# Differences in Characteristics, Left Atrial Reverse Remodeling, and Functional Outcomes after Mitral Valve Replacement in Patients with Low-Gradient Very Severe Mitral Stenosis

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*Background:* The discrepancy between planimetered mitral valve area (MVA) and mean diastolic pressure gradient (MDPG) has not been studied extensively in patients with mitral stenosis. The purpose of the present study was to investigate differences in characteristics and outcomes after mitral valve replacement (MVR) between low- and high-MDPG groups in patients with very severe mitral stenosis (VSMS). The hypothesis was that the low-MDPG group would have different characteristics and would be associated with poor clinical outcomes after MVR.

*Methods:* In total, 140 patients who underwent isolated MVR because of pure VSMS (planimetered MVA $\leq$ 1.0 cm$^2$) were retrospectively reviewed, and follow-up echocardiography was performed for $\geq$12 months after MVR. Patients were divided into two groups according to preoperative MDPG (low gradient [LG], <10 mm Hg; high gradient [HG], $\geq$10 mm Hg). Strain and strain rate analysis was performed using speckle-tracking echocardiography of the left ventricle before MVR in a subgroup of 56 patients.

*Results:* There were 82 patients (59%) in the LG group and 58 patients (41%) in the HG group. The LG group was older and demonstrated a higher prevalence of female gender, diabetes mellitus, and atrial fibrillation ($P$ < .05 for all). When comparing the LG and HG groups, the left atrial volume index was larger (105.1 $\pm$ 51.9 vs 87.8 $\pm$ 42.9 mL/m$^2$, $P$ < .001), and strain rate during isovolumic relaxation of the left ventricle was lower (0.17 $\pm$ 0.08 vs 0.29 $\pm$ 0.09 sec$^{-1}$, $P$ < .001) in the LG group. After MVR, the percentage left atrial volume index reduction after MVR was significantly smaller in the LG group ($-$29.9 $\pm$ 15.1% vs $-$43.5 $\pm$ 16.4%, $P$ < .001). Persistent symptoms after MVR were more common in the LG group compared with the HG group ($P$ = .004), even though preoperative functional class was similar between the groups.

*Conclusions:* Compared with those with HG VSMS, patients with LG VSMS were older, more often female, and more frequently had diabetes mellitus and atrial fibrillation. They also had greater impairment of isovolumic relaxation, less favorable left atrial reverse remodeling, and a greater risk for persistent symptoms after MVR. These data might suggest other concurrent mechanisms for left atrial enlargement and symptom development in LG VSMS, such as atrial fibrillation and diastolic dysfunction, as well as valvular stenosis. (J Am Soc Echocardiogr 2016;■:■-■.)

*Keywords:* Mitral stenosis, Mitral valve replacement, Left atrium

Mitral stenosis (MS) is the narrowing of the mitral valve orifice, and very severe MS (VSMS) is defined as mitral valve area (MVA) $\leq$ 1.0 cm$^2$. Hemodynamic severity is usually characterized by two-dimensional (2D) planimetry and calculated from diastolic pressure half-time. However, diastolic pressure half-time overestimates MVA in patients with impaired left ventricular (LV) compliance, because it is dependent on the degree of mitral obstruction as well as the compliance of the left ventricle.[1,2] Mean diastolic pressure gradient (MDPG) is reliably assessed by Doppler echocardiography, but this is not considered the best marker of MS severity, because it is dependent on MVA along with other factors that influence transmitral flow rate, heart rate, cardiac output, and associated mitral regurgitation.[3] Therefore, the severity of MS is determined by integrating all parameters, such as MVA, MDPG, and pulmonary artery (PA) systolic pressure.

MVA $\leq$ 1.0 cm$^2$ usually corresponds to an MDPG of >10 mm Hg at a normal heart rate in patients with MS.[4] In clinical practice, discrepancy between planimetered MVA and MDPG is not uncommon in patients with VSMS, suggesting the presence of low-gradient (LG) VSMS.

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**Abbreviations**

**2D** = Two-dimensional

**AF** = Atrial fibrillation

**BSA** = Body surface area

**Cn** = Net atrioventricular compliance

**FC** = Functional class

**HG** = High-gradient

**IVC** = Inferior vena cava

**LA** = Left atrial

**LAVI** = Left atrial volume index

**LG** = Low-gradient

**LV** = Left ventricular

**MDPG** = Mean diastolic pressure gradient

**MS** = Mitral stenosis

**MVA** = Mitral valve area

**MVR** = Mitral valve replacement

**OMV** = Open mitral valvotomy

**PA** = Pulmonary artery

**PHT** = Pulmonary hypertension

**PMV** = Percutaneous mitral valvotomy

**RA** = Right atrial

**$SR_{IVR}$** = Strain rate during isovolumic relaxation

**TR** = Tricuspid regurgitation

**VSMS** = Very severe mitral stenosis

However, few studies have evaluated the clinical implication of this discrepancy in patients with VSMS. Therefore, we investigated the differences in characteristics and outcomes after mitral valve replacement (MVR) between low- and high-MDPG groups of patients with VSMS. The main objectives of the study were to assess the mechanism of LG VSMS and to evaluate its influence on the outcome of LG VSMS.

## METHODS

### Study Population

We retrospectively reviewed 259 patients who underwent isolated MVR because of rheumatic MS at Severance Cardiovascular Hospital from January 2004 to December 2013. Among them, patients who did not undergo follow-up echocardiography <12 months after MVR, patients with >1+ mitral valve regurgitation, >1+ aortic valve regurgitation, and/or more than mild aortic stenosis on preoperative or follow-up echocardiography, patients with MVA > 1.0 $cm^2$, patients with cardiomyopathy or coronary artery disease requiring concurrent bypass surgery, patients with other combined congenital heart disease requiring concurrent surgical correction, and patients with atrial fibrillation (AF) with rapid ventricular rate (heart rate ≥ 100 beats/min) were excluded. MVA results were first screened using clinical reports, and all images were reviewed by two experienced echocardiographers, who were unaware of patients' clinical data, to confirm the inclusion criteria. As a result, 140 patients who underwent isolated MVR because of VSMS (MVA ≤ 1.0 $cm^2$ by 2D planimetry)[5] constituted the study population. During the recruitment period, 52 patients with VSMS were sent for percutaneous mitral valvotomy (PMV). The choice of surgery or PMV was determined by physicians. In general, PMV was performed in patients with favorable morphology for the procedure and Wilkins scores ≤ 8.[6]

Twenty-eight patients (20%) and seven patients (5%) had histories of PMV and surgical open mitral valvotomy (OMV), respectively. The median interval between MVR and PMV or OMV was 15 years (interquartile range, 11–18 years), and all these patients underwent the procedure >1 year before the echocardiographic examination. MVR was considered in 139 patients who were not candidates for PMV because of unfavorable valve morphology for PMV or left atrial (LA) clot and in one patient because of failure of PMV. Concurrent tricuspid annuloplasty was performed in patients with more than mild TR (tricuspid regurgitation) and tricuspid annular dilation according to the American College of Cardiology and American Heart Association guideline. Tricuspid annular dilation is defined as >40 mm on transthoracic echocardiography or >70 mm measured by the distance between the anteroseptal and anteroposterior commissures on direct intraoperative measurement. Patients were divided into two groups according to preoperative MDPG (LG, <10 mm Hg; high gradient [HG], ≥10 mm Hg). New York Heart Association functional class (FC) was assessed before surgery and at follow-up. Echocardiographic image acquisition for speckle-tracking analysis was performed in subgroup of 56 consecutive patients who fulfilled the enrollment criteria from March 2010 to December 2013. This study was approved by the institutional review board of Yonsei University, Severance Hospital (Seoul, Korea).

### Echocardiographic Measurement

Clinical and echocardiographic assessments were performed before MVR and 12 months after MVR. The echocardiographic images of the included patients were reanalyzed by two experienced echocardiographers who were blinded to patients' histories. LV internal diameter, septal thickness, and LV posterior wall thickness were measured at end-diastole from the parasternal short-axis view. LV mass was calculated using the formula recommended by the American Society of Echocardiography,[7] and LV mass was indexed to body surface area (BSA). LA volume was calculated from the parasternal long-axis view and apical four-chamber view using the prolate ellipse method[8] and indexed to BSA. The percentage LA volume index (LAVI) change between preoperative period and follow-up was calculated. MVA was assessed using 2D planimetry.

The MDPG was measured from a continuous-wave Doppler signal across the mitral valve by tracing its envelope. The severity of TR was assessed using color flow imaging and regurgitant jet area.[9] The calculated systolic PA pressure was defined as 4 × (maximum velocity of TR jet)$^2$ + right atrial (RA) pressure. RA pressure was estimated by measuring the inferior vena cava (IVC) diameter and its response to inspiration. IVC diameter ≤ 2.1 cm that collapses by >50% with inspiration suggests a normal RA pressure of 3 mm Hg, whereas IVC diameter > 2.1 cm that collapses by <50% with inspiration suggests a high RA pressure of 15 mm Hg. When IVC diameter and collapse did not fit this paradigm, a value of 8 mm Hg was used.[10]

Stroke volume was calculated using the Doppler method with LV outflow tract diameter and velocity-time integral and indexed to BSA. Cardiac output was calculated as the product of stroke volume and heart rate. Cardiac index was defined as cardiac output divided by BSA. Mitral valve effective orifice area was determined using the stroke volume measured in the LV outflow tract divided by the velocity-time integral of the mitral valve transprosthetic velocity during diastole and divided by BSA. Because patients with more than mild mitral and aortic regurgitation were excluded, mean diastolic flow rate was defined as the ratio of LV stroke volume to diastolic filling time. Net atrioventricular compliance (Cn) was determined as follows: Cn (mL/mm Hg) = 1,270 × (planimetric MVA/E-wave downslope).[11] Systolic mitral annular (Sm) and early diastolic mitral annular (Em) velocities were assessed using pulsed-wave Doppler tissue imaging of the septal mitral annulus from the apical four-chamber view. Pulmonary hypertension (PHT) was defined as a systolic PA pressure ≥ 35 mm Hg on echocardiography. Patients were stratified