Interpapillary muscle distance independently affects severity of functional mitral regurgitation in patients with systolic left ventricular dysfunction

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Objectives: Surgical papillary muscle (PM) imbrication has been reported to be effective to relieve leaflet tethering in patients with functional mitral regurgitation (FMR). However, the mechanism that contributes to improvement of FMR by shortening the interpapillary muscle distance (IPMD) has not been well investigated. The purpose of the present study was to investigate whether IPMD can affect MR severity independently of PM tethering distance in patients with left ventricular dysfunction (LVD) using multislice computed tomography.

Methods: We analyzed volumetric multislice computed tomography images of mitral apparatus in 83 patients with LVD (ejection fraction <50%): 37 patients with FMR and 46 patients without FMR. By using the original software, we assessed the 3-dimensional geometry of mitral apparatus including IPMD, tethering distances, and mitral tenting volume at end-systole. The severity of FMR was assessed using vena contracta (VC) width by 2-dimensional echocardiography.

Results: Posterior and anterior tethering distance and IPMD were increased significantly in patients with FMR than in those without FMR. Patients with IPMD in the highest tertile had a significantly higher degrees of MR (mean $\pm$ standard error VC width, 4.5 $\pm$ 0.3 mm) compared with patients in the lowest and the middle tertiles, adjusting for PM tethering distance (mean $\pm$ standard error VC width, 3.0 $\pm$ 0.4 and 2.9 $\pm$ 0.3 mm; $P < .001$, respectively). Multivariate analysis showed that anteroposterior annular diameter and IPMD were the strongest determinants of FMR severity and mitral tenting volume.

Conclusions: IPMD, which affects leaflet tethering independently of PM tethering distance, was the major determinant of mitral tenting volume and FMR severity in patients with LVD. (J Thorac Cardiovasc Surg 2014;148:434-40)

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Functional mitral regurgitation (FMR) is a common complication in patients with ischemic heart disease, which occurs as a consequence of regional or global left ventricular dysfunction (LVD).[1] Although the exact mechanism causing FMR is still elusive, leaflet tethering by the displaced papillary muscles (PMs) has been shown as an essential pathway of FMR.[2,3] Accordingly, the distance between posterior PM tips and anterior annulus has been reported to be a major determinant of FMR severity.[4] On the other hand, previous clinical studies have shown that reducing the distance between anterior and posterior PMs (interpapillary muscle distance [IPMD]) with the PM imbrication technique was effective to relieve leaflet tethering and correct subvalvular geometry.[5-8] However, because this technique inevitably corrects the posterior PM location with shortening of PM tethering distance to a certain extent, it is unclear whether shortening the IPMD has an additive effect on reducing FMR beyond correcting the posterior PM tethering distance.

Mediolateral displacement of anterior and the posterior PMs potentially can lift up the central portion of the anterior and posterior leaflets and increase the tethering of whole leaflets with increasing IPMD (Figure 1, middle panel). In contrast, apical displacement of both PMs without increasing the IPMD does not lift up the central portion of both leaflets and result in less leaflet tethering (Figure 1, right panel). Therefore, we hypothesized that the IPMD may affect leaflet tethering independently of the effect of the increased PM tethering distance.

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Abbreviations and Acronyms

ANCOVA	= analysis of covariance
AP	= anteroposterior
DCM	= dilated cardiomyopathy
FMR	= functional mitral regurgitation
IPMD	= interpapillary muscle distance
LVD	= left ventricular dysfunction
MSCT	= multislice computed tomography
PM	= papillary muscle
SE	= standard error
3D	= 3-dimensional
2D	= 2-dimensional

Recent advances in 3-dimensional (3D) imaging techniques such as echocardiography,[9] magnetic resonance imaging,[10,11] and multislice computed tomography (MSCT)[12] have provided a better understanding of geometric changes in patients with FMR. In these imaging modalities, MSCT has been reported to be valuable in studying precise mitral valvular and left ventricular (LV) geometry, including PM positions.[8,12] We previously developed an anatomic image creation software system for MSCT, which provides 3D visualization of the mitral apparatus including subvalvular geometry.[13] In addition, this system can measure mitral tenting volume, which has been thought to be the strongest determinant of MR severity. Accordingly, the purpose of the present study was to investigate whether IPMD can affect mitral valvular tenting and MR severity independently of PM tethering distance using MSCT in patients with LVD by using of our anatomic image creation software system.

METHODS

Patient Population

We retrospectively analyzed 108 consecutive patients who underwent MSCT coronary angiography with retrospective gating, which allows reconstruction of the data at desired phases of the cardiac cycle and were diagnosed by echocardiography as having regional or global LVD (ejection fraction <50%). The indication for MSCT coronary angiography was suspected or known coronary artery disease in all patients. After we excluded patients with the following: (1) structurally abnormal mitral valve, (2) technically inadequate images to allow analysis of 3D geometry, or (3) atrial fibrillation, 83 patients were subjected to the 3D analysis; 66 patients with old myocardial infarction and 17 patients with nonischemic dilated cardiomyopathy (DCM). Of these, 37 patients (25 old myocardial infarction and 12 DCM patients) had significant (≥moderate) FMR, referred to as FMR(+), and 46 patients (41 old myocardial infarction and 5 DCM patients) did not, referred to as FMR(−). Figure E1 represents patient selection for the study. A total of 6 patients were excluded because images were technically inadequate to allow analysis of 3D geometry.

This study was approved by the Institutional Review Board of Kobe City Medical Center General Hospital.

MSCT Protocol

All of the patients underwent scanning on the 64-slice MSCT scanner (VCT, GE Medical Systems, Wis), which is the same protocol as for standard MSCT coronary angiography. The electrocardiogram was recorded simultaneously to allow retrospective gating and reconstruction of the data at desired phases of the cardiac cycle. To study 3D geometry of the mitral apparatus, the end-systolic data set was reconstructed with a slice thickness of 0.625 mm and a reconstruction interval of 0.35 mm at 30% to 40% of the RR (R wave to R wave) interval. No additional radiation exposure or contrast agent with specific imaging protocol was necessary for mitral valve analysis.

Echocardiography

LV end-diastolic volume, end-systolic volume, and ejection fraction were measured as previously described with 2-dimensional (2D) transthoracic echocardiography.[14] MR severity was assessed semiquantitatively according to the recommendation of the American Society of Echocardiography[15] as none, mild, moderate, or severe. In addition, MR was quantified by the vena contracta width or the narrowest jet origin in a parasternal or apical long-axis view perpendicular to the coaptation line.[16,17]

Mitral Annular Area and Geometry of Mitral Apparatus

All images were analyzed by 2 experienced readers (K.K. and S.K.). We analyzed the end-systolic data set. A 3D reconstruction was performed using a commercially available Digital Imaging and Communications in Medicine (DICOM) viewer and the image analysis was performed with our 3D computer software, which is based on MATLAB (The MathWorks, Inc, Natick, Mass). Details of the technique recently were reported.[13] We created anatomic 3D images of the mitral annulus, leaflets, and PMs to measure annular geometry, leaflet tethering, tenting height, and tenting volume. Anteroposterior (AP) annular diameter, commissure–commissure annular diameter, and mitral annular area were evaluated as previously reported.[10,13] The maximum tenting height was defined as a distance from the level of the annular plane to the most tethered leaflet site. The tenting volume was calculated as a volume enclosed between the annulus and mitral leaflets. The leaflet tethering distances were measured as the distances between both the PM tips and the saddle horn and the IPMD was measured as the distance between the tips of the PMs. If PM heads were equally separated, each PM head was assessed separately and the mean position was used for the analysis. In addition, 3D coordinates of these points were determined on these images using a reference system with the origin of the centroid of the annular markers, the positive anterior axis in the annular plane passing from the middle of the posterior annulus to the midanterior annulus marker, and the positive apical axis perpendicular to the annular plane. The annular plane was determined as the least-squares fitting plane to the annulus. With this 3D coordinate system, positions of PM tips were resolved into their apical and nonapical (posteromedial or posterolateral) components (Figure E2).

Statistical Analysis

Continuous variables are described as means ± standard deviations. Categoric variables were compared with the chi-square test or the Fisher exact test as appropriate. Group comparison of continuous variables was performed by one-way analysis of variance with the Tukey post hoc test.

We assessed univariate regression analysis with tenting volume and MR severity as dependent variables, and we assessed mitral geometric measurements as independent variables. Then, multivariate analysis based on stepwise multiple linear regression was performed among variables with significant univariate correlations ($P < .05$). Because an association was present between the IPMD and posterior PM tethering distance, a multiple regression analysis was used to adjust for posterior PM tethering distance. To assess whether a threshold was present, multivariate models using analysis of covariance (ANCOVA) were used to estimate the mean (standard error [SE]) VC width and tenting volume across tertiles of IPMD.

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