ware
Strain/ Strain rate	• Measures tissue deformation and its time course	• Independent of tethering • Detects subclinical disease • Correlates with fibrosis • Viability /ischaemia with stress echo	• Strain age and load dependent • Technically difficult and time consuming • Currently mainly research tool
Dyssynchrony	• Multiple techniques	• Quantitative monitor for CRT	• Modest correlation to CRT benefit
Real time 3D	• Acquires full volume data set • Global and regional quantification	• Eliminates geometrical assumptions • Identifies true LV apex • Low intra/inter observer variability	• Not readily available/ accessible • Time consuming with offline analysis

AMI = acute myocardial infarction, AF= atrial fibrillation, BP = blood pressure, CAD = coronary artery disease, CRT= cardiac resynchronisation therapy, HR = heart rate, HF = heart failure, LV = left ventricular, TDI = tissue Doppler imaging, TTE = transthoracic echocardiogram, U/S = ultrasound.

restrictive filling[62] and decreased diastolic TDI velocities[63] are associated with poor prognosis in systolic HF. An E/Ea > 15 is a powerful prognosticator for adverse cardiac events[64] and is an independent predictor of cardiac mortality and HF hospitalisation[65]. However, these diastolic parameters will not be discussed in this current review.

Dyssynchrony

Uncoordinated ventricular motion or "mechanical dyssynchrony" is often present with LV dysfunction and is associated with a prolonged QRS complex. However, not all patients with a wide QRS complex exhibit dyssynchrony[66]; 30–50% of patients with a narrow QRS complex may have echocardiographic dyssynchrony that benefits from cardiac resynchronisation therapy (CRT)[67,68]. Echocardiography is the most widely used modality for dyssynchrony and techniques include M-mode, TDI, speckle tracking, and real-time 3D echocardiography (RT3DE).

The simplest method for evaluating dyssynchrony is M-mode analysis of posterior wall to septal delay with ≥ 130 ms predicting HF improvement with CRT[69]. Pulsed-wave TDI is performed on line and generally considered more difficult and time-consuming. CTDI is most commonly used and measures time from QRS onset to peak systolic velocity (TPSV). Bax and colleagues defined dyssynchrony as the maximum difference in TPSV between the four basal (anterior, inferior, septal, lateral) segments[70] and TPSV difference of 65 ms had a sensitivity and specificity of 80% for predicting reduction in death and HF hospitalisation. Yu, *et al*. developed a 12-segment model involving six basal

and mid segments from the three apical views and deriving the standard deviation (SD) between the 12 measurements, thereby creating a dyssynchrony index[71]. A SD ≥ 32 msec identified dyssnchrony and correlated with a favourable CRT response[72,73]. Similarly, speckle tracking can assess dyssynchrony[74] as also RT3DE that examines the time to minimum systolic volume (TMSV)[75,76].

LV torsion

LV twist or torsion describes the wringing motion of the LV and represents the net difference in clockwise and counterclockwise rotation of the LV apex and base[77]. Torsion occurs because of the varying orientation of the myocardial fibres; subendocardial fibres have a longitudinal orientation (~80°) relative to the mid-wall where the fibres are circumferentially orientated (0°), and changes to an oblique orientation (-60°) subepicardially[78].

During isovolumic contraction, the LV apex shows brief clockwise rotation that reverses rapidly and becomes counterclockwise during LV ejection[79,80], followed by untwisting (clockwise rotation) during early diastole. In contrast, rotation of the base is lower in magnitude and opposite in direction. Torsion is a function of LV contractility and varies linearly with EF[81] while "untwisting" correlates with the relaxation time constant (τ)[82]. Both TDI and speckle tracking can measure torsion and correlate with MRI[83,84]. Twist mechanics can be applied in disease states; in hypertension, diastolic LV untwisting was delayed and reduced in parallel to the severity of LV hypertrophy[85], while in AMI patients, apical LV twist was severely depressed[86].

Real time 3D echocardiography

RT3DE employs matrix array transducers that acquire real time full volume data sets[87]. The recently validated RT3DE volumetric quantification of global and regional LV function[88] overcomes limitations of 2D echocardiography as it eliminates geometric assumptions, identifies the true LV apex and evaluates wall motion encompassing all planes[89]. Jenkins, *et al*.[90] demonstrated the correlation of RT3DE to MRI with lower intra and inter observer variability, whilst comparing it to computed tomography, Sugeng, *et al*.[91] have shown its superiority in LVEF and volume measurement. RT3DE can assess LV dyssynchrony and demonstrated a greater improvement from CRT with RT3DE guided LV lead placement[92]. RT3DE is superior in ischaemic MR quantification as it visualises the true vena contracta and proximal flow convergence[93] especially with eccentric MR.

Role of echocardiography in therapeutic intervention

Echocardiography has a valuable role in guiding and monitoring HF therapies as discussed below.

Medical therapy

Current ACCF/AHA HF guidelines[6], recommend ACE inhibitors for patients with current or prior symptoms of HF and reduced LVEF while beta-blockers are recommended in stable patients (level A evidence). The addition of an aldosterone antagonist is recommended in patients with moderate to severe HF. In the SOLVD echo substudy[94], Enalapril significantly reduced LV volumes and mass while Carvedilol decreased LV volumes and increased LVEF in the ANZ HF Collaborative Group[95]. The Val-HeFT echo substudy[10] showed similar changes in LV dimension and LVEF with valsartan therapy. Aldosterone antagonists (Spironolactone and Elprenone) have shown mortality reduction in NYHA class III and IV HF patients with EF ≤ 35%[96] and in post AMI patients with EF ≤ 40%[97].

By the same token, echocardiography can be used to monitor the deleterious effects of cardiotoxic medications such as anthracycline chemotherapy[98], and treatment can be discontinued based on reduction in LV function.

Cardiac resynchronisation therapy

Cardiac resychronisation therapy (CRT) has emerged as a therapy for advanced HF patients on optimal medical treatment that favourably affects symptoms, hospitalisation and mortality rate[99,100]. A meta-analysis confirmed a 30% decrease in hospitalisations and mortality benefit (24–36%)[101] with LV reverse remodelling, improved EF and reduced MR predicting improved survival[102]. Current guidelines[103] recommend CRT for patients on optimal medical therapy with EF ≤ 35%, in NYHA class III or IV with QRS ≥ 120 ms although a subgroup of patients with QRS < 120 ms can benefit from CRT[104]. Single centre studies of CRT response in HF found that improvement was more likely in patients with echocardiographic dyssynchrony at baseline[70,105,106]. However, two multicenter studies, the PROSPECT[107] and ReThinQ trials[108], used echocardiographic criteria for patient selection and found only modest correlation between echocardiographic indices and CRT benefit. Additionally, a consistent finding from CRT trials, is a lack of benefit in approximately one third of patients (CRT nonresponders)[109].

ICD implantation

In HF patients with reduced EF and previous cardiac arrest, ICD has shown mortality benefits despite optimal medical therapy. The AVID[110], CIDS[111] and CASH[112] trials established that ICD improved survival compared with antiarrhythmic agents for secondary prevention of sudden cardiac death (SCD). Other randomised, multicentre studies including MADIT I[19] and II[113], MUSTT[114] and the SCD-HeFT[115], established ICD therapy as effective for primary prevention of SCD in selected patient populations. The LVEF cut offs used in these trials were < 40% in MUSTT, < 35% in MADIT I and SCD-HeFT and < 30% in MADIT II. Based on these trials, present guidelines[116] recommend an echocardiographic LVEF 30–40% for ICD implantation in specific patient groups.

Many patients eligible for CRT also meet criteria for ICD implantation. The COMPANION trial demonstrated the benefit of combined therapy with CRT and ICD over optimal medical therapy in patients with LVEF ≤ 35% with prior hospitalisation for HF[117].

Correction of ischaemic MR/ MV surgery

Ischaemic MR following an AMI is associated with increased mortality as demonstrated in the CADILLAC trial[118] where those with MR had higher mortality rates at 30 days and at one year. A similar increase in mortality over the longer term (five years) with ischaemic MR was reported[26]. Ischemic MR also predicts the development of HF in AMI patients with a little or no symptoms at base-

line[119] and HF risk with moderate to severe MR was ~50% at two years in one series[120].

Evaluation of ischaemic MR is integral to post AMI assessment, particularly if surgical revascularisation is being considered[121]. Echocardiography both peri- and intra-operatively can assess the mechanism and severity of MR and provide information as to the suitability for valvuloplasty or replacement. Intra-operative TOE tends to downgrade MR severity as a consequence of altered loading conditions under anaesthesia[122]. Mitral valve repair rather than replacement should be attempted in experienced centres[123,124]; however, the advantages of valve repair must be weighed against technical expertise and MR recurrence.

Conclusion

The evolving echocardiographic technologies have made it an indispensable modality of non-invasive cardiac imaging in the assessment of systolic HF providing information for diagnosis, quantification, therapeutic decision making and for monitoring treatment response. Newer echocardiographic modalities such as TDI, speckle tracking, twist mechanics, as well as RT3DE hold promise for improved accuracy of LV function assessment that would translate into benefits for HF patients by improved clinical care.

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