Geometric Deformity of the Mitral Annulus in Patients With Ischemic Mitral Regurgitation: A Real-time Three-Dimensional Echocardiographic Study

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Background and aim of the study: **Saddle-shaped non-planarity of the mitral annulus has been investigated previously. The study aim was to further clarify the configuration of the mitral annulus in ischemic mitral regurgitation (MR) by using transthoracic real-time three-dimensional (3-D) echocardiography.**

Methods: **Twenty-five patients with previous myocardial infarction and left ventricular dysfunction (ejection fraction <50%), and 10 healthy control subjects, were examined using real-time 3-D transthoracic echocardiography. The patients were allocated to either a non-MR group or an MR group. By using real-time 3-D echocardiography, the configuration of the mitral annulus was reconstructed in end-systole, and the height of the saddle-shaped mitral annulus calibrated (non-planar index).**

Results: In controls, the mitral annulus appeared as non-planar 'saddle shape', with a non-planar index of 5.5 ± 1.7 mm. The mitral annulus was flattened in both the non-MR and MR groups. The non-planar index was significantly smaller in the MR group than in the non-MR group (1.7 ± 1.8 mm versus 3.8 ± 1.2 mm, $p < 0.05$). The systolic annular area was significantly larger in the MR group than the non-MR group.

Conclusion: **The 'saddle shape' of the mitral annulus was deformed in patients with ischemic MR. Mitral annulus deformation may play a role in ischemic MR in conjunction with mitral valve tenting. These results suggest that a non-planar saddle-shaped annuloplasty ring would contribute to successful mitral valve repair durability in patients with ischemic MR.**

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Ischemic mitral regurgitation (MR) is known to occur in patients with systolic left ventricular (LV) dysfunction due to ischemic heart disease, with structurally normal mitral valve leaflets (1). A recent clinical study reported that the existence of ischemic MR is associated with excess mortality and risk even after surgical valve repair (2). According to previous experimental and clinical studies, mitral annulus dilatation, tethering of mitral leaflets secondary to LV dilatation, and reduced transmitral pressure to coapt the leaflets are implicated as mechanisms for ischemic MR (3-8). Saddle-shaped non-planarity of the mitral annulus has been investigated previously using rotated, two-dimensional (2-D) or multi-plane transesophageal echocardiography (9,10) in human studies, and by marker radiography or sonomicrometry in animal studies (11,12). A recent computer-based simulation study demonstrated successfully that the saddle-shape of the mitral annulus is a more subtle form to optimize mitral leaflet curvature, which minimizes peak mitral leaflet stress (13). On this basis, changes in the geometric form of the mitral annulus may be one of the causative mechanisms of functional MR, and results have supported the hypothesis that the non-planar saddle-shaped annuloplasty ring would increase the efficacy and durability of mitral valve repair. Recent advances in three-dimensional (3-D) transthoracic echocardiographic techniques have allowed visualization and analysis of the geometric configuration of the complex, non-planar mitral annulus non-invasively in humans. The aim of the present study was to establish further that deformity in the mitral annulus is indeed present in patients with ischemic MR secondary to ischemic heart disease.

Clinical material and methods

Patients

Twenty-five consecutive patients (17 males, eight

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females; mean age 67 ± 17 years) with previous myocardial infarction who presented with impaired global LV systolic function (biplane ejection fraction (EF) <50%) were studied prospectively. The exclusion criteria were: acute myocardial infarction; structural mitral valve or subvalvular lesions, such as mitral valve prolapse or rheumatic disease; atrial fibrillation or atrial flutter; and other cardiac disease such as organic valvular, pericardial, congenital or infiltrative heart disease. The underlying infarct regions were anteroseptal (n = 8), inferior (n = 10), posterior (n = 1) and anteroseptal + inferior (n = 6). Ten healthy subjects were also examined as a control group. All participants provided their written, informed consent to the study protocol, which was approved by the Committee for the Protection of Human Subjects in Research at Kawasaki Medical School.

Echocardiography

All echocardiographic examinations were performed using a SONOS 7500® instrument (Philips, Inc.) fitted with an S3 probe for 2-D images, and with an X4 probe for real-time 3-D images.

Global LV function

All subjects underwent a standard 2-D echocardiographic examination. LV end-diastolic and end-systolic dimensions were measured in the parasternal long-axis view. The EF (%) was measured using the biplane (modified) Simpson method.

Evaluation of MR

MR was evaluated using color Doppler echocardiography. In patients with MR, the regurgitant orifice area (ROA) was calculated using the proximal isovelocity surface area (PISA) method. In patients with no or trivial MR (as assessed using color Doppler), the ROA was assumed to be null. The patients were allocated to two groups: a non-MR group (n = 15) with ROA <0.1 cm^2, and an MR group (n = 10) with ROA ≥0.1 cm^2.

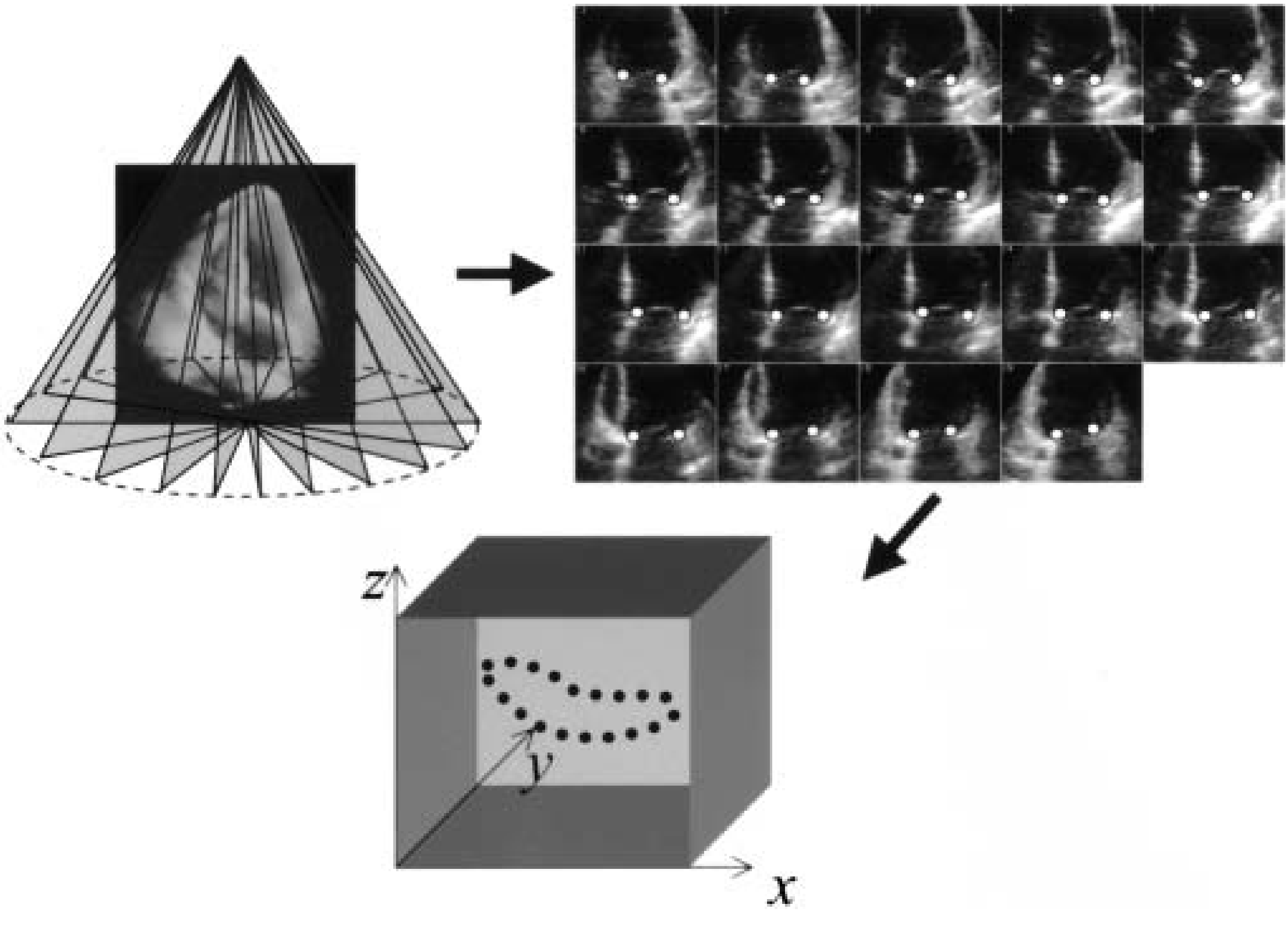


Figure 1: Three-dimensional data were automatically cropped into 18 equally spaced radial planes. The mitral annulus was marked in each cropped image in end-systole. Configuration of the mitral annulus was reconstructed by using MATLAB software.

Deformation of the mitral valve complex by 2-D echocardiography

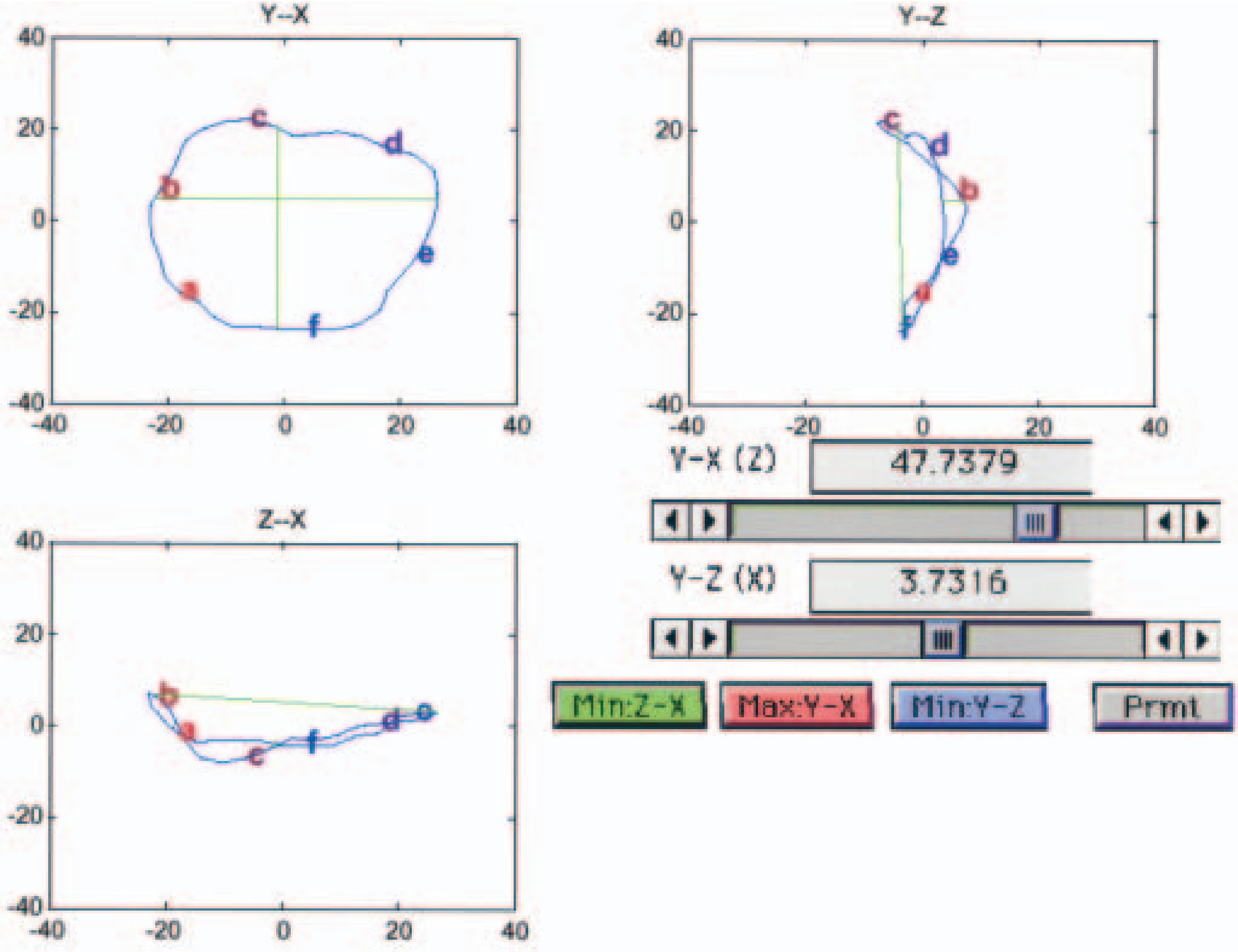
The mitral valvular tenting area and tenting length were measured by the area enclosed between the annular plane and mitral leaflets from the parasternal long-axis view at late systole. The distance from the mitral annulus to the posterior papillary muscle was measured in modified long-axis views obtained from the apex (tethering length).

3-D mitral annulus configuration

By utilizing real-time 3-D echocardiography, transthoracic volumetric images (full volume mode) with the apical view were obtained in all subjects. The volumetric frame rate was 16-22 per second, with an imaging depth of 12-16 cm. All volumetric images were stored digitally on compact disk and transferred to a personal computer for offline analysis. After setting the central point of the mitral annulus in each volumetric image, the 3-D data were automatically cropped into 18 radial planes spaced 10º apart. The mitral annulus was marked in each cropped image. Configuration of the mitral annulus was reconstructed using MATLAB (MathWorks Inc., Natick, Massachusetts, USA) in end-systole (Fig. 1). From the 3-D data (Fig. 2), the heights of the mitral annulus were measured to appreciate the non-planarity (non-planar index). The circumferences and annular projection areas of the mitral annulus were also calculated. These data were compared between the three groups.

Statistical analysis

Data were expressed as mean ± SD (or percentages). Group comparisons were made using Student's *t*-test. A p-value <0.05 was considered to be statistically significant.



Y-X (Z) 47.7379

Y-Z (X) 3.7316

Figure 2: Configuration of the mitral annulus was reconstructed by using MATLAB software three-dimensionally. Heights, circumferences and annular projection areas of the mitral annulus were calculated from these data.

Results

Among control subjects the average EF was 64 ± 3%, while the LV end-diastolic and end-systolic dimensions were 49.0 and 28.8 mm, respectively. There were no significant differences in EF between the MR and non-MR groups (36 ± 6% versus 34 ± 11%). The LV end-diastolic and end-systolic dimensions were significantly greater in the MR group than in the non-MR group (end-diastolic dimension 61.7 ± 9.4 mm versus 55.0 ± 4.3 mm ($p < 0.05$); end-systolic dimension 51.8 ± 12.2 mm versus 44.4 ± 3.9 mm ($p < 0.05$), respectively). In the MR group, the average regurgitant volume was 47.3 ± 28.7 ml, and the ROA 0.3 ± 0.2 cm^2.

Deformation of the mitral complex

The mitral valve tenting area and tenting length were significantly greater in the MR group than in the non-MR group (tenting area 3.6 ± 0.8 mm^2 versus 1.9 ± 0.6 mm^2 ($p < 0.05$); tenting length 17.1 ± 2.6 mm versus 9.3 ± 1.7 mm ($p < 0.05$)).

Configuration of the mitral annulus

In healthy control subjects, the configuration of the mitral annulus appeared as a non-planar 'saddle shape', with its high (farthest from apex) point located anteriorly near the aortic root and posteriorly near the posterior LV wall, while its low points were located at the anterior and posterior commissures. In both the non-MR and MR groups, configuration of the mitral annulus appeared as a planar shape in systole. In the MR group, the annulus shape was no longer 'saddle shaped'; rather, it appeared generally flat, but warped in some cases (Fig. 3). The non-planar index was 5.5 ± 1.7 mm in normal subjects, 3.8 ± 1.2 mm in the non-MR group ($p < 0.05$ versus controls), and 1.7 ± 1.8 mm in the MR group ($p < 0.05$ versus controls, $p < 0.05$ versus non-MR group).

Discussion

The saddle-shaped non-planarity of the mitral annulus has been investigated previously in animal models using sonomicrometry or marker radiography (11,12), and in human studies by using hand-rotated 2-D or multi-plane transesophageal echocardiography (9,10). This unique characteristic of mitral annulus configuration is thought to be a more subtle form of optimizing mitral leaflet curvature, which minimizes peak mitral leaflet stress (13). Hence, this curvature might contribute to the mechanisms of avoiding MR, as part of the 'mitral complex'. Ischemic MR is known to occur in patients with systolic LV dysfunction due to ischemic heart disease, with structurally normal mitral valve leaflets. It has been reported that the existence of ischemic MR is associated with excess mortality, and mitral valve repair using annuloplasty rings is recommended (2,14). However, plane rings have been widely used in mitral annuloplasty for over 20 years, despite the complex geometry of the actual mitral annulus. Yamaura et al. have reported that mitral annular configuration and dynamics are more physio-

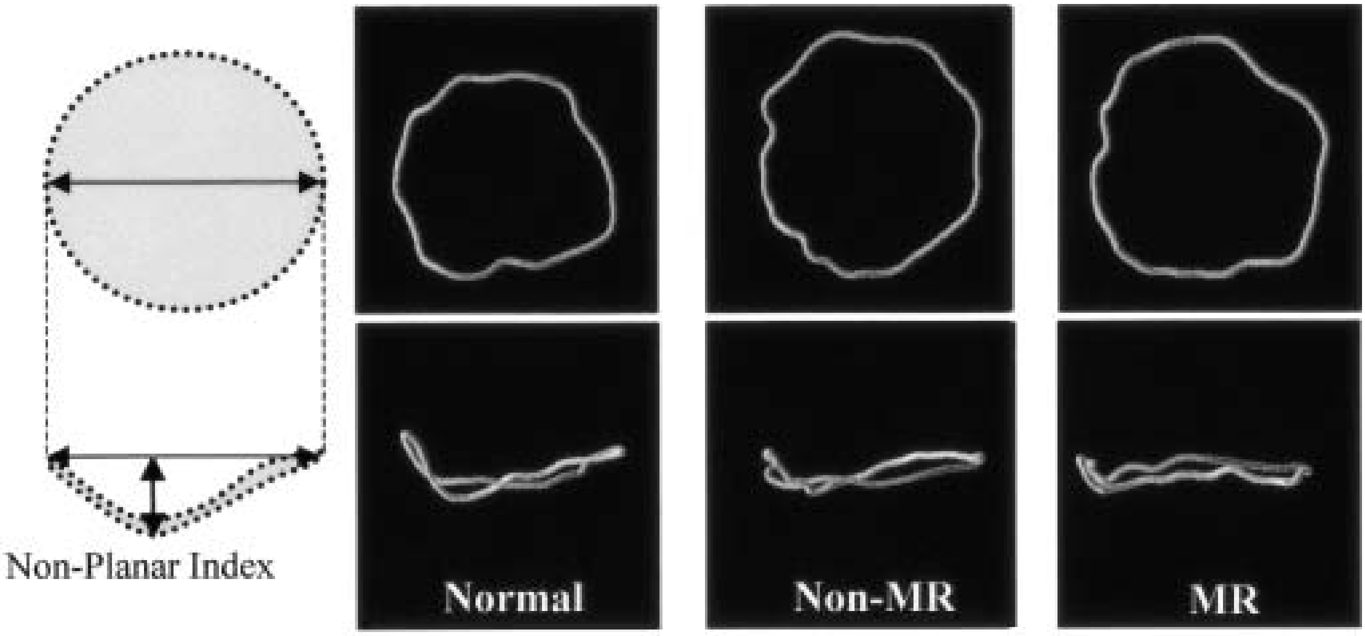


Figure 3: In control subjects, configuration of mitral annulus appeared as non-planar 'saddle shape'. In both non-MR and MR groups, the mitral annulus appeared as a planar shape. In the MR group, the shape of mitral annulus was no longer 'saddle-shaped', but appeared almost flat.

logical in patients with a flexible annuloplasty ring than in those with a rigid ring (10,15,16). The results of several animal studies have shown the presence of annulus deformation in the regional ischemia or in chronic ischemic MR (11,17), and new surgical strategies to restore the saddle shape of the mitral annulus have been proposed and investigated recently (18-20). The saddle shape of the mitral valve would be much more physiological, and contribute to successful mitral valve repair in patients with ischemic MR. However, the actual geometric changes in the mitral annulus configuration in patients with ischemic MR have not yet been investigated. In the present study, geometric deformity of the mitral annulus was successfully demonstrated by utilizing a newly developed software system with transthoracic, real-time 3-D echocardiography.

Configuration of the mitral annulus

In normal subjects, it was possible to demonstrate the curvature of mitral annulus, which appeared as a saddle shape. The mitral annulus had its highest point anteriorly near the aortic root, and posteriorly near the posterior LV wall, while its low points were located at the anterior and posterior commissures, as reported previously (1,9,10). In patients with an infarcted left ventricle and with LV dysfunction, the saddle shape deformed to a flat shape, and further deformation was found in those patients with ischemic MR. This deformation would increase the peak mitral leaflet stress, and might be followed by incomplete coaptation of the mitral valve.

Possible mechanisms of mitral annulus deformity

In the present study, the LV diastolic and systolic dimensions were greater in MR patients than in non-MR patients, despite there being no significant intergroup differences in the EF. Calculated circumferences and annular projection areas (using 3-D data) showed an enlarged annulus in ischemic MR patients. The mitral valve tenting area and tenting length were larger, and the mitral valve tethering length longer, in the MR group than the non-MR group. These findings were compatible with those mechanisms reported previously for ischemic MR (1,3,5,7). In other words, the geometric deformity and flattened mitral annulus might be initiated by LV remodeling and tethering of the mitral valve, which finally results in the occurrence of functional MR. The present results suggested that the physiological curvature of the mitral annulus should be taken into account when assessing the mechanisms of ischemic MR, whilst a 3-D analysis of annulus shape permits a suitable curvature to be defined when designing non-planar annuloplasty rings.

Study limitations

In the present study, both MR volume and ROA were estimated using the PISA method, but in some patients with small or trivial regurgitation, proximal convergence flow images could not be obtained by color Doppler echocardiography, and the existence of MR in the process of data analysis was ignored. Furthermore, MR severity was estimated in patients with two jets by the summation of two jets, as performed by Kwan et al. (21), though this method has not yet been validated. A second limitation was that, although possible mechanisms of annulus deformity were discussed, and the suggestion made that this contributed to the occurrence of ischemic MR as part of the mitral complex, this theory remained speculative and the actual mechanism was not clarified. An additional weakness was that the present study population was relatively small, and no investigations were made of any geometric differences of the mitral annulus among patients with a different infarct region. Also, although the annulus shape was only examined at end-systole, the saddle shape may change during the cardiac cycle, and further investigation is required in this respect. Finally, the accuracy of the original analysis software system used with real-time 3-D echocardiography for the mitral annulus has not been validated in vitro or in vivo. In order to validate the precision and accuracy of this method, simultaneous measurements in animals using a previously established method (e.g. marker radiography or sonomicrometry) would be required.

In conclusion, the previously described ‘saddle shape’ of the mitral annulus was deformed in patients with ischemic MR. Changes in annulus configuration play a role in ischemic MR in conjunction with mitral valve tenting. The present results suggest that a non-planar, saddle-shaped annuloplasty ring would contribute to successful mitral valve repair in patients with ischemic MR.

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