## Quantitative Modeling of the Mitral Valve by Three-Dimensional Transesophageal Echocardiography in Patients Undergoing Mitral Valve Repair: Correlation with Intraoperative Surgical Technique

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*Background:* Mitral valve (MV) repair is the procedure of choice for patients with degenerative MV disease (DMVD) with severe mitral regurgitation. The aim of this study was to identify specific quantitative MV parameters from preoperative three-dimensional (3D) transesophageal echocardiography that are associated with the length of the mitral annuloplasty band implanted and the performance of leaflet resection in patients with DMVD undergoing MV repair.

*Methods:* Ninety-four patients (mean age,  $60 \pm 11$  years; 68% men) referred for MV surgery with adequatequality preoperative 3D transesophageal echocardiographic studies were retrospectively identified. Parametric maps of the MV were generated using semiautomated MV modeling software. Annular and valvular parameters were measured and indexed to body surface area. The implanted annuloplasty band size and leaflet resection were determined on the basis of surgical reports.

*Results:* Three-dimensional annular circumference correlated best (r = 0.74) with the implanted annuloplasty band length and remained an independent predictor on multivariate linear regression analysis. A third of our cohort (n = 33) had posterior leaflet resection. On receiver operating characteristic curve analysis, P2 segment length  $\ge 20$  mm (area under the curve, 0.86; sensitivity, 88%; specificity, 74%) and P2 leaflet area  $\ge 3.4$  cm<sup>2</sup> (area under the curve, 0.84; sensitivity, 85%; specificity, 74%) best discriminated the need for leaflet resection.

*Conclusions:* In DMVD, quantitative 3D annular circumference obtained from semiautomatically generated parametric maps of the MV from 3D transesophageal echocardiographic data was associated with the surgically implanted annuloplasty band length, while P2 leaflet length  $\geq$  20 mm and area  $\geq$  3.4 cm<sup>2</sup> were associated with the performance of leaflet resection. These parameters should be further investigated for preoperative planning in patients with DMVD undergoing MV repair. (J Am Soc Echocardiogr 2015;28:1083-92.)

*Keywords:* Degenerative mitral valve disease, Three-dimensional transesophageal echocardiography, Quantitative valve modeling, Leaflet resection, Annuloplasty

Degenerative mitral valve (MV) disease (DMVD) affects approximately 2% of the population and is the leading cause of mitral regurgitation (MR) in developed countries.<sup>1</sup> In patients requiring surgery

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Copyright 2015 by the American Society of Echocardiography. http://dx.doi.org/10.1016/j.echo.2015.04.019 for severe MR due to DMVD, American and European societal guidelines recommend valve repair over replacement, provided that the valve is suitable and that the institution has surgeons with appropriate expertise.<sup>2,3</sup> Valve repair as opposed to replacement is associated with improved event-free survival.<sup>3</sup> Two important aspects of MV repair are the choice of mitral annuloplasty ring or band size and the decision regarding leaflet modification. These decisions are most often made intraoperatively on the basis of surgical experience and judgement.<sup>4</sup> This reduces reproducibility. Several tools such as ring sizers have been used to help make this process more objective, but they too have limitations.<sup>4</sup>

Echocardiography is the modality of choice for the assessment of MV disease. Specifically, three-dimensional (3D) transesophageal echocardiography (TEE) allows superior visualization of the MV anatomy and morphology, allowing better assessment of the lesion, its complexity, and its suitability for repair compared with two-dimensional (2D) TEE.<sup>5</sup> In addition, 3D MV modeling generates

#### Abbreviations

**ALPM** = Anterolateralposteromedial

**DMVD** = Degenerative mitral valve disease

**ICD** = Intercommissural distance

- **ITD** = Intertrigonal distance
- LV = Left ventricular
- **MR** = Mitral regurgitation

**MV** = Mitral valve

**SAM** = Systolic anterior motion

**TEE** = Transesophageal echocardiography

**3D** = Three-dimensional

**2D** = Two-dimensional

surements of the MV obtained in its physiologic state.<sup>6-8</sup> This offers an opportunity for preoperative surgical planning and individualizing the surgical approach to the patient. However, before using 3D MV modeling for surgical planning, it is important to first demonstrate associations between measurements obtained by preoperative 3D modeling and components of the surgical technique. The aim of our study was to identify specific quantitative parameters on a preoperative 3D TEE using a semiautomated MV modeling technique that would correlate with the annuloplasty band length used and the performance of leaflet resection in patients with DMVD who

a plethora of quantitative mea-

underwent MV repair. We hypothesized that mitral annular and leaflet parameters commonly measured and used intraoperatively along with novel 3D parameters can be obtained by 3D TEE-based semiautomated MV modeling preoperatively and will correlate with the annuloplasty band length used and the performance of leaflet resection during the surgery.

#### **METHODS**

## Patients

We retrospectively identified all adult patients referred to an expert surgeon (T.D.), who underwent MV repair for severe MR secondary to DMVD between 2010 and 2013 at Toronto General Hospital (Toronto, Ontario, Canada). Patients who had diagnostic-quality pre- or intraoperative 3D TEE, received annuloplasty bands, and underwent predischarge echocardiography were included. The study protocol was approved by the institutional research ethics board.

#### Echocardiography

All patients underwent preoperative transthoracic echocardiography. Left ventricular (LV) volumes and ejection fraction were measured using the biplane Simpson method.<sup>9</sup> The severity of MR was graded per American Society of Echocardiography guidelines<sup>10</sup> using a multiparametric approach. All patients then underwent clinical 2D TEE using an iE33 system (Philips Medical Systems, Andover, MA) equipped with an X7-2t transesophageal probe. Three-dimensional assessment of the MV was performed using fullvolume (median volume rate, 20 volumes/sec; interquartile range, 16-26 volumes/sec) or real-time (median volume rate, 9 volumes/ sec; interquartile range, 7-13 volumes/sec) 3D acquisitions of the MV from either the midesophageal four- or three-chamber view. Four-beat gated acquisitions were used for the full-volume data sets. Withholding of respiration was performed whenever possible. All patients underwent predischarge transthoracic echocardiography from which the MV peak and mean gradients and residual MR were assessed by two level 3-trained echocardiographers (F.P., P.T.) using

the integrative approach, as recommended by the American Society of Echocardiography.<sup>10</sup> The result of the surgical repair was considered optimal on the basis of a  $\leq$ 5mm Hg mean transvalvular gradient, mild or less MR, and absence of systolic anterior motion (SAM) or LV outflow tract obstruction on predischarge echocardiography.

## **Three-Dimensional Quantitative Measurements**

The 3D transesophageal echocardiographic data sets were first assessed for gating artifacts by examining the studies in a plane perpendicular to the plane of acquisition. Studies with gating artifacts were excluded. The studies were then analyzed offline by a single operator (A.C.) blinded to clinical, echocardiographic, and surgical findings using semiautomated valve software (eSie Valves; Siemens Medical Solutions USA, Inc, Mountain View, CA) which has been previously described in detail.<sup>11</sup> In brief, first 3D Digital Imaging and Communications in Medicine data were loaded. A midsystolic frame was chosen for analysis because it was where leaflet billowing and/or prolapse was best visualized, and on the basis of the annular dynamics, it was felt to represent the average measure of annular circumference (smallest circumference at early systole and largest at end-systole). The valve was segmented automatically using a machine learning algorithm.<sup>11</sup> The position of the valve and its orientation and dimension in the image are first detected. This forms a region of interest, within which key landmarks (e.g., trigones and commissures) as well as the annulus and leaflet free edges are detected. Then an average surface model of the anterior and posterior leaflets is fitted to the landmarks. These contours are then deformed to match the atrial side of the leaflets in the image (Figure 1A). To facilitate automated computation of complex measurements, the surface model returned by eSie Valves is represented uniformly. This is established from a landmark-based resampling procedure. Each vertex of the valve surface model is uniquely defined by two coordinates, the u-coordinate, tangential to the valve circumference, from anterior to posterior, and the v-coordinate, perpendicular to the valve circumference, from annulus to free edge (Figure 1B). Each stage of the automated valve modeling is performed by robust detectors trained on a large database of cases covering a wide range of normal and pathologic patient data. When computing the annular circumference, the application goes through the vertices of the anterior leaflet defined by a zero v-coordinate, creating the anterior perimeter, followed by the same process for the posterior leaflet. The total circumference is then the sum of the anterior and posterior perimeters. Leaflet segments are defined using geometric features to cope with the lack of clear image features. More precisely, the A1 to A3 and P1 to P3 segments were defined by dividing the leaflets at the u-coordinates 0 to 1/3, 1/3 to 2/3 and 2/3 to 1.

Once the valve is modeled, to confirm the predetermined landmarks and edit the segmented valve, different work-flow options were available. First, commonly used valve orientations (long axis through A2 to P2, commissural view, and en face view) are displayed for editing (Figure 2A). To view the model in more detail, parallel sagittal and coronal or rotational cut planes (which go through a 360° rotation of the valve) are used (Figures 2B and 2C). Using those planes, data sets in which shift and stitch artifacts interfered with the modeling were excluded. Quantitative parameters automatically generated from the geometric model included (1) 3D annular measurements: total area, anterior, posterior, and total circumference; (2) anteroposterior and anterolateral-posteromedial (ALPM)



Figure 1 Geometric modeling and quantitative measurements of the MV. (A) After a frame is selected (*white arrow*), an automated multiplanar reconstruction of the MV is created on the basis of detected landmarks such as the trigones, commissures, annulus, and free edges; the en face model is then displayed within the 3D volume data as seen in the right lower corner. (B) Quantitative measurements are based on the represented model where the algorithm goes through vertices on the v- and/or u-coordinate, depending on the parameter defined (described further in the text).



**Figure 2** Semiautomated quantitative 3D MV modeling work flow. Work-flow options to confirm and edit automated landmark detection: (**A**) left to right from the upper panel: commissural view, two consecutive sagittal planes through the anterior lateral (AL) and posterior medial (PM) commissure, cross-sectional plane, midsagittal and two subvalvular cross-sectional planes; (**B**) parallel cut planes: sagittal from AL to PM and coronal planes from posterior to anterior leaflet; (**C**) rotational planes: starting from the midsagittal (commissural view) plane. Anterior leaflet, *blue*; posterior leaflet, *green*; annulus, *yellow*; trigone, *pink* squares.

diameter; (3) 3D leaflet measurements: anterior and posterior leaflet areas, A1 to A3 leaflet segment areas and lengths, P1 to P3 leaflet segment areas and lengths; (4) intertrigonal distance (ITD); and (5) inter-commissural distance (ICD) (Figure 3). The annular and leaflet measurements were true 3D surface measurements. For example, the area measurements of the leaflet were true 3D surface area, and the length of the leaflets included 3D length of the prolapsing segment.

## **Surgical Technique**

Surgical repair was performed by a single experienced surgeon (T.D.) blinded to all quantitative 3D transesophageal echocardiographic MV data. Grading of DMVD was based on the intraoperative leaflet and annular changes seen during surgical inspection.<sup>12</sup> Mild myxomatous degeneration was defined as leaflets that were thin, were fairly normal in size, were transparent (except for the prolapsing segment), and had chordae tendineae that were thin and attenuated. This included Carpentier fibroelastic deficiency and cases with minimal myxomatous changes. Moderate degeneration was defined as opaque leaflets due to myxoid infiltration of the spongiosa, increased leaflet size but still elastic and not excessively thick (<3 mm thick), and myxoid infiltration of the chordae tendineae. Severe degeneration was considered to exist when leaflets were voluminous, aneurysmal, and thickened ( $\geq$ 3 mm), the annulus was massively dilated (i.e.,  $\geq$ 40 mm), and often posterior displacement of the mitral annulus  $\geq$ 5 mm, with thick and obviously myxomatous chordae tendineae.<sup>12</sup>

MV repair was performed with or without neochord placement or leaflet resection, followed by annuloplasty band placement using a Medtronic Simplici-T band (Medtronic, Inc, Minneapolis, MN).<sup>12-14</sup> Prolapse of the anterior leaflet and of the commissural areas was corrected with chordal replacement.<sup>13</sup> Posterior leaflet prolapse was corrected mostly with neochords, when the leaflet was normal in size or when its height was not significantly increased (<20 mm); however, partial resection of the base and occasional triangular resection of the free margin were done in patients with excessively large posterior leaflets (height > 20 mm).<sup>13</sup> The Simplici-T annuloplasty band has been used exclusively by our surgeon since October 2005.<sup>14</sup> No pre- or intraoperative measurements are used to determine the length of the band used.<sup>13</sup> First annuloplasty sutures are placed through the posterior mitral annulus from the lateral to the medial fibrous trigones. Then the annuloplasty band is secured to these sutures. Annular reduction is performed by passing the sutures closer together in the band in areas of commissures, false



Figure 3 Three-dimensional TEE-derived quantitative parameters. (A) The 3D shape of the mitral annulus and leaflets automatically generated from a geometric model, from which all parameters were derived. (B) Total annular circumference, anterior circumference (*blue outline*), and posterior circumference (*magenta outline*); the commissural landmarks serve as the border between the anterior and posterior annulus). (C) Anteroposterior (AP) diameter (*black dashed line*) and ALPM diameter (*red dashed line*). (D) ITD (*dotted magenta line*) and ICD (*dotted black line*). (E) Anterior leaflet parameters: total anterior leaflet area; anterior leaflet area and length (*dotted black lines*) by segment: A1 (*yellow*), A2 (*pink*), A3 (*cyan*). (F) Posterior leaflet parameters: total leaflet area; posterior leaflet area and length P1 to P3, color segmentation as previous.

Table 1Baseline characteristics of included patients ( $n = 94$ )				
Variable	Value			
Age (y)	$60\pm11$			
Men	64 (68%)			
BSA (m <sup>2</sup> )	$1.91\pm0.23$			
NYHA class				
L	37 (39%)			
II	46 (49%)			
III	11 (12%)			
IV	_			
Hypertension	32 (35%)			
Diabetes	5 (5%)			
Atrial fibrillation*	15 (16%)			
2D echocardiography				
LV end-diastolic diameter (cm)	$5.3\pm0.5$			
LV end-systolic diameter (cm)	$\textbf{3.3}\pm\textbf{0.5}$			
LV ejection fraction (%)	$61\pm7$			
RVSP (mm Hg)	$36\pm13$			

*BSA*, Body surface area; *NYHA*, New York Heart Association; *RVSP*, right ventricular systolic pressure.

Data are expressed as mean  $\pm$  SD or as number (percentage).

\*None of the patients were in atrial fibrillation at the time of echocardiography.

commissures, or partially resected segments, on the basis of subjective observation of disproportion between the sizes of the leaflets and the mitral annulus. The excess length of the 100-mm band is then cut.<sup>12-15</sup>

#### Interobserver and Intraobserver Variability

For intraobserver variability, 10 randomly selected studies were reanalyzed by the same observer (A.C.) 3 to 5 months after the initial analysis, blinded to the original measurement or the precise frame used previously. For interobserver variability, the measurements were repeated by a second observer (F.P.) blinded to the original measurements and to the precise frame used. Variability was assessed for relevant annular and leaflet parameters.

## **Statistical Analysis**

Categorical variables are expressed as frequencies and continuous variables as mean  $\pm$  SD or median and interquartile range, depending on normality. Univariate and multivariate linear regression analysis was performed to identify 3D transesophageal echocardiographic parameters associated with the annuloplasty band size used in patients with optimal surgical repair (defined above) using the bootstrap resampling method (10,000 samples). The bias-corrected and accelerated method was used to generate CIs.<sup>16</sup> In the multivariate model, the best parameters on univariate analysis and other parameters that are clinically used intraoperatively to determine annuloplasty band size length were included.<sup>4</sup> A partial *F* test was used to compare a model with single parameter with a more comprehensive model using all the parameters commonly used intraoperatively to determine annuloplasty band size. Comparisons between patients with and those without leaflet resection were performed using Pearson's  $\chi^2$ tests for categorical variables and Student's unpaired t test or the Wilcoxon signed rank sum test for continuous data. Receiver operating characteristic curves were created to assess the discriminatory value of P2 length and P2 area for the need for leaflet resection.

Quantitative 3D parameter	All (n = 94)	No resection ( $n = 61$ )	Resection ( $n = 33$ )	P <sup>†</sup>
Annular dimensions (indexed to BSA*)				
Annular area (cm <sup>2</sup> )	14.2 $\pm$ 3.7 (7.5 $\pm$ 1.9)	13.6 $\pm$ 3.3 (7.5 $\pm$ 1.9)	15.5 ± 4.0 (7.7 ± 1.8)	.03
Anterior circumference (mm)	$63 \pm 8 \ (33.6 \pm 5.1)$	62 ± 8 (33.8 ± 5.5)	66 ± 8 (33.1 ± 1.2)	.01
Posterior circumference (mm)	75 $\pm$ 11 (39.6 $\pm$ 6.7)	73 $\pm$ 10 (40.2 $\pm$ 6.9)	77 $\pm$ 12 (38.6 $\pm$ 6.2)	.09
Total annular circumference (mm)	138 $\pm$ 17 (73.2 $\pm$ 10.7)	135 $\pm$ 17 (74.0 $\pm$ 11.5)	144 $\pm$ 17 (71.6 $\pm$ 9.1)	.02
AP diameter (mm)	$37 \pm 5 \ (19.5 \pm 3.1)$	35 $\pm$ 5 (19.6 $\pm$ 3.3)	$39\pm 6~(19.4\pm 2.9)$	.003
ALPM diameter (mm)	$44 \pm 6 \ (23.4 \pm 3.7)$	$43 \pm 6 \ (23.6 \pm 4.0)$	$46\pm 6~(22.9\pm 3.3)$	.04
ITD (mm)	$27\pm3~(14.6\pm2.2)$	$27 \pm 4$ (14.8 $\pm$ 2.4)	$29 \pm 3 \ (14.3 \pm 1.7)$	.02
ICD (mm)	$27\pm5~(14.5\pm2.9)$	$27\pm5~(14.6\pm3.0)$	$29 \pm 5 \; (14.3 \pm 2.5)$	.09
Leaflet measurements (indexed to BSA*)				
A1 length (mm)	$16 \pm 3 \ (8.7 \pm 1.8)$	16 $\pm$ 3 (8.9 $\pm$ 1.9)	$17 \pm 3 \ (8.2 \pm 1.6)$	.58
A1 area (cm <sup>2</sup> )	$2.2 \pm 0.7~(1.2 \pm 0.4)$	$2.1 \pm 0.7 \ (1.2 \pm 0.5)$	$2.3\pm0.7$ (1.1 $\pm$ 0.3)	.29
A2 length (mm)	$22 \pm 4$ (11.8 $\pm$ 2.7)	22 $\pm$ 4 (12.1 $\pm$ 3.0)	$22 \pm 4$ (11.2 $\pm$ 2.2)	.36
A2 area (cm <sup>2</sup> )	$3.3 \pm 1.0~(1.8 \pm 0.6)$	$3.2 \pm 0.8 \ (1.8 \pm 0.5)$	3.6 $\pm$ 1.2 (1.8 $\pm$ 0.6)	.12
A3 length (mm)	17 $\pm$ 3 (8.9 $\pm$ 1.9)	16 $\pm$ 3 (9.0 $\pm$ 1.9)	18 $\pm$ 4 (8.9 $\pm$ 1.8)	.13
A3 area (cm <sup>2</sup> )	$2.0 \pm 0.7 \ (1.1 \pm 0.7)$	$1.9 \pm 0.6 \ (1.0 \pm 0.4)$	$2.2\pm0.9$ (1.1 $\pm$ 0.4)	.04
Anterior leaflet area (cm <sup>2</sup> )	7.5 $\pm$ 2.2 (4.0 $\pm$ 1.2)	7.2 $\pm$ 1.9 (4.0 $\pm$ 1.2)	8.2 $\pm$ 2.7 (4.1 $\pm$ 1.2)	.11
P1 length (mm)	16 $\pm$ 5 (8.4 $\pm$ 2.5)	15 $\pm$ 5 (8.2 $\pm$ 2.6)	18 $\pm$ 5 (8.7 $\pm$ 2.3)	.003
P1 area (cm <sup>2</sup> )	$2.8 \pm 1.2 \ (1.5 \pm 0.6)$	$2.7$ $\pm$ 1.0 (1.5 $\pm$ 0.6)	$3.0 \pm 1.4 \ (1.5 \pm 0.7)$	.32
P2 length (mm)	19 $\pm$ 6 (8.2 $\pm$ 2.6)	17 $\pm$ 5 (9.5 $\pm$ 2.9)	24 $\pm$ 5 (12.0 $\pm$ 2.2)	<.001
P2 area (cm <sup>2</sup> )	$3.4 \pm 1.4 \ (1.8 \pm 0.7)$	$2.8 \pm 1.1 \ (1.6 \pm 0.7)$	$4.5\pm1.4$ (2.2 $\pm$ 0.6)	<.001
P3 length (mm)	$16 \pm 4 \ (8.3 \pm 2.4)$	15 $\pm$ 4 (8.1 $\pm$ 2.5)	17 $\pm$ 4 (8.6 $\pm$ 2.3)	.003
P3 area (cm <sup>2</sup> )	$2.7 \pm 1.1 \; (1.5 \pm 0.6)$	$2.5\pm1.1$ (1.4 $\pm$ 0.6)	$3.1 \pm 1.1 \ (1.5 \pm 0.6)$	.02
Posterior leaflet area (cm <sup>2</sup> )	$8.9 \pm 3.3~(4.8 \pm 1.8)$	$8.0 \pm 2.8~(4.5 \pm 1.8)$	10.5 $\pm$ 3.5 (5.2 $\pm$ 1.6)	<.001

#### Table 2 Preoperative quantitative 3D echocardiographic parameters in patients with versus without leaflet resection

AP, Anteroposterior; BSA, body surface area.

Data are expressed as mean  $\pm$  SD.

\*Indexed measurements (area in square centimeters per square meter, length and circumference in millimeters per square meter).

<sup>†</sup>No resection versus resection group.

Inter- and intraobserver variability was assessed using the intraclass correlation coefficient<sup>17</sup> and the coefficient of variation. A level of significance of .05 was used. All statistical analyses were conducted using SPSS version 20 (SPSS, Inc, Chicago, IL).

#### RESULTS

#### **Patient Population and Baseline Characteristics**

A total of 285 patients had MV repair during the study period. Among these patients, preoperative 3D TEE was performed in 189 patients. The proportion of patients undergoing 3D TEE increased over time, extending from 42% in 2010 to 91% in 2013, reflecting availability of equipment and experience of the operators. Among these cases, only 106 patients had available Digital Imaging and Communications in Medicine data for analysis. However, 12 were excluded because of low volume rates of acquisition ( $\leq$ 5 volumes/ sec). A total of 94 patients with a mean age of 60 ± 11 years, 68% of whom were men, were included. Among the patients, 61% had New York Heart Association functional class  $\geq$  II symptoms at the time of surgery, with normal LV size (end-systolic diameter < 40 mm) in 86% and normal function (LV ejection fraction  $\geq$  60%) in 62%. Baseline characteristics of the 94 patients are summarized in Table 1. The 12 excluded patients had similar clinical characteristics

(mean age, 56  $\pm$  15 years; New York Heart Association class  $\geq$  II in 42%; no LV dilatation; and normal LV function in 83%).

## Preoperative Quantitative 3D Echocardiography

Automated valve modeling was performed in <1 min, but additional time was necessary for manual editing of annular landmarks and leaflet contours. The latter required on average 8 min, given that 50% of our patients had bileaflet disease, and 65% had moderate to severe myxomatous valvular changes. Quantitative annular and leaflet measurements are summarized in Table 2.

## Surgical Findings

Single-leaflet disease was seen in 50%, with the posterior leaflet more commonly affected (Table 3). The degree of myxomatous disease was moderate or severe in 65% of the patients. Eighty-seven patients (93%) underwent neochord implantation (13  $\pm$  7 chords/patient), and all patients underwent annuloplasty band (mean size, 66  $\pm$  7 mm) placement. Posterior leaflet resection was performed in 33 patients (35%). Compared with the group without resection, these patients had more severe myxomatous changes (moderate or greater changes in 82%) and had longer annuloplasty bands implanted (Table 3).

Variable	All (n = 94)	No resection (n = 61)	Resection (n = 33)	<b>P</b> *
Leaflet involvement				.06
Isolated anterior	9 (10%)	9 (15%)	0	
Isolated posterior	38 (40%)	23 (38%)	15 (45%)	
Bileaflet	47 (50%)	29 (48%)	18 (55%)	
Myxomatous change				.04
Mild	33 (35%)	27 (44%)	6 (18%)	
Moderate	44 (47%)	25 (41%)	19 (58%)	
Severe	17 (18%)	9 (15%)	8 (13%)	
Total number of chords placed	12.6 ± 7.1	11.9 ± 6.2	14.1 ± 8.7	.25
Simplici-T band length (mm)	66 ± 7	64 ± 6	69 ± 8	.009

Table 3	Surgical	findings in	i patients	with	and	those	without
MV leafl	et resect	ion					

Data are expressed as number (percentage) or as mean  $\pm$  SD. \*No resection versus resection group.

## Predischarge Echocardiography

On the basis of predischarge 2D transthoracic echocardiography, optimal early postoperative results were seen in 86 patients (91%). The remaining eight had mild to moderate residual MR (n = 3) or transmitral gradients > 5 mm Hg (n = 5; mean gradient, 5.7 ± 0.3 mm Hg; mean heart rate, 80 ± 4 beats/min) (Table 4). When patients with mean gradients  $\leq$  5 mm Hg (n = 89) were compared with those with gradients  $\geq$  5 mm Hg (n = 5, 31 of 89 patients with gradients  $\leq$  5 mm Hg underwent MV leaflet resection, while two of five with elevated gradients underwent leaflet resection. The mean length of the annuloplasty band in patients with elevated gradients was 62 ± 8 mm, while in the other group it was 66 ± 7 mm.

## Association between TEE-Based 3D MV Parameters and Annuloplasty Band Length

Among the 94 patients, the 86 with optimal postoperative results were used to identify parameters associated with the implanted annuloplasty band size (Table 5). All 3D transesophageal echocardiographic parameters and the annuloplasty band size were indexed to body surface area. The implanted band size ranged from 48 to  $84 \text{ mm} (24-51 \text{ mm/m}^2)$ . There was a modest to good correlation between the implanted band size and annular and leaflet parameters commonly used intraoperatively (ICD, ITD, anterior leaflet area, and A2 length<sup>4</sup>) to determine annuloplasty ring size. The strongest correlation (r = 0.74) was with 3D annular circumference. On univariate regression analysis, body surface area-indexed 3D annular circumference, ITD, and ALPM annular diameter had the strongest correlations with implanted band size (Table 5). Among these parameters, 3D annular circumference accounted for the largest ( $R^2 = 0.55$ ) variability in implanted band size (Figure 4). When the other commonly used intraoperative parameters for annuloplasty sizing were included in a multivariable analysis, only ITD and 3D annular circumference remained significant (Table 5). Also, on the basis of the partial F test, adding the other most commonly used intraoperative parameters to a model consisting of 3D annular circumference did not significantly improve the model (P = .08).

Variable	All (n = 94)	No resection (n = 61)	Resection (n = 33)	<b>P</b> *
Mean transmitral gradient (mm Hg)	3.3 ± 1.0	3.3 ± 1.0	3.2 ± 1.1	.36
Peak transmitral gradient (mm Hg)	8.3 ± 2.9	$8.3\pm3.2$	$\textbf{8.2}\pm\textbf{2.4}$	.81
MR severity				.99
None or trivial	75 (80%)	49 (80%)	26 (79%)	
Mild	16 (17%)	10 (16%)	6 (18%)	
Moderate	3 (3%)	2 (3%)	1 (3%)	

Table 4 Predischarge echocardiographic findings

Data are expressed as mean  $\pm$  SD or as number (percentage).

\*No resection versus resection group.

# Parameters Associated with the Need for Leaflet Resection

A third of the patients had leaflet resection (Table 2). These patients had larger annular areas, anterior and total circumferences, anteroposterior and ALPM diameters, and ITDs. Among the anterior leaflet parameters, only A3 area was significantly larger in the resection group. However, among the posterior leaflet parameters there were several differences. The P2 leaflet length ( $24 \pm 5$  vs 17  $\pm 5$  mm, P < .001) and area ( $4.5 \pm 1.4$  vs  $2.8 \pm 1.1$  cm<sup>2</sup>, P < .001), and total posterior leaflet area ( $10.5 \pm 3.5$  vs  $8.0 \pm 2.8$  cm<sup>2</sup>, P < .001), were most significantly larger in the resection group.

Receiver operating characteristic curve analysis demonstrated an area under the curve of 0.86 (95% CI. 0.79–0.93) for the P2 segment length to discriminate the performance of leaflet resection, with a length  $\geq 20$  mm having sensitivity and specificity of 88% and 74%, respectively. Similarly the P2 leaflet area had an area under the curve of 0.84 (95% CI, 0.76–0.92) to discriminate the performance of leaflet resection, with a P2 leaflet area of  $\geq 3.4$  cm<sup>2</sup> having sensitivity and specificity of 85% and 74%, respectively.

#### Reproducibility

Analysis of inter- and intraobserver variability for the MV measurements obtained demonstrated good agreement between observations (Table 6).

## DISCUSSION

In a cohort of 94 patients with DMVD, using preoperative 3D transesophageal echocardiographic data sets, we demonstrate the ability to semiautomatically model the MV and obtain 3D parameters that were associated with the mitral annuloplasty band length used intraoperatively (3D annular circumference, ALPM diameter, and ITD) and the performance of leaflet resection (P2 length and area). Three-dimensional annular circumference had the best association with surgically implanted annuloplasty band length, while a P2 leaflet length of  $\geq$ 20 mm and an area  $\geq$  3.4 cm<sup>2</sup> best discriminated the performance of intraoperative leaflet resection.

#### Role of Echocardiography in MV Repair

Preoperative echocardiography has an important role in the assessment of valvular anatomy and the severity and mechanism of

	Univariate m	odel		Multivariate model	
	Correlation coefficient (95% CI)	$\beta$ coefficient* (95% Cl)	<b>R</b> <sup>2†</sup>	P <sup>‡</sup>	
3D annular dimensions/BSA					
Annular area	0.57 (0.41–0.69)	1.44 (0.96–1.96)	0.32	_	
Annular circumference	0.74 (0.62–0.83)	0.32 (0.25–0.38)	0.55	<.001	
ICD	0.60 (0.44–0.72)	0.91 (0.61–1.18)	0.36	.20	
ALPM annular diameter	0.72 (0.60–0.81)	0.86 (0.65–1.04)	0.52	-	
ITD	0.72 (0.60–0.81)	1.50 (1.14–1.84)	0.52	.002	
3D leaflet dimensions/BSA					
Anterior leaflet area	0.57 (0.45–0.69)	2.15 (1.45–3.08)	0.33	-	
A2 length	0.60 (0.43–0.74)	0.97 (0.66–1.27)	0.37	.92	
A2 area	0.56 (0.41–0.69)	4.44 (2.89–6.24)	0.32	_	

BSA, Body surface area.

\*All *P* values < .001.

<sup>†</sup>Linear regression analysis.

<sup>‡</sup>*P* value for multiple regression weights.

MR.<sup>18</sup> Using 2D TEE, we have previously defined predictors of unsuccessful and nondurable MV repair.<sup>15,19</sup> Three-dimensional TEE further improves the visualization and identification of segmental MV anatomy  $^{20,21}$  and allows preoperative determination of the complexity of MV repair.<sup>18,20,22,23</sup> The latter can then trigger referral to the best skilled surgeon for that repair (Figure 5).<sup>24</sup> In addition, 3D MV modeling can provide more objective measures of various valvular and annular parameters that have been validated surgically by us and others.<sup>7,20</sup> However, to date, there are very few data on the use of 3D TEE-based quantitative MV parameters for preoperative planning of MV repair.<sup>6</sup> This may reflect the limitations of 3D MV modeling approaches, which have predominantly been a manual process,<sup>25</sup> and the absence of studies that have demonstrated associations between 3D quantitative parameters and components of the surgical technique. Preoperative planning is important to minimize unnecessary MV replacement in DMVD and to minimize postoperative complications such as mitral stenosis or early recurrence of MR.<sup>24,25</sup> We illustrate the use of a semiautomated technique relying on robust discriminative learning algorithms to rapidly model the MV automatically. With ongoing improvement, routine clinical application will be feasible. In addition, the associations we have shown between quantitative 3D parameters and components of MV repair is the first step toward designing studies that can prospectively examine value of these parameters for preoperative surgical planning.

## Leaflet Resection in DMVD

The goals of MV repair in DMVD are to maintain leaflet motion, provide adequate leaflet coaptation surface, and stabilize the annulus.<sup>24,26</sup> The two main surgical approaches are resection of the abnormal tissue and leaflet preservation with the use of neochords.<sup>14,24,27</sup> Although the primary approach at our center is leaflet preservation, one third of our patients still required resection, a proportion similar to those seen in other studies.<sup>28,29</sup> There is currently limited objective guidance as to when leaflet resection should be performed with leaflet preservation approaches. Although decisions regarding leaflet resection may be seem to be obvious on the basis of intraoperative measurements, highly experienced centers have shown postoperative SAM in up to 8% of patients requiring intervention.<sup>29</sup> Therefore, there is room for echocardiography-based preoperative planning to improve surgical outcomes. Previous work has demonstrated that posterior leaflet length > 15 mm on 2D echocardiography was an independent predictor of SAM<sup>29</sup> and that P2 scallop length measured using manual 3D MV quantification software was a determinant of posterior leaflet sliding.<sup>30</sup> The latter study did not provide a threshold of P2 length that was associated with leaflet sliding. In our study, on the basis of 3D modeling, we identified larger P2 length and area in the patients who underwent leaflet resection. Using optimal postoperative results (no SAM or MR) by a reference MV surgeon, we identified that P2 area and length of  $\geq$ 3.4 cm<sup>2</sup> and  $\geq$ 20 mm, respectively, discriminated the performance of intraoperative leaflet resection. Whether using these parameters for decision regarding resection will affect short- and long-term surgical outcomes will need to be determined prospectively.

#### **Annuloplasty Sizing**

Following leaflet correction, an annuloplasty ring or band is used to restore annular shape and allow sufficient leaflet coaptation. Several annuloplasty rings and bands are available, the selection of which varies among surgeons and is controversial.<sup>4</sup> Manufacturer-provided sizers are used intraoperatively to determine the appropriate ring size on the basis of the measurement of ITD, ICD, and anterior leaflet surface area or length. Reproducible intraoperative identification of these landmarks under nonphysiologic conditions during cardioplegic arrest, especially in advanced DMVD, can be challenging.<sup>4,31</sup> Also, there are inconsistencies in the methods of sizing among manufactures and expert surgeons. Furthermore, these sizers were not designed on the basis of optimal surgical outcomes. Regardless of the type, appropriate sizing is crucial to reduce the risk for residual MR, SAM, and mitral stenosis and to ensure long term durability of the repair.<sup>4</sup>

Ender *et al.* showed that superimposition of computerized models of Carpentier-Edwards Physio annuloplasty rings onto live 3D transesophageal echocardiographic zoom images was superior to 2D



Figure 4 Linear regression of body surface area–indexed annuloplasty band size versus 3D mitral annular circumference. A good correlation is seen between the two parameters, with an r value of 0.74.

measurement of ICD or the length of the anterior mitral leaflet in predicting annuloplasty ring size in 50 patients undergoing MV repair.<sup>6</sup> However, in the presence of excessive leaflet billowing, or multisegment involvement and/or annular displacement, visualization of the annulus may be challenging and limit the superimposition of the ring model on an en face view. Also, the use of an "eyeball method" for ring sizing still poses a risk for subjectivity and variability. In this study, we have demonstrated that 3D parameters derived from modeling of the 3D transesophageal echocardiographic data sets of the MV obtained in its physiological state correlated with the length of the annuloplasty band implanted during surgery. Threedimensional body surface area-indexed annular circumference, a measurement not available by 2D echocardiography and challenging intraoperatively, correlated best with the length of the annuloplasty band implanted (R = 0.74). The lack of a stronger correlation is likely a reflection of the wide spectrum of DMVD studied and the fact that ring implantation does not aim to bring back original annular dimensions but to restore a proper geometric relationship. The latter is an "art" that is challenging to determine preoperatively. However, given that there are currently no established methods to determine the length of the Simplici-T annuloplasty band used for MV repair,<sup>13</sup> our work demonstrates a potentially novel method to test prospectively. Unlike sizers used to size rings, our work uniquely provides a regression formula (Figure 4) based on optimal surgical outcomes of a reference MV surgeon to determine the size of the Simplici-Tannuloplasty band length. Therefore, our findings are a step forward in the potential future use of preoperative imaging to help guide components of MV repair surgery.

#### Limitations

In complex or severe DMVD, the software to model the MV is not fully automated and would require manual editing. However, semiautomation represents a substantial progress compared with manual reconstruction methods.

<b>Table 6</b> Reproducibility analysis ( $n = 10$ ): ICC and coefficient
of variation

	Interobserver variability		Intraobserver variability	
Variable	ICC	Coefficient of variation (%)	ICC	Coefficient of variation (%)
Annular measurements				
Annular area	0.99	1.7	0.99	1.0
ALPM diameter	0.99	1.9	0.97	1.3
ITD	0.93	4.6	0.96	2
Annular circumference	0.99	1.2	0.99	1.7
Leaflet measurements				
A2 area	0.91	3.2	0.97	2.8
A2 length	0.83	3.3	0.95	2.1
Anterior leaflet area	0.91	4.5	0.97	2.4
P2 length	0.89	9.9	0.92	4.6
P2 area	0.96	8.3	0.98	4.9
Posterior leaflet area	0.97	6.1	0.99	2.8
ICD	0.92	5.8	0.94	3.4

ICC, Intraclass correlation coefficient.

We chose a midsystolic frame for our analysis, and the associations with surgical findings may have been different had a different phase of the cardiac cycle been used. However, we have justified our reason for our choice and do not feel that this affects the validity of our findings.

Because of the retrospective nature of our study, we did not have surgical measurements to compare with our 3D measurements. However, our group has previously shown associations between 3D TEE and intraoperative measurements.<sup>20</sup>

Our sample size was modest; however, to our knowledge, this is the largest study to date assessing the use of 3D modeling of the MV preoperatively to identify parameters associated with components of the surgical technique.

Our findings are based on a single experienced surgeon and practice at one center, which may not be applicable widely, especially with regard to the use of the annuloplasty band type and the surgical skill for repair. Further studies are needed to assess associations with other bands and rings and surgical approaches used at other centers and 3D echocardiographic parameters. However, the use of a single expert surgeon ensured uniformity in the types of procedures performed and allowed a "reference standard" comparison that would otherwise not have been available. Also, although centers with experience in MV repair may have different approaches to repair, the concept of choosing an annuloplasty ring or band and leaflet resection are universal. Therefore, the present study is a proof of concept that demonstrates the association between 3D echocardiography-derived parameters and components of the surgical technique used by an experienced MV surgeon. Whether providing such information to a less experienced MV surgeon will improve surgical outcomes needs to be assessed prospectively.

Finally we used MV gradients as a surrogate measure of the effective mitral orifice area, because we did not have postoperative MV area measurements obtained by 2D or 3D planimetry. However, gradients are routinely used as a surrogate of effective MV orifice area, and planimetry of the orifice is challenging after MV repair given that the orifice does not conform to one plane.



Figure 5 Two-dimensional and 3D echocardiographic parameters that can help surgical planning of MV repair on the basis of existing literature and the present study. In addition, commonly used intraoperative measurements to determine various aspects of surgery are provided. Left panel shows the currently used parameters, which are measured intraoperatively; right panel shows the 2D and 3D echocardiographic parameters that can be measured and provided to the surgeon preoperatively. Parameters in red are the parameters that correlated best with intraoperative technique in our study.<sup>4,13,20,22-24,27,33-37</sup> NA, Currently no available data.

#### **Clinical Implications**

In the era of MV repair in asymptomatic patients with severe MR, there is no room for suboptimal repair or unnecessary MV replacement. Although sizers and intraoperative measurements can be used to determine ring size or need for leaflet resection, this is predominantly experience driven and hence not reproducible.<sup>4</sup> Even in the best hands, moderate to severe MR recurs in 1% to 2% of patients per year, and postoperative SAM is seen in up to 8%.<sup>15,29</sup> Therefore, preoperative planning may help further reduce the risk for these suboptimal outcomes. Also, despite the demonstrated benefits of MV repair in DMVD, a significant proportion of patients (50% to 60%) still undergo MV replacement.<sup>24</sup> Provision of objective surgical parameters to guide certain scientific aspects of MV repair may promote more widespread adoption of MV repair.<sup>4</sup> Although the "art of MV surgery" cannot be taught, certain objective parameters can provide guidance to the surgeon. We demonstrate two such parameters that should be assessed prospectively for this role. We have also summarized all other existing echocardiographic parameters available in the literature that can be used for preoperative surgical planning in a flow diagram (Figure 5). Although the use of these parameters may be less relevant to a reference MV surgeon, it can be particularly helpful to surgeons in training, those who are in the early stages of their careers, and surgeons who work at centers with lower surgical volumes. In fact, recent data demonstrate that the majority of MV repair in the United States occurs are low-volume centers.<sup>32</sup> Another important potential application of our findings is in minimally invasive surgical approaches (e.g., thoracoscopic and robotic MV repair) or emerging percutaneous approaching to MV repair or replacement in which direct surgical visualization will not be possible. Finally, the most important benefit of preoperative planning will be when these parameters can be shown to minimize the complications of MV repair and have an impact on the surgery itself (e.g., reduce pump time). This remains to be determined prospectively.

## CONCLUSIONS

In patients with DMVD undergoing MV repair for severe MR, 3D TEE can have an important role in the preoperative assessment of the complexity of the MV repair. However, important decisions, such as the need for leaflet resection and the annuloplasty band size, are made intraoperatively on the basis of surgical experience. Although this approach is effective in the hands of a reference MV surgeon, it has limitations at smaller volume centers. Our study demonstrates the association between objective quantitative parameters obtained using 3D TEE–based modeling of the MV and the annuloplasty band length used and the performance of leaflet resection. The demonstration of such association is an important first step to promote prospective studies that could assess the value of such 3D modeling in predicting various components of surgical technique and potentially affecting surgical and long-term outcomes.

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