Mitral valve anatomy and function: new insights from three-dimensional echocardiography

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By integrating volumetric rendering with motion in real-time, three-dimensional (3D) echocardiography is the most suited imaging technique for assessing heart valves. Today, the rapidly advancing 3D technology allows us to perform a virtual ‘dissection’ of the heart intra vitam and to discover unprecedented, realistic views of cardiac valves in just a few minutes. The mitral valve is the cardiac structure easiest to visualize by transthoracic or transesophageal approach. 3D echocardiography is able to display the non-planar valve leaflets and annulus, the complex subvalvular apparatus and their spatial relationships with the surrounding structures. The complementary use of 3D colour flow adds data about valve integrity and allows the quantitation of valvular diseases. Accumulating evidence suggests that 3D echocardiography is emerging as the reference technique to assess mitral valve morphology and function and guide valvular procedures of mounting complexity. The purpose of this review is to provide an update on the current clinical applications of 3D echocardiography for assessing mitral valve and stressing the incremental benefits of 3D echocardiography over conventional two-dimensional echocardiography.

Introduction

Three-dimensional echocardiography (3DE) is the most suited imaging technique for assessing heart valves, by integrating volumetric rendering with motion in real time. Today, the rapidly advancing 3D technology allows us to perform a virtual ‘dissection’ of the heart intra vitam and to discover unprecedented, impressive views of cardiac valves in just a few minutes (Fig. 1). In particular, the mitral valve is the cardiac structure easiest to adequately visualize by transthoracic or transesophageal (3DTEE) approach. 3D is able to display the non-planar valve leaflets and annulus, the complex subvalvular apparatus and their spatial relationships with the surrounding structures. The complementary use of 3D colour Doppler flow adds data about valve integrity and allows the quantitation of valvular diseases.\textsuperscript{1} 3DTEE can either supplement the transthoracic 3DE with new information and greater anatomic detail of mitral valve anatomy (Fig. 2), or replace it when transthoracic imaging is unfeasible (e.g. inadequate acoustic window for 3DE, intraoperative monitoring, etc). Since the cumbersome mental reconstruction from separate tomographic mitral valve views is no longer required, 3DE is rapidly gaining more advocates within the echocardiography field and especially among cardiovascular surgeons, for its unique capability to display a realistic mitral valve anatomy in the beating heart and for the striking similarity with their perspective on the operating table. Accumulating evidence suggests that 3D is emerging as the reference technique to assess mitral valve morphology and function, and guide valvular procedures of mounting complexity.\textsuperscript{2,3}

Examination of normal mitral valve by three-dimensional echocardiography

Normal mitral valve function depends on the structural integrity and optimal interaction among all components of the mitral valve apparatus: the leaflets, the subvalvular apparatus (chordae tendineae and papillary muscles), the annulus and the left ventricle (LV).

Mitral leaflets

Conversely to conventional two-dimensional (2D) technique, which displays the mitral valve leaflets en face only from the left-ventricular perspective, 3D enables their visualization from both left-ventricular and left atrial perspectives (Fig. 3).\textsuperscript{1} The latter is also known as ‘surgical view’, since it resembles the intraoperative image when the surgeon approaches the mitral valve from the right side of the patient, by opening the left atrium. Furthermore, 3DE allows practically any cut plane of the data set to obtain conventional or unconventional display. 

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of mitral valve leaflets, both from apical and parasternal approaches.

The anterior leaflet appears larger and it is attached to about one-third of the annular circumference. The posterior leaflet has a quadrangular shape and it is attached to the other two-thirds of the annulus. For surgical repair purposes, both leaflets are divided into three individual segments (scallops): $A_1$, $A_2$, $A_3$, the anterior; and $P_1$, $P_2$, $P_3$, the posterior (from left to right, respectively) (Fig. 1). The posterior mitral valve leaflet is best visualized from parasternal window, whereas the anterior leaflet can be well appreciated from both apical and parasternal windows.

Subvalvular apparatus

The anatomic and functional integrity of mitral valve subvalvular apparatus can be well appreciated from longitudinal cut planes (Fig. 4). En face views of the mitral valve from the left-ventricular perspective allow to evaluate the chordal insertions on mitral valve leaflets. Conversely, chordal rupture with flail/prolapse can be well visualized from ‘surgical’ view (Fig. 5) and from selected longitudinal cut planes across corresponding scallops (i.e. $A_1$-$P_1$, $A_2$-$P_2$, $A_3$-$P_3$).

Mitral annulus

The normal mitral annulus is oval and saddle-shaped, with its lowest points located at the commissures, and its highest points near the aortic root and near the posterior wall. The elliptical shape of mitral valve annulus is best appreciated from the surgical view of the mitral valve, encompassing the whole annular circumference in...
Mitral valve anatomy and function Muraru et al.

one view (Fig. 1). Performant tools to precisely quantitate the size, shape and degree of non-planarity of mitral valve annulus have been developed in order to better understand mitral valve mechanics and to assist the surgeon in evaluating the feasibility of mitral valve repair (Fig. 4). Evidently, 2D echocardiography (2DE) is not able to provide data about the shape of mitral valve annulus, since mental reconstruction from separate 2D views cannot provide the same information as the volume-rendered 3D reconstruction.

The mitral valve annulus is a dynamic structure and it has been noted that it undergoes dynamic changes, with cyclic changes in area and longitudinal displacement toward the apex during systole. A comprehensive description of these dynamic changes by transthoracic 3DE and the reference values of parameters describing the geometry of mitral valve apparatus have been reported. In healthy individuals, the mitral leaflets appear nearly flat with minimal tenting in mid-systole, and the mitral annular surface area reaches the largest value during the rapid left-ventricular filling phase. During the systolic phase, the steepening of the saddle shape and the descent of the annulus toward the apex seem to favour the normal apposition of the mitral valve leaflets. Using perioperative 3DTEE, a thorough understanding of the mechanisms of mitral valve regurgitation – including the loss of annular dynamic changes caused by ventricular remodelling or valve degeneration – may help to select the best approach for mitral valve repair. As a practical consequence of the dynamic changes in annular area, the annulus sizing should also take into account the timing of the cardiac cycle in which measurements are performed (most 3DE studies using automated quantification in mid-systolic frame).

Mitral-aortic coupling

As previously described, mitral valve and aortic valve are coupled via fibrous tissue connecting the two annuli. Thanks to the introduction of 3DTEE, it has recently become possible to study the two valves simultaneously by using a non-invasive imaging method with adequate spatial and temporal resolution. The fibrous continuity between the two valves has a dense fibrous structure, acting as an anchor for the anterior part of the mitral annulus, whereas the posterior part is more dynamic, being mainly formed by muscular components. Consequently, mitral valve annulus deforms during cardiac cycle, its area reaching its largest dimension in early diastole when the projected aortic area is minimal, and vice versa during systole. This coupled reciprocal behaviour of the two valves contributes to the efficiency of the heart as a pump. A decreased angle between the two valves during ejection has been also noted and identified as an additional factor potentially facilitating blood ejection. Veronesi et al. recently demonstrated that mitral valve repair with annuloplasty ring can alter aortic valve pulsatility and its longitudinal excursion, highlighting the concept of the two valves functioning as a unique apparatus.

Left ventricle

The normal motion and contraction of the LV also contribute to maintain the mitral valve competence. Any change in ventricular geometry that affects papillary muscle position can change the axial relationship of the chordae and leaflets, resulting in poor coaptation (Fig. 4). 3DE allows a comprehensive qualitative assessment of left-ventricular shape and regional function and an accurate quantitation of left-ventricular volumes, geometry and systolic performance. In addition, observing leaflet mobility on 3D images can discriminate between normal leaflet mobility and tethered leaflet(s) due to regional wall motion abnormalities or global left-ventricular enlargement with increased sphericity, resulting in functional mitral regurgitation.
Mitral regurgitation
Three-dimensional echocardiography has a great potential to complement the conventional 2DE for a more accurate diagnosis and a tailored treatment of mitral regurgitation (Table 1).

Degenerative mitral regurgitation
The common mechanism of degenerative mitral regurgitation is leaflet prolapse due to chordal elongation or rupture, with secondary leaflet malcoaptation during systole. The echocardiographic findings cover a wide spectrum in correspondence with the pathologic changes: simple chordal rupture with one prolapsing scallop (usually P2) in fibroelastic deficiency; thickening and expansion of one scallop with long-standing prolapse in secondary myxomatous degeneration; Barlow’s disease with large valve size and severely dilated annulus, excess leaflet tissue involving multiple segments and diffuse chordal elongation and prolapse of multiple segments with normal valve size in forme fruste (Fig. 5). Three-dimensional transthoracic echocardiography (3DTTE) determines the exact localization and extent of prolapsing segments with an overall accuracy of 95%, whereas 3DTTEE has the highest accuracy (97%).

Table 1  Comparison of diagnostic yield of 2D and 3D echocardiography in patients with mitral valve disease

<table>
<thead>
<tr>
<th>Authors</th>
<th>Population</th>
<th>Echo modality</th>
<th>Reference method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biaggi et al.16</td>
<td>50 pts with surgical repair for MVP-related MR</td>
<td>2D and 3D TEE</td>
<td>Surgical inspection</td>
<td>3D TEE was more accurate (92–100%) than 2D TEE (80–96%) in identifying prolapsed segments</td>
</tr>
<tr>
<td>La Canna et al.17</td>
<td>222 pts with surgical repair for MVP-related MR</td>
<td>2D and 3D TTE, 2D and 3D TEE</td>
<td>Surgical inspection</td>
<td>3D TEE was more accurate (92%) in identifying prolapsed segments than 2D TEE (78%), 3D TEE (80%) and 2D TEE (54%) and a superior quantitative recognition of dominant (≥5-mm displacement) and secondary (2 to &lt;5 mm displacement) lesions</td>
</tr>
<tr>
<td>Ben Zekry et al.18</td>
<td>40 pts referred for MV repair</td>
<td>2D and 3D TTE, 2D and 3D TEE</td>
<td>Surgical inspection</td>
<td>All modalities were equally reliable in identifying the mechanism of MR (functional vs. organic). 3D TEE was superior in localizing the disease and identifying anterior leaflet prolapse</td>
</tr>
<tr>
<td>Tamborini et al.19</td>
<td>200 pts with severe MVP-related MR</td>
<td>3D TTE</td>
<td>Surgical inspection</td>
<td>Accurate characterization (95%) of all MV lesions, including the identification of simple vs. complex lesions</td>
</tr>
<tr>
<td>Pepi et al.20</td>
<td>112 pts with MVP and severe MR</td>
<td>2D and 3D TTE, 2D and 3D TEE (reconstruction 3D TEE)</td>
<td>Surgical inspection</td>
<td>3D TEE showed similar accuracy as 2D TEE (90 vs. 87%); 3D TEE showed superior accuracy (95%), whereas 2D TEE was the least accurate modality (77%)</td>
</tr>
<tr>
<td>Garcia-Orta et al.21</td>
<td>81 pts with severe MR</td>
<td>2D vs. 3D TEE (reconstruction 3D TEE)</td>
<td>Surgical inspection</td>
<td>3D TEE was more concordant than 2D TEE (100 vs. 88%) with surgical findings. Particularly about A1 and commissural lesions</td>
</tr>
<tr>
<td>Grewal et al.22</td>
<td>42 pts with severe MR</td>
<td>2D vs. 3D TEE (real-time 3D TEE)</td>
<td>Surgical inspection</td>
<td>3D TEE superior to 2D TEE imaging in the diagnosis of P1, A2, A3, and bileaflet disease Agreement between the 2 modalities was k = 0.93</td>
</tr>
<tr>
<td>Gutierrez-Chico et al.23</td>
<td>41 pts with MVP</td>
<td>3D TTE vs. 2D TEE</td>
<td>2D TEE</td>
<td>surgical findings. Particularly about A1 and commissural lesions</td>
</tr>
</tbody>
</table>

2D, two-dimensional; 3D, three-dimensional; MR, mitral regurgitation; MVP, mitral valve prolapse; pts, patients; TEE, transoesophageal; TTE, transthoracic.
Mitral valve anatomy and function Muraru et al. 5

diagnose complex lesions (medial and lateral scallops or commissural involvement) and to predict the complexity of surgical technique or need for mitral valve replacement.25 Having surgical inspection as reference, a quantitative morphologic analysis of mitral valve prolapse by 3DTEE (e.g. 3D billowing volume and billowing height) allowed a reliable identification of mitral valve prolapse from normal mitral valve and the discrimination between different causes of degenerative mitral regurgitation (Barlow disease and fibroelastic deficiency).26 All these parameters can be quantified by 3DE.27

In myxomatous mitral valve disease, the annulus is very enlarged but maintains its dynamic changes throughout the cardiac cycle; yet its dynamic pattern is different from normal individuals, showing a loss of early systolic area contraction and of the deepening of its saddle shape, despite a similarly normal ventricular contraction as in controls.9

Functional mitral regurgitation has been described as a ‘ventricular’ disease – typically occurring in patients with ischaemic or idiopathic dilated cardiomyopathy – with compromised geometry of the mitral valve apparatus. The annulus becomes larger and flatter with reduced dynamic changes, whereas the leaflets exhibit an enhanced apical tethering with restriction to closure.27 3DE data sets enable the measurement of different parameters describing the abnormal geometry of mitral annulus and papillary muscle displacement, mitral valve leaflet tethering and tenting in 3D space (tenting volume) (Fig. 4). Quantifying differences in mitral valve geometry and mitral regurgitation jet characteristics between ischaemic mitral regurgitation and functional mitral regurgitation in dilated cardiomyopathy can help to better understand the different pathophysiological mechanisms involved in these two types of mitral regurgitations.28 In comparison with functional mitral regurgitation due to dilated cardiomyopathy, ischaemic mitral regurgitation is characterized by smaller 3D mitral annular surface area, larger annular pulsatility (maximal change of mitral annular surface area expressed in percentage) and asymmetrically displaced papillary muscles.27 The extreme form of ischaemic mitral regurgitation is caused by papillary muscle rupture, usually the postero-medial one, given its single-vessel blood supply.29

In cases of inferior wall infarction, the predominant tethering involves the P3 scallop of the mitral valve, whereas tethering of multiple leaflet segments (both anterior and posterior) occurs after anterior infarction. By quantifying the extent of leaflet redundancy, billowing volume and displacement of mitral valve coaptation line, 3DE may identify a high risk of developing systolic anterior motion (SAM) after mitral valve repair and open new therapeutic ways of approaching functional mitral regurgitation (leaflet area modification).26

Quantification of mitral regurgitation severity is essential for clinical decision-making. 3DE enables an integrated approach, based on specific findings (mitral valve lesions), supportive findings (left-ventricular and left atrial volumes with increased accuracy and reproducibility than 2DE) and quantitative findings (regurgitant volume and regurgitant orifice area). The identification of mitral valve flail (Fig. 5), ruptured papillary muscle or a large, wall-impinging colour jet is highly suggestive for a severe mitral regurgitation. In cases with discrepant results from conventional 2DE (TTE and/or TEE), 3DE can complement the diagnosis work-up with additional information about mitral regurgitation severity.

Calculation of regurgitant orifice area and regurgitant volume by 2DE is based on geometric assumptions of a circular regurgitant orifice shape, and several factors (alignment, aliasing velocity, jet eccentricity) may cause underestimation or overestimation of regurgitant orifice area. Quantification of mitral regurgitation by 2DE using the vena contracta assumes that the regurgitant orifice shape is circular, which cannot be reliably verified with 2D imaging. It has been documented that vena contracta is not circular, but rather elliptical in most patients, especially in those with functional mitral regurgitation,30 and that 3D is significantly superior over 2D assessment, especially in patients with eccentric mitral regurgitation.31 3DE may overcome some of these limitations, and can accurately depict non-planar, slit-like or multiple anatomic regurgitant orifices which are most challenging for a 2D quantification approach. In preliminary studies, vena contracta area, 3D PISA-derived effective orifice area and regurgitant volumes by 3DTEE were reported to improve the accuracy in quantifying mitral regurgitation severity.32–34

Mitral valve stenosis

The therapeutic decision in mitral valve stenosis – balloon valvuloplasty (PMV) or mitral valve replacement – relies on two major informations about mitral valve obtained by echocardiography: accurate quantitation of residual mitral valve orifice and lesion morphology (commissural fusion, calcification, mobility, etc) to derive anatomic scores predictive for the feasibility of PMV.

Three-dimensional echocardiography enables a comprehensive anatomic characterization of leaflet, commissural and chordal involvement from any (un)conventional plane. Using transversal cut planes from the ventricular perspective it is possible to localize and planimeter the narrowest valvular orifice, by orienting the cut plane position according to the spatial orientation of mitral valve opening (symmetric/eccentric) (Fig. 6). Occasionally, multiple orifices of the stenotic mitral valve can be individualized and planimetered by 3DE.

Doppler methods for calculating mitral valve functional area have known intrinsic limitations (highly dependent on proper alignment and haemodynamic conditions,
Two-dimensional echocardiography has good sensitivity to detect pathologic masses and to assess their mobility, due to its high temporal and spatial resolution. However, its 2D nature and limited views induce inherent uncertainties and errors regarding the maximal size and the insertion point of these masses. Vegetations and tumours of the mitral valve apparatus can be nicely characterized as shape, size (maximal and minimal diameters, and total volume, irrespective of their shape), and insertion more readily and accurate with 3DE. 3DE can also depict leaflet perforations and colour Doppler supports the diagnosis with informations on mitral regurgitation mechanism and severity.

**Congenital mitral valve diseases**

Detailed anatomic analysis of mitral valve complex congenital abnormalities for diagnosis and planning mitral valve reconstructive surgery is not always possible with 2D transthoracic images. 3DE enables an intuitive delineation of mitral valve anatomy for a better understanding of the mechanisms responsible for mitral valve dysfunction, obviating the need for the difficult mental 3D reconstruction from separate 2D views. Dynamic mitral valve 3D offers unprecedented in-vivo images of mitral valve congenital pathology. In patients with mitral valve cleft, 3DE may quantify the width and depth of the cleft, informations that cannot be obtained from 2DE. In addition, 3DE also provides qualitative information regarding the degree of fibrosis and edge retraction, and the presence and impact of accessory chordae on the left-ventricular outflow tract and mitral valve motion. Other abnormalities, as double-orifice mitral valve, parachute mitral valve, anomalous insertion of mitral valve apparatus, unicuspid mitral valve and so on, all can be responsible for valvular dysfunction (stenosis and/or regurgitation) and 3DE is particularly suitable for their diagnosis through unlimited number of imaging planes and orientations.37

**Mitral valve repair and mitral prostheses**

Three-dimensional echocardiography, particularly 3DTEE, provides unparalleled views of both bioprosthetic and mechanical valve components, including leaflets and discs, rings and struts (Fig. 7). Excellent views can be obtained from various perspectives, even though acoustic shadowing may affect the proper visualization of mechanical mitral valve from the LV. 3DE is able to delineate the site, size and shape of the peri-prosthetic leaks, and it can be applied for accurate prosthetic valvular planimetry. 3D orifices area of valvular prostheses correlated better than Doppler orifice area with manufacturer orifice area,38 and may be able to better differentiate pathologic obstruction from severe patient–prosthesis mismatch.

Prosthetic valve thrombosis is a fearful complication of mitral mechanical prostheses and a prompt diagnosis is essential for patient care. 2DTEE is the standard for diagnosis, yet it is limited to certain cross-sectional views of the prosthesis. 3DTEE can display the entire circumference of the suture ring and the surface of discs in a

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**Fig. 6**

Rheumatic mitral stenosis. Two-dimensional (a, b) and three-dimensional (ventricular view, c; atrial view, d) echocardiographic visualization of characteristic abnormalities of rheumatic mitral valve stenosis: valve thickening and retraction, reduced opening with valve doming, commissural fusion (arrows). Please remark that the anatomical mitral valve area (AVM) obtained by two-dimensional echocardiography is significantly larger than by three-dimensional method.
single view (i.e. from left atrial or ‘surgical’ perspective), therefore allowing a precise evaluation of thrombosis and disc mobility. 3DE can delineate thrombosis localization and extension, as well as thrombus mobility and true size. The latter is particularly important in highly irregular 3D-shaped thrombi, in which the limited tomo-graphic views of 2DTEE cannot adequately delineate their maximal dimensions. The thrombotic load, apart from symptomatic status, can change the patient indication from conservative treatment to thrombolysis or even redo surgery; therefore an accurate diagnosis is warranted.

Three-dimensional transoesophageal echocardiography has a unique potential to become the standard for non-invasive echo monitoring during catheter-based interventions. For mitral valve balloon valvuloplasty, visualization of the entire length of the intracardiac portion of the guiding catheter, as well as continuous demonstration of the catheter tip is feasible, allowing clear delineation of the spatial orientation of the catheter and the balloon in the left atrium and their relation to the mitral valve orifice. For mitral valve clipping, proper positioning and orientation of the clip relative to the closure line of the mitral valve can be more easily assessed by 3DE than by 2DE. For both interventions, 3DTEE also allows the accurate quantification of the severity and location of the resultant mitral regurgitation, if present.

3DE may also be useful to localize and quantitate areas of dehiscence. Seen as a separation of the mitral valve annuloplasty ring, the dehiscence appears to be dynamic in systole and diastole. It can be differentiated from dropout because of its smooth edge, whereas dropout has irregular borders. In addition, 3D colour flow can be valuable in differentiating a dehiscence, because colour flow can be seen traversing through this area of missing tissue. Percutaneous closure of prosthetic valve dehiscence can also be guided by 3DTEE with successful results.

**Limitations of three-dimensional echocardiography and technical tips for challenging situations**

Obtaining a proper 3D rendering of mitral valve for a reliable clinical use is highly dependent on a good quality of the acoustic window and on the quality of acquisition. Although there is no current solution to improve the former, several tips can be applied to achieve optimal results for the latter.

Multibeat acquisitions of the mitral valve are subject to artifacts related to probe motion, patient’s respiration or irregular heart cycles. In these challenging situations, real-time scanning or narrow angle single-beat data sets may be alternatively used, with the noted shortcomings related to the small field and relatively lower frame-rates, respectively. Reducing the number of stitched subvolumes (to two or three) or waiting for a sequence of fairly equal cycles can be attempted in the setting of arrhythmias.

Limited temporal resolution may be problematic with some 3D equipments, but seems adequate to study valve morphology using the latest 3D transthoracic and transoesophageal technology (able to provide 10–15 vps in single-beat and 60–70 vps in multibeat acquisition modality – depending on the volume size – while maintaining a satisfactory spatial resolution). Reducing the dimensions of the 3D volume acquisition to the minimum size that encompasses the entire mitral valve, eliminating neighbouring structures from the field of interest and using six (or seven) beat full-volumes will ensure the highest temporal resolution.

Dropout artifacts in very thin valves and acoustic shadowing in heavily calcified valves/annuli or prostheses cannot be avoided by 3D ultrasound modality. During acquisition, it is advisable to set the gain/compression in the mid-range, with a slightly higher time gain compression setting; this is because there are limits to how much gain and/or compression can be added or removed after the 3D acquisition has been completed. As with 2D approach, optimizing the image with the best lateral–axial resolution and respiratory manoeuvres remains equally important during 3DE acquisition.
Colour Doppler, either 2D multiplane or 3D, can be of help when artifacts vs. true pathology is in question. As with 2D, 3D off-angle cut-planes can lead to faulty conclusions and/or measurements. Multiplane 2D imaging (side-by-side simultaneous display of the structure of interest from two or three angles) using 3D probe may verify and correct for this error. 

Last but not the least, the completion of a learning curve in image acquisition and interpretation of mitral valve morphology in various pathologies with the supervision of an expert in 3DE, as well as the training for a proper use of 3D scanner controls and softwares, will ensure the best outcome.

Conclusions

Although 3DE is not flawless, transthoracic 3DE and 3DTEE add unquestionable advantages and a wealth of critical informations, and they will probably become the techniques of choice and the standard of care in mitral valve pathology. The systematic training in 3DE of present and future generations of echocardiographers will enable an accurate identification of complex lesions of present and future generations of echocardiographers mitral valve pathology. The systematic training in 3DE of present and future generations of echocardiographers will enable an accurate identification of complex lesions of present and future generations of echocardiographers.
Mitral valve anatomy and function Muraru et al.


