Quantification of Mitral Valve Morphology With Three-Dimensional Echocardiography
– Can Measurement Lead to Better Management? –
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The mitral valve (MV) has complex 3-dimensional (3D) morphology and motion. Advance in real-time 3D echocardiography (RT3DE) has revolutionized clinical imaging of the MV by providing clinicians with realistic visualization of the valve. Thus far, RT3DE of the MV structure and dynamics has adopted an approach that depends largely on subjective and qualitative interpretation of the 3D images of the valve, rather than objective and reproducible measurement. RT3DE combined with image-processing computer techniques provides precise segmentation and reliable quantification of the complex 3D morphology and rapid motion of the MV. This new approach to imaging may provide additional quantitative descriptions that are useful in diagnostic and therapeutic decision-making. Quantitative analysis of the MV using RT3DE has increased our understanding of the pathologic mechanism of degenerative, ischemic, functional, and rheumatic MV disease. Most recently, 3D morphologic quantification has entered into clinical use to provide more accurate diagnosis of MV disease and for planning surgery and transcatheter interventions. Current limitations of this quantitative approach to MV imaging include labor-intensiveness during image segmentation and lack of a clear definition of the clinical significance of many of the morphologic parameters. This review summarizes the current development and applications of quantitative analysis of the MV morphology using RT3DE.

Key Words: Echocardiography; Imaging; Mitral regurgitation

In the past 5 years, advances in real-time 3-dimensional echocardiography (RT3DE) have revolutionized the imaging of the mitral valve (MV). Many studies have consistently shown the superiority of 3D transesophageal echocardiography (TEE) over 2D TEE for visualizing MV morphology. RT3DE has become the imaging modality of choice for guiding MV surgery and catheter-based intervention. Currently, RT3D imaging of the MV involves mainly visualization and qualitative interpretation of volume-rendered images. This “qualitative” approach typically involves few quantitative measurements of MV morphology, and is prone to subjectivity that introduces bias, low reproducibility, and high dependency on imaging expertise.

Quantitative cardiac imaging has growing importance for several reasons: (1) as imaging becomes more digital, the opportunity will create the need; (2) automated approaches to intervention and surgery design and planning are emerging from the laboratory and entering the clinic; (3) algorithm-driven analysis yields faster and more reproducible results; and (4) a variety of users (eg, cardiac anesthetists) wants to use the repeatable methodology offered by quantitative methods. Image-processing tools provide characterization of the complex 3D morphology and motion of the MV. Combined with the properties of the imaging modality and knowledge of anatomy, this yields quantitative descriptions that are useful in diagnostic and therapeutic decision-making. This review summarizes the current development and applications of quantitative analysis of the MV morphology using RT3DE.

**Anatomic Consideration**

**MV Leaflets**
The anterior leaflet (AL) is in fibrous continuity with the aortic valve and guards one-third of the anterior mitral annulus. Fine demarcations divide the AL into 3 smaller scallops. The posterior leaflet (PL) is crescent-shaped and spans the posterior...
two-third of the mitral annulus. The 3 scallops of the PLs are usually distinct and sometimes separated by prominent cleft-like indentations, which normally never reach the annulus. The 2 leaflets converge at the anterolateral and posteromedial commissures and maintain a coaptation reserve to prevent mitral regurgitation (MR) during systole; a coaptation length of 5 mm is considered a minimum to ensure adequate leaflet function. In normal valves, ALs are on average 2.3-fold longer and 1.5-fold larger than the PLs.

Mitral Annulus
The mitral annulus is a ring-like structure in continuity with the fibrous skeleton of the heart. Its portion between the central fibrous body and anterolateral commissure is in continuity with the aortomitral curtain. The intercommissural width of the annulus is normally longer than the anteroposterior diameter, giving the annulus an elliptical shape. The surface area of both leaflets taken together is 140% of the annular area, indicating a large natural surplus of leaflet surface to cover the mitral orifice by normal valves.

Subvalvular Apparatus
The chordae tendineae are of 3 types: primary, secondary, and tertiary. Primary chordae arise from the papillary muscles and fan out to anchor the edge of both leaflets to prevent their prolapse. Secondary chordae are usually thicker and fewer in number and arise from papillary muscle tips to attach to the ventricular side of the leaflet body. Tertiary chordae arise from the ventricular wall and attach to the ventricular side of the PL close to the annulus. The chordae tendineae can be pathologically elongated or ruptured, leading to significant MR. In a dilated or distorted left ventricle (LV), the outwardly displaced ventricular wall pulls the chordae apically and posteriorly, teth- ering the leaflets and resulting in functional MR.

Technology of RT3DE
Prior to the development of matrix-array transducers, reconstruction of the MV was primarily based on a stack of sequentially-scanned 2D images acquired manually or mechanically. Previous techniques produced questionable image quality because of motion artifacts, under-sampling, and noisy signals. Advances in technology have allowed miniaturization of the matrix-array transducers, achieved by fitting thousands of fully sampled elements into the tip of the 3DE transducer, which not only circumvents the reconstruction issues but also facilitates the visualization of geometry (3D) and motion (4D) of the heart in vivo.

3DE image acquisition of the MV for quantitative analysis is usually performed in the apical 4-chamber views on transthoracic echocardiography, or in mid-esophageal views on TEE. There are generally 2 approaches to 3DE data set acquisition:
(1) RT or live 3D imaging and (2) gated acquisition with non-RT reconstruction. In live 3D imaging, a volumetric data set of a relatively narrow pyramidal sector is acquired and displayed in RT. Live imaging is generally a frame-rate of display >20 frames/s, and preferably >30 frames/s. In ECG-gated 3DE acquisition, pyramidal data sets of 4–6 consecutive heartbeats are merged to obtain a wider volumetric image that is displayed offline. Choice of the mode of imaging is a trade-off between frame-rate, image quality, size of the field-of-view, and image-processing time (RT or non-RT). Recently, high volumetric rate 3D ultrasound imaging enables the volumetric region being imaged to be sparsely subsampled by scanning beams, with spatial locations between beams filled in with interpolated values or interleaved with acquired data from other 3D scanning intervals. A full-volume RT3DE data set can then be obtained in a single heartbeat, which is particularly useful when imaging patients with arrhythmias.

Computer Techniques for Segmentation of the MV

The full volumetric data sets acquired by RT3DE are processed within the computer’s memory and then 3-dimensionally rendered on the computer screen. An optimal view is then selected to allow the most favorable segmentation of the image. In computer vision, segmentation is the process that partitions an object into various regions based on their similarities. These similar regions are grouped into a set of pixels (2D) or voxels (3D), which exhibit similar distinguishable characteristics such as gray-level intensity, texture, edge information, etc. The segmented regions can then be taken to quantify the relevant morphological parameters of a structure, the MV for instance, manually or automatically. Currently, the 2 most commonly used software systems for MV analysis are the Mitral Valve Navigator (MVN) (previous versions were called MVQ; Germany). These software packages allow manual or semi-automatic detection of major anatomic landmarks with subsequent surface modeling using a geometric mesh. Morphological quantification of the MV can be computed according to the final model (Figure 1). On the other hand, fully automated extraction of morphological parameters remains challenging because signal dropout, speckle noise, and low tissue contrast currently limit the quality of RT3DE images, and there is a wide variety of normal and pathological MV geometry. It is now possible to have the annular and leaflet geometry and their motion dynamics quantitatively analyzed using RT3DE with minimal human intervention (Figure 2). Nevertheless, without prior knowledge and human input, automatic segmentation of the coaptation zone, scallops, chordae tendineae, and papillary muscles remains difficult, mainly because RT3DE of these structures has even lower signal-to-noise ratio (ie, blurrier).

MV Pathophysiology: Lessons From RT3DE

Degenerative MR

3DE shows that the mitral annulus has a non-planar hyperbolic paraboloid configuration analogous to a saddle. The annular height-to-width ratio (AHCWR) of this saddle-shape is consistent across mammalian species, suggesting an evolutionary advantage. A RT3DE-derived computational model shows that a saddle-shaped annulus may offer extra mechanical support by adding curvature to the leaflet surface. Minimum leaflet stress occurs when the AHCWR is in the range of 15–25%. In humans, we recently undertook a quantitative RT3DE study in patients with MV prolapse (MVP) with a wide spectrum of MR severity to characterize the link between MV morphology and MR severity. For the first time in humans, we demonstrated that annular flattening is strongly associated with progressive leaflet billowing, higher frequencies of chordal rupture, and greater effective regurgitant orifices (ERO) (Figure 3). The lower limit of the AHCWR in a healthy population appears to be 15%, and a ratio <15% is strongly associated with moderate or severe MR among patients with MVP. Importantly, annular height and AHCWR are reduced even in patients with MVP and no or mild MR, suggesting the possibility of a primary annular abnormality. Such annular flattening was not observed in patients with organic MR because of nonprolapsed leaflet pathologies. This study, together with other quantitative RT3DE studies of annular dynamics, supports annular flattening as a novel mechanism in the pathogenesis of degenerative MR. From the surgical point of view, MV repair with a saddle-shaped anuloplasty ring allows better leaflet coaptation by not hoisting the papillary muscles towards the posterior annulus. A quantitative RT3DE study performed by Otani et al showed that the nonprolapsed MV leaflets are often apically tethered as a result of LV dilatation attributed to primary MVP-associated MR, and that secondary tethering further exacerbates malcoaptation and contributes to a vicious cycle getting more MR (Figure 4B). In P2 prolapse, AL tenting volume shows good correlation with left ventricular mid-systolic volume and papillary muscle displacement. Multivariate analysis has identified both leaflet tenting volume and prolapse...
Functional or Ischemic MR
Functional MR can be defined as MR secondary to left ventricular remodeling in the absence of a primary abnormality of the MV (Figure 4C). Leaflet malcoaptation in functional MR is attributed to annular flattening and dilatation, leaflet tethering, reduced rate of rise of LV pressure, as well as systolic dyssynchrony. RT3DE with quantitative software that manually or semi-automatically tracks the annular motion has been used by several researchers to study the annular mechanism of functional MR. Both Grewal et al and Levack et al found that an ischemic annulus is less dynamic than normal, with significantly diminished area contraction, anteroposterior diameter shortening, and saddle-shape accentuation during systole. Topilsky et al studied in detail the relationship between phasic changes of annular geometry and ERO. Their study showed that different mechanisms contribute to different systolic phases of functional MR, with inadequate early-systolic annular contraction and saddle-shape accentuation determining early-systolic ERO, whereas asymmetric papillary tips movement determining mid- and late-systolic ERO. Differences in MV geometry are observed in the asymmetric and symmetric tethering patterns of ischemic MR. For the same degree of tethering, an asymmetric pattern is associated with increased MR severity. RT3DE was also used to measure the surface area of mitral leaflets and discovered that the leaflets may enlarge in adaptation to chronic tethering secondary to LV remodeling because of ischemia/infarction, dilated cardiomyopathy, and chronic aortic regurgitation. These observations challenge the current concepts relating functional MR solely to LV remodeling. RT3DE may be the ideal method for noninvasively monitoring and understanding this leaflet adaptive process, potentially leading to new therapeutic measures to prevent functional MR.

Figure 3. Illustrative examples of mitral valve (MV) deformation in MV rollaple (MVP). (A) Control subject with a saddle-shaped annulus (AHCWR=23%). (B) Patient with mild MVP and mild mitral regurgitation (MR). RT3DE reveals P2 billowing (arrow). Morphological quantification shows a decreased saddle-shape of the annulus (AHCWR=18%), and a light-red hue localized to P2 with a billow volume of 0.2 ml. (C) Patient with chordal rupture, flail P2 and severe MR. The ruptured chord (arrowheads) can be visualized on RT3DE. The annular saddle-shape is lost (AHCWR=14%). Leaflet topography shows a deep-red hue at P2, indicating P2 prolapse with a large coaptation gap (*). Leaflet billow volume=0.8 ml. (D) Patient with the severe MR of Barlow’s disease. The annulus is extremely flat (AHCWR=10%), and there is diffuse deep-red discoloration over multiple scallops, indicating extensive leaflet billowing (billow volume=7.8 ml). AHCWR, annular height-to-width ratio; RT3DE, real-time 3-dimensional echocardiography. Reproduced with permission from Lee AP, et al. Circulation 2013; 127: 832–841.

volume as independent contributors to the MR vena contracta area. These findings suggest a pathophysiologic rationale for early surgical repair.
Rheumatic MV Disease

In rheumatic mitral stenosis (MS), the MV orifice area measured by 3D planimetry is more accurate than 2D planimetry and Doppler assessment. Direct visualization of the MV commissures by 3DE allows morphological evaluation of commissural fusion and calcification, which is underestimated by 2DE in approximately one-fifth of patients. RT3DE has revealed that valve shape, not just the size of the orifice, has a potential effect on the flow dynamics across a valve. The coefficient of contraction (=effective/anatomic orifice area) and the related net pressure loss are importantly affected by leaflet geometry in patients with MS. With the use of 3DE and stereolithography, Gilon et al confirmed that variations in the 3D geometry of the MV led to varying pressure gradients that were up to 40% higher for the flattest valves for the same anatomic area and flow rate compared with “funnel”-shaped valves. Their findings suggested that morphological quantification could address uniquely 3D questions to provide insight into relations between cardiac structure, pressure, and flow. Areas of the annulus and the anterior and PLs were larger in rheumatic MR than in normal controls (Figure 4D). A large anteroposterior annulus diameter and small PL angle were independently associated with rheumatic MR severity. Morphological quantification of the LV and subvalvular apparatus found that misalignment of the papillary muscles and a narrowed interchordal angle also contribute to rheumatic MR. Valve repair of rheumatic MR is more challenging when leaflet retraction coexists with misalignment of papillary muscles, and morphological quantification will be helpful to guide valve repair, if contemplated.

Mitral-Aortic Valve Coupling

The morphology and function of the mitral and aortic annuli are interdependent through their fibrous connection, a phenomenon known as mitral-aortic coupling (MAC). MAC may be an integral part of normal cardiac physiology. Importantly, pathology or surgery of the MV may affect the aortic valve, and vice versa, through MAC. RT3DE has allowed noninvasive assessment of MAC in normal subjects, patients with degenerative MVP, and after annuloplasty. Mitral annuloplasty not only reduces systolic contraction of the mitral annulus area, but also affects the normal annular dynamics of the untreated aortic valve. Tsang et al recently demonstrated that aortic stenosis can affect the MV because of calcification of the aortomitral curtain. These results have important implications both when planning intervention and when developing new annuloplasty rings with the goal of preserving physiologic MAC.

Current Clinical Applications of Morphological Quantification of the MV

Diagnosis of MVP

Diagnosis of MVP on 2D echocardiography is defined as leaflet displacement ≥2 mm above the annular plane in the parasternal long-axis view. This definition takes into consideration the saddle-shaped annulus, which explains why MVP can be over-diagnosed if the apical 4-chamber view is used. In the parasternal long-axis plane, however, the most frequently imaged segments are A2 and P2, making the diagnosis of prolapse of other segments challenging on 2DE. Color-coded parametric 3D display of the MV provides information about the contours and displacement of all 6 segments of the leaflets relative to the saddle-shaped annulus, and may improve diagnostic accuracy (Figures 2,4B,48,49). In addition, 3D MV quantification could allow better recognition of secondary lesions of MVP such as mitral clefts (defined as extending ≥50% of leaflet height) and subclefts (<50% of leaflet height).

Surgical Planning for MV Repair

Quantitative analysis of the MV could objectively identify repairable disease and guide surgical intervention. Morphological analysis in assessing MV billowing revealed significant quantifiable differences between normal, fibroelastic deficient, and Barlow’s disease patients. Billowing height with a cutoff value of...
of 1.0 mm distinguishes MVP from normal subjects, and a billowing volume with a cutoff value 1.15 ml differentiates between fibroelastic deficiency (simpler repair expected) and Barlow’s disease (complex repair expected). Combining quantitative and qualitative RT3DE imaging of the MV improves repair rates. Complexity of a degenerative MV repair can be predicted from quantifiable parameters including commissural width and the number of prolapsing segments.51

Functional MR repair is associated with high rates of recurrence.53 Understanding the coaptation deficiency preoperatively, and modeling the coaptation anatomy likely to result after a certain repair strategy remain the ultimate promise of 3D imaging. Quantitative 3DE allows precise calculation of the leaflets’ angles, tenting volume, leaflet area, and interpapillary muscle distances.52 Tenting area and A2 bending angle are both independently correlated with complexity of functional MR repair.51 In patients undergoing undersized annuloplasty for ischemic MR, a PL angle ≥45° predicts poor post-annuloplasty outcome.55 In patients with dilated cardiomyopathy undergoing annuloplasty for functional MR, we have demonstrated that postoperative mitral competence is highly dependent on distal AL mobility. For a distal AL angle >25°, the positive and negative predictive values in predicting recurrent MR are 82%, and 93%, respectively.5 Although 2DE is used to measure the leaflet tethering angles, 3DE may provide more precise measurements (Figure 5). Fattouch et al reported that by modeling the 3D anatomy of the subvalvular apparatus preoperatively as a “truncated cone”, the new position of surgically relocated papillary muscle heads desirable to achieve adequate leaflet coaptation can be pre-calculated.54

Guiding Transcatheter MV Intervention and Development of New Devices

During percutaneous transcatheter mitral valvotomy (PTMV), Anwar et al55 propose a semiquantitative RT3DE score with higher points indicating increasing MV thickness, immobility, calcification, and subvalvular involvement. At 1 year after PTMV, the rate of re-stenosis, significant MR or re-intervention in patients with a favorable RT3DE score was 17%, but 48% by Wilkins’s score. Accordingly, using the RT3DE score may identify more patients with unsuitable anatomy for PTMV.55

Accurate assessment of gap and width as well as billowing height and volume is necessary for selection of potential candidates for percutaneous MV repair using the MitraClip system.56 Besides the site of prolapse, 3D TEE could provide a more precise quantification of the prolapse gap and width than 2D imaging (Figure 6).57 Post-intervention, 3DE quantification of the area of the double-orifices is feasible to assess MS as an adjunct to Doppler assessment.58

Figure 5. (A) Mitral valve (MV) geometry measurement in the parasternal long-axis view. A, anterior annulus; C, coaptation point; AP, annular diameter; CD, coaptation depth; LA, left atrium; P, posterior annulus; and S, secondary chordae insertion. Tethering of the basal anterior leaflet (AL) by secondary chordae can be quantified by the angle between the annular plane and AL body (ALAbase); tethering of the distal AL is quantified by the angle between the annular plane and a line joining the anterior annulus and coaptation point (distal AL angle [ALAtip]). The mobility of the posterior leaflet (PL) is quantified by the angle between the annular plane and the PL (PLA). (B) Patient with functional mitral regurgitation (MR) complicating heart failure. Upper panel: TEE long-axis view shows asymmetric tethering of PL (green arrow) and bending of the AL body in association with severe eccentric MR. The distal AL seems not to be tethered, touching the annular plane during systole. Lower panel: 3DE shows tethering of P2 (green arrow). (C) Color-coded topographic display reveals AL tethering limited to the body of the AL (*), hence its bending on 2DE. ALAtip (# Ant) is small (12°), whereas PLA is large (53°). ALAtip <25° is predictive of successful repair for nonischemic functional MR by undersized annuloplasty.5 Post-annuloplasty MV functions as an unicuspid valve but because the AL tip is not tethered, good leaflet coaptation is achieved despite basal AL tethering (lower panel; note the bending of AL persists). 2DE, 2-dimensional echocardiography; 3DE, 3-dimensional echocardiography; TEE, transesophageal echocardiography. Modified with permission from Lee AP, et al. Circulation 2009; 119: 2606–2614.
Limitations and Future Directions

The main limitation of quantitative MV imaging is that the procedure involved in segmentation of the valve is currently too time-consuming to be incorporated into routine clinical use. Moreover, manual input to define the anatomic landmarks of the MV tends to introduce bias, measurement errors and variability. Automated morphological quantification using intelligent algorithms for anatomic recognition will likely improve efficiency and reproducibility of the MV modeling process to a degree optimal for day-to-day diagnostic use. Advances in hardware and software leading to improvement in the 3DE image quality will also enhance the robustness of the segmentation process. Furthermore, morphologic segmentation provides the biomechanical basis for novel application of computer modeling and simulation techniques that will allow study of the MV in even more detail.

More importantly, future studies should aim to identify which of the numerous parameters are of clinical significance, provide cutoff values for decision-making, and define the effect on patient outcome.

Conclusions

“You can’t manage what you don’t measure.” It is an old business management adage that may also be true in understanding and managing complex diseases such as those of the MV. Recent advances in surgical and transcatheter intervention techniques for MV disease have created an unprecedented clinical need to describe the MV morphology and function in precise and quantifiable detail. The question of “What to measure and how?” should be answered by future studies. Quantitative dynamic 3D imaging techniques such as RT3DE of the MV will likely become an important tool guiding decision-making for the most appropriate management of individual patients to achieve the best outcome.

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References


