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3D transthoracic echocardiography for left ventricular assessment- ready for prime time?

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Take Home Messages

- 3D transthoracic echocardiography (3D TTE) is as accurate as cardiovascular magnetic resonance (CMR) to derive left ventricular ejection fraction (LVEF).
- 3D TTE LVEF has lower inter- and intra-observer variability than 2D LVEF.
- 3D TTE LVEF has utility for patients who require serial imaging (i.e. recipients of cardiotoxic chemotherapy).
- 3D stress echocardiography results in more rapid acquisition and analyses of data when compared with 2D.

Introduction

Two-dimensional (2D) transthoracic echocardiography (TTE) has been pivotal in the surveillance and management of a number of cardiovascular conditions including heart failure (1), coronary artery disease (2) and valvular heart disease (3). The accuracy of left ventricular (LV) function assessment using 2D TTE has been questioned due to a number of limitations including geometrical assumptions, apical foreshortening, operator subjectivity and poor endocardial definition (4). Cardiac magnetic resonance imaging (CMR) has been considered a gold-standard to assess LV systolic function and cardiac chamber volumes (5,6). However, its use has been limited due to high cost, low availability and logistical barriers (e.g. claustrophobia, long procedure duration, cardiac devices). Three-dimensional transthoracic echocardiography (3D TTE) is a promising alternative to combine the benefits of CMR and 2D TTE, whilst overcoming their limitations.

The development of fully sampled matrix array transducers, the ability to visualise real-time datasets and accessible post-processing packages has resulted in 3D TTE being more easily accessible and usable in the clinic. Notwithstanding this, the majority of departmental echocardiograms carried out today remain 2D with significant issues affecting the adoption of 3D assessment. In this editorial I will look at the utility of 3D transthoracic echocardiography for the assessment of left ventricular function.

Left ventricular assessment

Left ventricular assessment involves assessing regional contractility, wall thickness, end-diastolic and end-systolic volume, as well as the LV ejection fraction (LVEF). LVEF is calculated by dividing the volume of blood pumped from the left ventricle per beat by the volume of blood collected in the left ventricle at end diastole.

2D TTE ventricular assessment involves scanning the LV from multiple planes (parasternal long and short axis, apical 4-, 3- and 2- chamber views). The modified Simpson's rule for estimating LVEF util-

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-ises the assumption that the left ventricle is a series of discs derived from tracing endocardial contours on apical 2- and 4- chamber views. This may result in errors in the presence of regional pathology such as wall motion abnormalities and aneurysms.

Most modern echocardiography machines have 3D capability but require the purchase of a 3D probe. The 3D assessment of the LV is best carried out from the apical window. To minimise the risk of fore-shortening it is recommended to use the full-volume dataset to create standard 2D images corresponding to the cut planes in the apical-4, -3 and -2 chamber views. Software packages are offered by most vendors allowing for online or offline quantitative analysis. The advantages and disadvantages of 3D TTE are included in Table 1. Acquiring LV volumes is quicker with 3D TTE compared with 2D TTE, whilst the analysis takes longer with 3D TTE (7). The main steps involved in analysis include:

1. identification of specific landmarks such as the mitral ring and the LV apex;

2. segmentation of the volumetric dataset into 2D orthogonal views; and

3. manual correction of endocardial and epicardial borders (8).

Compare and contrast

3D TTE LVEF and volumes assessment has been reported to be accurate and reproducible when compared with cardiovascular magnetic resonance (CMR) in a myriad of pathologies and in healthy volunteers (7,9,10) or quantitative gated single-photon emission computed tomography in patients with coronary artery disease (11) and superior to 2D TTE (7,9–11). A meta-analysis of 23 studies, including 1638 TTE datasets, confirmed that 3D TTE is superior to 2D TTE but underestimated volumes when compared with CMR (12). Chukwo et al. (2008) report this phenomenon to be more likely in patients with larger end-diastolic volumes (13), possibly due to the fact that large ventricles may not fit within the probe's scanning sector and issues with accurate endocardial border detection (10). Despite this caveat, 3D TTE is superior to 2D TTE in providing better reproducibility and precision (12).

The use of intravenous contrast agents has been recommended to better delineate LV trabeculations and papillary muscles, as they are at times poorly visualised with 3D TTE (7,14). This is one of the reasons postulated for the underestimation of LV volumes with 3D TTE when compared with CMR, as with 3D TTE it may be difficult to differentiate between the endocardial border and trabeculations or papillary muscles. These are commonly excluded on LV volumes and LVEF estimation with CMR (7,14,15).

Besides being an accurate modality for LV ejection fraction (LVEF) estimation, 3D TTE derived LVEF has superior prognostic utility when compared with 2D LVEF according to two single centre studies (16,17). The first study reported that in 455 patients 3D LVEF had superior incremental value when compared with 2D LVEF in stepwise Cox regression analyses to predict all-cause death or cardiac hospitalisation at 6.6±3.4 years follow-up (16). The second study reported similar findings in 724 patients at 3.7±1.1 years follow-up (17).

There are a number of disadvantages associated with 3D TTE. The size of most 3D transducer probes is large and makes it challenging to avoid acoustic interference from the ribs. Recent advances have resulted in smaller probes being marketed by multiple vendors. 3D TTE has lower spatial and temporal resolution when compared with 2D TTE. Temporal resolution can be improved by using smaller sector widths and stitching (i.e. merging) the volumes together. Artefacts may be generated if the volumes that are merged together have differing R-R intervals (e.g. ectopic beats, atrial fibrillation).

Left ventricular mass

2D echocardiography derived LV mass is an independent predictor of cardiovascular events and mortality (18). 3D TTE derived LV mass compared well with CMR (19,20) than 2D TTE with stronger correlation with CMR than 2D TTE(19) , reduced bias using Bland-Altmann analysis than with 2D TTE (20). 3D TTE had lower bias and interobserver variability than 2D TTE in explanted hearts (21). Thus, 3D TTE has utility in assessing patients where the clinical question is if there is left ventricular hypertrophy (e.g. hypertension, hypertrophic cardiomyopathy, chronic kidney disease). No prognostic studies have been carried out to date with 3D TTE derived LV mass.

Table 1. Advantages and disadvantages of 3D Transthoracic echocardiography

Advantages	Disadvantages
Provides easily recognisable images.	Requires specific training to acquire and analyse.
A comprehensive and time-volume analysis of LV function can be obtained from a single 3D TTE dataset.	Arrhythmia makes 3D (multi-beat) acquisition challenging.
Avoids foreshortening associated with 2D TTE.	Limited by poor acoustic windows.
Measurements do not require geometric assumptions about shape.	Good image quality is required for accurate LV ejection fraction quantification.
LVEF assessment is accurate and reproducible compared to CMR.	Lower spatial and temporal resolution compared to 2D TTE.
Better reproducibility and precision compared with 2D TTE.	LV volumes underestimated compared to CMR.

CMR cardiac magnetic resonance, LV left ventricular, LVEF left ventricular ejection fraction, TTE transthoracic echocardiography.

Serial imaging in cardiovascular oncology

Serial imaging is recommended in recipients of cardiotoxic chemotherapy to identify a reduction in LVEF (22). 3D TTE has been reported to have lower test-retest variability (i.e. how close 2 repeated measures on the same subject are) than 2D TTE (12). In a longitudinal study in 56 patients 3D TTE LVEF was reported to be superior to 2D TTE (with or without contrast agents) for inter- and intra- observer variability or for serial imaging (repeated imaging every 6 months, 1 year, etc.) (23). In fact the 2016 European Society of Cardiology position paper on cancer treatments and cardiovascular toxicity (22) recommends 3D TTE for LVEF estimation, where available.

An interesting point is that whilst chemotherapy related cardiac dysfunction is defined as a decrease in the LVEF of 10% from baseline, to a value below the lower limit of normal; Thavendiranathan et al. (2013) reported that the minimal identifiable difference by 2D TTE (biplane method of LVEF estimation) is 9%, contrast use did not significantly alter this difference (9.8%) whilst 3D TTE LVEF was reported to have a minimal identifiable difference of 4.8%. This has important implications for echocardiography departments involved in following up oncology patients.

Post myocardial infarction

Two small studies (n=50 in each study) assessing post myocardial infarction patients demonstrated that 3D TTE LVEF was better correlated with CMR LVEF than 2D TTE (24,25). The authors concluded that if serial imaging was indicated 3D TTE was the preferred modality. Current guidelines recommend LVEF assessment to guide implantable cardioverter defibrillator therapy (e.g. 6-12 weeks post MI) (26) or mineralocorticoid receptor antagonists (2), however they do not specify which modality to use. These studies are hypothesis inducing, but more work is required to investigate the prognostic role of 3D TTE LVEF for outcomes and whether it is superior to 2D TTE LVEF.

Cardiac dyssynchrony and resynchronisation therapy

Cardiac dyssynchrony, characterised by a prolonged QRS duration (greater than 120 ms) on electrocardiography, can be assessed using echocardiography by measuring the time to maximal contraction of each cardiac segment (27). An advantage of 3D TTE is the simultaneous assessment of all cardiac segments. In a small study of 47 patients undergoing cardiac resynchronisation therapy (CRT), 3D TTE was used to guide LV lead placement, by identifying the myocardial segment with the slowest time to peak contraction (i.e. most dyssynchronous) (28). At one year follow-up patients who had an optimally placed LV lead demonstrated an improvement in LVEF of 10±2% and a reduction in systolic volumes (32±7 ml) when compared with patients with sub-optimal lead placement (improvement in LVEF: 6±3 %, reduction in systolic volume: 13±6 ml). Subsequent studies have also reported that 3D TTE can predict which patients may respond to CRT at 6 months (29,30) and at 1 year (31).

Stress echocardiography

One of the main strengths of 3D TTE is in its application to stress echocardiography and the ability to acquire the whole LV volume in one heartbeat. It is useful to perform simultaneous evaluation of multiple segments from a single data set. 2D TTE requires the acquisition of at least 5 different image planes, which are acquired over different heart beats, at different time points in peak stress, or in the rest phase. Disadvantages include lower temporal and spatial resolutions which might influence identifying end-systole and end-diastole accurately. LV contrast is commonly used to improve border opacification especially at peak stress (32). Pharmacological stress testing (e.g. dobutamine) and exercise stress testing (e.g. ergometer, treadmill) have been used with 3D TTE. Acquisition of a full 3D dataset enables the heart to be assessed in multiple views avoiding foreshortening and increases reproducibility of scan planes. 3D stress echocardiography has been demonstrated to be as rapid to acquire and analyse and offers equal accuracy as 2D TTE (33).

Conclusion

The European Association of Cardiovascular Imaging and the American Society of Echocardiography recommend that 3D TTE should be the imaging modality of choice for LV assessment, in patients with good acoustic windows (8). Whilst these recommendations were made several years ago there are still hurdles to overcome before 3D TTE can be more widely available in echocardiography departments throughout the United Kingdom, not the least being lack of training for registrars and sonographers and lack of availability of 3D probes. Whilst there are advantages to 3D TTE, there is a lack of data from clinical trials investigating its superiority to 2D TTE at this point in time. Looking to the future I would expect post-MI and heart failure trials to make use of 3D TTE for imaging end-points which would develop a robust evidence base for the use of 3D TTE in the clinic.

Disclosures

None.

Box 1. Glossary

Fully sampled matrix array transducers: ultrasound probes (transducers) with a matrix made of piezoelectric crystal elements which electronically acquire a 3D volume.

Temporal resolution: the minimal movement of an object that can be detected over time (number of frames per second).

Spatial resolution: the minimal distance that can be resolved between 2 points.

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