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Assessment of mitral valve geometric deformity in patients with ischemic heart disease using three-dimensional echocardiography

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Abstract *Background:* A full understanding of the geometry of the nonplanar saddle-shaped mitral annulus can provide valuable information regarding the pathophysiology of mitral regurgitation (MR).

Aim of the work: To investigate mitral annular geometric deformities using three-dimensional echocardiography among patients with ischemic coronary illness with and without mitral regurgitation.

Methods: Three-dimensional transesophageal echocardiographic data were acquired intraoperatively from patients with ischemic heart disease with or without associated mitral regurgitation who experienced coronary artery bypass grafting and normal control subjects. The mitral annulus was analyzed for differences in geometry using QLAB software.

Results: Left ventricular ejection fraction was reduced in patients with ischemic heart disease and MR (n = 21; Group 1) and without MR (n = 7; Group 2) compared with that in normal subjects (n = 14; Group 3) (43.4% ± 11.8% and 35.9% ± 13.6% vs. 52.6% ± 9.3%, respectively; p = 0.015). Mitral annular height and mitral annular saddle-shaped nonplanarity were significantly lower in Group 1 compared to Group 2 and Group 3 (6.00 ± 1.07 mm, 7.96 ± 0.93 mm and 8.31 ± 1.12 mm; $p < 0.0001$) and (0.19 ± 0.04, 0.26 ± 0.04 and 0.26 ± 0.03; $p < 0.0001$) respectively while mitral annular ellipsicity and Mitral valve tenting volume were significantly higher in the same group (1) (114.82% ± 22.47%, 100.21% ± 9.87% and 97.29% ± 14.37%; p = 0.0421) and (2.73 ± 1.11, 2.20 ± 1.39 and 0.87 ± 0.67) respectively. Vena contracta diameter was inversely correlated with the mitral annular height (r = −0.82; $p < 0.0001$) and saddle-shaped nonplanarity of the annulus (r = −0.68; $p < 0.0001$).

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Conclusion: Among patients with ischemic heart disease, there are significant increases in mitral valve tenting volume and height, and those with mitral regurgitation exhibited a reduced mitral annular height, a shallower saddle shape annulus and losses of ellipsicity of the annulus.

1. Introduction

After myocardial infarction, mitral regurgitation occurs roughly in ten to twenty percent of patients.[1] The mechanisms underlying ischemic mitral regurgitation are multiple and complex and are yet to be fully elucidated; they remain the subject of considerable debate. However, surgical procedures for the mitral valve demand the precise analysis of its anatomy.

The normal mitral annulus has a nonplanar saddle shape[2–5] that is higher at its anterior and posterior points and lower at the anterolateral and posteromedial commissures.[6] Normal annular motion throughout the cardiac cycle helps in leaflet coaptation and valve competence[7], and it has been suggested that this is valuable for reducing mechanical stress on the chordae tendineae and mitral leaflets.[8]

Recent data show that restrictive annuloplasty for the treatment of mitral regurgitation during a coronary artery bypass graft is associated with persistent mitral regurgitation early after the operation in 10–20% of cases and with a higher rate of recurrent mitral regurgitation in 50–70% of cases at the 5-year follow-up.[9,10] These imperfect results highlight the need to create options or concomitant surgical procedures that specifically focus on the causal mechanisms of the condition. Any tool that can potentially help in the development of annuloplasty rings to restore a diseased mitral valve annulus back to a truly normal geometry will be highly beneficial.

Recent advances in technology resulted in high temporal and spatial resolution of the three-dimensional (3D) echocardiography that aids in the quantitative analysis of mitral valve geometry.[11] The aim of this study was to use 3D echocardiographic analysis to investigate mitral annular geometric deformities in patients with ischemic heart disease with and without mitral regurgitation.

2. Subjects and methods

2.1. Study population

This study was conducted between March 2014 and August 2015 (as prospective observational study). We screened 32 consecutive patients who underwent coronary artery bypass grafting. As a control group, we also screened 19 subjects who were referred for a transesophageal echocardiographic study for various etiologies but were found to have no underlying structural cardiac disease. We excluded nine of the screened patients because of the presence of a stitching artifact, aortic valve disease, structural mitral valve disease (flail leaflets or torn chordae), mitral prolapse, atrial fibrillation, or technically inadequate studies; this left 28 patients ischemic heart disease and 14 healthy control subjects, who were enrolled in the study. The study was approved by our institutional review board. Informed written consent was obtained from all the subjects.

2.2. Procedure

Transesophageal echocardiographic images were obtained for all the enrolled subjects, and static mitral annular parameters were accordingly measured at end-systole. Mitral regurgitation was assessed through the measurement of the diameter of the vena contracta which was taken from long-axis at mid-esophageal view and defined as the narrowest part of the mitral regurgitation jet. Vena contracta was defined as severe, moderate, or mild for vena contracta diameters $\geqslant 0.7$ cm, 0.3–0.69 cm, and < 0.3 cm, respectively.[12] The measured annular parameters were compared between patients with ischemic heart disease with mitral regurgitation, patients with ischemic heart disease with no mitral regurgitation, and control subjects. Left ventricular internal dimensions and ejection fraction, were acquired preoperatively within one week of the study by 2 D echocardiographic examination.

2.3. Image acquisition

Complete (two and three dimensional) transesophageal echocardiographic examinations were performed according to recommendations of the American Society of Echocardiography[13] after the induction of general anesthesia, using a Philips iE33 Ultrasound Machine (Philips Healthcare, USA) equipped with a fully sampled 3D X7-2t xMATRIX array transducer (Philips Healthcare).

3D images of the mitral valve were acquired using the full-volume acquisition method. Images were acquired with R-wave gating over four beats; the images covered the entire mitral complex, including the annulus, leaflets, papillary muscles, and aortic valve. An adequate image was defined as en face surgical views of the mitral valve without artifacts.[14]

2.4. Image analysis

Offline quantitative mitral valve analysis was performed on an Xcelera Workstation (Philips Healthcare) equipped with custom software (QLAB MVQ, version 10.3, Philips).

To build a model of the mitral valve annulus, mitral valve images were presented on a quad screen, including three orthogonal planes representing the orthogonal anatomic planes derived from the 3D dataset. To start the analysis, end-systole was tagged on the cine-loop (the end-systolic frame defined as the frame just before aortic valve closure). Image alignment was achieved and a multiplanar projection model was produced by rotating the image on orthogonal planes and aligning the red, blue, and green lines to adjust the mitral valve where it was bisected by the two long-axis planes. The four major annulus reference points were tagged on the appropriate planes to define the anterolateral, posteromedial, anterior, and posterior reference points in the two- and four-chamber views. With regard to editing the nadir and aortic points, we chose the lowest point at the tip of the mitral valve leaflets and the point at the level of the aortic valve cusps in the five-chamber view, respectively.

The reconstructed valve was displayed as a 3D-rendered surface presented as a topographical map. The parameters to be measured were automatically generated from the resultant model.[14,15]

2.5. Parameter measurement

The following mitral valve annular dimensions were measured in mm or mm^2 (Fig. 1): the mitral valve commissural diameter (anterolateral to posteromedial diameter of the mitral annulus), mitral valve anteroposterior diameter (anterior to posterior diameter of the mitral annulus), mitral annular 3D circumference (perimeter of the mitral annulus), mitral annular 2D circumference (circumference of the mitral annulus in the projection plane), mitral annular 2D area (area of the mitral annulus in the projection plane), and mitral annular 3D minimal area (area of the minimal surface spanning the mitral annulus).

The shape of the mitral valve annulus was defined by the following measurements: height of the annulus (defined as the vertical distance between the lowest and the highest points on the annulus); ellipsicity of the annulus (%), given by the ratio of the anteroposterior diameter to the commissural width; and saddle-shaped nonplanarity of the annulus (%), given by the ratio of the annular height to the commissural width, where a higher percentage represents a deeper saddle shape [16] (Fig. 1).

The mitral valve leaflets were defined by the following Parameters: the angle of the anterior leaflet, angle of the posterior leaflet, nonplanar angle of both leaflets[14,15], mitral valve tenting volume (in mL; volume of the leaflets' tent), and maximal mitral valve tenting height (mm) (Fig. 2).

2.6. Statistical analysis

Data were expressed as mean ± standard deviation or percentage, as appropriate. All continuous data were tested for normality using the Kolmogorov–Smirnov test, and distributions were compared across groups using analysis of variance (ANOVA) or the Fisher's exact test, as appropriate. When ANOVA results were significant ($p < 0.05$), the Tukey test for multiple comparison was used to examine the differences between groups. Pearson correlations between all continuous variables were calculated, with non-normally distributed variables log-transformed prior to analysis. Statistical analyses were performed using Stata S.E. 13.1 (StataCorp, College Station, TX, USA).

3. Results

3.1. Patient characteristics

Table 1 summarizes the characteristics of patients that were divided into three groups for comparison and analysis: Group 1 ($n = 21$), those with ischemic heart disease and mitral regurgitation; Group 2 ($n = 7$), those with ischemic heart disease but without mitral regurgitation; and Group 3 ($n = 14$), the control group. The mean ages of Groups 1 and 2 were greater than those of the control group (Group 1, 59.8 ± 9.4 years; Group 2, 62.4 ± 12.6 years; and Group 3, 41.6 ± 11.9 years; $p < 0.0001$), but no other demographic differences were found between the groups.

In the patients with ischemic heart disease (Groups 1 and 2) the left ventricular systolic function was reduced compared with that in the normal subjects but did not differ significantly between Groups 1 and 2.

3.2. Mitral annulus dimensions and shape

Table 2 summarizes the measured and derived mitral annular parameters. Most of these did not significantly differ between the groups; however, significant differences were found in three parameters:

Mitral annulus height was significantly lower in Group 1 (6.00 ± 1.07 mm) than in Group 2 (7.96 ± 0.93 mm) and Group 3 (8.31 ± 1.12 mm; $p < 0.0001$). The saddle-shaped nonplanarity of the annulus was significantly lower in Group 1 (0.19 ± 0.04) than in Group 2 (0.26 ± 0.04) and Group 3 (0.26 ± 0.03; $p < 0.0001$). Mitral annular ellipticity was significantly higher in Group 1 (114.82% ± 22.47%) than in Group 2 (100.21% ± 9.87%) and Group 3 (97.29% ± 14.37%) $p = 0.0421$ (Table 2).

The vena contracta diameter was inversely correlated with both mitral annulus height ($r = -0.82$; $p < 0.0001$; Fig. 3) and saddle-shaped nonplanarity of the annulus ($r = -0.68$; $p < 0.0001$; Fig. 4).

3.3. Mitral leaflet angles and volume

Table 3 summarizes the measured and derived mitral leaflet parameters. The only significant differences between the groups were for mitral valve tenting volume and height. Mitral valve tenting volume was significantly higher in Groups 1 and 2 (2.73 ± 1.11 and 2.20 ± 1.39 mL, respectively) than in Group 3 (0.87 ± 0.67 mL; both $p = 0.0001$). The difference in tenting volume between Groups 1 and 2 was not significant. Similarly, the mitral annular tenting height was greater in Groups 1 and 2 (5.78 ± 2.54 and 5.76 ± 2.61 mm, respectively) than in Group 3 (4.01 ± 0.86 mm; $p = 0.054$) but without a significant difference between Groups 1 and 2 (see Fig. 5).

4. Discussion

Possible mechanisms by which ischemia can cause mitral regurgitation include asymmetric annular dilatation, leaflet tethering and restricted motion, alteration in papillary muscle contraction, and distortion of left ventricular geometry due to regional or global left ventricular remodeling.[17–19] This can explain why a simple downsized annuloplasty ring used during coronary artery bypass grafting, irrespective of individual mitral valve geometry, is likely to be responsible for persistent mitral regurgitation after surgery.[20,21] Three-dimensional transesophageal echocardiography empowers direct representation of the mitral valve from any point and mapping of the mitral valve without the requirement for mental reconstruction.[22] A 3D echocardiography-based surgical plan

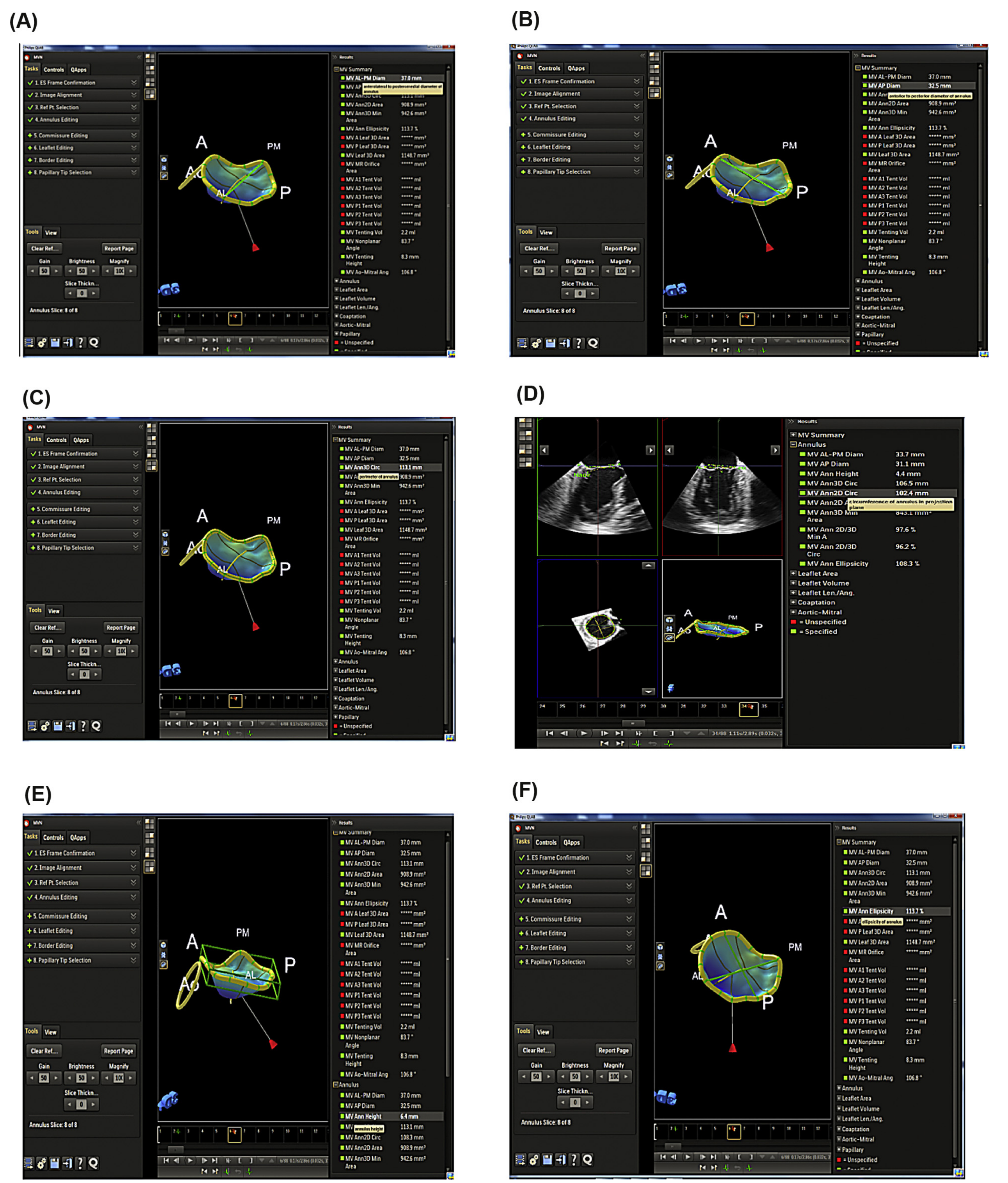

Figure 1 Illustrative example of three dimensional quantitative analysis of mitral annular dimensions: (A) Anterolateral to posteromedial diameter, (B) Anterior to posterior diameter, (C) Mitral annular 3D circumference, (D) Mitral annular 2D circumference, (E) Mitral annular height, (F) ellipsicity of the annulus.

aiming to insert an annuloplasty ring that can restore normal mitral annular geometry may lead to better results.[23]

Previous studies have focused on the potential benefit of 3D mitral valve quantitative analysis that compared static and dynamic changes in ischemic mitral regurgitation with those in normal subjects.[6–14] Others have studied changes in mitral valve prolapse.[15,16] However, the present study is the first to compare 3D mitral valve changes between patients with

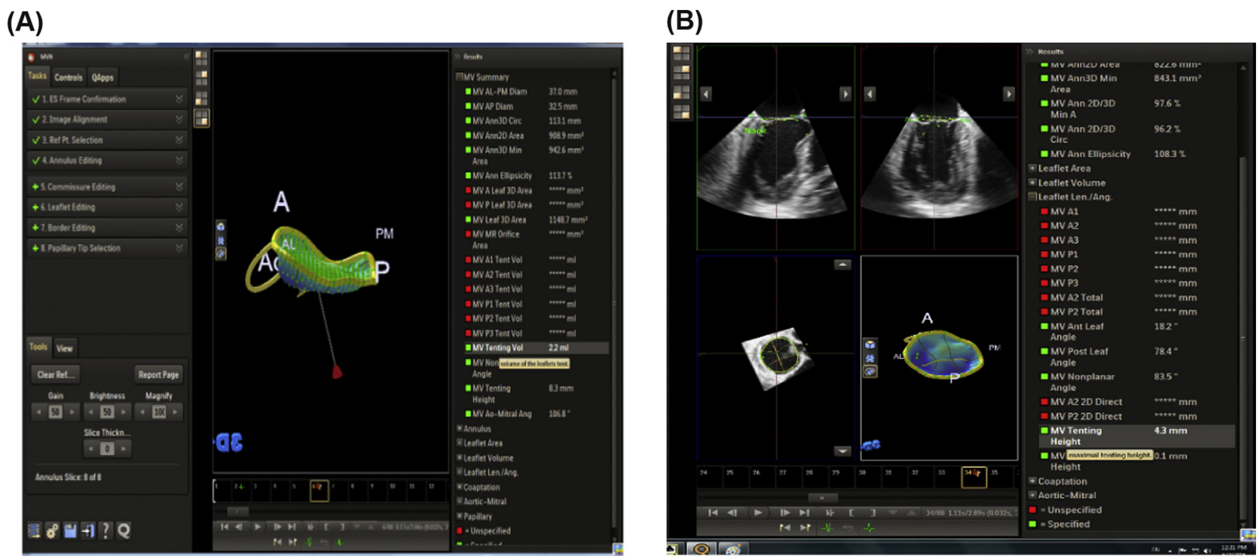

Figure 2 Illustrative example of Three dimensional analysis Mitral leaflet tenting: (A) Mitral valve leaflet tenting volume, (B) Mitral valve leaflet tenting height.

Table 1 Baseline patients characteristics.

Variable	Groups			ANOVA *p*-value
	Group 1 (n = 21)	Group 2 (n = 7)	Group 3 (n = 14)	
Age, y	59.81 ± 9.39[*]	62.43 ± 12.55[*]	41.57 ± 11.85	< .0001
Males, n (%)	13 (61.90)	6 (85.71)	27 (62.29)	0.564[^]
Body surface area (m^2)	1.81 ± 0.17	2.01 ± 0.07	1.84 ± 0.31	0.114
Ejection fraction (%)	43.38 ± 11.83[*]	35.86 ± 13.64[*]	52.57 ± 9.30	0.015
Vena contracta (mm)	0.40 ± 0.19	0	0	
Degree of mitral regurgitation n (%)				
Mild n (%)	10 (47.61)	0 (0)	0 (0)	
Moderate n (%)	9(42.85)	0 (0)	0 (0)	
Severe n (%)	2 (9.52)	0 (0)	0 (0)	

Note:
[*] $p < .05$ versus normal subjects; [&] $p < .05$ versus MR-group.
[^] Value from the Fisher's exact test.

Table 2 Mitral annular dimensions and shape.

Variable	Groups			ANOVA *p*-value
	Group 1 (n = 21)	Group 2 (n = 7)	Group 3 (n = 14)	
Anterolateral postmedial diameter, mm	33.24 ± 3.48	32.87 ± 3.47	32.14 ± 3.13	0.494
Antero-posterior diameter, mm	28.83 ± 4.14	29.16 ± 3.42	30.94 ± 2.41	0.542
3-D circ, mm	109.83 ± 13.73	114.06 ± 12.46	111.14 ± 13.37	0.771
2-D circ, mm	105.09 ± 12.91	109.17 ± 11.66	105.21 ± 13.07	0.749
2-D area, mm^2	820.24 ± 175.17	884.10 ± 162.31	811.43 ± 123.78	0.068
3-D Min area, mm^2	868.86 ± 195.11	923.89 ± 162.77	843.86 ± 112.04	0.064
Height, mm	6.00 ± 1.07[*,&]	7.96 ± 0.93	8.31 ± 1.12	< 0.0001
ellipsicity%	114.82 ± 22.47[*,&]	100.21 ± 9.87	97.29 ± 14.37	0.0421
Annular saddle-shaped nonplanarity	0.19 ± 0.04[*,&]	0.26 ± 0.04	0.26 ± 0.03	< .0001

Note:
[*] $p < .05$ versus normal subjects.
[&] $p < .05$ versus MR- group.

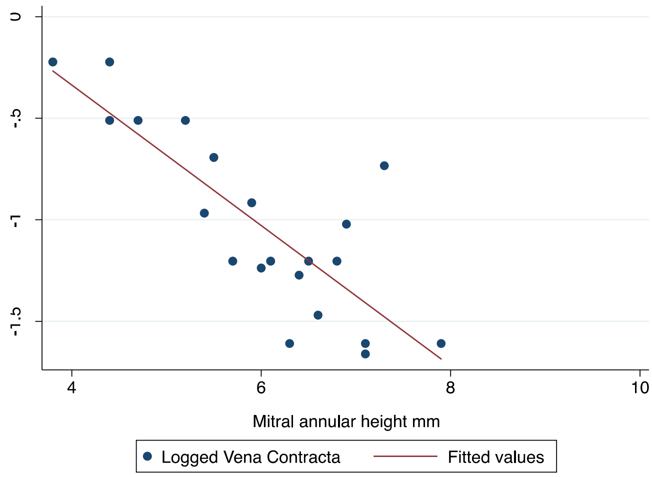

Figure 3 Two-way scatter plot of vena contra and mitral annular height, mm with line of best fit ($r = -0.82$).

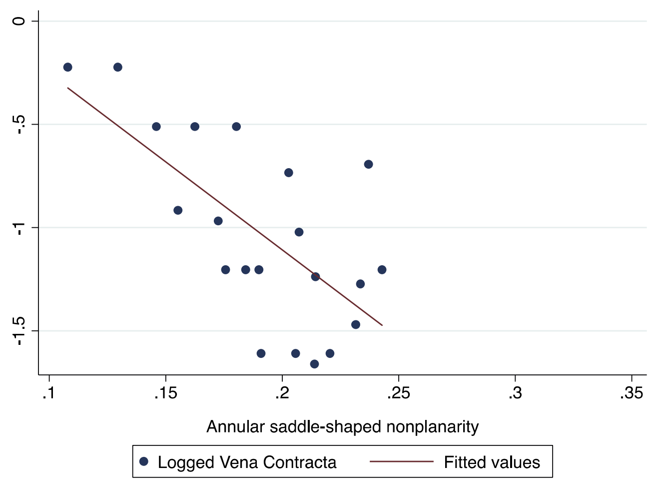

Figure 4 Two-way scatter plot of vena contra and annular saddle-shaped nonplanarity with line of best fit ($r = -0.68$).

ischemic heart disease with and without mitral regurgitation, in addition to comparing these with normal control subjects. As previous studies have concluded that diastolic changes of a small magnitude are insignificant in comparison with marked systolic changes[16] due to the natural mitral valve annulus confirming its saddle shape in systole,[24] we comprehensively analyzed end-systolic mitral valve anatomy to investigate mitral annular geometric deformity in our patients. Mitral valve 3D echocardiographic analysis allowed us to obtain a 3D quantitative analysis of the mitral annulus dimension and shape and a quantitative measurement of the mitral leaflet.

4.1. Mitral annulus dimensions and shape

As previously described, ischemic mitral regurgitation may be attributed to annular dilation caused by annular and subvalvular remodeling[25,26], annular shape change,[6] or leaflet tethering.[27,28]

In the present study, compared to patients with ischemic heart disease without mitral regurgitation, those with mitral regurgitation exhibited significantly reduced height and saddle-shaped nonplanarity of the mitral annulus, indicating a shallower saddle shape of the annulus in this subset of patients. This can lead to poor leaflet coaptation in these patients because of the loss of the mitral annular saddle shape phenomenon[2], i.e., early systolic contraction and shortening of anteroposterior distance without intercommissural change, which prompts the profound saddle shape of the annulus and strengthens coaptation.

This is in accordance with the findings of Levack et al.[29], who highlighted the adynamic nature of ischemic mitral annulus which loses its capacity to change its shape all through the cardiac cycle as it enlarges and flattens. Furthermore, the present study showed that at end-systole, the ratio of antero lateral–postero medial diameter to anteroposterior diameter (ellipsicity of the mitral annulus) was increased in patients with ischemic mitral regurgitation; this finding suggests that the mitral annulus loses its symmetry in this group of patients even without a significant dilatation in dimensions. Three-dimensional echocardiography can provide a detailed analysis of morpho-anatomic changes in the mitral valve to allow its quantification prior to mitral repair in patients with ischemic heart disease; this is important for the selection of a surgical strategy.

4.2. Mitral leaflets

In the present study, mitral valve tenting volume and tenting height were greater in patients with ischemic heart disease than in controls. This can be explained by the tethering of papillary muscle in patients with ischemic heart disease due to left ventricular remodeling.[30] These results support those of Watanabe et al.[31], who examined ischemic mitral annular geometric

Table 3 Mitral valve leaflet angles and volume.

Variable	Groups: Group 1 ($n = 21$)	Group 2 ($n = 7$)	Group 3 ($n = 14$)	ANOVA p-value
Anterior leaflets angle ^{O}	28.80 ± 7.61	32.94 ± 8.14	25.05 ± 6.18	0.068
Posterior leaflets angle ^{O}	62.51 ± 14.27	62.64 ± 9.78	63.79 ± 9.96	0.954
Nonplanarity angle ^{O}	88.27 ± 7.60	88.09 ± 6.80	91.21 ± 7.99	0.492
Mitral valve tenting volume, ml	2.73 ± 1.11*	2.20 ± 1.39*	0.87 ± 0.67	0.001
Mitral valve tenting height, mm	5.78 ± 2.54*	5.76 ± 2.61*	4.01 ± 0.86	0.054

Note:
* $p < .05$ versus normal subjects, & $p < .05$ versus MR-group.

Figure 5 Example of mitral annular height in examined groups: (A) Mitral annular height in normal subject, (B) Mitral annular height in ischemic heart disease patient without mitral regurgitation, and (C) Mitral annular height in ischemic heart disease patient with mitral regurgitation.

deformities in ischemic mitral regurgitation attributable to anterior or inferior myocardial infarction and concluded that there were significant increase in leaflet tenting in ischemic mitral regurgitation.

4.3. Limitation of the study

In this study, due to small sample size, we did not subclassify mitral regurgitation (anterior, posterior, early systolic, mid or late systolic) to compare the annular deformity in different subtypes of mitral regurgitation.

4.4. Conclusion

In patients with ischemic heart disease, there are significant increases in mitral valve tenting volume and height due to leaflet tethering, and there are significant differences in the mitral annular geometry in patients with associated mitral regurgitation, in the form of reduced mitral annular height, a shallower saddle shape of the annulus and loses of annular ellipticity.

4.5. Clinical implication

The present study suggests that 3D mitral valve analysis can address full details regarding the morpho-anatomic changes of the mitral valve in patients with ischemic mitral regurgitation.

4.6. Recommendation

We recommend the use of detailed 3D mitral valve morphological analysis before the surgical repair of ischemic mitral regurgitation because of its potential help in surgical decision-making and the selection of annuloplasty rings. Further studies are needed to compare the morpho-anatomic changes in different subtypes of mitral regurgitation.

Conflict of interest

There is no conflict of interest.

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