New insights into the surgical treatment of mitral regurgitation

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Chapter 4

Preoperative Three-Dimensional Valve Analysis Predicts Recurrent Ischemic Mitral Regurgitation after Mitral Annuloplasty

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Abstract

BACKGROUND: Valve repair for ischemic mitral regurgitation (IMR) with undersized annuloplasty rings is characterized by high IMR recurrence rates. Patient-specific preoperative imaging-based risk stratification for recurrent IMR would optimize results. We sought to determine if prerepair three-dimensional (3D) echocardiography combined with a novel valve modeling algorithm would be predictive of IMR recurrence 6 months after repair.

METHODS: Intraoperative transesophageal real-time 3D echocardiography was performed in 50 patients undergoing undersized ring annuloplasty for IMR (and in 21 patients with normal mitral valves). A customized image analysis protocol was used to assess 3D annular geometry and regional leaflet tethering. IMR recurrence (≥grade 2) was assessed with two-dimensional transthoracic echocardiography 6 months after repair.

RESULTS: Preoperative annular geometry was similar in all IMR patients, and preoperative leaflet tethering was significantly higher in patients with recurrent IMR (n=13) than in patients in whom IMR did not recur (n=37) (tethering index 3.91 ± 1.01 vs. 2.90 ± 1.17, P=0.008; tethering angles of A3 (23.5 ± 8.9° vs. 14.4 ± 11.4°, P=0.012), P2 (44.4 ± 8.8° vs. 28.2 ± 17.0°, P=0.002), and P3 (35.2 ± 6.0° vs. 18.6 ± 12.7°, P<0.001)). Multivariate logistic regression analysis revealed preoperative P3 tethering angle as an independent predictor of IMR recurrence with an optimal cut-off value of 29.9° (AUC 0.92, 95%CI 0.84-1.00, P<0.001).

CONCLUSIONS: 3D echocardiography combined with valve modeling is predictive of recurrent IMR. Preoperative regional leaflet tethering of segment P3 is a strong independent predictor of IMR recurrence after undersized ring annuloplasty. In patients with a preoperative P3 tethering angle of 29.9° or larger, chordal-sparing valve replacement rather than valve repair should be strongly considered.
**Introduction**

Ischemic mitral regurgitation (IMR) is common and its presence strongly affects prognosis [1,2]. Even a mild degree of IMR adversely affects survival, with a strongly graded relationship between severity and reduced survival [1,2]. Although mitral valve repair with undersized ring annuloplasty has become the preferred treatment [3-5], the persistence and recurrence rate of moderate or severe IMR remains high, at up to 30% after 6 months [6,7].

Current annuloplasty rings treat annular dilatation, but do little to improve (and may potentiate) leaflet tethering [8,9]. Limited repair durability and IMR recurrence may explain the difficulty in demonstrating a survival benefit of annuloplasty for IMR [10].

Recent results from the Cardiothoracic Surgical Trials Network (CTSN) multicenter randomized trial suggest that a patient-specific approach to treatment guided by preoperative risk stratification for recurrent IMR would be useful for optimizing the results of surgical intervention for IMR [11].

We hypothesized that the degree of preoperative mitral leaflet tethering determines the risk of IMR recurrence after undersized ring annuloplasty. Three-dimensional (3D) transesophageal echocardiography (TEE), combined with advanced image analysis and a custom computerized valve modeling algorithm, was used for quantitative preoperative assessment of annular geometry and regional leaflet tethering in patients undergoing undersized ring annuloplasty for IMR. The ability of these preoperative geometric parameters to predict IMR recurrence 6 months after valve repair was prospectively evaluated.

**Methods**

The Institutional Review Boards of the University of Pennsylvania, the University of Pittsburgh, and the Beth Israel Deaconess Medical Center approved this study. Written informed consent was obtained from all patients.

**Patients and Image Acquisition**

Fifty patients with severe IMR underwent mitral valve repair with an undersized annuloplasty ring (Table 1). Ring type selection was at the discretion of the surgeon.

Two-dimensional (2D) transthoracic echocardiography was performed preoperatively and six months after repair. Images were acquired through a transthoracic apical four-chamber view. Severity of IMR was determined semi-quantitatively with color Doppler by assessing the area of the regurgitant jet as a percentage of left atrial area in the
Table 1. Preoperative and intraoperative patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal (n = 21)</th>
<th>Non-recurrent IMR (n = 37)</th>
<th>Recurrent IMR (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>66.1 ± 14.4</td>
<td>68.0 ± 9.0</td>
<td>62.5 ± 13.0</td>
</tr>
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<td>Female</td>
<td>8 (38)</td>
<td>11 (30)</td>
<td>6 (46)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>32.2 ± 8.0</td>
<td>28.5 ± 4.4</td>
<td>29.4 ± 6.5</td>
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<tr>
<td>Medical history</td>
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<td></td>
<td></td>
</tr>
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<td>Hypertension</td>
<td>11 (52)</td>
<td>29 (78)</td>
<td>9 (69)</td>
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<tr>
<td>Diabetes</td>
<td>6 (29)</td>
<td>18 (49)</td>
<td>5 (38)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>3 (14)</td>
<td>8 (22)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2 (10)</td>
<td>14 (38)c</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (10)</td>
<td>4 (11)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>3 (14)</td>
<td>14 (38)</td>
<td>5 (38)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>2 (10)</td>
<td>6 (16)</td>
<td>5 (38)</td>
</tr>
<tr>
<td>NYHA class, 1-4 scale</td>
<td>2.4 ± 0.8</td>
<td>2.4 ± 0.8</td>
<td>2.7 ± 0.8</td>
</tr>
<tr>
<td>IMR grade, 0-4 scale</td>
<td>0.3 ± 0.5</td>
<td>3.2 ± 0.7c</td>
<td>3.3 ± 0.8d</td>
</tr>
<tr>
<td>Basal aneurysm/dyskinesis</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>7 (54)b,d</td>
</tr>
<tr>
<td>Inferior wall motion abnormality</td>
<td>0 (0)</td>
<td>32 (86)</td>
<td>10 (77)</td>
</tr>
<tr>
<td>Left ventricular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic diameter, cm</td>
<td>4.7 ± 0.8</td>
<td>5.7 ± 0.8c</td>
<td>6.0 ± 1.0d</td>
</tr>
<tr>
<td>End-systolic diameter, cm</td>
<td>3.2 ± 0.8</td>
<td>4.6 ± 0.8c</td>
<td>5.1 ± 1.2d</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>65.2 ± 10.1</td>
<td>38.2 ± 14.7c</td>
<td>32.3 ± 12.5d</td>
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<tr>
<td>Annuloplasty ring</td>
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<tr>
<td>Profile 3D ring</td>
<td>-</td>
<td>23 (62)</td>
<td>12 (92)</td>
</tr>
<tr>
<td>CE Physio II ring</td>
<td>-</td>
<td>7 (19)</td>
<td>1 (8)</td>
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<td>CG Future band</td>
<td>-</td>
<td>6 (16)</td>
<td>0 (0)</td>
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<tr>
<td>St. Jude tailor flexible ring</td>
<td>-</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ring size, mm</td>
<td>-</td>
<td>29.0 ± 1.7</td>
<td>28.6 ± 1.3</td>
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<tr>
<td>Concomitant procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>6 (29)</td>
<td>25 (68)c</td>
<td>8 (62)</td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>14 (67)</td>
<td>4 (11)c</td>
<td>0 (0)d</td>
</tr>
<tr>
<td>Tricuspid valve repair</td>
<td>0 (0)</td>
<td>4 (11)</td>
<td>2 (15)</td>
</tr>
<tr>
<td>Atrial maze</td>
<td>0 (0)</td>
<td>7 (19)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Atrial septal defect closure</td>
<td>1 (5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

a Data are presented as mean ± standard deviation or number (%).

b P < 0.05 recurrent vs non-recurrent, c P < 0.05 non-recurrent vs normal,
d P < 0.05 recurrent vs normal.

CABG = coronary artery bypass grafting; IMR = ischemic mitral regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.
apical four-chamber view. The following grading scale was used: grade 0, no IMR; grade 1, less than 20%; grade 2, 20% to 40%; grade 3, 40% to 60%; and grade 4, more than 60% [12]. Recurrent IMR 6 months after repair was defined as IMR grade 2 or higher.

Left ventricular (LV) wall motion abnormalities were also assessed on the preoperative echocardiograms (aneurysm, dyskinesis, akinesia, and hypokinesis). Criteria for inferior basal aneurysm were evidence of thinning and localized LV dilatation or distortion. Dyskinesis was the presence of outward displacement of the LV wall during systole. Inferoposterior aneurysm and dyskinesis were combined in one variable.

Real-time 3D TEE was performed before mitral valve repair. Preoperative imaging data sets were acquired in the operating room after induction of general anesthesia and before sternotomy in all 50 patients with IMR and also in 21 patients with normal mitral valves and normal LV function who required cardiac operations for indications other than mitral valve disease. Images were acquired through a mid-esophageal view with a Philips ie33 (Philips Medical, Andover, MA) ultrasound system equipped with a 2-7 MHz X7-2t TEE matrix transducer.

Image Segmentation and Annular Leaflet Modeling

Each full-volume preoperative 3D TEE data set was exported to an Echo-View 5.4 (TomTec Imaging Systems, Munich, Germany) software workstation. All analyses were performed at midsystole. Techniques of annular segmentation and modeling (Fig. 1) and leaflet segmentation and modeling (Fig. 2) have been described previously [13-15]. The Cartesian (x, y, z) coordinates of each data point were exported from TomTec to Matlab software (The Mathworks, Natick, MA) to perform quantitative reconstruction of the valve.

Determination of septolateral diameter (SL), intercommissural width (CW), and mitral transverse diameter (MTD) are shown in Fig. 1C-E. Mitral annular area (MAA) (the area enclosed by the 2D projection of an annular data set onto its corresponding least-squares plane (Fig. 1E)) and mitral annular circumference were also determined.

Mitral valve tethering area (MVTa) was defined as the area enclosed by the mitral annular plane (white dashed line) and the mitral leaflets for a given point along the intercommissural axis (Fig. 2B). MVTa was calculated at known intervals (0.1 mm), Δc, along the intercommissural axis. Mitral valve tethering volume (MVTv) was calculated as the sum of the incremental regional volumes (MVTa x Δc). Mitral valve tethering index (MVTI (MVTv divided by MAA)) was also calculated for each data set. Anterior tethering angle (ATA) and posterior tethering angle (PTA) were computed at known intervals (0.1 mm) along the entire length of the intercommissural axis by measuring the angle formed by
Figure 1. Annular segmentation technique

(A) 3D echocardiographic volume containing the mitral valve with cross-sectional planes at 10-degree increments. (B) Representative 2D cross-section with green dots representing the selected annular points. Oblique (C), intercommissural (D), and transvalvular (E) annular views of a single real-time 3D-derived mitral annular model with annular landmarks and the 36 annular data points (circles). The least-squares plane has been superimposed on the annulus in each view. The least-squares plane is depicted by a horizontal line in C and D and by the check boxes in E.

AA = anterior mitral annulus; AC = anterior commissure; AL = anterolateral annulus; AML = anterior mitral leaflet; AoV = aortic valve; CW = commissural width; L = lateral aspect of the annulus; LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; MTD = mitral transverse diameter; MVO = mitral valve orifice; PA = posterior mitral annulus; PC = posterior commissure; PM = posteromedial annulus; PML = posterior mitral leaflet; S = septal aspect of the annulus; SL = septolateral diameter.

Figure 2. Leaflet segmentation technique

(A) Template of transverse cross-sections every 1 mm along intercommissural axis. (B) One of the 2D cross-sections represented by the white dashed line in A; the atrial surface of the mitral valve leaflets and the coaptation zone is interactively marked (green curves), resulting in a data set of 500 to 1,000 points for each valve. The white and red dashed lines are both within least-squares annular plane. Determination of (B) the MVTa, (C) the ATA and the PTA are shown.

AC = anterior commissure; AML = anterior mitral leaflet; AoV = aortic valve; ATA = anterior tethering angle; Coapt = coaptation; LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; MVTa = mitral valve tethering area; PC = posterior commissure; PML = posterior mitral leaflet; PTA = posterior tethering angle.
the anterior or posterior leaflet tangent relative to the mitral annular plane (Fig. 2C). Segmental (mean) tethering angles were determined by dividing the valve into equal thirds along the intercommissural axis to conform to the standard 6 anatomic leaflet segments (A1, A2, A3; P1, P2, P3) and by calculating the mean segmental tethering angle for each specific segment based on computed tethering angles at 0.1 mm intervals (along the intercommissural axis).

Statistical Analysis
Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as percentages. Comparisons between groups were performed using Pearson’s χ² test or Fisher’s exact test (two-sided) as appropriate for categorical variables and the independent samples t-test or Mann-Whitney U test (two-sided) as appropriate for continuous variables. Univariate 3D echocardiographic variables with P<0.10 were included in the multivariate analysis. Age and gender were included in all multivariate models. Multivariate logistic regression analyses by means of a forward stepwise algorithm (cut-off for entry and removal 0.05) were performed to identify independent predictors of IMR recurrence. Odds ratios were reported with 95% confidence intervals (CI). Goodness-of-fit of the final logistic regression model was assessed with the Hosmer-Lemeshow statistic.

A receiver operating characteristic (ROC) curve was calculated for continuous independent predictors to single out the optimal cut-off value of predicting IMR recurrence. The statistical significance of difference of area under the curve (AUC) from the "no discrimination line" was evaluated by the Mann-Whitney U statistic.

All calculations were performed using commercially available statistical packages (IBM SPSS Statistics 21.0; IBM Corporation, Armonk, NY and Stats Direct 2.8.0; StatsDirect Ltd, Cheshire, UK). Statistically significant differences were established at P<0.05.

Results

Patient Characteristics
Recurrent IMR occurred in 13 patients (26%) 6 months after undersized annuloplasty. These findings were used to divide patients in recurrent and non-recurrent IMR groups. Preoperative and intraoperative patient characteristics are presented in Table 1. Data from 21 patients with normal mitral valves and normal LV function are included in Table 1 as a reference. The preoperative degree of IMR, LV size and LV ejection fraction (LVEF) were similar in the non-recurrent and recurrent IMR groups. The basal aneurysm/dyskinesis rate
Table 2. Preoperative 3D echocardiographic annular and leaflet tethering variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal (n = 21)</th>
<th>Non-recurrent IMR (n = 37)</th>
<th>Recurrent IMR (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septolateral diameter, mm</td>
<td>28.7 ± 5.1</td>
<td>31.3 ± 3.7c</td>
<td>31.3 ± 5.1</td>
</tr>
<tr>
<td>Commissural width, mm</td>
<td>31.4 ± 3.2</td>
<td>32.9 ± 5.0</td>
<td>32.4 ± 6.5</td>
</tr>
<tr>
<td>Mitral transverse diameter, mm</td>
<td>34.6 ± 3.9</td>
<td>37.4 ± 4.4c</td>
<td>36.9 ± 4.8</td>
</tr>
<tr>
<td>Mitral annular area, mm²</td>
<td>786 ± 155</td>
<td>943 ± 210c</td>
<td>924 ± 260</td>
</tr>
<tr>
<td>Annular circumference, mm</td>
<td>103 ± 11</td>
<td>114 ± 13c</td>
<td>115 ± 14d</td>
</tr>
<tr>
<td>Mitral valve tethering volume, mm³</td>
<td>1771 ± 689</td>
<td>2812 ± 1499c</td>
<td>3744 ± 1541d</td>
</tr>
<tr>
<td>Mitral valve tethering index</td>
<td>2.25 ± 0.70</td>
<td>2.90 ± 1.17c</td>
<td>3.91 ± 1.01b,d</td>
</tr>
</tbody>
</table>

Segmental tethering angle, °

- A1: 18.4 ± 9.2 19.4 ± 8.6 24.7 ± 6.8d
- A2: 15.0 ± 8.2 26.9 ± 11.6 33.3 ± 10.6d
- A3: 9.5 ± 6.4 14.4 ± 11.4 23.5 ± 8.9b,d
- P1: 16.5 ± 8.5 24.0 ± 12.3c 30.6 ± 6.3d
- P2: 17.9 ± 12.0 28.2 ± 17.0c 44.4 ± 8.8b,d
- P3: 14.0 ± 7.6 18.6 ± 12.7 35.2 ± 6.0b,d

* Data are presented as mean ± standard deviation.

b P < 0.05 recurrent vs non-recurrent, c P < 0.05 non-recurrent vs normal,
d P < 0.05 recurrent vs normal.

IMR = ischemic mitral regurgitation.

was significantly higher in the recurrent IMR group than in the non-recurrent IMR group (54% vs. 3%, P=0.001).

Annular Geometry

Annular variables are summarized in Table 2. Preoperative annular variables were similar for patients with and without recurrent IMR. The annuli in all patients with IMR were significantly dilated relative to patients with normal mitral valves.

Leaflet Tethering

Leaflet tethering variables are summarized in Table 2. Preoperative global and regional leaflet tethering was more severe in patients with recurrent IMR after annuloplasty than in patients without recurrent IMR. The preoperative MVTI and the preoperative tethering angles of A1, A3, P2, and P3 were significantly higher in patients with recurrent IMR. Preoperative regional mitral valve tethering is shown in Fig. 3, with data from 21 patients with normal mitral valves included for reference. The preoperative MVTa is higher in all regions, most significantly towards the PC (A2-P2 and A3-P3 regions), for patients with
IMR, especially in patients who will develop recurrent IMR (Fig. 3A). The preoperative MVTa is significantly higher in the A3-P3 region for patients with recurrent IMR compared with patients without recurrent IMR (Fig. 3B). 3D echocardiographic-derived virtual renderings of representative mitral valves [16] demonstrate annular dilatation and flattening in IMR valves as well as augmented leaflet tethering towards the PC in valves that will develop recurrent IMR (Fig. 3C). Preoperative regional ATA and PTA are shown in Fig. 4. For reference, data from 21 patients with normal mitral valves is included in Fig. 4. Preoperative ATA and PTA are higher in all regions for patients with IMR, especially in patients who will develop recurrent IMR (Fig. 4A,C). Preoperative ATA is significantly higher in the A3 region for patients with recurrent IMR compared to patients without recurrent IMR (Fig. 4B). Preoperative PTA is significantly higher in the P2-P3 region for patients with recurrent IMR compared with patients without recurrent IMR (Fig. 4D).

Predictors of IMR Recurrence

Univariate and multivariate logistic regression analyses of IMR recurrence are reported in Table 3. Multivariate analysis revealed preoperative regional tethering of segment P3 (preoperative P3 tethering angle) as an independent predictor of IMR recurrence after undersized annuloplasty (odds ratio 1.28 (95% CI 1.11-1.49), Wald $\chi^2$ 11.14, $P=0.001$). The Hosmer-Lemeshow goodness-of-fit test was non-significant, indicating that this multivariate model is a good fit ($\chi^2=2.13$, df=8, $P=0.977$). A ROC curve was calculated for preoperative P3 tethering angle to single out the optimal cut-off value of predicting IMR recurrence (Fig. 5). The optimal cut-off value was 29.9° with an area under the curve (AUC) of 0.92 (95% CI 0.84-1.00, $P<0.001$), a sensitivity of 84.6% and a specificity of 89.2%.

Comment

Mitral valve repair with undersized ring annuloplasty is currently the preferred treatment strategy for IMR [3-5]; however, the overall persistence and recurrence rate of moderate or severe IMR within 12 months of the operation has been consistently reported to affect approximately a one-third of the treated patients [6,7,11]. We observed a similar incidence of recurrent IMR in this study of 26%. The high incidence of recurrent IMR after repair may explain the difficulty in demonstrating a survival benefit of annuloplasty for IMR over coronary revascularization alone [10,11,17]. The negative clinical implications of recurrent IMR were confirmed by the recent randomized multicenter study conducted by the CTSN, which evaluated the relative benefits and risks of repair versus replacement in patients with
3D VALVE ANALYSIS PREDICTS RECURRENT IMR AFTER ANNULOPLASTY

Figure 3. Preoperative regional mitral valve tethering
(A) Regional mitral valve tethering area (MVTa) distribution for patients with normal valves (light gray) and those with recurrent (medium gray) and non-recurrent (black) IMR. The MVTa is plotted as a function of intercommissural distance, expressed as a percentage of the distance travelled from the anterior commissure (AC). The positions of the AC and posterior commissure (PC) are, respectively, 0% and 100%. (B) Regional MVTa for patients with non-recurrent and recurrent IMR. Dashed lines represent standard deviations. Shaded areas indicate regions where MVTa differs significantly between groups. (C) Three-dimensional echocardiographic virtual models of a representative normal mitral valve and preoperative mitral valves that will and will not develop recurrent IMR after undersized ring annuloplasty: (top row) oblique commissure-to-commissure view, (middle row) oblique septolateral view, (bottom row) left ventricular view.

AC = anterior commissure; IMR = ischemic mitral regurgitation; PC = posterior commissure.

Figure 4. Preoperative regional tethering angles.
(A) Regional anterior tethering angle (ATA) distribution for patients with normal valves (light gray) and those with recurrent (medium gray) and non-recurrent (black) IMR. ATA is plotted as a function of intercommissural distance. (B) Regional ATA for patients with non-recurrent and recurrent IMR. Dashed lines represent standard deviations. Shaded areas indicate regions where ATA differs significantly between both groups. (C) Regional posterior tethering angle (PTA) distribution for patients with normal valves and those with recurrent and non-recurrent IMR. (D) Regional PTA for patients with non-recurrent and recurrent IMR.
IMR = ischemic mitral regurgitation.
### Table 3. 3D Echocardiographic predictors of IMR recurrence by univariate and multivariate logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
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<tr>
<td>Septolateral diameter, mm</td>
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<td>0.86-1.17</td>
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<tr>
<td>Commissural width, mm</td>
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<tr>
<td>Mitral transverse diameter, mm</td>
<td>0.97</td>
<td>0.84-1.12</td>
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<tr>
<td>Mitral annular area, mm²</td>
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<td>1.00-1.00</td>
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<tr>
<td>Annular circumference, mm</td>
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<td>Segmental tethering angle, °</td>
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<td></td>
</tr>
<tr>
<td>A1</td>
<td>1.09</td>
<td>1.00-1.19</td>
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<td>A2</td>
<td>1.05</td>
<td>0.99-1.12</td>
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<td>1.02-1.19</td>
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<td>P2</td>
<td>1.13</td>
<td>1.04-1.22</td>
</tr>
<tr>
<td>P3</td>
<td>1.28</td>
<td>1.11-1.49</td>
</tr>
</tbody>
</table>

CI = confidence interval; IMR = ischemic mitral regurgitation; OR = odds ratio.

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**Figure 5.** Receiver operating characteristic (ROC) curve for preoperative P3 tethering angle as a predictor of IMR recurrence after undersized mitral ring annuloplasty (optimal cut-off value: 29.9°).
IMR [11]. The CTSN study demonstrated no significant difference in LV volume or survival at 12 months between repair and replacement groups; however, the recurrence of moderate or severe IMR after 12 months was 33% in the repair group [11]. Subgroup analysis demonstrated that repair patients with recurrent IMR had no reduction in LV volume, whereas repair patients without recurrence experienced LV volume reduction that was superior to patients who underwent valve replacement [11]. These results suggest that a patient-specific approach to treatment guided by preoperative imaging-based risk stratification that is predictive of recurrent IMR would be useful for optimizing surgical results. Such a tool would allow patients at high risk for recurrent IMR to have valve replacement, whereas low risk patients would continue to receive valve repair.

Several 2D echocardiographic imaging studies have suggested that variables such as leaflet tethering height, tethering area, anterior and posterior tethering angles, interpapillary muscle distance, and systolic sphericity index are associated with IMR persistence or recurrence after annuloplasty [8]. Although these variables are associated with recurrent IMR, there is substantial heterogeneity in their reported ability to predict recurrent IMR. The inadequacy of preoperative 2D echocardiographic variables to predict recurrent IMR was most recently demonstrated by a subgroup analysis of the CTSN trial [17]. In that analysis of 116 patients, leaflet tethering was determined to be the cause of recurrent IMR; however, none of the baseline 2D echocardiographic measures of leaflet tethering were predictive of recurrent IMR [17]. Of note, results from our study and the CTSN trial suggest basal aneurysm/dyskinesis, which reflects severe LV ischemic remodeling and mitral valve tethering, is an important determinant of IMR recurrence [17].

The current study has demonstrated that real-time 3D echocardiography combined with custom image analysis and valve modeling algorithms provides a useful tool for quantifying the complex geometry of the entire mitral valve and, more importantly, is able to effectively predict the risk of recurrent IMR after undersized ring annuloplasty. Unlike 2D echocardiography, this method is not influenced by viewing plane selection, regional asymmetry, or localized annular distortions and, therefore, represents a reliable and clinically relevant technique for quantitative in vivo assessment of global and regional mitral valve pathology.

In IMR, annular dilatation (Carpentier type I dysfunction) and leaflet tethering (Carpentier type IIIb dysfunction) both reduce leaflet coaptation and render the mitral valve incompetent [8]. Several studies have shown a high degree of variability in the pathologic anatomy of IMR [18-21], with annular and leaflet distortions demonstrating a high degree of regional heterogeneity. In this study, the preoperative annular size was similar in patients
with and without recurrent IMR. However, preoperative mitral valve 3D tethering was significantly more severe in patients with recurrent IMR than in patients without recurrent IMR, especially towards the posterior commissure (segments P2 and A3-P3). These findings confirm the complex 3D pathologic anatomy of IMR and its variability between patients and within different regions of mitral valve.

Undersized ring annuloplasty is effective in reducing annular area but does little to improve - and may actually exacerbate - leaflet tethering by displacing the posterior annulus anteriorly, which leads to increased posterior leaflet tethering [9]. Therefore, it is likely that the relative contribution of annular dilatation and leaflet tethering to IMR in individual patients determine the clinical response to annuloplasty. Patients with annular dilatation and relatively limited tethering are likely to respond best to valve repair, whereas those with severe tethering are more likely to develop recurrent IMR after annuloplasty. The group with severe tethering may be better off with chordal-sparing valve replacement. Because IMR is caused not only by annular dilatation, but also by leaflet tethering and the outward displacement of papillary muscles [22], patients at risk of recurrent IMR may also benefit from annuloplasty combined with subvalvular techniques targeting the chordae and papillary muscles [8]. The imaging and modeling methodology used in the current study has the potential to provide the surgeon with the ability to perform a detailed, in vivo three-dimensional valve analysis preoperatively that will complement standard intraoperative valve analytic techniques by quantitatively determining the relative contributions of (regional) annular dilatation and leaflet tethering, thereby helping to direct surgical intent to either valve repair or replacement.

In summary, preoperative regional leaflet tethering of segment P3 is a strong independent predictor of IMR recurrence after undersized mitral ring annuloplasty. In patients with a preoperative P3 tethering angle of 29.9° or larger, chordal-sparing valve replacement rather than valve repair should be strongly considered.

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References


