Characterization of Degenerative Mitral Valve Disease Using Morphologic Analysis of Real-Time Three-Dimensional Echocardiographic Images

Objective Insight Into Complexity and Planning of Mitral Valve Repair

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Background—Presurgical planning of mitral valve (MV) repair in patients with Barlow disease (BD) and fibroelastic deficiency (FED) is challenging because of the inability to assess accurately the complexity of MV prolapse. We hypothesized that the etiology of degenerative MV disease (DMVD) could be objectively and accurately ascertained using parameters of MV geometry obtained by morphological analysis of real-time 3D echocardiographic (RT3DE) images.

Methods and Results—Seventy-seven patients underwent transesophageal RT3DE study: 57 patients with DMVD studied intraoperatively (28 BD, 29 FED classified during surgery) and 20 patients with normal MV who were used as control subjects (NL). MVQ software (Philips) was used to measure parameters of annular dimensions and geometry and leaflet surface area, including billowing volume and height. The Student t test and multinomial logistic regression was performed to identify parameters best differentiating DMVD patients from normal as well as FED from BD. Morphological analysis in the DMVD group revealed a progressive increase in multiple parameters from NL to FED to BD, allowing for accurate diagnosis of these entities. The strongest predictors of the presence of DMVD included billowing height and volume. Three-dimensional billowing height with a cutoff value of 1.0 mm differentiated DMVD from NL without overlap, and billowing volume with a cutoff value 1.15 mL differentiated between FED and BD without overlap.

Conclusions—Morphological analysis as a form of decision support in assessing MV billowing revealed significant quantifiable differences between NL, FED, and BD patients, allowing accurate classification of the etiology of MV prolapse and determination of the anticipated complexity of repair. (Circ Cardiovasc Imaging. 2011;4:24-32.)

Key Words: mitral valve • echocardiography • 3D imaging • Barlow disease • fibroelastic deficiency • degenerative mitral valve disease

Mitral regurgitation represents a pathophysiological spectrum of functional and structural defects of the mitral valve (MV) apparatus. Specifically, degenerative mitral valve disease (DMVD) frequently includes different degrees of annular dilation, leaflet redundancy, and chordal dysfunction, which result in variable cardiovascular morbidity and mortality. DMVD encompasses 2 broad categories, fibroelastic deficiency (FED) and Barlow disease (BD). Accurate diagnosis of these entities along with their specific location and complexity is important because they require different surgical planning, which necessitates careful matching of the complexity of reparable with surgical expertise. Differential diagnosis in DMVD is challenging because it relies on qualitative evaluation that requires a high level of clinical echocardiographic expertise. Quantitative decision support would be useful in assessing key anatomic features of DMVD.

Clinical Perspective on p 32

In contrast to 2D echocardiography, real-time 3D echocardiography (RT3DE) using matrix 3D transesophageal technology, with its improved spatial resolution compared with previously used sparse array transducers, has resulted in enhanced visualization of the pathomorphology of the mitral valve, particularly in DMVD. We hypothesized that RT3DE-derived measurements of valvular anatomy could be

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used to characterize DMVD objectively. The goals of this study were (1) to describe the pathomorphology of the MV in DMVD and (2) to identify specific quantitative 3D echocardiographic parameters that accurately characterize DMVD and therefore could be used to differentiate patients with normal, FED, and BD valves, estimate the complexity of disease, and thus optimize treatment strategy.

Methods

Patients
A total of 80 patients were prospectively studied. Three patients were excluded because of difficulties encountered with 3D transesophageal echocardiographic (TEE) acquisition and offline postprocessing. Thus, we enrolled into the study a total of 77 patients. This included 57 consecutive patients with primary DMVD and severe mitral regurgitation (MR), defined as effective regurgitant orifice area $>$0.40 mm$^2$ and/or vena contracta $>$0.7 cm,13 meeting indication for surgical repair, and 20 control subjects randomly selected from a pool of patients undergoing TEE for clinical indications other than MV disease, who did not have any discernible MV pathology. Patients with MV prolapse associated with connective tissue disorders, Marfan syndrome, rheumatic heart disease, and hypertrophic cardiomyopathy were excluded. The patients with DMVD underwent intraoperative TEE after induction of general anesthesia and endotracheal intubation but before cardiopulmonary bypass. At the time of surgery, these patients were classified by the surgeon as either BD or FED, based on the criteria listed in Table 1,14 rather than the 2D TEE findings that were available to the surgeon, but who was blinded to the 3D TEE images and the results of 3D analysis. This resulted in 28 patients with BD and 29 with FED. The research study was approved by the institutional review board, and every patient signed an informed consent before the TEE study.

Table 1. Surgical Criteria for the Classification of Degenerative Mitral Valve Disease

<table>
<thead>
<tr>
<th>Anulus</th>
<th>FED</th>
<th>BD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaflets</td>
<td>Normal or near normal valve size (anulus $&lt;$32 mm)</td>
<td>Severely dilated annulus</td>
</tr>
<tr>
<td>Chords</td>
<td>Elongated in the affected segment, w/ or w/o rupture</td>
<td>Thickened, calcified, elongated, restricted w/ or w/o rupture</td>
</tr>
<tr>
<td>Billowing characteristics</td>
<td>No billowing of the adjacent segments</td>
<td>Multisegmental billowing</td>
</tr>
</tbody>
</table>

Statistical Analysis

Statistical analysis was performed using Microsoft Excel with R 2.8. Continuous variables were expressed as mean±SD and plotted for each group. Intergroup differences were compared using unpaired Student $t$ test. Statistical significance was indicated by a probability value of $<$0.05. Multinomial logistic regression was performed to determine which measurements are best predictors of complexity of DMVD, specifically, which parameters are best at distinguishing normal from FED and from BD patients. A classification tree analysis using recursive partitioning was developed to distinguish normal patients from those with BD and FED and to indicate a preliminary indication of an optimal cutoff value for the presence of DMVD and specifically, FED versus BD. In addition, receiver operating characteristic (ROC) analysis was performed to assess the superiority of these predictors. The area under the curve (AUC) was calculated for these parameters. The agreement between the qualitative analysis of 2D and 3D TEE images by 2 experts with surgical experience, who were blinded to the surgical designations. These intraobserver agreement, were tested using Student $t$ test. Statistical significance was indicated by a probability value of $<$0.05. Multinomial logistic regression was performed to determine which measurements are best predictors of complexity of DMVD, specifically, which parameters are best at distinguishing normal from FED and from BD patients. A classification tree analysis using recursive partitioning was developed to distinguish normal patients from those with BD and FED and to indicate a preliminary indication of an optimal cutoff value for the presence of DMVD and specifically, FED versus BD. In addition, receiver operating characteristic (ROC) analysis was performed to assess the superiority of these predictors. The area under the curve (AUC) was calculated for these parameters. The agreement between the qualitative analysis of 2D and 3D TEE images by 2 experts with surgical experience, who were blinded to the surgical designations. These
statistics. The calculated $k$ coefficients were judged as follows: 0 to 0.2, low; 0.21 to 0.4, moderate; 0.41 to 0.6, substantial; 0.61 to 0.8, good; and $>0.8$, excellent.

**Reproducibility Analysis**

Reproducibility of the 3D morphological parameters was assessed in 20 patients, including 10 patients with FED and 10 patients with BD. Intraobserver variability was assessed using repeated measurements performed by the same observer a month later, whereas interobserver variability was evaluated by repeating the analysis by a second independent observer, blinded to the results of all prior measurements. Variability was expressed in terms of coefficients of variation between repeated measurements expressed as a percentage of their mean.

**Results**

DMVD patients were initially compared with the normal control subjects. Patient characteristics for the study group are shown in Table 2. As expected, the FED patients were on average older than BD patients. Figure 2 shows surgical views, zoomed RT3DE images, and their respective color-coded parametric 3D renderings of the MV obtained in 2 patients with different types of DMVD.

**Figure 1.** Three-dimensional morphological analysis of a normal mitral valve. Mitral annulus is manually initialized in 1 plane (A) and then repeated in multiple rotated planes and interpolated (B); MV leaflets are manually traced from commissure to commissure in multiple parallel planes (C); the resultant surface is displayed as a color-coded, 3D-rendered valve surface (D).

**Figure 2.** Examples of views of the MV from the left atrial perspective obtained in 2 patients with DMVD. Top, FED with a P2 flail leaflet and ruptured chords; bottom, BD with multisegmental billowing: A, surgical views; B, zoomed 3D echocardiographic views; and C, corresponding 3D-rendered, color-coded images.
There was a significant and progressive increase in 3D annular geometry, leaflet surface area and prolapse characteristics is shown in Table 3.

**Anunnar Geometry**

There was a significant and progressive increase in 3D annular dimensions from control subjects to FED and even further in BD patients (Figure 3A and 3B). There was a significant increase in mean 3D annular area in DMVD patients versus the normal control subjects (Table 3). In addition, both AP and CC diameters were increased in the DMVD patients compared with control subjects. However, the ratio of CC to AP dimension was reduced to 1.06±0.30 in BD patients, reflecting the more circular shape of the mitral annulus compared with the more oval shape in control subjects and FED patients (Table 3). Although no intergroup differences were noted in 3D annular height and aortic-mitral angle, a significant increase in the nonplanar angle was evident in BD patients.

**Leaflet Area**

The total leaflet surface area was increased in FED and BD patients (Table 3). Both anterior and posterior leaflet areas were increased in DMVD patients (BD significantly greater than FED) compared with the normal valves; there was no discernible difference in the degree of enlargement of the anterior versus the posterior leaflet area in the 2 DMVD subgroups.

**Predictors of Complexity**

The $t$ test analysis identified multiple parameters that distinguished DMVD from control subjects. Of these, billowing height and volume were the strongest predictors, because other parameters had considerable intergroup overlapping ranges diminishing their predictive power. Billowing height demonstrated minimal overlap and therefore was the strongest discriminator between control subjects and DMVD (Figure 3C). However, this parameter was not a strong discriminator between the FED and BD patients. Billowing volume, identified by $t$ test as a statistically significant parameter, demonstrated minimal overlap between FED and BD, serving as the strongest identifier of DMVD geometric complexity in these patients (Figure 3D). Multinomial regression similarly identified leaflet billowing height and volume as strong predictors for the detection of DMVD and evaluation of its etiology and complexity. Again, billowing height was found to be paramount in separating control subjects from DMVD patients, and billowing volume was the strongest parameter distinguishing between the 2 DMVD subgroups. As expected, multisegmental prolapse was evident in BD patients with all segments billowing to a greater degree than their counterparts FED patients. In BD patients, the P2 scallop demonstrated the greatest degree of billowing in the posterior leaflet, followed by P1 and P3 scallops (Table 3).

**Optimal Cutoff Values**

Classification tree analysis using recursive partitioning demonstrated that patients with billowing volumes of $<$1.15 mL and with billowing heights of $<$1 mm were normal; in contrast, patients with a billowing volumes of $<$1.15 mL and prolapse heights of $>$1 mm had FED, whereas those with billowing volumes $>$1.15 mL had BD (Figure 4). Indeed, the highest billowing height in the data set for normal patients was 0.9 mm, and the lowest for a DMVD patient was 1.1 mm. Similarly, the highest billowing volume among FED patients was 1.1 mL, while the lowest prolapse volume among BD patients was 1.15 mL. The use of these cutoff values resulted in an algorithm for objective, quantitative differential diagnosis of DMVD (Figure 5).

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**Table 2. Clinical Characteristics of the Patients With Degenerative Mitral Valve Disease (29 Patients With Fibroelastic Deficiency and 30 Patients With Barlow Disease) and 20 Control Subjects**

<table>
<thead>
<tr>
<th></th>
<th>Control Subjects (n=20)</th>
<th>FED (n=29)</th>
<th>BD (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, %</td>
<td>46</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>63±13</td>
<td>61±7</td>
<td>53±9‡</td>
</tr>
<tr>
<td>Mean BSA, kg/m</td>
<td>1.71±0.24</td>
<td>1.76±0.31</td>
<td>1.81±0.19</td>
</tr>
<tr>
<td>Mean heart rate, bpm</td>
<td>73±13</td>
<td>77±14</td>
<td>75±15</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td>143/83±27/16</td>
<td>123/76±22/9*</td>
<td>129/67±27/11*</td>
</tr>
</tbody>
</table>

BSA indicates body surface area.

* $P<0.05$ versus normal control subjects; ‡ $P<0.05$ versus FED.

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**Table 3. Summary of Volumetric Measurements of Mitral Valve Anatomy in Patients With Degenerative Mitral Valve Disease (29 Patients With Fibroelastic Deficiency and 28 Patients With Barlow Disease) and the 20 Control Subjects**

<table>
<thead>
<tr>
<th></th>
<th>Control Subjects</th>
<th>FED</th>
<th>BD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three-dimensional annular area, mm²</td>
<td>797±152</td>
<td>1154±261*</td>
<td>1834±432†</td>
</tr>
<tr>
<td>Two-dimensional annular area, mm²</td>
<td>769±148</td>
<td>1122±250*</td>
<td>1792±426†</td>
</tr>
<tr>
<td>AP diameter, mm</td>
<td>28±3</td>
<td>34±5*</td>
<td>44±8†</td>
</tr>
<tr>
<td>CC diameter, mm</td>
<td>33±3</td>
<td>40±4*</td>
<td>45±9†</td>
</tr>
<tr>
<td>CC/ AP ratio</td>
<td>1.21±0.1</td>
<td>1.21±0.1</td>
<td>1.06±0.3*</td>
</tr>
<tr>
<td>Three-dimensional perimeter, mm</td>
<td>103±10</td>
<td>128±17*</td>
<td>158±19†</td>
</tr>
<tr>
<td>Leaflet area, mm²</td>
<td>943±218</td>
<td>1453±354*</td>
<td>2302±455†</td>
</tr>
<tr>
<td>Anterior leaflet area, mm²</td>
<td>472±109</td>
<td>722±178*</td>
<td>1162±276†</td>
</tr>
<tr>
<td>Posterior leaflet area, mm²</td>
<td>419±102</td>
<td>735±214*</td>
<td>1175±306†</td>
</tr>
<tr>
<td>Aortic-mitral angles, degrees</td>
<td>120±10</td>
<td>124±8</td>
<td>123±10</td>
</tr>
<tr>
<td>Nonplanar angles, degrees</td>
<td>124±11</td>
<td>129±18</td>
<td>155±20†</td>
</tr>
<tr>
<td>Billowing height, mm</td>
<td>0.27±0.23</td>
<td>4.10±2.37*</td>
<td>8.41±2.91†</td>
</tr>
</tbody>
</table>

A1, A2, and A3 are scallops 1 through 3 of the anterior leaflet; P1, P2, and P3 are scallops 1 through 3 of the posterior leaflet.

* $P<0.05$ versus normal control subjects; † $P<0.05$ versus FED.
ROC Results

ROC curve analysis revealed high AUC values for 2 parameters: (1) AUC for 3D measurements of billowing height with cutoff value of >1.0 mm was 0.98; and (2) AUC for 3D measurement of billowing volume with cutoff of >1.15 mL was 1.0.

Qualitative 2D Versus 3D Evaluation

In the subset of 20 patients tested for diagnostic accuracy of 2D versus 3D TEE images using surgical inspection as the gold standard, accurate scallop involvement was identified by 2D TEE in 76% (46/61, \( P < 0.05 \)) and by 3D in 92% (56/61, \( P > 0.05 \)). Surgical agreement with 2D TEE findings was highest for P2 and A2 segments and lowest for P3, A1, and A3 segments. Commissural involvement was ascertained surgically in 4 of 20 patients. In none of these 4 patients, the diagnosis was made by 2D TEE images, whereas with 3D TEE images, the diagnosis was made in 3 of 4 cases by both observers. Fifteen of the 20 patients met the criteria for complex mitral valve disease, based on surgical inspection. Of these, observer 1 diagnosed using 2D images 10 patients as having complex MV disease (\( \kappa = 0.50 \)), whereas observer 2 identified 9 patients (\( \kappa = 0.43 \)). Using 3D images, observer 1 diagnosed 14 patients (\( \kappa = 0.88 \)) and observer 2 diagnosed 13 (\( \kappa = 0.77 \)) as having complex disease. In addition, interobserver agreement identifying lesions by 2D versus 3D morphological analysis was 78% (\( \kappa = 0.56 \)) and 91% (\( \kappa = 0.80 \)), respectively.

Reproducibility of Quantitative 3D Analysis

The mean interobserver and intraobserver variability values are summarized in Table 4. As expected, the interobserver variability was greater than the intraobserver variability in both FED and BD patients. In both groups, for all 4

Figure 3. Graphic representation of measurements of MV geometry in the 57 patients with DMVD (29 patients with FED and 28 patients with BD) and the 20 control subjects. Solid squares with error bars represent mean \( \pm \) SD; diamonds represent maximal and minimal values. \( * P < 0.05 \) versus normal; \( \dagger P < 0.05 \) versus FED. AP indicates anteroposterior. See text for details.

Figure 4. Scatterplots demonstrating the cutoff values of 1.0 mm for billowing height (vertical dashed line) and cutoff value of 1.15 mL for billowing volume (horizontal dashed line) in differentiating patients with BD versus FED.
DMVD, namely BD and FED. This finding could support and, more importantly, between the 2 different etiologies of DMVD patients. However, the severity and magnitude of prolapse has been difficult to accurately determine preoperatively using 2D TEE, especially in valves with multisegmental lesions.20,21 This is probably the case because 3D TEE is less operator-dependent than 2D TEE that relies on fine adjustments of the TEE probe and mental integration of a limited number of 2D imaging planes to delineate MV pathology. Analysis in a subset of our patients demonstrated higher agreement between qualitative assessment of 3D images and surgical findings when compared with 2D images. Additionally, the interobserver variability for the localization of involved mitral valve scallops was lower with 3D compared with 2D. These observations further reinforce the advantages of 3D echocardiography in identifying lesions in P1, A2, and A3 segments and bileaflet lesions. However, the lack of reliable preoperative assessment frequently leads to inadequate match between the complexity of disease and the surgical expertise which becomes obvious only in the operating room. As a result, difficulties with presurgical planning and decision support may lead to either unsuccessful repair or conversion to replacement with poor outcome in patients with complex valvar disease.15–17 Accordingly, we sought to and successfully demonstrated the feasibility of using RT3DE-derived volumetric measurements of valvar anatomy to objectively evaluate MV annular and leaflet distortion in patients with DMVD before surgery. Furthermore, we found that this morphological analysis was able to differentiate between degenerative and normal valves, and, more importantly, between the 2 different etiologies of DMVD, namely BD and FED. This finding could support reliably preoperative automated clinical decision-making and thus have important surgical implications.

Although slight bulging of the MV leaflets into the left atrium during MV closure is normal, in its exaggerated state, termed “billowing” by Barlow, it is usually associated with a midsystolic click, excess tissue, and loss of leaflet apposition.18 Prolapse is defined by the failure of MV leaflet edge coaptation, usually as a result of substantial billowing, chordal rupture or elongation, frequently resulting in MR. Two-dimensional echocardiography has no specific criteria for differentiating normal from pathological billowing. A severely prolapsed or flail leaflet is relatively easy to identify on 2D echocardiography by experts with the exception of certain segments, and even easier with 3D echocardiography.19 RT3DE TEE has been shown to be better than 2D TEE in identifying lesions in P1, A2, and A3 segments and bileaflet lesions. However, difficulties with presurgical planning and decision support may lead to either unsuccessful repair or conversion to replacement with poor outcome in patients with complex valvar disease.15–17 Accordingly, we sought to and successfully demonstrated the feasibility of using RT3DE-derived volumetric measurements of valvar anatomy to objectively evaluate MV annular and leaflet distortion in patients with DMVD before surgery. Furthermore, we found that this morphological analysis was able to differentiate between degenerative and normal valves, and, more importantly, between the 2 different etiologies of DMVD, namely BD and FED. This finding could support reliably preoperative automated clinical decision-making and thus have important surgical implications.

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Our results suggest a systematic approach to differentiating DMVD from normal valves and importantly BD from FED preoperatively. In the proposed algorithm, DMVD can be differentiated from normal valves based on presence of abnormal billowing height, whereas billowing volume can be used to distinguish between BD and FED patients. Use of this quantitative algorithm makes early differentiation feasible and the diagnosis more objective and less experience-dependent. In addition, the 3D morphological analysis provides adjunctive information on the location and severity of extent of prolapse or billowing and degree of annular remodeling.

One might argue that in up to 20% of the patients, a clear distinction between BD and FED is not possible.\textsuperscript{23,24} Although there is an overlap between FED and BD in certain parameters, the billowing volume clearly separated these 2 populations in our group of patients. Though etiologic differentiation alone may not always be sufficient in determining complexity, precise quantification may help differentiate surgically straightforward FED patients from those with more complex pathology, for example, forme fruste. Most importantly, large increase in billowing volume is associated with more complex repair as is known to be the case in patients with BD.

Besides obviating the need for anticoagulation and decreasing the risk of endocarditis, MV repair allows preservation of left ventricular function by maintaining the integrity of the subvalvular apparatus.\textsuperscript{25} As the procedure of choice, surgical repair of MV prolapse requires a clear understanding of the relationship between the etiology of DMVD, the anatomic and functional features related to the etiology, and, importantly, the short- and long-term impact of any alterations on the MV anatomy.\textsuperscript{26} The success and planning of surgical correction rests on accurate MV anatomic assessment and the detection of those lesions that may predict unsuccessful repair, such as extensive bileaflet disease or anterior leaflet pathology.\textsuperscript{27} Our findings supported a more accurate assessment of the complexity and localization of segmental lesions with RT3DE imaging. Furthermore, quantification of prolapsing or billowing volume, in addition to morphology, can distinguish between more complex lesions versus secondary, less important lesions.

Addressing the geometric distortion evident especially in BD patients is indispensable for a successful MV repair. Reshaping of the mitral annulus via annuloplasty can be achieved by measuring the length of insertion of the anterior leaflet, the area of the anterior leaflet, or a combination of both. Our finding of larger annuli in BD patients was consistent with previous findings.\textsuperscript{28} Normally, the AP to CC diameter ratio is 3:4 during systole.\textsuperscript{22} Our data demonstrated an increase in the ratio as well as a change in annular shape from oval to more circular. Correct sizing and customizing the shape of the prosthetic annuloplastic ring may be essential for the restoration of the physiological ratio and preservation of leaflet mobility. Because the typical size of the annuloplastic ring is between 36 and 40 mm, it may be clinically helpful to customize the rings in patients with especially large annuli,\textsuperscript{28} as evident in some of our patients. Although the issue of sizing of prosthetic rings remains controversial,\textsuperscript{29} accurate sizing may be essential toward preventing systolic anterior MV motion and MR\textsuperscript{28} and thereby, avoiding resection of the anterior leaflet, which is integral to maintenance of MV geometric relationships. Conversely, if morphological analysis reveals a large anterior MV surface area, multisegmental or bileaflet involvement, a longer and more complicated surgical procedure might be anticipated in advance, thereby steering the patient to centers of expertise in complex MV repair.

The MV annulus has been shown to be nonplanar and saddle-shaped.\textsuperscript{30} In our study, 3D morphological analysis revealed a decrease in nonplanarity as evidenced by the increased nonplanar angle in BD patients. Restoration of normal geometry would probably occur with the insertion of a customized annuloplasty ring that would reinstate normal geometric AP relationships, elevate the posterior annulus, and improve leaflet coaptation, all essential toward maintenance of normal valvular physiology.

One of the consequences of inadequate MV repair is the development of systolic anterior motion,\textsuperscript{31–34} resulting in MR. Known risk factors contributing to recurrent MR include bileaflet prolapse or billowing, the absence of anuloplasty ring, chordal shortening, and limited posterior annular dilation.\textsuperscript{35} By quantifying the extent of the excess anterior and posterior leaflets’ length, surface area, and billowing volume, morphological analysis could help identify patient at risk for developing systolic anterior motion. The long-term freedom from MR and avoidance of reoperation is less achievable and variable from center to center in cases of DMVD involving the anterior leaflet.\textsuperscript{36,37} One of the goals of MV repair is restoration of a large surface area of coaptation, which is challenging when confronted with considerable billowing, especially when the anterior leaflet is involved.\textsuperscript{38}

Limitations

Measurements performed in this study are time-consuming, rely on adequate image quality, and require a learning period for both imaging and data analysis. Although RT3DE zoomed acquisition can be difficult to perform in patients with an exceedingly large annulus, only 1 of the 57 DMVD patients who were screened was excluded from our study for this reason. Because surgical inspection is performed in an immobile, flaccid state, as opposed to echocardiographic assessment, which visualizes the valve in a dynamic state, it can potentially result in discrepancy between the methodologies,\textsuperscript{39} one might construe that using surgical findings as the gold standard reference might be a limitation of our study. However, this ability of morphological analysis to detect small, not easily visible areas of billowing, whereas increasing the sensitivity of RT3DE is likely to be diagnostically inconsequential. In addition, it is known from prior studies that there are annular changes in geometry during systole\textsuperscript{40}; however, small multiphasic variations in annular size are not likely to affect the diagnosis of DMVD. Nevertheless, to address this potential pitfall, all measurements in our study were performed at the same phase of the cardiac cycle, that is, end-systole.

Our methodology using billowing height was able to distinguish between the 2 forms of DMVD disease, but there
may be forme fruste degenerative valves that may be incorrectly classified using our stratified approach based on cutoff values. However, a congruent approach that incorporates all the morphological and quantitative findings observed in our study may still be sufficient to guide the treatment strategy and timing of surgery. The applicability of this methodology in patients with other MV pathologies needs to be assessed in future studies.

In summary, our results show that 3D analysis depicts a spectrum of pathomorphologic abnormalities that can be used to accurately differentiate degenerative from normal valves, and, importantly, FED from BD patients, as reflected in this study by the close agreement between 3D TEE and the surgical determinations. Moreover, this analysis facilitates not only the confirmation of etiology, but also highlights quantitative anatomic differences between the groups and provides a framework for preoperative assessment of the complexity of repair. As quantification tools become more automated and less reliant on expertise, they may be used to support clinical decision-making by a wider group of physicians.

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Disclosures
Drs Salgo, Cardinale, and Settemriere are employees of Philips Healthcare.

References

Chandra et al  Morphologic Analysis of Degenerative Mitral Valve Disease 31
Degenerative mitral valve disease (DMVD) frequently includes different degrees of annular dilation, leaflet redundancy, and chordal dysfunction, which result in variable cardiovascular morbidity and mortality. DMVD encompasses 2 broad categories, fibroelastic deficiency and Barlow disease. Accurate diagnosis of these entities along with their specific location and complexity is important because they require different surgical planning, which necessitates careful matching between the complexity of reparability and surgical expertise. Differential diagnosis in DMVD is challenging because it relies on qualitative evaluation that requires a high level of expertise. Quantitative decision support would be useful in assessing key anatomic features of DMVD and therefore guide appropriate surgical strategy. This is the first comprehensive study to characterize DMVD objectively using real-time 3D echocardiography. We sought to describe the pathomorphology of the MV in DMVD and to identify real-time 3D echocardiography parameters that can accurately characterize DMVD. Our results have yielded a systematic approach to differentiating DMVD from normal valves and importantly Barlow disease from fibroelastic deficiency before surgery. In the proposed algorithm, DMVD can be differentiated from normal valves based on billowing height, whereas billowing volume can be used to distinguish between Barlow disease and fibroelastic deficiency patients. Use of this quantitative algorithm makes early differentiation feasible and the diagnosis more objective and less experience-dependent, highlights quantitative anatomic differences between the groups, and provides a framework for preoperative assessment of the complexity of repair. As quantification tools become more automated and less reliant on expertise, they may be used to support clinical decision-making by a wider group of physicians.
Characterization of Degenerative Mitral Valve Disease Using Morphologic Analysis of Real-Time Three-Dimensional Echocardiographic Images: Objective Insight Into Complexity and Planning of Mitral Valve Repair


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