Mechanism of Asymmetric Leaflet Tethering in Ischemic Mitral Regurgitation

3D Analysis With Multislice CT

It has been reported that patients with ischemic mitral regurgitation (IMR) caused by inferoposterior myocardial infarction have asymmetric leaflet tethering associated with regional and inferior left ventricular (LV) remodeling (1). This report suggests that asymmetric medial papillary muscle (PM) displacement with inferior myocardial infarction causes asymmetric leaflet tethering in the medial side of the whole leaflets. However, asymmetric leaflet tethering accompanied by regional LV dilation in patients with functional mitral regurgitation (FMR) has not been well investigated.

Medial displacement of posterior PM can potentially shift whole leaflets medially and result in approximately equal tethering mediolaterally (Fig. 1A, middle panel). In contrast, apical displacement of posterior PM may predominantly tether medial side of leaflets and result in asymmetrically predominant tethering in this side (Fig. 1A, right panel). Therefore, we hypothesized that asymmetric apical displacement of PMs leads to asymmetric leaflet tethering.

Conversely, recent advances in 3-dimensional (3D) imaging techniques such as echocardiography (2), multislice computed tomography (MSCT) (3), and magnetic resonance imaging (4) have allowed a better understanding of geometric changes in patients with FMR. Therefore, the purpose of the present study was to: 1) compare the geometry of the mitral apparatus including the symmetry of mitral leaflet tethering; and 2) investigate the mechanism of asymmetric leaflet tethering in patients with significant FMR caused by ischemic cardiomyopathy (ICM [regional LV remodeling]) and dilated cardiomyopathy (DCM [global LV remodeling]), with use of our anatomical image creation software system and MSCT.

Of patients undergoing 64-slice MSCT coronary angiography from 2006 to 2009, we retrospectively analyzed 74 consecutive patients who were diagnosed by echocardiography as having significant FMR (moderate or greater) caused by regional or global LV dysfunction (ejection fraction <45%). After excluding the patients with: 1) structurally abnormal mitral valve; 2) technically inadequate images to allow analysis of 3D geometry; and 3) atrial fibrillation, 41 patients underwent analysis: 28 old inferoposterior myocardial infarction patients with regional LV dysfunction (ICM-MR) and coronary artery disease (CAD), confirmed by coronary angiography in all patients; and 13 DCM patients with global LV dysfunction and without coronary artery disease, confirmed by coronary angiography (n = 6) and MSCT (n = 13). Patients with global LV dysfunction due to left anterior descending or multivessel CAD were excluded from the study. Supplementary Figure 1 represents patient selection of the study. In addition, 20 patients with normal mitral valve and normal LV function, and without significant MR were included as control subjects. All patients were examined by MSCT for suspected coronary artery disease.

A conventional echocardiographic study was obtained, and MR was quantified by the vena contracta width or the narrowest jet origin in a parasternal or apical long-axis view. We chose the end-systolic phase for MSCT data analysis rather than mid-systolic phase, as it is better for minimizing cardiac motion. The 3D reconstruction was performed using a commercially available DICOM viewer, and the image analysis was performed with our 3D computer software, which is based on MATLAB (The MathWorks Inc., Natick, Massachusetts). Details of the 3D measurements are summarized in the Online Appendix and Supplementary Figure 2.

We determined the threshold of difference between medial and lateral tenting volume as 20% of the mean regional tenting volume in FMR patients (DCM-MR and ICM-MR), which is equal to 0.3 ml. Accordingly, FMR patients were classified as medial-dominant (medial-lateral ≥0.3 ml), lateral-dominant (lateral-medial ≥0.3 ml), and balanced tenting patterns. Supplementary Table 1 summarizes patient characteristics and geometry of mitral apparatus. Total tenting volume and medial and lateral tenting volume were significantly larger both in DCM-MR and in ICM-MR compared with controls. Example images of mitral apparatus in patients with asymmetric and symmetric leaflet tethering are shown in Figure 1B through 1G. Among ICM-MR patients, there were 9 with medial-dominant, 19 with balanced, and none with lateral-dominant tenting pattern; among DCM-MR patients, there were no patients with medial-dominant, 12 with balanced, and 1 with lateral-dominant tenting pattern (p = 0.03).

In FMR patients, the difference between medial and lateral tenting volume (medial-lateral tenting volume) was well correlated with differences of apical displacement between both medial and lateral PM tips (r = 0.67, p < 0.001), whereas differences of medial-lateral or posterior displacement did not show significant correlations.

Previous study has demonstrated that the pattern of mitral leaflet deformation was asymmetric in ICM-MR patients using 3D echocardiography (1). Delgado et al. (3) also demonstrated a more pronounced leaflet tethering at the central and medial site in FMR patients with heart failure. However, the relationship between leaflet deformation and displacement of PMs due to LV remodeling remains uninvestigated. In the present study, asymmetric leaflet tethering was strongly associated with asymmetric apical displacement of PMs rather than medial-lateral displacement. In addition, almost two-thirds of ICM patients with FMR had symmetric leaflet tethering. That is consistent with previous reports.
showing asymmetric and/or symmetric mitral leaflet tethering of FMR in ICM patients (1). The present study further demonstrated partial mechanism of asymmetric medial tethering in relation to apical displacement of medial PM. These symmetric or asymmetric leaflet tethering may have a different impacts on MR severity.

Several surgical techniques including chordal cutting and PM relocation have been introduced to reduce FMR. Because these reconstructive techniques aim at reducing leaflet tethering due to PM displacement, it seems to be important to know the precise leaflet deformation, especially whether leaflet tethering and PM positions are symmetric or asymmetric. Our system could provide detailed mitral geometry including annular dilation, leaflet deformation, and PM displacement, which could clearly demonstrate symmetry of leaflet tethering in relation to PM positions.

In conclusion, symmetric leaflet tethering is predominant in DCM-MR, and even in patients with ICM-MR, and asymmetric apical displacement of PM tips leads to asymmetric leaflet tethering in patients with IMR. These anatomic variations can potentially guide therapies aimed at reducing FMR by PM repositioning.

Kitae Kim, MD, Shuichiro Kaji, MD,* Yoshimori An, MD, Hidetoshi Yoshitani, MD, Masaaki Takeuchi, MD, Robert A. Levine, MD, Yutaka Otsuji, MD, Yutaka Furukawa, MD

*Department of Cardiovascular Medicine, Kobe City Medical Center General Hospital, 2-1-1 Minatojima-minamimachi, Chuo-ku, Kobe 650-0047, Japan. E-mail: skaji@theia.ocn.ne.jp
doi:10.1016/j.jcmg.2011.08.023

REFERENCES


► APPENDIX
For MSCT protocols and 3D measurements, supplementary figures 1 and 2, and a supplementary table, please see the online version of this article.

OCT-Verified Neointimal Hyperplasia Is Increased at Fracture Site in Drug-Eluting Stents

Although drug-eluting stents dramatically reduce stent restenosis, in-stent restenosis still occurs in approximately 10% of sirolimus-eluting stent (SES) implantation cases. Optical coherence tomography (OCT) has the potential to assess neointima hyperplasia precisely in vivo (1). However, the morphological features of stent fracture in OCT imaging have not yet been reported, and there is no OCT study that clarifies the relationship between stent fracture and neointimal hyperplasia in SES. We investigated the morphological features of stent fracture in OCT to clarify the relationship between stent fracture and neointimal hyperplasia in SES.

We enrolled 110 adequately expanded SES (BxVelocity platform) stents from 70 patients. For overlapped stents (n = 41), we confirmed complete overlapping in the post-procedural angiography. The scheduled coronary angiography and OCT imaging were performed at 11 ± 6 months after SES implantation. According to the presence of stent fracture in breath-hold fluoroscopy, stents were divided into a fractured stent group and a nonfractured stent group. Binary restenosis was defined as a >50% stenosis by the CMS-QCA system (CMS-MEDIS, Medical Imaging Systems, Leiden, the Netherlands). An OCT 0.016-inch catheter (ImageWire, LightLab Imaging, Westford, Massachusetts) was used, and all OCT image acquisitions were performed with the continuous-flushing method (2). To coregister OCT images and coronary angiograms on an individual stent basis, we used the distance from each stent edge, the tip of guiding catheter, and anatomical landmarks. Stent area, lumen area, and neointima area were measured according to a previous report (3). In case stent struts cannot be recognized, substitute stent area, which was an average stent area of both broken edges of the fractured stent, was applied (Fig. 1). Neointimal area was assessed in multiple slices, incrementally spaced by 1 mm from fracture site to distal and proximal sites. To assess the distribution pattern of neointima within the stent, neointimal hyperplasia was repartitioned along the stent length into 18 segments.

Stent fracture was observed in 14 (12.7%) of 110 stents. The fractured stent group showed higher binary in-stent restenosis (29% vs. 6%, p = 0.02) and percent diameter stenosis (44.8 ±