VALVE DISEASE AND 3-D ECHO-CARDIOGRAPHY

Three dimensional echocardiography in valvular heart disease

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ABSTRACT

Although cardiac structures exist in three dimensions, two dimensional (2-D) echocardiography only provides information in a single tomographic plane, the orientation of which is determined by the ultrasound window. Accordingly the use of geometric assumptions and/or mental integration of information from multiple 2-D images are needed to assess cardiac function and structure. Advances in ultrasound technology and image reconstruction have opened up the possibility of using three dimensional (3-D) techniques in both quantitative applications such as measurement of ventricular volumes and qualitative applications such as the assessment of valve stenosis or regurgitation. Further technical improvements in terms of real-time 3-D imaging and development of 3-D transoesophageal echo (TOE) probes; have opened up further applications including intra-operative guidance of percutaneous valve interventions.

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INTRODUCTION AND TECHNOLOGY OVERVIEW

This article aims to give an overview of the applications of 3-D echocardiography in the assessment and treatment of valvular disease in adults in current clinical practice. There has been considerable evolution in technology since the initial description of three-dimensional (3-D) echocardiography several decades ago.[1] The first generation of 3-D probes performed gated acquisition with static rendering of images, but not in real time. The second generation did to an extent allow real-time imaging but the relatively low density of active elements (approximately 300) resulted in low sampling rate and compromise to image quality. Current 3-D probes, due to the high element count (>3000), deliver the high sampling rates necessary to achieve clinically useful real-time 3-D imaging with high image resolution and satisfactory frame rates.

Imaging in 3-D essentially involves the acquisition of a volume data-set over one or more heartbeats, depending on volume size. In "full-volume" acquisitions, typically four or more sub-volumes, are acquired with ECG gating and are stitched together to create a larger volume. This is used for larger structures, for example in assessment of left ventricular function and volumes. "Full-volume" acquisition can also be performed with colour Doppler to assess origin and shapes of flow jets in 3-D. This often requires more sub-volumes and ECG-cycles (typically seven), and the total volume acquired is often smaller than the "full volume" without colour Doppler. As might be expected, the major limitation of this approach is "stitching" artefacts that are created when the sub-volumes are not aligned. This occurs in two situations - firstly when the heart rhythm is irregular, e.g. ectopic beats or atrial fibrillation and secondly when there is significant translational motion of the heart with, for example, respiration or other patient movements. Single heart beat large volume acquisitions are under development; however a limitation of current technology is that as the volume of interest increases in size, image quality is compromised in terms of spatial and temporal resolution. If a smaller 3-D volume is obtained, then live or real time 3-D imaging with good resolution and frame rates is possible. This is useful for studying a single structure of interest such as the mitral valve or atrial septum and removes the problem of irregular heart rhythms. However, currently there is no colour Doppler available with live 3-D imaging. As with all echo techniques, 3-D methods are still dependent on obtaining an adequate echo window.

An image on a flat plane monitor is created by using two-dimensional (2-D) "pixels". In 3-D imaging, "voxels" or volume pixels are acquired and for the operator to appreciate all three dimensions on a 2-D display, the perception of "depth" is achieved by shading techniques. The volumetric datasets can be "cropped" in either standard tomographic planes or oblique planes to remove unwanted structures and display the regions of interest. Measurements can be made of distance or area from any 2-D plane within the 3-D dataset, but direct measurements from the 3-D image display are currently not possible although an appreciation of size can be made by overlaying a grid of known dimensions.

CLINICAL APPLICATIONS OF 3-D

Imaging in 3-D provides clear appreciation of the true shape of cardiac structures and the spatial relationships between them. Full evaluation of valvular heart disease, whether for diagnosis or planning of an intervention, requires accurate delineation of the actual valve pathology but also assessment of any consequent cardiac dysfunction including assessment of ventricular size and function (see below). 3-D methods can also be used for assessment of ventricular dyssynchrony and for morphological assessment in congenital lesions, but these applications will not be discussed further in this review. Table 1 shows common clinical applications of 3-D-transthoracic and transoesophageal echo. The clinical utility of 3-D echocardiography in valvular disease is well illustrated by its use in mitral valve disease, which will be covered in more detail. Once the reader has grasped these concepts they will be able to apply the principles to other valve lesions.

THE LEFT AND RIGHT VENTRICLES

Assessment of left ventricular systolic function by 2-D echo has several potential sources of error, including geometric assumptions that do not account for wall motion abnormalities or irregular ventricular shapes, and acquisition of foreshortened images, both of which can result in significant inter-observer and inter-study variability. 3-D echo avoids these problems and current equipment allows LV-image acquisition over a few heartbeats and semi-automated post processing within a few minutes. Using cardiac magnetic resonance imaging (MRI) as gold standard, several studies have compared 2-D and 3-D echo methods of assessing LV volumes and mass. 2-D methods appear to underestimate LV volumes but overestimate LV mass, whereas 3-D echo shows good agreement with MRI.[2-4] Recently the additional assessment of left ventricular volumes by 3-D echo in unselected patients in a multi-centre setting was shown to be quick (five extra minutes on average), and altered the management of significant numbers of patients compared to estimation of systolic function by 2-D echo alone.[5] The accuracy of 3-D echo and ability to detect small but significant changes in systolic volumes is likely to contribute to decisions regarding optimum timing of valve surgery. This may be particularly advantageous in difficult clinical situations such as the asymptomatic patient with apparent severe valvular disease.

The right ventricle presents difficulties in assessment of systolic function due to its unique shape. Comparison of 3-D echo with MRI has shown good agreement for RV volumes, but not mass.[6,7] Right ventricular volumes have been measured by 3-D echo in a 200 patient series with a variety of conditions by Tamborini et al., who reported that this appears feasible with a mean of 3 minutes for image acquisition and 4 minutes for analysis. They also reported good correlation of 3-D ejection fraction with conventional indices of RV function such as tricuspid annulus plane systolic excursion (TAPSE).[8]

TABLE 1: Clinical applications of 3-D

Advantages of 3-D echo
Qualitative
Accurate depiction of anatomy
Demonstration of spatial relationships between cardiac structures
Quantitative
Accurate and reproducible chamber volumes and mass (TTE FV)
Regional timings and dys-synchrony (TTE FV)
Accurate mitral valve area planimetry (TTE FV & RT TOE)
Precise multi-dimensional measurements of defects such as PFO/ASD (RT TOE)
Indications of 3-D echo
Established indications
Accurate left ventricular volumes and ejection fraction
Assessment of mitral regurgitation/stenosis
Intra-operative guidance of transcatheter interventional procedures
Assessment of prosthetic valve function/dysfunction
Assessment of congenital heart disease
Emerging indications
Assessment of aortic stenosis/regurgitation
Accurate right ventricular volumes and ejection fraction
Intra-operative guidance of mitral valve surgery
Assessment for cardiac resynchronisation
Useful in theory but no clear indication yet
Assessment of tricuspid/pulmonary valve disease

RT = real-time. FV = full volume. ASD = atrial septal defects. PFO = patent foramen ovale.

THE MITRAL VALVE

The mitral valve with its complex geometry comprising the annulus, leaflets and sub-valve apparatus is ideally suited to 3-D assessment. The mitral annulus is saddle shaped, with high points at the anterior and posterior regions and low points at the leaflet commissures. The posterior leaflet inserts into two-thirds of the mitral annular circumference, while the anterior leaflet is larger by area and approximately accounts for two-thirds of the total valve area. The posterior leaflet is divided into 3 regions P1 (anterolateral), P2 (middle) and P3 (posteromedial), and the anterior leaflet is divided into opposing segments A1-A3.

MITRAL REGURGITATION

Mitral regurgitation can arise from several mechanisms – classified by Carpentier. Type I - leaflet motion is normal, but regurgitation arises from reduced coaptation (e.g. mitral annular dilatation); Type II – leaflet motion is excessive (e.g. myxomatous or flail leaflets); and Type III – leaflet motion is restricted (e.g. ischaemic papillary muscle dysfunction). Guidelines emphasise the benefits of valve preservation by repair on patient outcomes.[9] An accurate description of the mechanism of valve failure is required to predict the techniques needed and likelihood of achieving successful mitral repair. This helps to guide the decision on the best time to intervene and offer surgery, as increasingly mitral repair is being performed in asymptomatic patients with severe mitral regurgitation.[10,11] However, if there is a high chance that the valve may be replaced then surgery is better delayed until symptoms develop or other parameters are met such as a dilating ventricle or falling left ventricular ejection fraction. Assessment of the mitral valve by 2-D echo requires the operator to obtain multiple views through all segments of the two leaflets. This requires considerable expertise and experience, but even then errors in interpretation may occur. By comparison 3-D echo (TTE or TOE), can give a rapid overview of the mitral valve using the en-face or "surgical view" of the mitral valve from the left atrium. The extent of any prolapsing or restricted leaflet segments, the commissures, leaflet coaptation line and mitral annulus can be seen and images can also be rotated to view the valve from the ventricular side. Figure 1 shows several examples of posterior mitral leaflet prolapse on 3-D echo and illustrates how this allows appreciation of differences between them. 3-D echo also gives the ability to perform accurate segment by segment analysis. Rapid online analysis can be performed by viewing the dataset in multiplanar reconstruction format to define short axis and long axis views of the mitral valve. Using established landmarks the entire coaptation line can be assessed from the anterolateral commissure, P1 and A1 segments through P2, A2 and then P3, A3 and the posteromedial commissure. The relationship of each segment to the annulus can be accurately assessed. Measurements can be made of segment prolapse or tenting in relation to the annulus. Suggested protocols for obtaining the surgical view and segmental analysis are summarised in Table 2, while

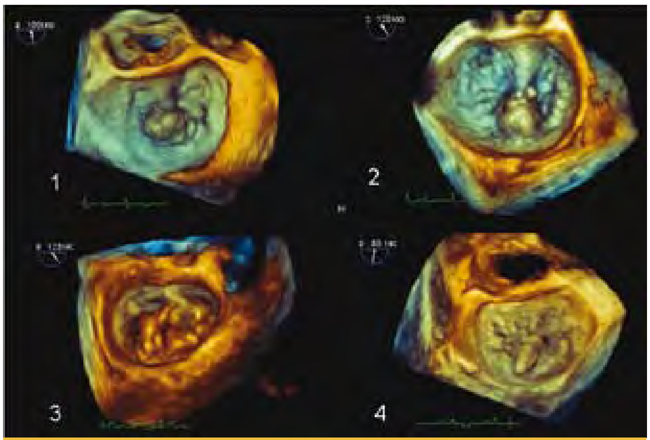

FIGURE 1: Surgical view of the mitral valve on transoesophageal echocardiography, showing 4 examples of P2 segment prolapse. **Image 1:** prolapse of the lateral portion of P2 and part of P1, with chordal rupture in that region. **Image 2:** central portion of P2 is flail with chordal rupture. The regurgitant jet tracks over A2 where a deep ridge is visible. **Image 3:** A lateral portion of P2 prolapse with chordal rupture. There is a deep "cleft" in the P2 segment, extending back to the annulus, on the right of the prolapse. **Image 4:** Central P2 segment prolapse with several points of chordal rupture.

TABLE 2: Suggested protocols for obtaining the surgical view and segmental analysis

Surgical view	
TTE	parasternal long axis-live 3-D data set
	or parasternal short axis-live 3-D data set
TOE	mid oesophageal long axis-live 3-D data set /zoom mode
	- rotate image to look on to mitral valve from left atrium
	- optimise image to see leaflets in entirety
Segmental analysis	
TTE	parasternal long axis-full volume 3-D data set
	or apical long axis-full volume 3-D data set
TOE	mid oesophageal long axis-live 3-D data set /zoom mode
	- biplane imaging
	- optimise image to see left atrium/leaflets/annulus/subvalve

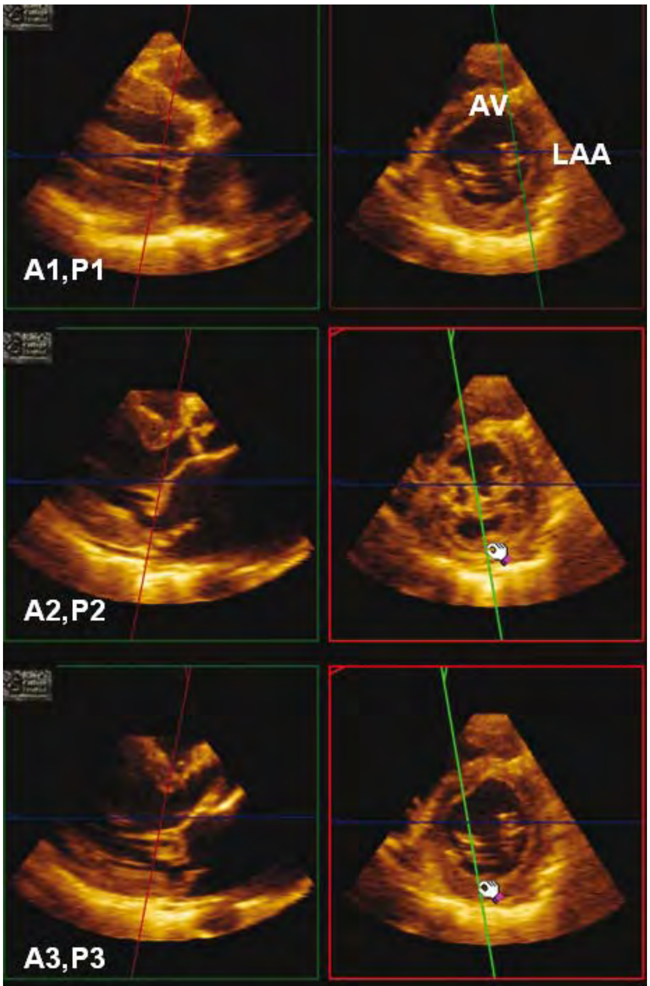

FIGURE 2: Segmental analysis of the mitral valve: Transthoracic full-volume 3-D dataset taken from the parasternal long axis window. Using multiplanar reconstruction format long axis and short axis views are displayed at three levels. The level of each segment is confirmed in short axis and then assessed during systole in long axis. The images shows P2 flail segment with additional prolapse of P3 and A3.

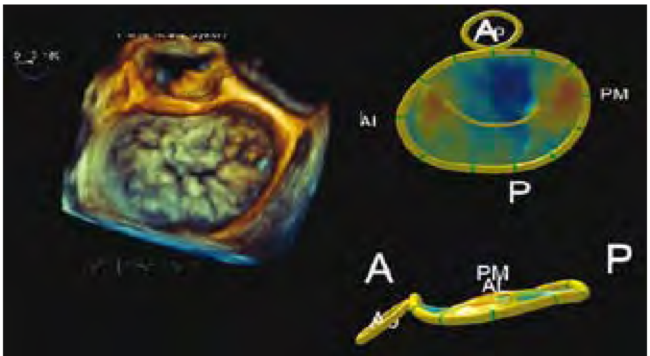

FIGURE 3: Severe mitral regurgitation was seen through a deep cleft in P2. Detailed analysis with MVQ software, showed a severely dilated annulus with total loss of its normal saddle shape and no significant prolapse - confirming that the primary lesions were the deep cleft in P2 and the annular dilatation.

Figure 2 gives an example of segmental analysis. Dedicated mitral valve quantification software (e.g. MVQ, Phillips Medical) is available for use with 3-D TOE datasets – an example is given in Figure 3. This can give a very detailed assessment with accurate measurements of the annulus and leaflets, papillary muscle position and aortic-mitral angles, and is likely to play an important role in pre-operative planning of mitral valve repair in the future.

The literature confirms the clinical utility of 3-D echo in mitral regurgitation and the comparison of real time 3-D TTE with 2-D TOE has shown comparable high sensitivity, specificity and accuracy for identifying prolapsing mitral segments.[12] However in that study a small proportion (11%) of patients were excluded due to insufficient image quality by transthoracic echo. Macnab et al. compared 2-D and 3-D TOE assessment of the mitral valve against the gold standard of surgical findings, and reported that 3-D TOE is more accurate at identifying the location and extent of leaflet prolapse – particularly at the most medial and lateral portions of the valve.[13] More recently, Grewal et al. performed a similar study and also found superior performance of 3-D TOE, particularly in identifying complex disease involving multiple segments or both leaflets.[14]

Assessment of the severity of mitral regurgitation by 2-D echo can be challenging, particularly with eccentric jets. 3-D colour Doppler allows better visualisation of the origin, size and shape of jets.[15,16] The vena contracta and proximal isovelocity surface area (PISA) methods are other common methods used to quantify severity of mitral regurgitation, the latter also allowing calculation of effective regurgitant orifice area and regurgitant volume.[17] The conventional PISA method assumes a hemispheric shape of the isovelocity surface, which very often is not the case. 3-D methods allow assessment of the true shape of proximal flow convergence region and also permit more accurate measurement of the PISA and vena contracta.[18,19]

In clinical practice 3-D used as part of the initial TTE study could largely replace the need for initial 2-D TOE as this allows more confident assessment of leaflet morphology, and hence the likelihood of successful repair and timing of intervention. Once the decision for surgery is made a TOE with 3-D imaging could be performed to accurately define valve anatomy and dimensions used for pre-operative planning.

While surgical repair remains the therapy of choice in severely regurgitant mitral valves, functional mitral regurgitation often involves significant left ventricular impairment. Such patients may face significant risk from conventional surgery and percutaneous approaches are currently being explored. MitraClip (Evalve Inc) is one example, based on the surgical Alfieri operation, and inserted using a transvenous approach and atrial septal puncture. The "clip" is positioned over the regurgitant orifice grasping both mitral leaflet free edges, creating a double orifice with significant reduction in mitral regurgition.[20] 3-D TOE imaging provides excellent assessment of the mitral annulus dimensions, location and extent of the regurgitant orifice and leaflet morphology; all essential in planning the procedure. During the procedure 3-D echo is also of considerable value.[21] The position of trans-septal puncture is crucial - if it is too high or too low on the atrial septum the delivery system may either not reach the valve or assume an awkward angle making clip deployment impossible. 3-D imaging allows a precise atrial-septal puncture, and accurate positioning over the mitral valve leaflets during clip deployment. Once successfully deployed, assessment of residual regurgitant jets and how this relates to valve anatomy can also be performed using 3-D.

MITRAL STENOSIS

The commonest cause for mitral stenosis is rheumatic heart disease. Stenosis severity is quantified in terms of mean transmitral gradient and mitral orifice area.[22] Methods that calculate the "effective" mitral orifice area include pressure half time measurement (PHT), continuity equation and PISA (proximal isovelocity surface area) methods. However these have their limitations - the Doppler derived mitral valve area is influenced by factors including tachycardia, heart rhythm, non-linear Doppler velocity curves, concomitant valvular disease, and is not applicable in the immediate period post balloon valvuloplasty.

Direct planimetry can be used to measure the true "anatomic" orifice area. This is considered to be the reference method in clinical practice having been shown to correlate more precisely to direct measurement of anatomic orifice at surgery than other Doppler methods.[23] However the mitral valve is often funnel-shaped and the stenotic orifice may be situated obliquely within the ventricle. 2-D planimetry is limited by difficulties in obtaining the minimum cross sectional area during planimetry measurements. This method demands considerable experience and expertise to define the correct orientation of the true mitral valve orifice. 3-D TTE helps locate the plane with the smallest mitral valve orifice as the image can be viewed using multi-planar reformatting to align with the orifice in long and short axis, (Figure 4). Use of 3-D has been shown to be an accurate method for assessing mitral valve area, faster and more reproducible than 2-D echo.[24,25] If the patient is in atrial fibrillation, rather than "full-volume", live 3-D imaging should be used. Invasive catheter measurements using Gorlin's method has also been compared to 3-D echo and the latter appears to correlate more closely to other non-invasive methods.[26] Another limitation of 2-D echo planimetry is the presence of significant calcification particularly when within the leaflets. This can be overcome by 3-D TOE imaging, as clear imaging of the orifice is possible from the left atrial en-

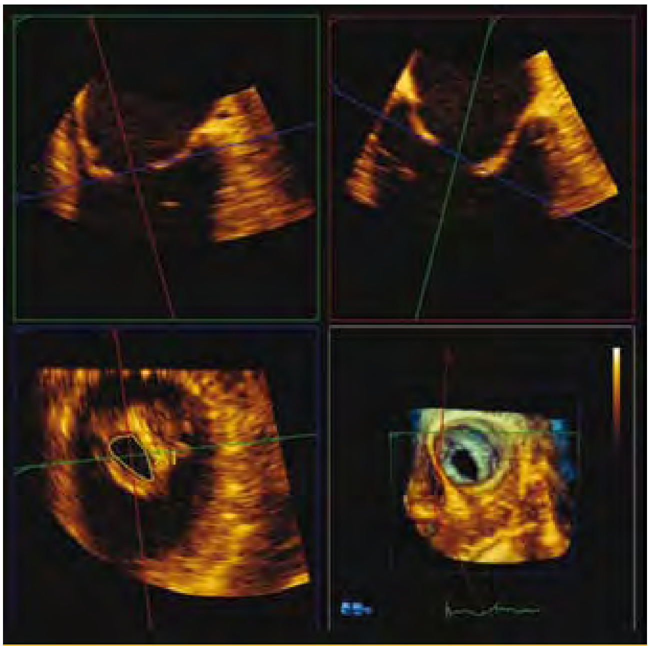

FIGURE 4: 3-D TOE live "zoom" mode of a stenotic mitral valve: Multiplanar reconstruction method to accurately locate and quantify true anatomic mitral valve orifice area by planimetry.

face view as calcific shadowing is cast into the left ventricle. Alternatively the use of 3-D TTE with colour Doppler is another solution.[27] It seems likely that 3-D techniques will become the new "gold standard" for quantifying mitral valve area.

Percutaneous balloon valvuloplasty is an effective treatment for appropriately selected patients with rheumatic mitral stenosis. 3-D TOE can provide accurate information on the functional significance and morphology of the valve to determine suitability for balloon valvuloplasty. Accurate peri-procedural evaluation of the mechanism and effect of valvuloplasty is also desirable - with 3-D assessment one can determine the increase in valve area and whether this has occurred due to commissural splitting as intended, or due to leaflet tearing. It is also recognised that Doppler-derived measures of mitral valve area are inaccurate immediately post valvuloplasty due to acute changes in left atrial compliance and transmitral gradient.[28] The most reliable method of assessing change in area is direct planimetry and 3-D TTE has been shown to correlate best immediately post procedure with invasive measurements.[29]

PROSTHETIC VALVE ASSESSMENT

When considering prosthetic valve function traditional methods focus on assessment of flow characteristics. 2-D Doppler parameters are used to describe the effective orifice area. However, not uncommonly we encounter the problem of "high velocities" across the valve. The differential diagnosis includes a normal finding for that particular valve type and size, patient prosthesis mismatch or valve malfunction e.g. due to pannus formation. Assessment of prosthetic valve morphology by 2-D echo is limited

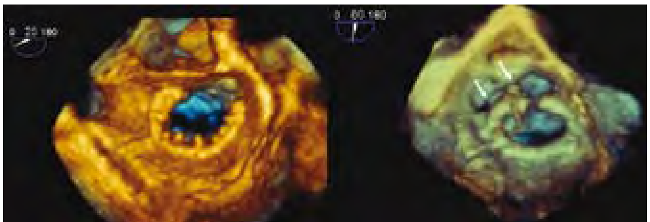

FIGURE 5: Left image shows a mitral valve repaired with an annuloplasty band. Right images show partial band dehiscence (white arrows) from the annulus with a visible unravelled suture.

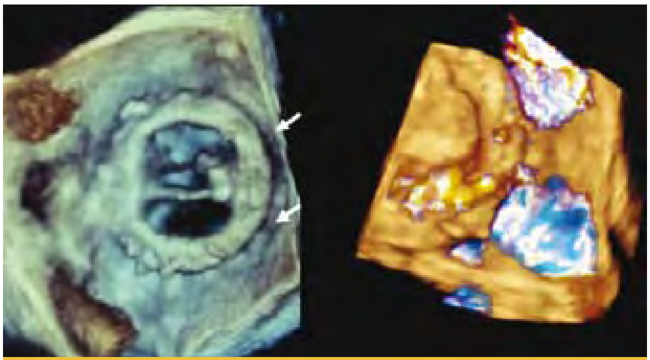

FIGURE 6: Left image St Jude's bi-leaflet mechanical valve with pannus formation over leaflets and two large regions of valve dehiscence (white arrows). Right image depicts paravalvular regurgitation identified with 3-D colour Doppler.

by artefact and shadows cast around the prosthesis, particularly with mechanical valves.

3-D TOE, and to a lesser extent 3-D TTE, can clearly demonstrate prosthetic valve morphology and disc/leaflet motion can be observed in real time.[30,31] 3-D echo also provides clear images of mitral repair and dehiscence of annuloplasty rings can be appreciated, (Figure 5). Para-valvular leaks can be identified by a combination of 3-D zoom and 3-D FV colour imaging, (Figure 6). Real time 3-D TOE has been shown to be superior in assessing the site and extent of para-valvular leaks as compared with 2-D TOE.[32]

AORTIC VALVE

In aortic stenosis, indices of severity include the peak jet velocity and mean transaortic gradient as well as effective orifice area (by the Doppler derived continuity equation).[22] However, continuity equation assessment of valve area makes assumptions over the LVOT tract shape, which can be more accurately measured with 3-D echocardiography. Hybrid measurements using 2-D Doppler derived aortic valve velocity time integral and 3-D derived LV stroke volume have shown promise in this regard.[33] Direct assessment of aortic valve area by 2-D echo is challenging since unequal restriction of leaflets can lead to the aortic valve opening becoming distorted and this is further compounded by the presence of calcification. Although the principles of 3-D valve planimetry can be applied to aortic stenosis,[34] the role of such measurements are limited and are not recommended except where Doppler methods are unavailable.[22] In one TOE study the aortic valve, was optimally visualised in only 18% of subjects as compared to >90% for the mitral valve.[35] However, the majority were normal aortic valves with thin pliable leaflets. Acoustic shadowing can limit the 3-D anatomic assessment of aortic stenosis.

Although one study has shown that the severity of aortic regurgitation can be accurately quantified by measuring the vena contracta area using 3-D echo (rather than width as in 2-D), and conceptually such an approach appears attractive, further studies are needed and currently this has not yet entered routine clinical use.[36] The additional morphological information gained from 3-D imaging of the aortic valve may also be useful where there is a discrepancy between clinical and echocardiographic data. A good example is in the presence of subaortic membranes, which can be easily missed by 2-D techniques.[37]

Transcatheter Aortic Valve Implantation (TAVI) is a novel minimally invasive treatment for aortic stenosis. 3-D TOE allows additional information about the left ventricular outflow tract and aortic annulus size before the procedure, as well as confirming the presence of a tri-leaflet aortic valve (a bicuspid valve is a relative contra-indication to TAVI due to increased risk of displacement of the prosthesis). 3-D TOE during the procedure can guide positioning of the valve to ensure that it will sit clear of nearby structures including the basal interventricular septum, anterior mitral valve leaflet and coronary arteries; the 3-D spatial orientation of these structures are not readily appreciated by fluoroscopy or 2-D imaging alone. 3-D TOE can also be invaluable in detecting complications immediately after deployment including the location and extent of paravalvular regurgitation.

RIGHT-SIDED VALVE DISEASE

It seems intuitive that the 3-D techniques described above in relation to the mitral and aortic valves would also be well suited to assessment of the right sided heart valves. However currently there are only a few reports in the literature so far regarding the use of 3-D techniques in assessment of tricuspid valve disease.[38,39]

FINAL COMMENTS

Traditional 2-D imaging emphasises acquiring specific on-axis views to produce standardised images, as chamber measurements made in these views are prognostic markers in many disease states. 3-D imaging requires a different approach to scanning. Since 3-D imaging offers enface views of cardiac structures it requires a clear understanding of cardiac anatomy. Appreciation of the orientation of the heart in 3-D within the chest and how cardiac structures are related to one other are essential to fully utilise the potential of 3-D echocardiography. As with all new techniques there is a significant learning curve and image quality is still dependent on echocardiographic windows. Once users become familiar with the technology, adding 3-D acquisitions onto a standard 2-D study typically requires only a few extra minutes, although further time may be required afterwards for "post-processing". 3-D echocardiography provides incremental information over standard 2-D techniques, allowing more accurate assessment of cardiac and in particular valvular disease. This can be used to refine the diagnosis and better guide the treatment of patients. Some of the common clinical applications of the technology have been described above, although the clinical uses of 3-D echocardiography will likely continue to grow.

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