Chapter 24

Advanced applications of 3-dimensional echocardiography

Arnold CT Ng, Victoria Delgado, Matteo Bertini, Gaetano Nucifora, Miriam Shanks, Nina Ajmone Marsan, Eduard Holman, Nico R.L. van de Veire, Dominic Y Leung, Jeroen J. Bax.

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ABSTRACT

Over the last few decades, advancements in ultrasound, electronic and computing technologies have permitted current second generation 3-dimensional (3D) echocardiography to display on-line 3D rendered images of the heart. Since various studies demonstrated its superiority over 2-dimensional echocardiography, there is growing enthusiasm to embrace this new 3D echocardiographic technology. With its increasing widespread clinical availability, 3D echocardiography is getting closer to routine clinical use. However, as with any new emerging technologies, clinical applications of 3D echocardiography should be based on current evidence. This review will focus on the evidence from clinical studies that form the scientific basis for the advanced applications of 3D echocardiography, from cardiac chamber volume assessments, left ventricular dyssynchrony assessments, quantifications of valvular abnormalities, to the role of 3D echocardiography during cardiac interventions.

INTRODUCTION

Over the last few decades, significant advances in ultrasound, electronic and computer technology have enabled on-line display of 3-dimensional (3D) rendered images of the heart. With increasing computer power and ease of data acquisition, current second generation real-time 3D echocardiography (RT3DE) is one-step closer to routine clinical use. Numerous studies have documented superior accuracy and reliability of RT3DE over 2-dimensional (2D) echocardiography. In this article, we review current status of 3D echocardiography and its advanced applications in imaging the heart.

3-DIMENSIONAL ECHOCARDIOGRAPHIC VOLUME, FUNCTION AND MASS ASSESSMENT

Quantification of left ventricular volumes and ejection fraction

Quantification of left ventricular (LV) volumes, mass and ejection fraction (EF) are one of the most common clinical requests in a busy cardiology practice. Risk stratification, prognosis and therapeutic management of cardiac patients rely on an accurate assessment of these parameters. 2D echocardiography is the most commonly utilized imaging modality for the evaluation of LV volumes and ejection fraction. Current guidelines recommend the modified Simpson's biplane method of discs to quantify LV volumes and EF.[1] However, its accuracy is reduced in the presence of foreshortened apical images and erroneous assumptions on LV geometry. RT3DE overcomes these limitations and has superior accuracy and reproducibility over 2D echocardiography.[2, 3] Although RT3DE-derived LV volumes are highly correlated with measurements derived from cardiac magnetic resonance (CMR) imaging, several studies have demonstrated that it still significantly underestimated LV volumes by up to 30% (Table 1).[2-10]

Several hypotheses have been proposed to explain this observation. First, accurate and reliable RT3DE measurements are highly dependent on the image quality. Compared to RT3DE, CMR has a higher spatial and contrast resolution, thus enabling better delineation of the endocardial border. Secondly, the different echocardiographic views required for endocardial border detection and the different software tacking algorithms may lead to significant biases in LV volume assessments. Currently, there are 3 different approaches commonly used for LV volume and EF quantification: 3D guided biplane analysis, direct volumetric analysis and real-time triplane quantification.

3D guided biplane analysis is based on the detection of anatomically correct, non-foreshortened apical 2- and 4-chamber views on RT3DE datasets (Figure 1).

Table 1. Comparison of correlations and agreements between real-time 3-dimensional echocardiography and cardiac resonance imaging left ventricular volumes assessment

Variable	Authors	Pts (N)	RT3DE	CMR	R	Bias
LVEDV	Mor-Avi et al.[13]	92	Direct Volumetric	SAX	0.91	-67 ± 46 ml
	Nucifora et al.[6]	24	Triplane	SAX	0.97	-4 ± 15 ml
	Soliman et al.[11]	53	Multiplane	SAX	0.98	-24 ± 10 ml
	Jacobs et al.[3]	50	Direct Volumetric	SAX	0.96	-14 ± 17 ml
	Jenkins et al.[121]	110	Direct Volumetric	SAX	0.78	-44 ± 35 ml
	Sugeng et al.[5]	31	Direct Volumetric	SAX+LAX	0.94	-5 ± 26 ml
	Kuhl et al.[9]	24	Multiplane	SAX	0.98	-14 ± 19 ml
LVESV	Mor-Avi et al.[13]	92	Direct Volumetric	SAX	0.92	-41 ± 46 ml
	Nucifora et al.[6]	24	Triplane	SAX	0.97	-6 ± 12 ml
	Soliman et al.[11]	53	Multiplane	SAX	0.99	-12 ± 9 ml
	Jacobs et al.[3]	50	Direct Volumetric	SAX	0.97	-6.5 ± 16 ml
	Jenkins et al.[121]	110	Direct Volumetric	SAX	0.86	-21 ± 28 ml
	Sugeng et al.[5]	31	Direct Volumetric	SAX+LAX	0.94	-5 ± 26 ml
	Kuhl et al.[9]	24	Multiplane	SAX	0.98	-13 ± 20 ml
LVEF	Mor-Avi et al.[13]	92	Direct Volumetric	SAX	0.81	-3 ± 22%
	Nucifora et al.[6]	24	Triplane	SAX	0.95	1 ± 6%
	Soliman et al.[11]	53	Multiplane	SAX	0.97	-0.8 ± 3.7%
	Jacobs et al.[3]	50	Direct Volumetric	SAX	0.93	-1 ± 6 %
	Jenkins et al.[121]	110	Direct Volumetric	SAX	0.64	-2 ± 10%
	Sugeng et al.[5]	31	Direct Volumetric	SAX+LAX	0.96	0.3 ± 4%
	Kuhl et al.[9]	24	Multiplane	SAX	0.96	0.9 ± 4%

CMR = cardiac magnetic resonance; RT3DE = real-time 3-dimensional echocardiography; LAX = longitudinal long-axis; SAX = short axis; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; R = correlation coefficient; Pts (N) = patient number

Using the biplane method of discs, LV volumes and EF are calculated. This approach improves accuracy over conventional 2D biplane volume quantification by reducing LV foreshortening. However, it still relies on LV geometric assumptions and the limits of agreement may be suboptimal in patients with an abnormal LV geometry.[3, 11] Recently, Soliman et al. compared the accuracy of two different RT3DE analysis algorithms for LV volumes and function assessments with CMR as the reference method: real-time 3D multiplanar interpolation and full volume reconstruction method.[11] The first approach calculated LV volumes by semiautomatic tracing of the endocardial surface in 8 planes while the second method calculated the LV volumes by performing automatic contour detection from the complete 3D dataset. Although both methods showed good correlations with CMR, values obtained by multiplanar interpolation were significantly lower compared to full volume reconstruction or CMR.[11]

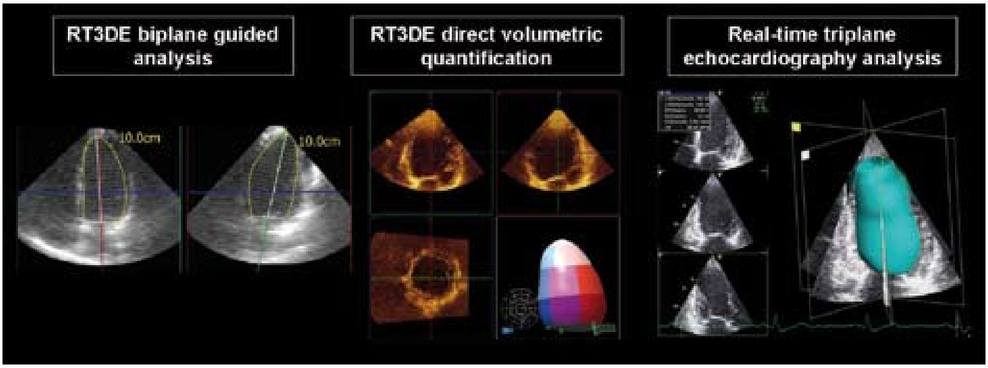

Figure 1. LV volumes and ejection fraction assessment with 3D echocardiography. Several methods of analyses are currently available: RT3DE biplane guided analysis (left), direct volumetric quantification (middle), and real-time triplane echocardiographic analysis (right).

Assessment of LV volumes and EF by RT3DE direct volumetric analysis is based on semiautomatic detection of the 3D endocardial surface using a deformable shell model (Figure 1).[3, 12, 13] LV volumes can be calculated at any desired phase or throughout the entire cardiac cycle. As this RT3DE surface detection algorithm is not affected by LV foreshortening and does not depend on geometric assumptions, recent studies have demonstrated superior accuracy and reproducibility of this method over 3D biplane guided LV volume analysis.[3] However, LV volume measurements by this method were still significantly lower as compared to CMR. To identify potential sources of measurement errors, Mor-Avi et al. conducted a multicentre study comparing RT3DE volumetric measurements with CMR.[13] A total of 92 patients with varying LVEF were recruited. In addition, phantom imaging, inter-modality analysis-related differences as well as differences in LV endocardial boundary identification were also evaluated. RT3DE volumetric quantification underestimated LV volumes due to: 1) insufficient spatial resolution of RT3DE to clearly delineate the endocardial trabeculae resulting in their inclusion within the myocardium rather than within the LV cavity; 2) inclusion of basal LV slices by CMR (which uses short-axis slices) whereas RT3DE (which uses long-axis views) avoided this problem.[13] As such, different imaging modalities have different reference values.

Finally, real-time triplane echocardiographic quantification of LV volumes may be of value in rapid acquisition and analysis of LV volumes and function.[6] This technique simultaneously acquires the 3 standard LV apical views within a single cardiac cycle, and has a relatively high temporal and spatial resolution (Figure 1). Real-time triplane echocardiographic measurements of LV volumes has been shown to be highly correlated with CMR measurements, showing small bias and narrow limits of agreement.[6]

Quantification of right ventricular volumes and function

The complex geometry of the right ventricle (RV) with its crescent shape and large infundibulum make quantifications of its volumes and function challenging. Often, RV systolic function is evaluated by the tricuspid annular systolic excursion index.[1] As before, 2D echocardiographic measurements of RV volumes are inaccurate due to the need for geometric assumptions. With the advent of

RT3DE, several studies have sought to establish the accuracy of this technique in RV volume and EF quantification.[14-17] Gopal et al. demonstrated the superiority of RT3DE over 2D echocardiography in RV volumes and EF assessment when compared to CMR in healthy subjects.[17] In that study, RV volumes and function quantification were performed by 2 different RT3DE analyses methods and compared against CMR: RT3DE volume by apical rotation and RT3DE volume by disc summation. In both methods, the analyses were performed on multiplanar reconstructions of RT3DE datasets and the endocardial boundaries were manually traced. RT3DE RV volumes, either by apical rotation or disc summation methods, showed a strong correlation with CMR. However, RV volumes by disc summation method had smaller bias and tighter limits of agreement compared to the apical rotation method. This observation may be explained by the fact that RT3DE volumes by disc summation took into account the RV inflow and outflow tracts, whereas the apical rotation method could not include data in which the contours appeared to overlap.[17] Recently, Niemann et al. evaluated RV volumes in 30 patients, of which 16 patients had major congenital heart disease.[14] Using 3 multiplanar (sagittal, 4-chamber and coronal) views, endocardial tracings performed in 1 plane were automatically duplicated in the other orthogonal planes. RV volumes calculated from the full volume datasets were compared with CMR. RT3DE RV volumes showed a good correlation with CMR RV volumes and both imaging techniques yielded similar values for RV end-diastolic (71.0 ± 15.0 ml vs. 70.1 ± 14.8 ml) and end-systolic volumes (39.8 ±10.4 ml vs. 39.1 ± 10.2 ml) (Figure 2).

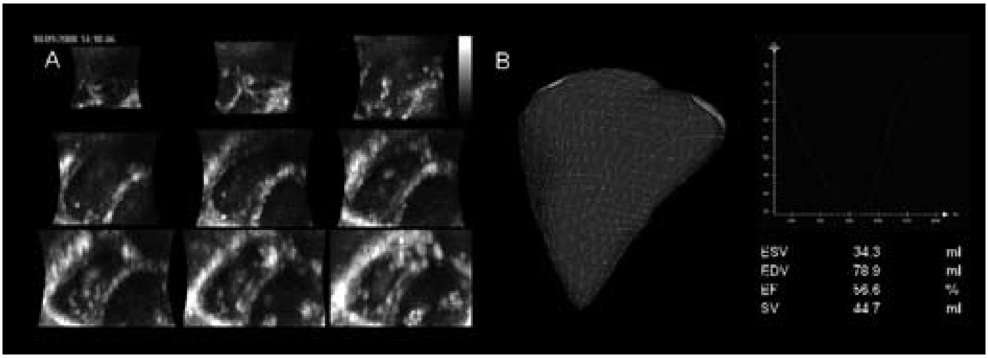

Figure 2. RT3DE right ventricular volumes and function assessment. Multi-slice (9-slice) 3D echocardiography obtained on-line by the full volume dataset shows multiple short-axis views of the right ventricle (panel A). Further off-line analysis of RT3DE datasets with dedicated software allows full-volume reconstruction of the right ventricle (panel B). The change in right ventricular volume during the cardiac cycle is presented graphically (right panel), with quantifications of end-diastolic and end-systolic volumes, ejection fraction and stroke volume.

Quantification of left and right atria

Enlarged left atrial (LA) volume predicts a poor clinical outcome in patients with chronic heart failure, valvular heart disease or arrhythmias. In addition, LA volume is a morphologic expression of LV diastolic dysfunction and indicates long-term elevation of LV diastolic filling pressures. 2D echocardiographic measures of LA volumes have been extensively compared with CMR,[1] and tend to un-

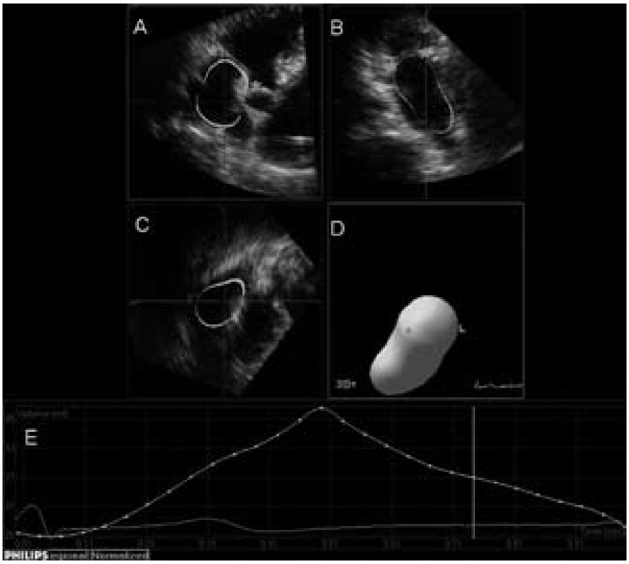

Figure 3. RT3DE assessment of left atrial volumes. Direct volumetric quantification of left atrium (LA) volumes can be performed from RT3DE datasets. By using 5 reference points (at the LA roof and at the mitral annulus) in 2 orthogonal planes of the LA (panel A and panel B), the algorithm automatically traces the endocardial surface. Panel C shows the endocardial tracing of the LA at short-axis slice. Panel D shows the reconstructed full volume of the LA. Changes in LA volumes throughout the cardiac cycle are plotted in a volume-time curve graph (panel E). LA: left atrium

derestimate LA volumes mainly due to geometric assumptions.[18] Recently, RT3DE has been introduced as a valuable method for LA volume and function assessment. Using CMR as a reference, Keller et al. demonstrated that RT3DE LA volume measurements based on multiplanar intersection algorithm were more accurate and reproducible than 2D echocardiographic measurements.[19] In addition, correlations between RT3DE LA volume values and CMR values were excellent, with small bias (5.3 ml) and tight limits of agreement (22.1 ml).[19] Phasic LA function can also be comprehensively and accurately assessed by RT3DE volumetric quantification (Figure 3).

Left atrial function includes LA conduit function, LA active contraction and LA reservoir function. The impact of therapeutic procedures, such as radiofrequency catheter ablation for atrial fibrillation, on LA volumes and function can be assessed by RT3DE with low inter- and intraobserver variability.[20, 21]

Finally, the accuracy and reproducibility of RT3DE on right atrial volume assessment has also been demonstrated.[19] RT3DE right atrial volume measurements correlated closely to CMR measurements. However, the bias and the limits of agreement were slightly higher (12.1 ml and 25.5 ml respectively) compared to the LA.[19]

Quantification of left ventricular mass

In patients with systemic hypertension, LV mass is an independent predictor for adverse cardiac events. Regardless the echocardiographic method used, all algorithms mathematically calculate LV mass by subtracting the LV cavity volume from the volume enclosed by the LV epicardial surface. The resultant LV volume (or shell volume) is then multiplied by the density of myocardium, yielding the LV mass.[1] Therefore, similar to quantifications of LV volumes, 2D echocardiographic measurements of LV mass can be limited by LV foreshortening and the need for geometric assumptions. As before, 3D echocardiography overcome these limitations and may constitute a suitable technique to obtain accurate and reliable estimates of LV mass. Previous studies have demonstrated superior accuracy of RT3DE over 2D echocardiography in LV mass estimations.[8] Similar to LV volume assessments, LV mass can be measured by either 3D guided biplane or direct volumetric quantification.[22-24] LV mass measured by RT3DE correlated well with CMR reference values ($r = 0.9$), with small bias (3%) and narrow limits of agreement (28%).[22] These findings were also confirmed in patients with abnormal LV geometries, severe LV hypertrophy or dilated cardiomyopathies.[4, 25] In addition, the interobserver and intraobserver variability of RT3DE LV mass measurements were lower than 2D echocardiography.

3-DIMENSIONAL CARDIAC OUTPUT AND SHUNT ASSESSMENT

Cardiac output measurement is an important clinical parameter that provides information on the cardiopulmonary circulatory status. The thermodilution and Fick methods are commonly used to determine cardiac output. The thermodilution method uses a Swan-Ganz catheter with a proximal port to inject a bolus liquid of known temperature and distal thermistor to determine the change in temperature over time. However, this technique is invasive with associated complications such as infections, and significant errors can occur in the settings of low cardiac outputs (especially <2.5 L/min), intracardiac or pulmonary shunts, or severe tricuspid regurgitation. The Fick method uses oximetric data obtained during cardiac catheterization and is also invasive. Thus, non-invasive echocardiographic measurements of stroke volume and cardiac output are attractive alternatives.

Stroke volume estimation by ventricular volume measurements

The most commonly used 2D echocardiographic method for cardiac output estimation is by volume determination using the Simpson's biplane method of discs. However, it is limited by assumptions of LV cavity geometry.[26] RT3DE has previously been utilized to determine stroke volume by ventricular volume measurements, and has been shown to be an accurate method of cardiac output measurement in vivo.[27] The correlation between 3D echo and CMR derived stroke volumes were shown to be excellent ($r = 0.92$, $p < 0.0001$), but 3D echocardiography still underestimated stroke volume by 13 ± 14 mL.[27] Common reasons for 3D echocardiographic underestimations of LV volumes and stroke volume include the limited pyramidal scan angle, low spatial resolution and low frame rates. Often, the entire LV cannot be imaged in patients with a dilated LV due to the limited pyramidal scan angle, and the low spatial resolution with 3D echocardiography can result in inadequate resolution of the LV endocardium. Furthermore, low frame rates can be problematic for the identification of the precise end-diastolic and end-systolic frames, especially in the presence of tachycardia.

Stroke volume estimation by Doppler echocardiography

Pulsed wave Doppler echocardiography can provide an estimate of cardiac output, and the most commonly used site for Doppler derived stroke volume is the LV outflow tract (LVOT). Flow passing through the LVOT (or any other sites) can be calculated as the product of the velocity-time integral and the cross-sectional area of the respective site. However, cardiac output determination by Doppler echocardiography is associated with multiple limitations such as geometric assumptions of the LVOT, angle dependency, and inaccuracies with LVOT velocity flow profile.

Assumptions of LVOT geometric shape

Current recommendations by the American Society of Echocardiography advocate either the LVOT or aortic annulus as the preferred sites for determining stroke volume and cardiac output.[28] Often, the cross-sectional area of the aortic annulus is assumed to be circular and is derived from the annular diameter in the parasternal long-axis view by $\pi \times (D/2)^2$. Aortic annular diameter is measured in early systole from the junction of the aortic leaflets with the septal endocardium, to the junction of the leaflet with the mitral valve posteriorly, using the inner edge to inner edge. However, studies utilizing 3D transthoracic echocardiography and multislice computed tomography have demonstrated the LVOT to be elliptical in shape (Figure 4).[29, 30] In our experience, calculated circular aortic annular area using transesophageal echocardiography underestimated planimetered cross-sectional area using multislice computed tomography by up to 16.4% (see Chapter 30).

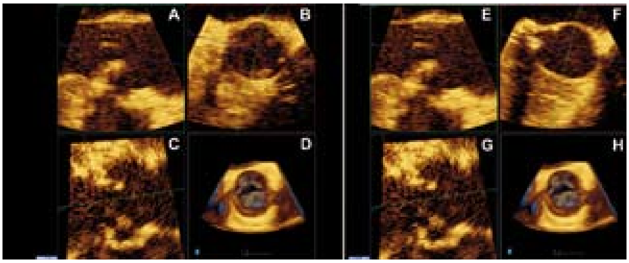

Figure 4. 3D transesophageal echocardiography with the 3-chamber long axis views shown in panels A and E during systole. Cross-sectional views showed an elliptical shaped aortic annulus (panel B) and left ventricular out flow tract (panel F).

Angle dependency of Doppler echocardiography

Doppler based techniques in quantifying blood flow velocities are based on the principles of Doppler shift. The higher the detected Doppler shift, the higher the measured velocity. Common to all Doppler based techniques are the angle dependency as described by a cosine relationship. Thus, the greater insonation angle, the lower the detected Doppler shift and the lower the measured velocity. Even though a Doppler angle of $<30^\circ$ is commonly used as the upper limit of acceptance, the measured velocity would still be underestimated by up to 13.4% (cosine $30^\circ = 0.866$).

Inaccuracies of LVOT velocity flow profile

Accurate determination of flow rates by conventional pulsed wave Doppler is dependent on the assumption of a laminar flow pattern and flat velocity profile in the LVOT. However, reconstructions of velocity flow profiles in the LVOT by magnetic resonance imaging demonstrated a non-flat, skewed velocity distribution and peak velocities measured in the center of the flow area overestimated the average velocities by 4% (range -1% to 10.8%, $p = 0.019$).[31] With current echocardiographic instrumentation, assessment of the flow profile or measuring the mean velocity of blood cells is difficult.

3-dimensional color flow Doppler

Determination of stroke volume by 3D color flow Doppler overcomes some of the inherent limitations associated 2D and Doppler echocardiography, including the assumption of a circular aortic valve geometry and the flat flow velocity profile over the aortic valve. 3D Doppler echocardiography allows direct measurements of stroke volume by integrating all the Doppler flow velocity vectors in the region of interest in the reconstructed cross-sectional image.[32, 33] In an animal study, when compared to the gold standard of cardiac output measurement by an ultrasonic flow probe placed in the aortic root, 3D Doppler derived cardiac output demonstrated excellent correlation ($R^2 = 0.99$) but slight overestimation of cardiac output (mean difference = 32 ± 46 mL/min). However, application of this technique is limited by the need for multiple cardiac cycles during data acquisition, and irregular cardiac rhythms or respiratory motion will lead to volume mismatches. Furthermore, turbulent flow due to the presence of significant valvular regurgitation or stenosis would make accurate stroke volume calculations difficult.

Shunt volume estimation by Doppler echocardiography

3D color flow Doppler echocardiography has also been applied to the quantification of shunt volumes in patients with atrial septal defects.[34] Using the mean shunt volume determined by conventional quantitative 2D Doppler echocardiography and the Fick method as the reference method, there was excellent correlation with 3D Doppler derived shunt volume ($r = 0.981$). However, due to the low frame rates, the presence of bidirectional shunting could not be assessed. Similarly, common to all Doppler-based measurements is the angle dependency limitation.

3-DIMENSIONAL ASSESSMENT OF REGIONAL FUNCTION AND MYOCARDIAL PERFUSION

Assessment of regional wall motion

Echocardiographic assessment of resting LV regional wall motion abnormalities (RWMA) carries important diagnostic, therapeutic and prognostic implications among patients with known or suspected coronary artery disease. For instance, among patients with ST-elevation myocardial infarction, the extent of RWMA before myocardial reperfusion therapy is related to the amount of myocardium at risk, and a wall motion score index greater than 1.7 was associated with LV myocardial perfusion defects larger than 20% as determined by technetium-99m sestamibi imaging.[35] Moreover, the extent of RWMA at pre-discharge is related to the occurrence of cardiac events during follow-up.[36, 37] Among patients with chest pain but non-diagnostic electrocardiogram, the absence of RWMA rules out the presence of myocardial ischemia with a very high negative predictive value (94-98%).[38] In addition, the absence of RWMA in this group of patients is associated with good prognosis, while their presence independently predicts cardiac events during follow-up.[39, 40] Similarly, the occurrence of RWMA during (exercise or pharmacological) stress echocardiography is helpful for the identification of patients having significant coronary artery disease.[41] In addition, the presence and extent of inducible RWMA portends a poorer prognosis.[41]

2D echocardiography is still the most routinely used imaging modality for the evaluation of regional LV systolic function at rest and during stress. However, several limitations hamper its accuracy and reproducibility: 1) the assessment of RWMA relies on visual assessments of endocardial motion and wall thickening, which is subjective and highly dependent on the experience of the reader and acoustic window;[42] 2) probe positioning error causes inadequate visualization of true LV apex and foreshortening of images, potentially leading to misinterpretation of regional wall motion;[42] 3) RWMA of myocardial regions not displayed in the standard imaging planes may be missed;[42] 4) during stress echocardiography, stress imaging planes may be different from baseline imaging planes, potentially leading to erroneous interpretations;[43, 44] 5) at peak stress, the images need to be acquired in a narrow time window in order to detect possible ischemia.[43, 44]

Recently, RT3DE has been proposed to overcome most of the above mentioned limitations of 2D echocardiography. Two different RT3DE imaging modes are available for the assessment of regional wall motion: multiplane (biplane or triplane) mode and full volume mode.[43, 44]

Multiplane mode

Multiplane mode allows the simultaneous acquisition and on-line visualizations of two (biplane) or three (triplane, usually with 60° increments) imaging planes (Figure 5).[44]

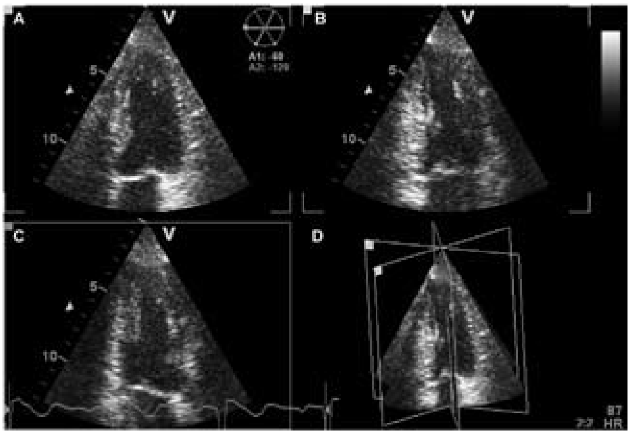

Figure 5. Multiplane (triplane) 3D echocardiography allows simultaneous visualization of 3 apical views. During image acquisition, a 4-chamber reference view (panel A) is chosen and displayed in the upper left corner of a quad-screen image display while secondary imaging planes (2-and 3-chamber views) are simultaneously displayed (panels B and C respectively). The interplane angles are chosen as 60° by default, but can be steered electronically to any desired angle (panel D).

As changing the probe position is no longer necessary during acquisition of the apical views, this potentially reduce image plane positioning errors and incorrect wall motion interpretations.[44] Previous studies have validated the feasibility of multiplane imaging technique during exercise [45] or dobutamine [46, 47] stress echocardiography (Table 2). The main advantage of this approach is the reduction of acquisition time (compared to serial scanning of different 2D image planes) without decreasing the image quality or compromising test accuracy.[45-47] As the use of multiplane imaging technique during exercise stress echocardiography permits the acquisition of post-stress images at higher heart rate, it potentially improves the ability to detect ischemia.[45]

Table 2. Feasibility and diagnostic accuracies of real-time 3-dimensional stress echocardiography

Authors	Pts (N)	3D imaging mode	Stress test	Feasi bility RT3DE	Feasi bility 2DE	Sens/ Spec RT3DE	Sens/ Spec 2DE
Sugeng et al.[45]	19	Biplane	Exercise	94%	93%	-	-
Yang et al.[47]	33	Biplane	Dobutamine	91%	100%	-	-
Eroglu et al.[46]*	36	Triplane	Dobutamine	97%	98%	93%/75%	93%/75%
Peteiro et al.[49]*	100	Full volume	Exercise	92%	99%	78%/73%	84%/76%
Yang et al.[47]	33	Full volume	Dobutamine	94%	100%	-	-
Ahmad et al.[52]*	90	Full volume	Dobutamine	-	-	88%/-	79%/-
Matsumura et al.[51 †]	56	Full volume	Dobutamine	89%	90%	86%/80%	86%/83%
Aggeli et al.[50]*	56	Full volume	Dobutamine	-	-	84%/72%	82%/83%

*Sens = sensitivity; Spec = specificity; RT3DE = real-time 3-dimensional echocardiography; 2DE = 2-dimensional echocardiography; Pts (N) = patient number; *coronary angiography as reference standard; † ^{201}Tl SPECT as reference standard*

Full volume mode

The full volume mode allows the acquisition of apical full volume 3D datasets by integrating, during a brief breath-hold, 8 R-wave-triggered sub-volumes into a larger pyramidal volume (90° by 90°) and allows complete capture of the LV.[43] Multiple LV short-axis views can then be automatically obtained on-line from the full volume datasets (Figure 6).[43]

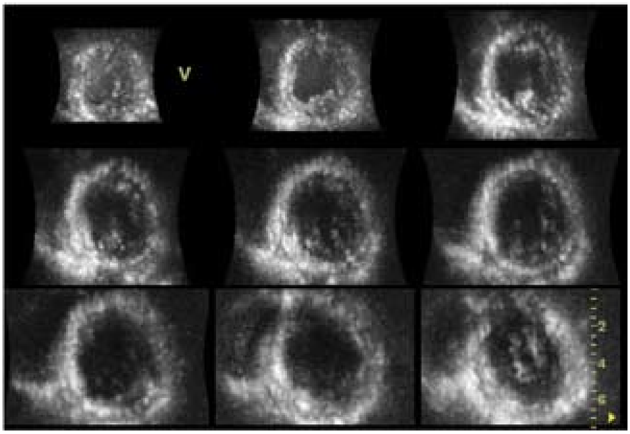

Figure 6. Multislice 3D echocardiography allows simultaneous visualizations of 9 short-axis images, progressing from apex (upper left) to base (lower right).

Further off-line analyses are performed using dedicated software that permits cropping of the dataset to display multiple short-axis and long-axis imaging planes in addition to the standard imaging planes (Figure 7). This allows the assessment of true LV apex and of regions/planes that may not be adequately visualized with 2D echocardiography.[43]

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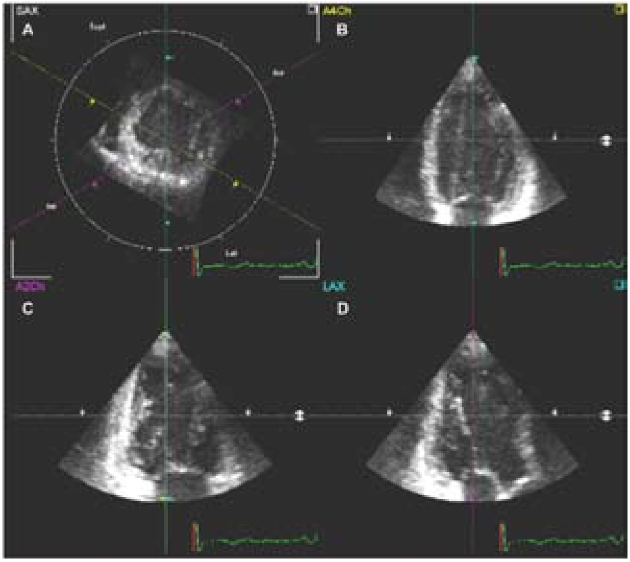

Figure 7. Off-line analysis of full volume 3D dataset performed using dedicated software. The software automatically displays a short-axis view (panel A) and the 3 apical views with the 4-chamber as a reference view (panel B) the 2- and 3-chamber views (panels C and D respectively). Further cropping of the 3D dataset can be performed to visualize any short-axis or long-axis imaging planes.

The potential clinical utility of qualitative assessment of regional LV function at rest using full volume RT3DE was first reported by Collins et al.[48], and further studies have evaluated the feasibility and accuracy of this approach during exercise and pharmacological stress testing (Table 2). However, Peteiro et al. showed that full volume mode was not optimal for exercise based stress echocardiography.[49] Although RT3DE during exercise had similar sensitivity and specificity for the detection of coronary artery disease compared to 2D echocardiography, the feasibility of RT3DE was significantly lower than 2D echocardiography at peak exercise (92% vs. 99%, $p < 0.05$) and post-exercise (95% vs. 100%, $p < 0.05$). Due to the need for multiple heart beat acquisition, heart rate variability as well as body and breathing motions that occur immediately after exercise may impair the feasibility of full volume RT3DE.[49]

In contrast, more promising results for full volume RT3DE were obtained for dobutamine stress echocardiography.[47, 50-52] Similar to the multiplane imaging technique, full volume 3D dobutamine stress echocardiography has been reported to be feasible and as accurate as 2D echocardiography for the diagnosis of significant coronary artery disease, but with significantly shorter image acquisition time.[47, 50-52] In addition, compared to the multiplane imaging technique, full volume mode has the advantage of acquiring the entire LV and thereby permitting off-line analyses and displaying of images in any imaging plane.

Despite these promising results, significant limitations still restrict the widespread use of RT3DE for the assessment of regional LV function. Of note, image quality with RT3DE is lower due to suboptimal spatial and temporal resolutions.[53, 54] A preliminary study by Collins et al. indeed demonstrated a lower percentage of visualized segments with RT3DE compared to 2D echocardiography (83% vs. 97%, respectively, $p < 0.001$), despite all the patients being recruited had optimal acoustic windows.[48] Other studies that explored the feasibility of RT3DE in unselected populations reported a prevalence of uninterpretable or poor quality RT3DE images in the range of 35%.[54-56] In this setting, the use of intravenous contrast agents for LV opacification during rest and stress RT3DE may increase the number of interpretable LV segments and may improve intra- and inter-observer agreement (Figure 8).[55, 57]

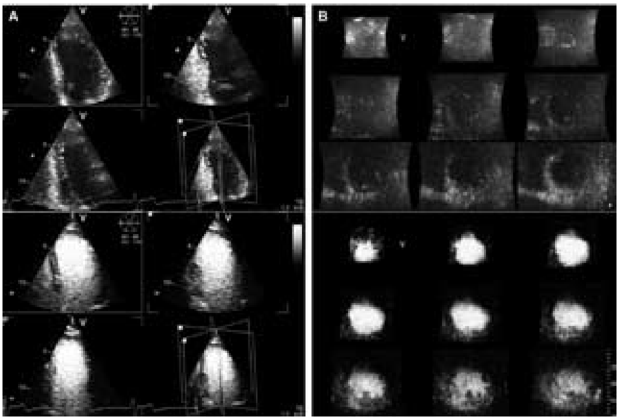

Figure 8. Examples of poor endocardial border definition during multiplane (triplane) 3D echocardiography (panel A, top) and during multislice 3D echocardiography (panel B, top). The use of intravenous echo-contrast significantly improves endocardial border definition (panel A and B, bottom), allowing the assessment of wall motion abnormalities.

Assessment of regional myocardial perfusion

Myocardial contrast echocardiography (MCE) is a relatively new imaging technique that allows non-invasive evaluation of myocardial perfusion. It requires intravenous infusion of micro-bubble perfusion agents that have unique properties such as stability, similar intravascular rheology as red blood cells and remaining solely within the intravascular space, thereby echocardiographically displaying the status of myocardial perfusion.[58, 59] Using dedicated software, assessments of myocardial perfusion using conventional 2D echocardiography can be performed by either qualitative visual interpretations of peak contrast intensity, or by off-line quantitative analyses. Quantitative MCE can provide meaningful information on coronary microcirculation: 1) capillary blood volume (represented by myocardial contrast intensity during continuous infusion of contrast and achievement of a steady-state); 2) myocardial blood velocity (represented by myocardial contrast replenishment after destruction of

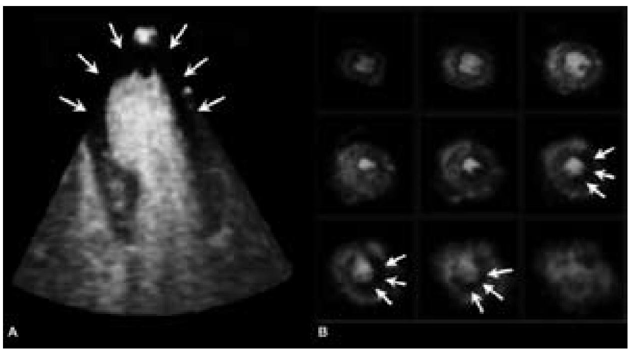

Figure 9. Panel A: Myocardial contrast 3D echocardiography obtained in a patient with left anterior descending coronary artery stenosis. Apical segments lacks contrast enhancement indicating a perfusion defect (arrows). Panel B: Short-axis slices at different levels of the left ventricle from apex to base extracted from a 3D dataset obtained in a patient with 90% stenosis in the proximal left circumflex coronary artery. Note the perfusion defect in the left circumflex artery territory (arrows). Reprinted from *Cardiol Clin* Vol. 25; Mor-Avi V and Lang RM[42]; Three-dimensional echocardiographic evaluation of the heart chambers: size, function, and mass, 241-251, Copyright 2007, with permission from Elsevier.[42]

micro-bubbles in the myocardium with high-energy ultrasound); and 3) myocardial blood flow (represented by the product of capillary blood volume x myocardial blood velocity).[58, 59]
While the clinical utility of myocardial contrast 2D echocardiography is well established (diagnosis of coronary artery disease in patients with stable and unstable chest pain complaints, identification of myocardial viability in patients with acute myocardial infarction and chronic ischemic LV dysfunction)[60], the feasibility of 3D assessment of myocardial perfusion is still under investigation (Figure 9). Myocardial contrast RT3DE has the potential to overcome many of the limitations of myocardial contrast 2D echocardiography. In particular, it would allow faster image acquisition and off-line assessments of infinite image planes.[61] However, few studies have provided preliminary data on its application in clinical practice.

Toledo et al. tested the applicability of myocardial contrast RT3DE in evaluating adenosine-induced changes in myocardial perfusion in eight healthy volunteers and found a two-fold increase in the measured perfusion index after adenosine infusion, as expected in a physiologic vasodilator response.[58] More recently, Iwakura et al. and Bhan et al. evaluated the feasibility of myocardial contrast RT3DE in clinical settings.[60, 61] Iwakura et al. performed 2- and 3D MCE after intracoronary injections of microbubbles in 47 patients who underwent primary percutaneous coronary intervention for acute myocardial infarction.[60] Myocardial perfusion assessed by myocardial contrast RT3DE correlated with infarct size (determined by peak creatine kinase) and predicted regional recovery at follow-up better than 2D myocardial contrast echocardiography. However, as shown by Bhan et al., the feasibility of myocardial contrast RT3DE is still lower than that of 2D myocardial contrast echocardiography.[61] In that study, 46 patients referred for dobutamine stress echocardiography underwent 2- and 3D MCE. Myocardial perfusion could be assessed in 95% of segments during RT3DE vs. 98% of segments during 2D echocardiography ($p = 0.006$).

Myocardial contrast RT3DE, although promising, still requires further validation before becoming part of routine clinical practice. In particular, its use for non-invasive evaluation of myocardial perfusion and diagnosis of coronary artery disease needs to be validated against reference techniques (i.e. single-photon emission computed tomography and invasive coronary angiography) in larger studies.

3-DIMENSIONAL LEFT VENTRICULAR DYSSYNCHRONY ASSESSMENT

Assessments of LV dyssynchrony by 2D echocardiography have been used with varying success in predicting response to cardiac resynchronization therapy. RT3DE provides a comprehensive model of systolic dyssynchrony assessment using multiple regions of the LV in a "wide-angle" volume-rendered cine loop that is captured from 4 to 7 continuous beats. Assessment of systolic dyssynchrony is based on off-line reconstructions of regional volumetric curves in a 16- (or 17-) segmental model as defined by the American Society of Echocardiography. From the regional volumetric curves, the time to minimal regional volume can be measured, and indices of systolic dyssynchrony calculated from 2-basal (septal and lateral), 6-basal, 12 (6-basal, 6-mid) or 16 (6-basal, 6-mid and 4-apical) segmental models. When compared with other 2D techniques, the assessment of LV dyssynchrony with RT3DE has the advantage of simultaneous acquisition of all LV segments, allowing for more extensive intersegment comparison, and avoiding the problem of heart rate variability during image acquisition.[62] A series of plots representing the change in volume in each of the 16 segments throughout a cardiac cycle can be obtained. In a synchronous LV, all regions reach their minimum volumes at approximately the same time during the end-systole. Conversely, when significant LV dyssynchrony occurs, a wide scattering of time to minimal regional volume points is observed (Figure 10).

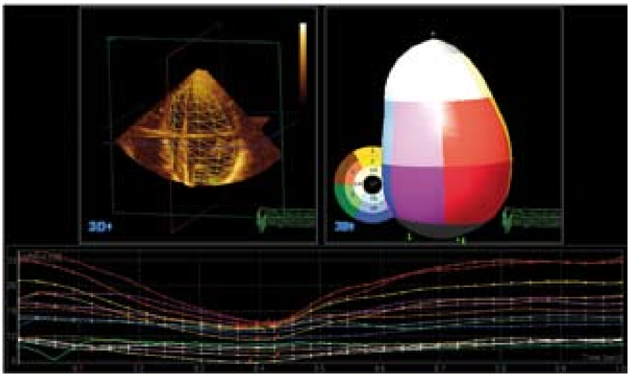

Figure 10. Example of patient with dilated cardiomyopathy with significant dyssynchrony (systolic dyssynchrony index 9.5%). Top left panel: 3-dimensional segmentation of left ventricle. Top right panel: color-coded representation of left ventricular segments. Bottom panel: time-volume curves of the 16 left ventricular segments. In each curve a red triangle is the marker of the peak of the minimum systolic volume.

Furthermore, parametric images derived from over 800 virtual waveforms provide a visual summary of regional LV contraction timings as a polar plot. In this polar plot presentation, global time to minimal regional volume is used as the timing reference. Segments with a time to minimal regional volume that is approximately the same as the global time to minimal regional volume are coded as green, while segments with an earlier or later time to minimal regional volume are coded in blue or red respectively (Figure 11). Kapetanakis et al. demonstrated good feasibility and reproducibility (<10%) in RT3DE-derived dyssynchrony index in 89 healthy volunteers and 174 unselected patients who were referred for routine echocardiography.[63] In the study, systolic dyssynchrony index (SDI) was defined as the standard deviation of the time taken to reach time to minimal regional volume using a 16-segment LV model, and was expressed as a percentage of the cardiac cycle. The authors demonstrated a logarithmic correlation between LVEF and SDI, independent of QRS complex duration (r = 0.79 and r = 0.77 for LVEF in patients with broad and narrow QRS complex respectively), and showed that mechanical dyssynchrony assessed by RT3DE became increasingly prevalent with worsening LV systolic function.

Gimenes et al. reported the largest study on the normal values of RT3DE-dyssynchrony indices (calculated from 6,12, and 16 segment models) in 120 healthy volunteers.[64] By considering normal values to be mean + 2 standard deviations, they found a RT3DE dyssynchrony index of 2.53%, 2.71% and 3.57%

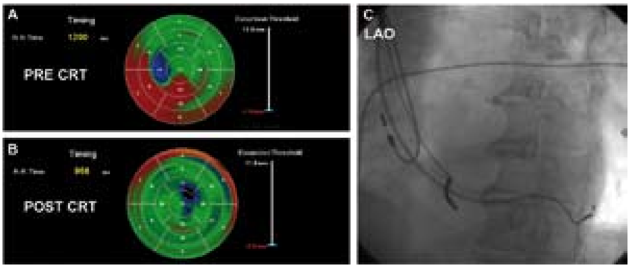

Figure 11. Example of parametric images obtained with in patient pre- and post-cardiac resynchronization therapy. Panel A: At baseline (PRE CRT) the most delayed segments (color-coded in red) were in the infero-posterior walls. Panel B: 6 months after cardiac resynchronization therapy (POST CRT) the most delayed segments were in the antero-septal walls. Panel C: left anterior oblique (LAO) view on fluoroscopy which showed left ventricular lead placement in the infero-posterior cardiac vein.

for the 6, 12, and 16 segment models respectively. Furthermore, in a recent analysis of 8 different parameters of mechanical synchrony performed in 2 institutions, SDI assessed with RT3DE together with radial strain synchrony derived from speckle-tracking echocardiography were the most reproducible parameters for the assessment of mechanical dyssynchrony in healthy subjects.[65]

RT3DE-dyssynchrony and cardiac resynchronization therapy

Like all dyssynchrony parameters, the use of SDI was first proposed to be a discriminator of patients' response to cardiac resynchronization therapy. Kapetanakis et al. recruited 26 patients referred for cardiac resynchronization therapy implantation found that clinical responders (reduction in New York Heart Association functional class at 10 months follow-up) had significantly larger SDI at baseline when compared to non-responders (16.6±1.1% vs. 7.1±2.0%, $p = 0.0005$).[63] Ajmone Marsan et al. subsequently investigated the predictive value of SDI for acute and chronic volumetric response to cardiac resynchronization therapy.[66, 67] The authors found that an SDI ≥5.6% had a sensitivity of 88% and a specificity of 86% to predict acute volumetric response to cardiac resynchronization therapy,[67] and an SDI ≥6.4% had a sensitivity of 88% and a specificity of 85% to predict reverse remodelling after cardiac resynchronization therapy at 6 months follow-up.[66] More recently, Soliman et al. reported a SDI cut-off value of 10% to have an optimal sensitivity and specificity of 93% and 91% respectively for the identification of volumetric response to cardiac resynchronization therapy at 12 months in 39 patients.[68] Although data on this field are emerging, most publications to date are only single-centre studies. As previously shown in the PROSPECT trial, predictive values of dyssynchrony parameters may yield a lower sensitivity and specificity in multicenter trials.[69] Consequently, future larger multicenter and randomized studies will have to demonstrate the value of this technique in the identification of responders to cardiac resynchronization therapy.

Advantages and limitations of RT3DE-dyssynchrony

RT3DE dyssynchrony parameter is a comprehensive and thorough measurement of LV mechanical dyssynchrony, providing an assessment of all LV segments. Furthermore, parametric images derived from over 800 virtual waveforms automatically provided by the software displays a visual summary of LV regional contraction timings as a polar map. This tool provides a rapid and intuitive assessment of the area of latest LV activation and may be of particular importance in guiding optimal LV lead placement in cardiac resynchronization therapy setting. However, the image quality of RT3DE is lower than 2D echocardiography and incomplete visualization of large ventricles may affect the quantitative analysis. At the same time, although RT3DE offers a more extensive assessment of the LV dyssynchrony, the temporal resolution is limited (20–25 Hz) and inferior compared to the temporal resolution of tissue Doppler imaging (>100 Hz). Furthermore, RT3DE requires a breath-holding time that is dependent on heart rate and may be difficult for highly symptomatic heart failure patients. Last but not least, cardiac rhythm disorders such as atrial fibrillation or frequent premature atrial or ventricular complexes may interfere with the full volume acquisitions.

3-DIMENSIONAL ECHOCARIOGRAPHIC VALVULAR ASSESSMENT

Recent developments in 3D echocardiography have also enabled real-time volumetric imaging of complex valvular anatomy, non-invasively elucidating the complex spatial relationships between various cardiac structures and displaying the images in unique perspectives previously only privy to surgeons, such as LA or LV views of the mitral valve.

Mitral valve

The mitral valve has a complex saddle-shaped configuration and its assessment by 2D echocardiography can be challenging. Previous first generation 3D echocardiography reconstructed 3D datasets from a series of 2D images and was instrumental in describing the saddle shaped mitral annulus, redefining the criteria for mitral valve prolapse.[70] Subsequently, a variety of mitral valvular abnormalities have been demonstrated using 3D reconstructions of transesophageal echocardiography images.[71] However, first generation 3D reconstruction methods were time consuming and labor-intensive. With the advent of RT3DE, the need for extensive off-line reconstructions was reduced and adequate visualizations of the mitral valve leaflets, commisures and orifice were feasible in up to 70% of patients.[72]

Mitral valve leaflets

The anterior mitral leaflet tends to be visualized better than the posterior leaflet on RT3DE, likely due to its larger size. While the anterior mitral leaflet is seen equally well from either the parasternal or apical window, the posterior leaflet is best visualized from the parasternal window. A previous study evaluated 41 patients with mitral valve prolapse found good agreement between transthoracic RT3DE and 2D tranessophageal echocardiography, with the highest accuracy achieved for the central scallops.[73] The transthoracic RT3DE findings were confirmed in the operating room in a subgroup of 15 patients. 3D transesophageal echocardiography has the ability to image different cardiac structures with excellent image quality, including the mitral valve apparatus with both anterior and posterior leaflets, annulus and subvalvular apparatus.[74]

A previous study comparing transthoracic RT3DE and 3D tranesophageal echocardiography on segmental analysis of mitral valve prolapse found that these 2 techniques yielded similar comparative accuracy for precise anatomic localization of the prolapsed segments.[73, 75] Another study reported higher concordance between 3D transesophageal echocardiography and surgery compared to 2D transesophageal echocardiography for the evaluation of mitral valve prolapse.[76] These findings suggest that 3D transesophageal echocardiography imaging may become the imaging modality of choice for pre-operative planning of mitral valve surgery (Figure 12).[77]

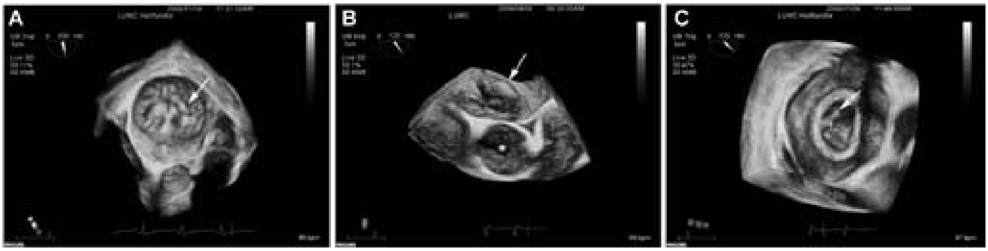

Figure 12. Panel A: RT3DE image of the mitral valve showing prolapse of the P2 (arrow). Panel B: RT3DE image of the mitral valve showing severe prolapse of the P2 with a large regurgitant orifice (arrow). Panel C: RT3DE image of the mitral valve with annuloplasty ring and prolapse of A1 and A2 (arrow). * aortic valve opened during systole.

Mitral annulus and subvalvular apparatus

Studies have shown that RT3DE measurements of mitral annular sizes were similar to those obtained by CMR.[78] Recent development of dedicated softwares have allowed advanced 3D rendering of valvular images from both transthoracic and transesophageal echocardiograms, permitting quantitative off-line analysis of mitral apparatus geometry (Figures 13 and 14).

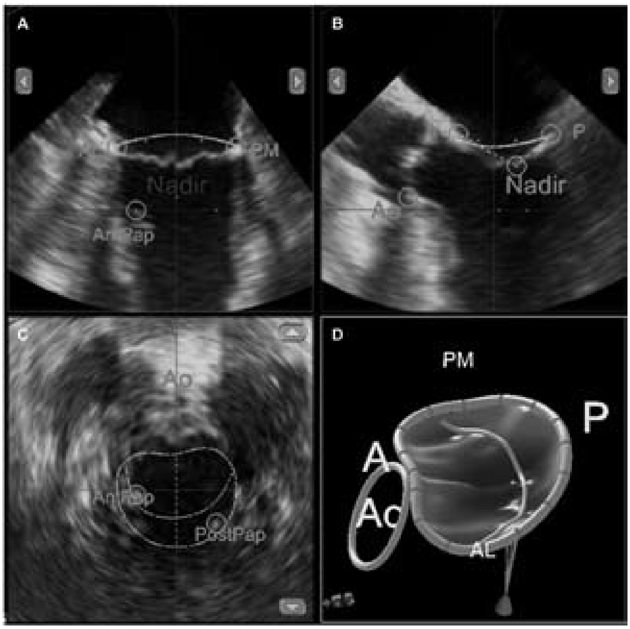

Figure 13. Using 3-dimensional transesophageal echocardiogram, Mitral Valve Quantification (MVQ) software generates a model of the mitral valve (panel D) by identifying manually placed reference points in the 2 chamber (panel A), 3 chamber (panel B) and short axis (panel C) multiplanar views. A: anterior; AL: anterolateral; P: posterior; PM: posteromedial; Ao: aorta; AntPap: anterolateral papillary muscle; PostPap: posteromedial papillary muscle.

Since its availability, several studies have aimed to improve characterization of the mechanisms causing mitral regurgitation.[77, 79-83] Both animal[82] and human[84-86] studies have evaluated the mitral valve apparatus in ischemic and non-ischemic cardiomyopathy, and have demonstrated changes in mitral annular geometries with associated increased inter-commissural and anteroposterior dimensions, increased leaflet tenting indicating chordal tethering, and reduced cyclic variations in annular shape and area compared to healthy individuals.[83, 86, 87] Further studies have shown differences in mitral apparatus changes between ischemic and non-ischemic cardiomyopathies.[83] Patients with non-ischemic cardiomyopathy had more global mitral annular dilatation compare to a predominantly anteroposterior and anterolateral to posteromedial dilatation in those patients with ischemic cardiomyopathy. Similarly, unequal papillary tethering lengths were observed in patients with ischemic cardiomyopathy compare to symmetrical tethering lengths in patients with non-ischemic cardiomyopathy.[87]

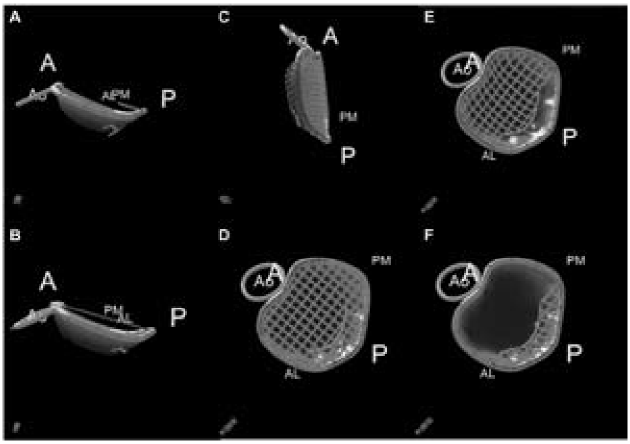

Figure 14. Examples of different measurements that can be generated from the Mitral Valve Quantification (MVQ) software. Panel A = posterior mitral leaflet (P2) to mitral annulus angle; Panel B = aorta to mitral annulus angle; Panel C = total mitral valve tenting volume; Panel D = total mitral annular area; Panel E = anterior mitral leaflet area; Panel F = posterior mitral leaflet area. A: anterior; AL: anterolateral; P: posterior; PM: posteromedial; Ao: aorta.

Using RT3DE, mitral annular area changes and apicobasal motions were compared between patients with hypertrophic cardiomyopathy, secondary LV hypertrophy (from hypertension and aortic stenosis), and normal controls.[88] There were no significant differences noted between the annular area and motions in patients with secondary LV hypertrophy compared to the controls. In contrast, annular apicobasal motion and annular area changes were reduced in patients with hypertrophic cardiomyopathy.[88]

Mitral regurgitation

In patients with non-ischemic cardiomyopathy, RT3DE have demonstrated symmetrical papillary muscle displacement with simultaneous enlargement of the mitral annulus leading to progressive chordal tethering and leaflet tenting, resulting in decreased leaflet coaptation and a predominantly central mitral regurgitation.[80, 81, 87] In contrast, studies evaluating mitral regurgitation in the patients with ischemic cardiomyopathy have demonstrated that the regurgitation occurs in parallel with LV remodeling. Unequal papillary tethering lengths related to regional wall motion abnormalities were observed in ischemic cardiomyopathy, resulting to eccentric mitral regurgitation.[83, 87] These observations have important implications in the surgical treatment of mitral regurgitation.

RT3DE color flow assessment of mitral regurgitation

Conventional Doppler echocardiographic methods of assessment for mitral regurgitation such as effective regurgitant orifice area are limited by dependence on geometric assumptions. Compared to 2D echocardiography, RT3DE color Doppler flow imaging permits unlimited image plane orientations and allow direct assessments of the size and shape of vena contracta from en face views. Several studies have studied the feasibility of visualizing valvular regurgitant jets with RT3DE color Doppler flow in humans.[89-93] Different vena contracta shapes from different MR etiologies have been demonstrated, with a non-hemispherical shape observed in the majority of the patients.[89, 90, 93] In particular, patients with functional MR often show a typical elongated semilunar-shaped vena contracta along the line of incomplete mitral leaflet closure caused by leaflet tethering (Figure 15).[93]

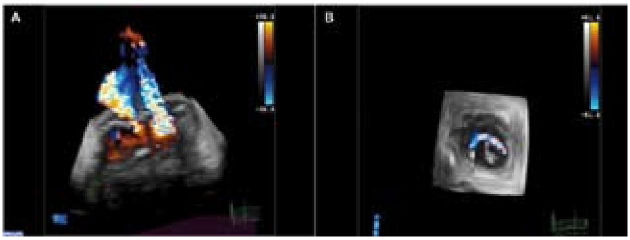

Figure 15. Example of non-hemispherical vena contracta. Panel A: 2-chamber view giving a false impression of 2 separate mitral regurgitant jets. Panel B: en face view of mitral regurgitation showing a semilunar-shaped vena contracta along the line of incomplete mitral leaflet closure.

On the other hand, a wide variety of irregularly shaped vena contracta was found in patients with organic mitral valve disease (Figure 16). As RT3DE color Doppler flow directly images the vena contracta without assuming a hemispherical geometry, it may be more accurate than 2D echocardiography for quantification of mitral regurgitation. This approach has been validated in vitro[94-96] and in animal model[97] against flow-meter standard[94-96] and CMR,[94] showing less regurgitant volume underestimation for all orifice shapes and regurgitant volumes tested compared to 2D flow-convergence method. Similar results have been replicated in the human studies that compared mitral regurgitation stroke volume measurements by RT3DE color flow against 2D echocardiography hemispheric and hemielliptic proximal isovelocity surface area methods[89, 91, 92, 94, 97] and CMR.[94]

Figure 16. Real-time 3-dimensional echocardiography showing mitral regurgitation color flow Doppler. Two different vena contracta widths in two orthogonal planes (Panel A: 4-chamber view; Panel B: 2-chamber view). En face view (Panel C) show an oval shaped vena contracta.

Mitral stenosis

The accuracy of RT3DE for assessment of mitral stenosis by direct planimetry of the mitral valve orifice area has been established in several studies.[98-102] Compared to traditional measurements such as 2D planimetry, pressure half-time and flow convergence, RT3DE planimetry area had the best agreement with mitral orifice area calculations derived from the Gorlin formula during cardiac catheterization.[98, 99, 101] While 2D planimetry may incorrectly display a tangential cross-section of the mitral valve orifice, RT3DE allows perpendicular en face views of the mitral valve depicting the tips of the leaflets. By slowly cropping the mitral funnel orifice, the smallest and most perpendicular view can be obtained. The theoretical advantage of planimetry is that it provides a relatively hemodynamic-independent assessment of the anatomical mitral valve area.[103] In addition, RT3DE provides detailed anatomical information, such as commissural splitting and leaflet tears immediately post-percutaneous balloon mitral valvuloplasty. Importantly, 3D measurements have lower intraobserver and interobserver variability.[98, 99, 101, 102]

Aortic valve

RT3DE imaging of the aortic valve can be challenging due to the often parallel angle of incidence of the ultrasound beam with the thin aortic leaflets, and drop-out artifacts from valvular calcifications.[77] Despite of these limitations, RT3DE has been shown to improve the accuracy during quantification of aortic stenosis severity. As previously described, RT3DE provides proper alignment of the imaging planes at the tips of the aortic leaflets, perpendicular to the aortic valve orifice. Direct planimetry of the aortic valve area with transthoracic RT3DE showed good agreement with standard 2D transesophageal echocardiography and invasive cardiac catheterization data, with the further advantage of improved reproducibility.[104, 105]

Standard 2D techniques for assessments of aortic valve stenosis incorrectly assume a circular geometry of the LVOT leading to underestimation of the calculated aortic valve area on continuity equation. RT3DE has demonstrated that the LVOT cross-sectional geometry is often elliptical in shape.[29] The discrepancies between 2D and 3D continuity equation derived areas were confirmed in animal model and humans, with the degree of upper septal hypertrophy being the sole predictor for underestimating the aortic valve area.[106] Thus, RT3DE is a feasible and reproducible method for assessing aortic stenosis by allowing direct planimetry of the aortic valve orifice and LVOT, therefore eliminating the need for geometrical assumptions (Figure 17). The utility RT3DE for imaging bicuspid aortic valves, prosthetic valves, vegetations, and subaortic pathologies remains to be determined in future studies.

Tricuspid valve

Initial experience on RT3DE imaging of tricuspid valves were limited to case reports such as tricuspid stenosis, cleft tricuspid valve, and a flail tricuspid leaflet.[107] Subsequent study focused on the assessment of tricuspid annulus by RT3DE found agreement between this technique and CMR measurements.[108] Newly developed quantitative analysis software has been utilized for comparison between tricuspid and mitral annular geometries, with the tricuspid annulus having a more planar

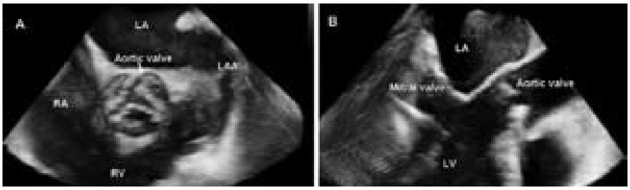

Figure 17. Real-time 3-dimensional echocardiography (RT3DE) allows for anatomic characterization of the aortic valve: panel A shows RT3DE short-axis view of a stenotic aortic valve (thickened and calcified leaflets). On panel B, a RT3DE long-axis view of the valve is presented. LA: left atrium; LAA: left atrial appendage; LV: left ventricle; RA: right atrium; RV: right ventricle.

shape. In another study, patients with functional tricuspid regurgitation were found to have even larger, more planar and more circular annulus compare to the mitral annulus.[109] In addition to annular dilatation, increased tenting volume has been documented in the patients with tricuspid regurgitation secondary to pulmonary hypertension.[110] Septal leaflet tethering, septal-lateral annular dilatation, and the severity of pulmonary hypertension were found to be the predictors of tricuspid regurgitation severity.[111] Improved quality of RT3DE images may allow more detailed assessments of the tricuspid leaflet thickness, mobility, calcification, and commissural width at the time of maximal tricuspid valve opening.

3-DIMENSIONAL ECHOCARDIOGRAPHY AND CARDIAC INTERVENTIONS

Transesophageal echocardiography is a valuable technique to guide several cardiac interventions such as surgical valve repair, atrial septal defect closure, LA appendage occlusion and transcatheter aortic valve implantation. 3D transesophageal echocardiography allows clear demonstration of the spatial relationships between cardiac structures that may not be evident on conventional 2D transesophageal echocardiography. Recent technological advances have permitted real-time acquisition and live 3D images using a 3D fully-sampled matrix array transesophageal echocardiography transducer.

Non-valvular interventions

The role of 3D transesophageal echocardiography in guiding several percutaneous non-coronary interventions has been previously demonstrated.[74, 112-114] For example, 3D transesophageal echocardiography improves the localization of the bioptome during RV endomyocardial biopsy, thereby reducing the number of procedural complications and increasing cardiac biopsy efficacy.[113] Similarly, during atrial septal defect closure with the Amplatzer device, 3D transesophageal echocardiography allows exact characterization of the shape and dimensions of the defect, contributes to selection of the optimal closure device, and allows assessment of the deployment and positioning of the Amplatzer device (Figure 18).[112]

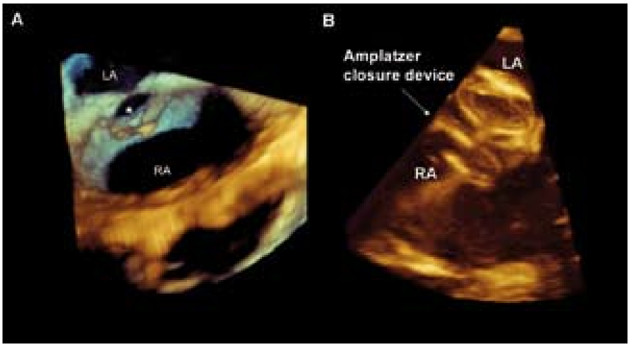

Figure 18. Three-dimensional transesophageal echocardiographic (TEE) imaging during atrial septal defect closure. In panel A, live 3D TEE demonstrates the right and left atria with an atrial septal defect (*). Panel B shows the deployed Amplatzer device closing the septal atrial defect. LA: left atrium; RA: right atrium.

Valvular interventions

Mitral valve interventions

Percutaneous mitral valve repair is a promising therapeutic option for patients with mitral valve regurgitation and high risk for surgery. Leaflet repair using the MitraClip system (Evalve Inc. Menlo Park, California), similar to the edge-to-edge Alfieri stitch, has been shown to be effective in selected patients with favourable anatomy (predominately in mitral valve prolapse and non-calcified valves).[115] 3D transesophageal echocardiography is a valuable diagnostic tool for patient selection by permitting exact localization of the prolapsed mitral leaflet (Figure 12). During the procedure, 3D transesophageal echocardiography also assists in transeptal cannulation into the left atrium. As the catheter system is positioned through the mitral valve, both anterior and posterior leaflets are opposed by the clip, thereby creating a double-orifice mitral valve and significantly reducing mitral regurgitation severity.[115]

In patients undergoing balloon valvuloplasty for mitral stenosis, 3D transesophageal echocardiography allows clear visualization of the mitral valve and has important therapeutic implications.[114] For example, prior to balloon valvuloplasty for mitral stenosis, 2D transesophageal echocardiography overestimated commissural fusion in 50% of the patients when compared to 3D transesophageal echocardiography. After the procedure, visualization of the commissures was feasible in all patients by 3D transesophageal echocardiography whereas the feasibility was only 67% by 2D transesophageal echocardiography.[114]

Aortic valve interventions

Over the last 10 years, more than 1000 transcatheter aortic valve implantations have been successfully performed in high-risk surgical patients with severe aortic stenosis.[116] 3D transesophageal echocardiography provides invaluable information before, during and immediately after the procedure. To minimize the risk of significant paravalvular regurgitation, selection of the appropriate prosthesis size is important. 3D transesophageal echocardiography allows exact characterization of the aortic annular geometry and diameters prior to selection of appropriate transcatheter valve size (Figure 4). Furthermore, 3D transesophageal echocardiography provides real-time continuous monitoring of the implantation procedure from crossing the aortic valve by the guidewire (Figure

19, panel A), balloon-dilatation of the native valve (Figure 19, panel B), to final deployment of the prosthesis (Figure 19, panel C). Procedural success and complications (such as significant central or paravalvular regurgitation, aortic dissection, or tamponade) can be also be evaluated immediately.

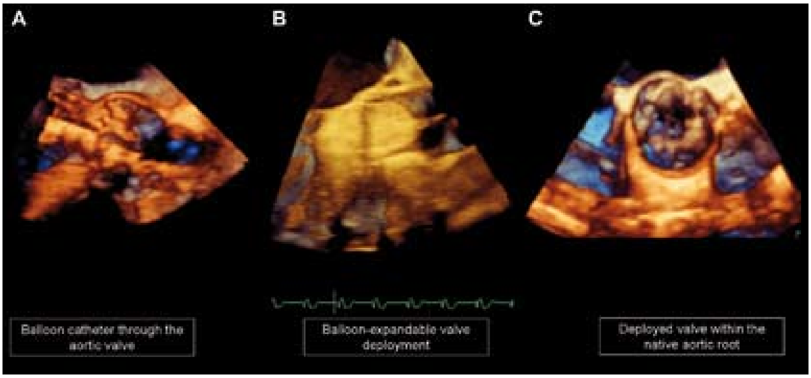

Figure 19. Three-dimensional transesophageal echocardiography during transcatheter aortic valve implantation procedure. First, the balloon catheter through the aortic valve is visualized (left panel) and subsequently, balloon dilatation of the aortic valve is performed. After deployment of the balloon-expandable prosthesis (middle panel), the function and position of the implanted valve can be assessed (right panel).

Transcatheter "valve-in-valve" procedure is a novel concept that has emerged as an alternative for replacement of aortic or mitral bioprosthesis. The morbidity and mortality risks of a redo operation for degenerated aortic or mitral bioprostheses are substantially higher. The feasibility of "valve-in-valve" procedure has been demonstrated experimentally[117] and to date, a few successful "valve-in-valve" procedures have been reported in humans.[118, 119]

Finally, percutaneous treatment of periprosthetic regurgitation is a promising alternative for patients with prosthetic valves at a high risk of reoperation. Initial case reports have described the feasibility of this procedure with mixed results.[120] The Amplatzer PDA occluder device is commonly used in these procedures. 3D transesophageal echocardiography may allow for exact localization of the periprosthetic regurgitation and assists in the occluder deployment during the procedure.

CONCLUSIONS

Current 3D echocardiography is close to routine clinical practice and is complementary to 2D imaging. As RT3DE does not rely on erroneous geometric assumptions of the heart, quantifications of chamber volumes and global functions from 3D datasets have superior accuracy and reproducibility over 2D echocardiography. Furthermore, RT3DE allows simultaneous assessment of regional myocardial function and perfusion, including the assessment of LV dyssynchrony in the context of cardiac resynchrnization therapy. RT3DE and 3D color Doppler echocardiography have improved our understandings of valvular anatomy, geometry and function, and allowed more accurate quantifications of the severity of valvular pathologies. Finally, the ability of 3D transesophageal echocardiography to provide real-time imaging is an invaluable tool before, during and after cardiac interventions such as transcatheter valve replacements. Future improvements including life 3D volumetric imaging with improved spatial and temporal resolutions will make 3D echocardiography an exciting ultrasound imaging modality.

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