Ischemic mitral regurgitation (MR) is known to occur in patients with systolic left ventricular (LV) dysfunction attributable to ischemic heart disease, with structurally normal mitral valve leaflets. Mitral annulus dilatation, tethering of mitral leaflets secondary to LV dilatation with outward displacement of papillary muscles, and reduced transmitral pressure to coapt the leaflets have been implicated as mechanisms for ischemic MR (1–8), and this common complication has been reported to benefit patients with functional mitral valve replacement (12–16), and annuloplasty is currently a common surgical strategy for ischemic MR, even if MR often persists after annuloplasty. Recently, chordal cutting surgery, which is based on the known mechanisms of ischemic MR (i.e., tethering of the mitral leaflet into the LV), has been expected to reduce chronic persistent ischemic MR after annuloplasty (17,18). However, in the clinical setting, the degree of geometric changes of the mitral leaflets and annulus has previously been assessed in a single slice of the mitral valve component by two-dimensional (2D) echocardiography (19,20), in spite of the unique configuration of the curved mitral valve and saddle-shaped mitral annulus (21–24). Hence, 2D imaging plane (i.e., parasternal long-axis view or apical four-chamber view), which is currently used for the measurement of tenting length (coaptation length) or tenting area in the clinical studies, may miss the maximum tethering site. Besides, present surgical approaches have been based on the beneficial result from animal experiments, ignoring the various three-dimensional (3D) geometric deformities in each patient in the clinical setting. If we can visualize 3D images of the whole mitral leaflets and annulus and analyze the degree of their deformation quantitatively, it will be helpful for the surgeon to know the precise mechanisms of the ischemic MR and to make a proper decision for the surgical strategy in each individual patient. In the present study, we sought to: 1) investigate the 3D geometric changes of the mitral leaflets and annulus by transthoracic real-time three-dimensional echocardiography.
Abbreviations and Acronyms

EDV = end-diastolic volume  
EF = ejection fraction  
ESV = end-systolic volume  
LV = left ventricle  
MI = myocardial infarction  
MR = mitral regurgitation  
PISA = proximal isovelocity surface area  
ROA = regurgitant orifice area  
3D = three-dimensional  
2D = two-dimensional

METHODS

Patients. We prospectively studied 12 patients with significant ischemic MR (regurgitant orifice area [ROA] ≥0.15 cm²) presenting with impaired global LV systolic function due to coronary artery disease (biplane ejection fraction [EF] <50%) from September 2003 to August 2004 (age 73 ± 6 years, 9 men). Inclusion criteria were: 1) structurally normal mitral valve; 2) technically adequate color flow Doppler image for proximal isovelocity surface area (PISA); 3) technically adequate real-time 3D echocardiographic image of the LV chamber and the mitral apparatus (annulus and leaflets) to allow analysis of 3D geometry; and 4) normal sinus rhythm. Exclusion criteria were: 1) acute MI; 2) structural mitral valve or subvalvular lesions, such as mitral valve prolapse or rheumatic disease; and 3) other cardiac disease, such as organic valvular, pericardial, congenital, or infiltrative heart disease. Ten healthy subjects were also examined as controls (age 65 ± 7 years, 7 men). All participants gave 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.

Echocardiographic protocol. All the echocardiographic exams were performed by SONOS 7500 (Philips Ultrasound, Bothell, Washington), with S3 probe for 2D images and X4 probe for real-time 3D images.

2D echocardiographic study. All subjects underwent a standard 2D echocardiographic examination. The LV end-diastolic volume (EDV) and LV end-systolic volume (ESV) were measured by the biplane Simpson method. Ejection fraction (%) was calculated by the equation 100 × (EDV − ESV)/EDV. Mitral regurgitation was evaluated by color Doppler echocardiography. Degree of MR was quantified by ROA using the PISA method.

3D echocardiographic study. VOLUMETRIC IMAGE ACQUISITION. Using a real-time 3D echocardiographic system, we obtained transthoracic volumetric images (full-volume mode) with the apical view in all the subjects. The volumetric frame rate was 16 to 22 frames/s, with an imaging depth of 12 to 16 cm. Before acquiring the full-volume image, we carefully adjusted the transducer position to be located at the apex in a biplane mode. All volumetric images were digitally stored on compact disk and transferred into a personal computer for offline analysis.

QUANTIFICATION OF MITRAL VALVE TENTING BY 3D ECHOCARDIOGRAPHY. We used our 3D computer software that is based on MATLAB (MathWorks Inc., Natick, Massachusetts) to analyze the volumetric image. First, in a cross-sectional plane of the mitral annulus, we defined the center of the mitral annulus in the volumetric image to set the axis through the transducer position and the center of the annulus. We also determined the anterior–posterior axis and commissure–commissure axis in the volumetric image. The 3D data were then automatically cropped into 18 radial planes spaced 10° apart. We manually marked the mitral annulus and leaflets in each cropped plane in mid-systole. From these data, anatomical 3D images of the mitral leaflets and annulus were reconstructed (Figs. 1 and 2A). Figure 2 shows the created 3D images by using the software system (normal subject). The anatomic 3D image (Fig. 2A) was created to observe the actual configuration of the annulus and leaflets with surface colorations, and this image can be observed from any direction. Figure 2A shows the anatomical 3D image from two different directions. Mitral leaflet configuration was then represented in contour as an actual 3D tenting image (Fig. 2B, left). For the quantitative measurements, the annular shape was approximated in the four quadrants. First, each quarter of the annulus that was projected on the X-Y plane was fitted to an ellipse equation and then annulus curvature toward the Z-axis was calculated by a power law function. Mitral annular area and mitral annular circumference were directly analyzed from the actual 3D tenting images. Height of the mitral annulus was also measured to appreciate the nonplanarity of the mitral annulus from the 3D data (Fig. 2B, right). For the 3D quantitation, the actual 3D tenting image was converted to the corrected 3D tenting image, in which the curved mitral annulus was stretched on a flat plane, keeping the distance from the leaflet to the surface of the annulus the same (Fig. 2C). In the corrected 3D tenting image, we measured maximum tenting length, mean tenting length, and tenting volume. The maximum tenting length was defined as a distance from the level of the 3D annular plane to the most tethered leaflet site in the 3D data. The mean tenting length was defined as an average distance from the level of the annular plane to the tethered leaflet into the LV. The tenting volume was calculated as a volume enclosed between the annular plane and mitral leaflets. These data were compared in the two groups.

MAPPING OF THE MAXIMUM TENTING SITE OF THE MITRAL LEAFLETS. In 12 studied patients with ischemic MR, we identified the sites of the most-tethered leaflet where the maximum tenting lengths were measured in the corrected 3D tenting image. Mitral leaflets were divided into six segments for the mapping of the maximum tenting site: lateral, central, and medial side of the anterior leaflet (AL, AC, AM); and lateral, central, and medial side of the
posterior leaflet (PL, PC, PM). The segments where the peak of the leaflet tenting positioned were determined on a schematic leaflet by the consensus of two experts by referring to the corrected 3D tenting image represented in contour.

Statistical analysis. Data are expressed as mean ± SD. Group comparisons used the Student t test. A value of p < 0.05 was considered significant.

RESULTS

Geometric measurements of the LV chamber, mitral annulus, and mitral leaflets in the two groups are summarized in Table 1.

Baseline characteristics. The 12 patients with ischemic MR included 3 patients with single-vessel disease, 6 patients with two-vessel disease, and 3 patients with three-vessel disease. Left ventricular dysfunction was severe with a wide range (EF 33.9 ± 9.1%, range 18% to 47%). The ROA was 0.29 ± 0.15 cm², ranging from 0.15 to 0.62 cm². Compared with the 10 control subjects, patients with ischemic MR showed no differences in age, gender, or body surface area, but LV volume significantly increased in patients with ischemic MR compared with normal subjects.

Mitral annular and leaflet geometry. Figures 2 and 3 show the 3D images created by using our system (Fig. 2: normal subject, Fig. 3: patient with ischemic MR). The anatomical 3D images (Figs. 2A and 3A) showed the configuration of the leaflet curvature with curved annulus ring. In normal controls, the mitral annulus appeared as a nonplanar “saddle shape,” with its farthest point from apex located near the aortic root and its near points from apex located at anterior and posterior commissure. Mitral leaflets appeared almost flat, with a little tethering into the LV. On the other hand, in patients with ischemic MR, the mitral annulus flattened compared with normal subjects, with apparent tenting of the mitral leaflets, which were tethered into the LV, showing mountain-shape leaflet bulging. Calculated annulus area and annulus circumference in actual 3D tenting images (Figs. 2B and 3B) were significantly larger in patients with ischemic MR compared with normal subjects. Annular height, which shows the nonplanarity of the mitral annulus, was significantly smaller in ischemic MR than normal subjects.

Calculated maximum tenting length, mean tenting length and tenting volume in corrected 3D tenting images (Figs. 2C and 3C) were significantly larger in patients with ischemic MR compared with normal subjects.

The site of the maximum tenting was located in the region of anterior leaflet in all 12 patients (4 in lateral side, 5 in central side, and 3 in medial side) (Fig. 4). No patient had the maximum tenting site in the region of posterior leaflet.

DISCUSSION

In the present study, our anatomical image creation software system used with transthoracic real-time 3D echocardiography could provide: 1) 3D geometric deformity of the mitral leaflets and annulus; 2) maximum tenting site of the mitral leaflet; and 3) quantitative measurements of mitral valve tenting and annular deformity in patients with ischemic MR.

Ischemic MR is a common complication in patients with systolic LV dysfunction due to ischemic heart disease with
structurally normal mitral valve leaflets. Clinically important ischemic MR occurs in 20% to 25% of such patients, and this complication has been reported to convey an adverse prognosis after MI, even after revascularization (9–11). A number of groups have investigated the mechanisms of ischemic MR, and their work has proven that displacement of the attached papillary muscles tethers the mitral leaflets into the LV and restricts their ability to coapt effectively at the level of mitral annulus, which may also dilate. Although annular size reduction is a current common surgical strategy for ischemic MR (12–16), reducing annular size alone is often ineffective, and MR often persists after annuloplasty. Recently, with the knowledge that ischemic MR is a disease of the entire mitral complex, new surgical strategies such as

Figure 2. Three-dimensional (3D) images of mitral annulus and leaflets in a normal subject. (A) Anatomical 3D image (views from two directions). Mitral annulus appeared as a nonplanar “saddle shape.” Mitral leaflets appeared almost flat, with a little tethering into the left ventricle. (B) Actual 3D tenting image. The annular shape was approximated for the 3D quantitation. Mitral leaflet configuration was represented in contour to appreciate the degree of tenting in the vertical view from left ventricle (left). Horizontal view provides the degree of annulus nonplanarity and actual tenting of the leaflet (right). Black dots indicate coaptation line. Circumferences, area, and height of the mitral annulus were measured from these 3D data. (C) Corrected 3D tenting image. The curved mitral annulus was stretched on a flat plane, keeping the distance from the annular surface to the leaflet. Mitral leaflet tenting from the level of 3D mitral annulus was represented in contour in the vertical view from the left ventricle (LV) (left). Horizontal view provides the degree of tenting of the leaflet from the level of mitral annulus (right). Black dots indicate coaptation line. Maximum tenting length, mean tenting length and tenting volume were measured from these 3D data. A = anterior; P = posterior; CL = antero-lateral commissure; CM = postero-medial commissure; LA = left atrium.
basal chordal cutting or papillary muscle repositioning have been expected to reduce chronic persistent ischemic MR (17,18,25). However, most of the previous studies done in the experimental setting using animal models and current surgical techniques have been developed on the basis of the beneficial result from animal experiments, ignoring the various 3D geometric deformities in each patient in the clinical setting. In the clinical setting, the degree of geometric changes of the mitral leaflets and annulus has previously been assessed by 2D echocardiography (19,20), but the unique configuration of the curved mitral valve and saddle-shaped mitral annulus (21–24). Precise and comprehensive understanding of the 3D geometric change of the whole mitral leaflets and annulus is needed for successful valve repair in the clinical setting. To our knowledge, this is the first report to: 1) provide 3D geometry of the mitral leaflets and annulus; 2) clarify the maximum tethering site of the mitral leaflet; and 3) quantify the degree of mitral valve tenting and annular deformity in humans.

**Mitral valve tenting in 3D images.** In normal subjects, mitral leaflets appeared almost flat, with small bulging from the level of the mitral annulus in the 3D images. The anterior leaflet near the aortic root was protruded toward the left atrium beyond the level of mitral annulus. However, in patients with ischemic MR, leaflet tenting was observed clearly with dramatic deformation tethered into the LV, showing a mountain-like configuration. With these 3D images, we can see the actual tethering site of the leaflets, which would help us in considering the proper surgical strategies in each individual. This system allows us to measure the maximum tethering length, mean tethering length, and tethering volume. To the best of our knowledge, this is the first report of 3D quantitative measurements of mitral valve tenting in a clinical setting. Calculated maximum tethering length, mean tethering length, and tethering volume were significantly larger in patients with ischemic MR compared with the normal subjects. Three-dimensional images of the mitral leaflets showed that they are tethered almost symmetrically in the patients with global LV dysfunction. However, the site of the peak-tenting leaflet was different in each individual. This result suggests that the single 2D plane (i.e., parasternal long-axis view or apical four-chamber view) that is currently used for the measurement of tenting length (coaptation length) or tenting area in the clinical studies can miss the maximum tethering site.

With variable clinical backgrounds, there should be different configurations in the various types of functional MR. Three-dimensional echocardiography is a promising technique that can provide precise 3D geometry, which is difficult to understand by conventional 2D echocardiography.

**Mitral annulus configuration.** In normal subjects, the mitral annulus appeared as nonplanar saddle shape, with its farthest point from apex located near the aortic root and its near points from apex located at the anterior and posterior commissure, as described previously in animal experiments and in human studies by using hand-rotated 2D or multi-plane transesophageal echocardiography (15,21,22,26). This unique characteristic of the mitral annulus configuration is thought to be a more subtle form to optimize mitral leaflet curvature, which minimizes peak mitral leaflet stress (23), and hence, new surgical strategies to restore the saddle shape of the mitral annulus have been recently proposed and investigated (i.e., nonplanar saddle-shaped annuloplasty ring, semirigid ring) (12,16). In the present study, we visually and quantitatively demonstrated dilated and flattened mitral annulus in patients with ischemic MR with the use of our new technique. Three-dimensional analysis of the mitral annulus geometry would contribute to further understanding of the 3D geometric changes of the whole mitral leaflets and annulus, in combination with the configuration of mitral leaflets.

**Study limitations.** Real-time 3D echocardiography that is currently available in the clinical setting provides images with lower quality than conventional 2D echocardiography. As the software system used in the present study requires identification of mitral annulus and leaflets for the manual tracing, technically inadequate real-time 3D echocardiographic images are not amenable for analysis.

In the present study, we did not access the degree of displacement of the papillary muscles. To understand 3D geometric changes of the mitral apparatus comprehensively, position of the papillary muscles should also be evaluated. Further improvement of this system is required to obtain a complete understanding of the entire mitral complex geometry.

We estimated MR severity in the patients with two jets by the summation of two jets by PISA method, although this method has not been validated.

We enrolled patients with significant ischemic MR presenting with impaired global LV systolic function (ischemic cardiomyopathy). However, it has been known that ischemic MR occurs in patients with regional, localized wall motion abnormality with displacement of papillary muscles in patients with inferior/posterior MI (20). Kwan et al. (27)
have investigated the asymmetrical mitral valve deformation in ischemic MR patients with regional wall motion abnormality from the measurements in the three 2D planes cropped from the 3D volumetric images. Further investigations are required in various types of patients with ischemic MR by using the present new technique to address the heterogeneity of the disease.

Conclusions. Three-dimensional geometric changes in the mitral leaflets and annulus were clearly demonstrated with novel software that allows anatomical image creation using transthoracic real-time 3D echocardiography in humans. This technique will be helpful in knowing the precise mechanisms of ischemic MR and in making a proper decision for the surgical strategy for each individual in the clinical setting.

**Figure 3.** Three-dimensional (3D) images of mitral annulus and leaflets in ischemic mitral regurgitation. (A) Anatomical 3D image (views from two directions). Mitral annulus flattened with apparent tenting of the mitral leaflets, which were tethered into the left ventricle (LV), showing mountain-shape leaflet bulging. (B) Actual 3D tenting image. Mitral leaflets are apparently tethered and annular height is shorter compared with normal. Mitral annulus is dilated. Black dots indicate coaptation line. (C) Corrected 3D tenting image. Mitral leaflets are tethered almost symmetrically from the level of mitral annulus (left). Maximum tenting length is longer than control (right). Black dots indicate coaptation line. The green mark indicates the maximum tenting site of the leaflet. In this particular patient, the maximum tenting site is located at middle of the anterior leaflet. Abbreviations as in Figure 3.
Figure 4. Mapping of the maximum tenting site in 12 patients with ischemic mitral regurgitation on a schematic leaflet. AL, AC, and AM indicate lateral, central, and medial side of the anterior leaflet; PL, PC, and PM indicate lateral, central, and medial side of the posterior leaflet, respectively. The site of the maximum tenting was located in the region of anterior leaflet in all 12 patients (4 in lateral side, 5 in central side and 3 in medial side).

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REFERENCES


