Journal of the American College of Cardiology
© 2005 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 46, No. 1, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.03.049

Papillary Muscle Dysfunction Attenuates Ischemic Mitral Regurgitation in Patients With Localized Basal Inferior Left Ventricular Remodeling

Insights From Tissue Doppler Strain Imaging

Takeshi Uemura, MD,* Yutaka Otsuji, MD, FACC,* Kenichi Nakashiki, MD,* Shiro Yoshifuku, MD,* Yuko Maki, MD,* Bo Yu, MD,* Naoko Mizukami, MD,* Eiji Kuwahara, MD,* Shuichi Hamasaki, MD,* Sadatoshi Biro, MD,* Akira Kisanuki, MD,* Shinichi Minagoe, MD,* Robert A. Levine, MD, FACC,† Chuwa Tei, MD, FACC*

Kagoshima, Japan; and Boston, Massachusetts

OBJECTIVES The purpose of this research was to test whether papillary muscle (PM) dysfunction attenuates ischemic mitral regurgitation (MR) in patients with left ventricular (LV) remodeling of a similar location and extent.

BACKGROUND Papillary muscle dysfunction could attenuate tethering and MR because of PM elongation. However, variability in the associated LV remodeling, which exaggerates tethering, can influence the relationship between PM dysfunction and MR.

METHODS In 40 patients with a previous inferior myocardial infarction but without other lesions, the LV volume, sphericity, PM tethering distance, PM longitudinal systolic strain, and MR fraction were quantified by echocardiography. The patients were divided into two groups: group 1 with significant basal inferoposterior LV bulging but without advanced LV bulging involving other territories, therefore with a similar location and extent of LV remodeling, and group 2 without significant LV bulging.

RESULTS The medial PM tethering distance was significantly correlated with the %MR fraction (r^2 = 0.64, $p < 0.01$), and multiple regression analysis identified an increase in the tethering distance as the only independent determinant of the MR fraction in all subjects and also in group 1. The PM longitudinal systolic strain had no significant relationships with MR fraction in all subjects with variable degrees of LV remodeling, but it had a significant inverse correlation with the MR fraction (r^2 = 0.33, $p < 0.01$) in group 1 with LV remodeling of a similar location and extent, indicating that PM dysfunction is associated with less MR.

CONCLUSIONS Papillary muscle dysfunction, reducing its longitudinal contraction to induce leaflet tethering, attenuates ischemic MR in patients with basal inferior LV remodeling. (J Am Coll Cardiol 2005;46:113–9) © 2005 by the American College of Cardiology Foundation

Ischemic mitral regurgitation (MR) is a common complication in patients with ischemic heart disease, and adversely affects their prognosis (1–3). Papillary muscle (PM) contractile dysfunction has previously been considered the main cause of ischemic MR with leaflet prolapse (4,5). However, isolated PM dysfunction failed to cause ischemic MR in animal models (6–9). In addition, mitral leaflet prolapse, which can be caused by PM dysfunction (4,5), is rare in patients with ischemic MR (10–12). Therefore, the relationship between PM dysfunction and ischemic MR has not been established.

Recent studies have demonstrated that the main cause of ischemic MR is augmented leaflet tethering by outward displacement of the PM due to left ventricular (LV) remodeling (Fig. 1, middle panel) (13–21). From the standpoint of leaflet tethering, remodeling of the adjacent LV wall to the PM in patients with ischemic heart disease can augment this tethering and MR (Fig.1, middle panel). However, in the presence of adjacent LV wall remodeling, PM dysfunction per se, with less systolic shortening in its long-axis direction, can potentially attenuate leaflet tethering and ischemic MR (Fig. 1, right panel). Therefore, ischemic MR basically relates to PM tethering, and PM dysfunction may not have a consistent relationship with MR in patients with variable degrees of adjacent LV wall remodeling. However, in selected patients with a similar degree of adjacent LV wall remodeling, PM dysfunction can potentially attenuate tethering and MR. Therefore, we hypothesized that ischemic MR basically relates to PM tethering but that PM dysfunction does not have a consistent relationship with the severity of MR in patients with variable degrees of LV remodeling. However, PM dysfunction may attenuate MR in patients with LV remodeling of a similar location and extent. The purpose of this study was to investigate the relationship between PM tethering, PM function, and ischemic MR in patients with prior inferior myocardial infarction (MI).

From the *First Department of Internal Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan; and †Massachusetts General Hospital, Boston, Massachusetts. Dr. Otsuji was supported by a Grant-in-Aid for Scientific Research 1559076 from Japan Society for the Promoting of Science, Tokyo, Japan.

Manuscript received July 30, 2004; revised manuscript received February 3, 2005, accepted March 15, 2005.

Abbreviations and Acronyms

EDV = end-diastolic volume
EF = ejection fraction
LV = left ventricle/ventricular
MAA = mitral annular area
MI = myocardial infarction
MR = mitral regurgitation
PM = papillary muscle
2D = two-dimensional

METHODS

Study patients. The study included 40 consecutive patients with prior inferior MI who were referred for echocardiographic examination between October 2003 and January 2004. The inclusion criteria were the presence of prior inferior MI diagnosed on the basis of a history of acute MI more than one month previously, serum creatine kinase activities more than twice the upper normal value, and segmental LV wall motion abnormalities in the inferior wall. The exclusion criteria were recent MI (<1 month), multiple MIs, MR caused by intrinsic mitral valvular lesions (including rheumatic changes, infective vegetations, and chordal or PM rupture), and other cardiac diseases, such as congenital defects, cardiomyopathy, aortic valve or pericardial diseases. This study was performed with the patients' written informed consent.

Echocardiography. Standard two-dimensional (2D) and Doppler echocardiography with tissue Doppler strain imaging was performed using a 3- to 4.5-MHz transducer (Vivid 7, GE Medical Systems, Milwaukee, Wisconsin). Recordings of the apical four- and two-chamber views were done with special attention paid to visualize the PM; LV end-diastolic and end-systolic cavity areas were traced in those views, and the LV end-diastolic volume (EDV) and ejection fractions (EF) were calculated by the method of discs. The LV shape, or sphericity, was assessed using the LV short-to-long axis dimension ratio in the mid-systolic apical two-chamber view (Fig. 2) (22), and the mid-systolic mitral annular area (MAA) was obtained by determining the annular dimensions in the apical four- and two-chamber views based on assuming an elliptical geometry (MAA = $d_1 \times d_2 \times \pi/4$) (23). The leaflet-tethering distance between the PM tip and the contralateral anterior mitral annulus was also measured in the apical four- and two-chamber views in mid-systole (Fig. 2, ℓ_1 and ℓ_2) (24). The mitral filling volume was measured by Doppler echocardiography as the product of the diastolic MAA and the time-velocity-integral of the mitral filling flow at the annular level, and the aortic ejection stroke volume was measured as the product of the aortic annular area and the time-velocity-integral of the ejection flow. The MR volume was then calculated as the difference between the mitral filling volume and the aortic ejection volume, and the MR fraction was obtained as the MR volume divided by the mitral filling volume (25,26).

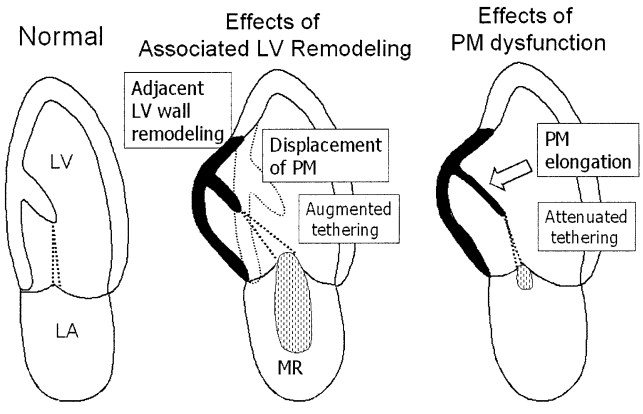

Figure 1. Expected potential and opposing effects of papillary muscle (PM) dysfunction resulting in exaggeration or attenuation of leaflet tethering and mitral regurgitation (MR). **(Middle panel)** Remodeling of the adjacent left ventricular (LV) wall, which accompanies PM dysfunction, causes outward displacement of the PM and thereby induces augmented leaflet tethering with MR. **(Right panel)** In the presence of adjacent LV wall remodeling, PM dysfunction per se results in systolic PM elongation or less shortening, which thus attenuates tethering and MR. LA = left atrium.

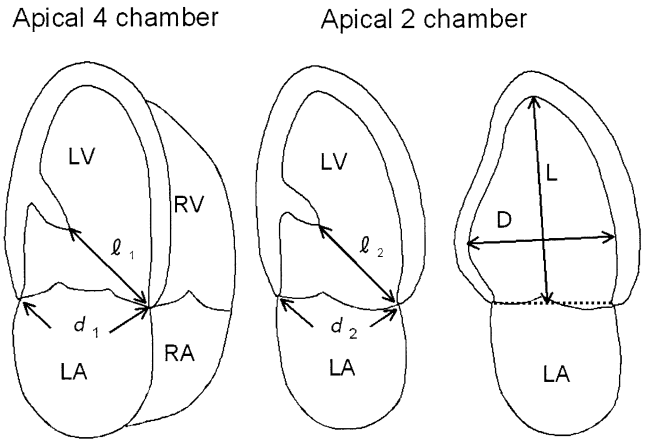

Figure 2. Quantitative measurements of the geometry of the left ventricle (LV) and mitral valve complex using two-dimensional echocardiography. D = short-axis dimension; d = mitral annular dimension; LA = left atrium; RA = right atrium; RV = right ventricle; L = long-axis dimension; ℓ_1 = lateral papillary muscle (PM) tethering distance; ℓ_2 = medial PM tethering distance.

Evaluation of PM function by 2D and Doppler echocardiography with tissue strain imaging. Papillary muscle systolic contraction generates tension in the chordae to maintain the systolic leaflet position or to prevent leaflet prolapse while the wall between the PM and mitral annulus contracts. Therefore, PM dysfunction was defined as PM contractile dysfunction in this study. Because PM contraction is spatially and temporally heterogeneous (27), PM dysfunction was further defined as peak systolic PM shortening in its long-axis direction or peak systolic PM thickening in its short-axis direction. Two methods were used to evaluate PM function. The end-diastolic and end-systolic medial or lateral PM width at its mid-portion was measured in the apical two- and four-chamber views to obtain systolic PM thickening by 2D echocardiography. Tissue Doppler imaging data was also recorded in these views to evaluate the medial and lateral PM longitudinal systolic strain (28).