Mitral tetrahedron as a geometrical surrogate for chronic ischemic mitral regurgitation

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CHRONIC ISCHEMIC MITRAL REGURGITATION (CIMR) is caused by geometrical derangement of the mitral complex owing to local or global chronic ischemia of the myocardium (5, 12). Ring annuloplasty, in addition to revascularization of the myocardium, is the standard treatment for CIMR. The recurrence rate after the surgical procedure, however, is high, even in medical institutions where many of these procedures are performed (10). Development of a more effective treatment requires comprehensive understanding of the relations between the structure of the mitral complex and CIMR. Although geometry of the mitral complex in CIMR can be quantified, data are still lacking. Yu et al. (17) demonstrated the feasibility of relating a mitral tetrahedron (MT) obtained from MRI to CIMR. In the present study, a more comprehensive analysis of geometrical indexes of MT was performed, and these indexes were compared in patients with and without CIMR. We aimed to test the hypothesis that geometrical analysis of MT could serve as a useful surrogate for assessment of CIMR.

MATERIALS AND METHODS

Study population. Fifty-eight subjects, including 40 patients with chronic ischemic heart disease and 18 age-matched healthy volunteers, comprised the study population (Fig. 1). They were divided into three groups according to left ventricular (LV) ejection fraction (LVEF) and the presence or absence of CIMR: LVEF ≥0.5 and negative CIMR (group 1, n = 28), LVEF <0.5 and negative CIMR (group 2, n = 12), and LVEF <0.5 and positive CIMR (group 3, n = 18). MT was defined by its four vertices at the anterior annulus, posterior annulus, and medial and lateral papillary muscle roots, determined by MRI at peak systole. The results showed no clear cutoff values of MT parameters between groups 2 and 1. In contrast, all MT indexes were significantly different between groups 3 and 2 (P < 0.05), and significant cutoff values differentiated the two groups. A scoring system employing parameters of the whole MT confirmed the absence of CIMR with values differentiated the two groups. 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DI_ML, DI_AL, DI_AM, DI_PL, and DI_PaM) were computed (Fig. 3). Additionally, the mitral area index (MAI) was determined from the area enclosed by the contour manually traced along the mitral annulus shown on the reconstructed images.

Indexes of surface triangles and whole tetrahedron. In addition to six edges, each MT consisted of four surface triangles: (1) the anterior triangle, defined by vertices A, M, and L; (2) the posterior triangle, defined by P, M, and L; (3) the medial triangle, defined by A, P, and M; and (4) the lateral triangle, defined by A, P, and L. Four boundary length indexes, Ti_M, Ti_P, Ti_A, and Ti_L, and four area indexes, Ai_A, Ai_P, Ai_M, and Ai_L, were then determined for anterior, posterior, medial, and lateral triangles, respectively. These eight indexes were categorized as the indexes of the surface triangles. For the whole tetrahedron, we computed the total edge length index (6-DI), total surface area index (4-AI), and volume index (VI). These three indexes were categorized as the indexes of the whole tetrahedron. Image analysis and data processing were performed with Matlab (MathWorks, Natick, MA).

Data normalization. For consistency of the indexes in different dimensions, volume data, including LVESV, LVEDV, and volume of the MT, were divided by body surface area (BSA), edge lengths of MT by BSA^{1/3}, and area data, including the area of the mitral annulus and areas of surface triangles of MT, by BSA^{2/3}. This procedure was different from that described in a previous study (9), in which volume and length data were normalized by BSA.

Statistics. Dichotomous data were compared by χ² test. Numeric data were compared with unpaired Student’s t-test between every two groups. Cutoff values of respective parameters for CIMR were selected using receiver operating characteristics (ROC) analysis with a tangent line with slope of 1.0 to the ROC curve. P < 0.05 was considered statistically significant. All statistical work was performed with SPSS for Windows (SPSS, Chicago, IL).

RESULTS

Demography of study population. Gender, age, and BSA were comparable between the three groups (Table 1). From group 1 to group 3, a significant decrease in LVEF and a significant increase in LVEDV and LVESV indexes (LVEDVI and LVESVI) were found (Table 1, Fig. 1). The percentages of coronary lesions involving the left anterior descending artery, right coronary artery, and left circumflex artery showed no significant difference between groups 2 and 3: 56.3 vs. 50.0% for the left anterior descending artery (P = 1.000), 50.0 vs. 50.0% for the right coronary artery (P = 1.000), and 56.3 vs. 20.0% for the left circumflex artery (P = 0.109). No significant difference was found in the percentages of old anterior infarct and old inferior infarct: 45.5 vs. 31.3% for old anterior infarct (P = 0.687) and 27.3 vs. 37.5% for old inferior infarct (P = 0.692).

Indexes of edge lengths and mitral area. All six edge length indexes and MAI differed significantly between groups 2 and 3, whereas only DI_AM and DI_PaM differed significantly between groups 1 and 2 (Fig. 3). Moreover, cutoff values with sensitivity and specificity >0.80 distinguished group 2 from group 3 in five edge length indexes (except DI_PaP) and MAI. Marked distinction was noted in DI_AM and DI_ML: for DI_AM, a cutoff value of 56.9 mm/BSA^{1/3} had sensitivity of 0.89 and specificity of 1.00; for DI_ML, a cutoff value of 27.0 mm/BSA^{1/3} had sensitivity of 0.94 and specificity of 1.00.

Boundary length indexes of surface triangles. Although there were differences in Ti_L, Ti_M, Ti_A, and Ti_P between groups 1 and 2, no clear cutoff values could be found (Fig. 4).
In contrast, TIL, TIM, TIA, and TIP were significantly greater in group 3 than in group 2: 149.6 ± 18.1 vs. 114.3 ± 14.2 mm/BSA$^{1/3}$ for TIL, 151.4 ± 12.9 vs. 120.4 ± 10.4 mm/BSA$^{1/3}$ for TIM, 154.2 ± 14.7 vs. 117.5 ± 12.6 mm/BSA$^{1/3}$ for TIA, and 141.1 ± 11.8 vs. 108.6 ± 10.3 mm/BSA$^{1/3}$ for TIP (all P < 0.001). Clear cutoff values differentiated group 2 from group 3 in these four indexes: 130.8 mm/BSA$^{1/3}$ for TIL (sensitivity 0.83 and specificity 0.92), 134.1 mm/BSA$^{1/3}$ for TIM (sensitivity 0.89 and specificity 0.92), 133.2 mm/BSA$^{1/3}$ for TIA (sensitivity 0.94 and specificity 0.92), and 117.6 mm/BSA$^{1/3}$ for TIP (sensitivity 1.00 and specificity 0.92).

Area indexes of surface triangles. Area indexes of surface triangles showed results similar to those for boundary length indexes (Fig. 5). No clear cutoff values for AIL, AIM, AIA, and AIP could be found between groups 1 and 2. However, clear cutoff values distinguished group 2 from group 3 in all area indexes: 702.7 mm$^2$/BSA$^{2/3}$ for AIL (sensitivity = 0.83 and specificity = 1.00), 641.0 mm$^2$/BSA$^{2/3}$ for AIM (sensitivity = 1.00 and specificity = 0.83), 592.4 mm$^2$/BSA$^{2/3}$ for AIA (sensitivity = 1.00 and specificity = 0.83), and 580.1 mm$^2$/BSA$^{2/3}$ for AIP (sensitivity = 0.94 and specificity = 1.00).

Indexes of the whole tetrahedron. Total edge length index (6-DI) was higher in group 2 than in group 1 (230.4 ± 21.1 vs. 206.0 ± 29.3 mm/BSA$^{1/3}$, P = 0.013), but the two groups could not be distinguished clearly with a cutoff value (Fig. 6). In contrast, 6-DI was significantly higher in group 3 than in group 2 (298.1 ± 26.1 vs. 230.4 ± 21.1 mm/BSA$^{1/3}$, P < 0.001), and a cutoff value with good sensitivity and specificity could be found (cutoff value of 268.1 mm/BSA$^{1/3}$ with sensitivity = 0.89 and specificity = 1.00). Total surface area index (4-AI) was higher in group 2 than in group 1, but no clear cutoff could be found (Fig. 6). In contrast, 4-AI was significantly higher in group 3 than in group 2 (3,513 ± 708 vs. 3,196 ± 385 mm$^2$/BSA$^{2/3}$, P < 0.001), and the two groups could be distinguished clearly by a cutoff value of 2,528 mm$^2$/BSA$^{2/3}$ (sensitivity = 1.00 and specificity = 1.00). Despite a 2.8-fold difference in LVESVI between groups 1 and 2 (18.4 ± 8.2 vs. 50.9 ± 26.0; Table 1), the difference in VI was only 1.4-fold: 3,351 ± 1,069 vs. 2,360 ± 1,058 mm$^3$/BSA (P = 0.010; Fig. 6). On the other hand, despite a 1.7-fold difference in LVESVI between groups 3 and 2 (87.3 ± 33.8 vs. 50.9 ± 26.0; Table 1), VI was 2.4 times greater in group 3 than in group 2: 8,141 ± 3,334 vs. 3,351 ± 1,069 mm$^3$/BSA (P <
A cutoff value of 5,089 mm/BSA distinguished group 2 from group 3 (sensitivity = 0.94 and specificity = 1.00).

**Scoring system for CIMR.** Three scoring systems for CIMR were developed on the basis of parameters related to individual edges: 1) six edge length indexes and MAI, 2) parameters related to individual surface triangles, i.e., four boundary length indexes and four area indexes, and 3) parameters related to the whole tetrahedron, i.e., 6-DI, 4-AI, and VI. The thresholds of each index used the cutoff values determined from the ROC analysis (Figs. 3–6). Among the three scoring systems (Fig. 7), the system employing parameters related to the whole tetrahedron could readily confirm the presence or absence of CIMR with the combination of the following thresholds: 6-DI = 268 mm/BSA, 4-AI = 2.528 mm²/BSA, and VI = 5,089 mm³/BSA. The sensitivity, specificity, positive predictive rate, and negative predictive rate were 1.0.

**DISCUSSION**

In the present preliminary study, we identified an analytic approach to quantitatively evaluate the geometrical alteration of LV in CIMR that is promising and merits further prospective evaluation in a larger sample of normal and abnormal subjects.

Geometrical alteration of the mitral complex in functional mitral regurgitation has been studied extensively. Several plausible mechanisms have been proposed, including dilation of the mitral annulus (1, 2, 14), a tethering effect on mitral leaflets by posterior displacement of the papillary muscles (2, 3, 12, 16, 17), spherization of the LV (13), and widening of the interpapillary distance (17) (Table 2). Owing to the multifactorial nature of CIMR, a comprehensive assessment of the geometry of the MT was performed and the relation of each geometrical index with CIMR was investigated in the present study. We found that the MT was an effective geometrical surrogate for CIMR. Specifically, a combination of 4-AI, 6-DI, and VI below their respective cutoff values could reliably indicate the absence of CIMR.

Although geometrical alteration of the MT leads to CIMR, it should be noted that volume overload induced by mitral regurgitation can cause secondary remodeling of the LV. Therefore, in the present study, geometrical alteration of the MT in group 3 should be considered a cause and a consequence of CIMR. Nonetheless, it is reasonable to conclude that an MT with all indexes below their respective cutoff values guarantees a normal structure without CIMR.

Complete ring annuloplasty is the most popular surgical procedure for repair of CIMR (2, 4, 10). Although the procedure is relatively simple and effective, a failure rate of ~30% has been reported at 6 mo (10). The findings in the present study provide an explanation for the moderate success rate of ring annuloplasty. In fact, this procedure corrects for only two of the MT indexes, namely, DIAp and DIAL. Our results from the present study provide an explanation for the moderate success rate of ring annuloplasty. Moreover, a successful outcome can be predicted if the procedure decreases the abnormal indexes so that 4-AI, 6-DI, and VI are below their respective cutoff values.
The present study showed a 1.4-fold difference in VI (3,351 ± 1,069 vs. 2,360 ± 1,058 mm³/BSA) and a 2.8-fold difference in LVESVI (50.9 ± 26.0 vs. 18.4 ± 8.2 mm³/BSA) between groups 1 and 2 and a 2.4-fold difference in VI (8,141 ± 3,334 vs. 3,351 ± 1,069 mm³/BSA) and a 1.7-fold difference in LVESVI (87.3 ± 33.8 vs. 50.9 ± 26.0 mm³/BSA) between groups 2 and 3. This peculiar finding might be explained by a functional division of the LV into anterior and posterior halves on the basis of their location with respect to the MT. The LV can be divided by an imaginary plane passing through the anterior mitral annulus, the medial papillary muscle root, and the lateral papillary muscle root (Fig. 8). It is clear that the MT is located in the posterior half of the LV. Although the anterior and posterior halves determine LVEF, only the posterior half is relevant to functional mitral regurgitation. Our finding suggests that corrective procedures for CIMR should focus on the posterior half of the LV.

Some experimental procedures used in the present study were different from those used previously. 1) Papillary muscle roots, rather than tips (9, 12), were used as one end of the annular-papillary distance, because papillary muscle tips usually branch. Therefore, error in length measurement can be reduced if papillary muscle roots are used. 2) A point on the mitral annulus between the medial and lateral trigones was chosen as the anterior annulus point. This is different from previous studies in which the medial trigone was used as the reference point (8, 9, 12, 16). 3) Instead of normalizing all parameters by BSA (1, 9), we normalized the length parameters by BSA^{1/3} and the area parameters by BSA^{2/3}. In this way, parameters in different dimensions could be weighted appropriately.

To serve as a control group with LVEF >0.5, we included 18 healthy volunteers and 10 patients in group 1. All the study parameters regarding LV volume and MT geometry were comparable between the healthy volunteers and the patients: 51.5 ± 14.5 vs. 54.6 ± 15.6 mm³/BSA (P = 0.614) for LVEDVI, 16.8 ± 7.3 vs. 21.1 ± 9.3 mm³/BSA (P = 0.186) for LVESVI, 0.67 ± 0.08 vs. 0.62 ± 0.10 (P = 0.202) for LVEF, 15.3 ± 5.8 vs. 16.8 ± 3.9 mm²/BSA^{1/3} (P = 0.494) for DI_{ML}, 204.1 ± 19.6 vs. 209.4 ± 42.7 mm²/BSA^{1/3} (P = 0.660) for 6-DI, 1,553 ± 347 vs. 1,660 ± 557 mm³/BSA^{2/3} (P = 0.533) for 4-AI, and 2,279 ± 1,016 vs. 2,509 ± 1,170 mm³/BSA (P = 0.590) for VI. Therefore, the parameters of the MT were averaged over these 28 subjects and used as normal control values.
Fig. 5. Two-dimensional parameters of the MT: surface area indexes (AI) of medial, lateral, anterior, and posterior triangles.

Fig. 6. Three-dimensional parameters of the MT: total edge length index (6-DI), total surface area index (4-AI), and volume index (VI).
Study limitation. The concept of an MT presented in this study does not take into consideration that the mitral leaflet might stretch to accommodate dilation of the mitral complex, as proposed in a previous study (1).

Because the original spatial resolution in the longitudinal direction was 10 mm in the present study, the leaflet structure and the coapting point between leaflets cannot be located precisely. Therefore, the tethering effect on the anterior leaflet and the corresponding downward displacement of the coapting point away from the mitral annular plane (8, 9) cannot be evaluated.

The effect of local ventricular perfusion status and viability on annular contraction and geometrical change of the MT was not investigated in the present study.

Conclusion. We have demonstrated that the MT is an effective quantitative geometrical surrogate for assessment of structural derangement of the mitral complex in CIMR. Thresholds of the MT parameters reported in the present study may serve as a guideline for presurgical planning and individualized correction.

GRANTS
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Table 2. Proposed mechanism for functional mitral regurgitation

<table>
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<tr>
<td>Dogs</td>
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<td>Increased tethering distance from posterior PM to anterior annulus, increased inter-PM distance</td>
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Mechanisms are listed in chronological order, from earliest (1983) to most recent (2004). DCM, dilated cardiomyopathy; MA, mitral annulus; PM, papillary muscle; 2D and 3D, 2- and 3-dimensional.
REFERENCES


