



LETTER TO THE EDITOR

Natural History of Mitral Stenosis in Patients With Mitral Annular Calcification

Mitral annular calcification (MAC) is an increasingly recognized cause of mitral stenosis (MS) (1). This study investigated the natural history of MS in patients with various degrees of MAC.

Patients with MAC of any severity were identified by searching Cleveland Clinic's echocardiography database for patients admitted between January 1996 and October 2013. Patients were included if they had MAC at their index study and had undergone ≥ 2 studies in the period of ≥ 2 years. Patients with prior mitral valve (MV) surgery, rheumatic heart disease, or other identifiable mitral disease were excluded. Mean and peak MV gradients, estimated right ventricular systolic pressure (RVSP), left atrium (LA) diameter measured by M-mode, and mitral valve area (MVA) determined by pressure half time were evaluated to determine the progression of MS. MAC was graded as mild if less than one-third of the circumference of the annulus; moderate if less than two-thirds; or severe if greater than two-thirds and/or was invading the adjacent myocardium. Patients with severe MAC at any point were allocated to the severe MAC group and the remaining patients to the nonsevere MAC group.

Continuous variables are reported as mean \pm SD or median \pm interquartile range (IQR). MS progression was assessed by applying a linear mixed effects model with unstructured covariance for random effects. All analyses were conducted using Stata version 14 software (StataCorp, College Station, Texas).

The study identified a total of 2,927 patients (index age: 71.2 ± 10.7 years of age; 49% females), and a total of 18,429 echocardiograms were analyzed. A total of 871 patients (29.7%) had severe MAC, and 2,056 patients (70.3%) had nonsevere MAC. Median follow-up time was 4.5 years (IQR: 2.9 to 7.2 years). Median number of echocardiograms per patient was 4 (IQR: 3 to 7 echocardiograms). Baseline mean and peak MV gradients were 4.54 ± 1.3 mm Hg and 11.1 ± 3.5 mm Hg, respectively. Mean MVA was 3.2 ± 0.6 cm², and mean LA size was 4.5 ± 0.5 cm. Overall mean gradient progression was 0.04 ± 0.0097 mm Hg/year ($p < 0.001$), with a higher progression observed in patients with severe MAC than in those with nonsevere MAC (0.112 ± 0.012 mm Hg vs.

0.008 ± 0.011 mm Hg, respectively; $p < 0.001$). Similar findings were observed for peak gradient (with a progression of 0.23 ± 0.025 mm Hg/year; severe vs. nonsevere MAC: 0.37 ± 0.030 mm Hg vs. 0.184 ± 0.029 mm Hg, respectively; $p < 0.001$), LA size (progression of 0.030 ± 0.002 cm/year; severe vs. nonsevere MAC 0.040 ± 0.003 vs. 0.029 ± 0.002 cm/year, respectively; $p = 0.002$); MVA (progression of 0.01 ± 0.006 cm²/year; severe vs. nonsevere MAC: 0.010 ± 0.007 cm² vs. 0.033 ± 0.007 cm², respectively; $p \leq 0.001$); and RVSP (progression of 0.75 ± 0.03 mm Hg/year; severe vs. nonsevere MAC 1.050 ± 0.045 mm Hg vs. 0.68 ± 0.039 mm Hg, respectively; $p < 0.001$) (Figure 1). In 2,013 patients with available aortic gradients, severe aortic stenosis (mean gradient: ≥ 40 mm Hg) was observed more often in patients with severe MAC than in those with nonsevere MAC (32.5% vs. 20.6%, respectively; $p < 0.001$).

A total of 142 patients (16.3%) developed severe MS and underwent surgical MV replacement. The baseline mean MV gradient was 6.6 ± 2.9 mm Hg in this subgroup. Their annual rate of progression was 0.51 ± 0.023 mm Hg/year, and the mean MV gradient at the time of surgery was 13.76 ± 4.15 mm Hg.

Although the overall progression of MS in patients with MAC was slow, severe MAC was associated with faster MS progression. The rate of mean gradient progression for patients with severe MAC was 0.112 mm Hg/year, still less than the rate of 0.19 mm Hg/year (2) seen in rheumatic MS in the modern era. Patients who underwent MV replacement appeared to have even faster rates of MS progression. The pressure half time method was unreliable for analyzing MVA in patients with severe MAC, likely due to reduced LV compliance (3-5), which is often seen in patients with severe MAC.

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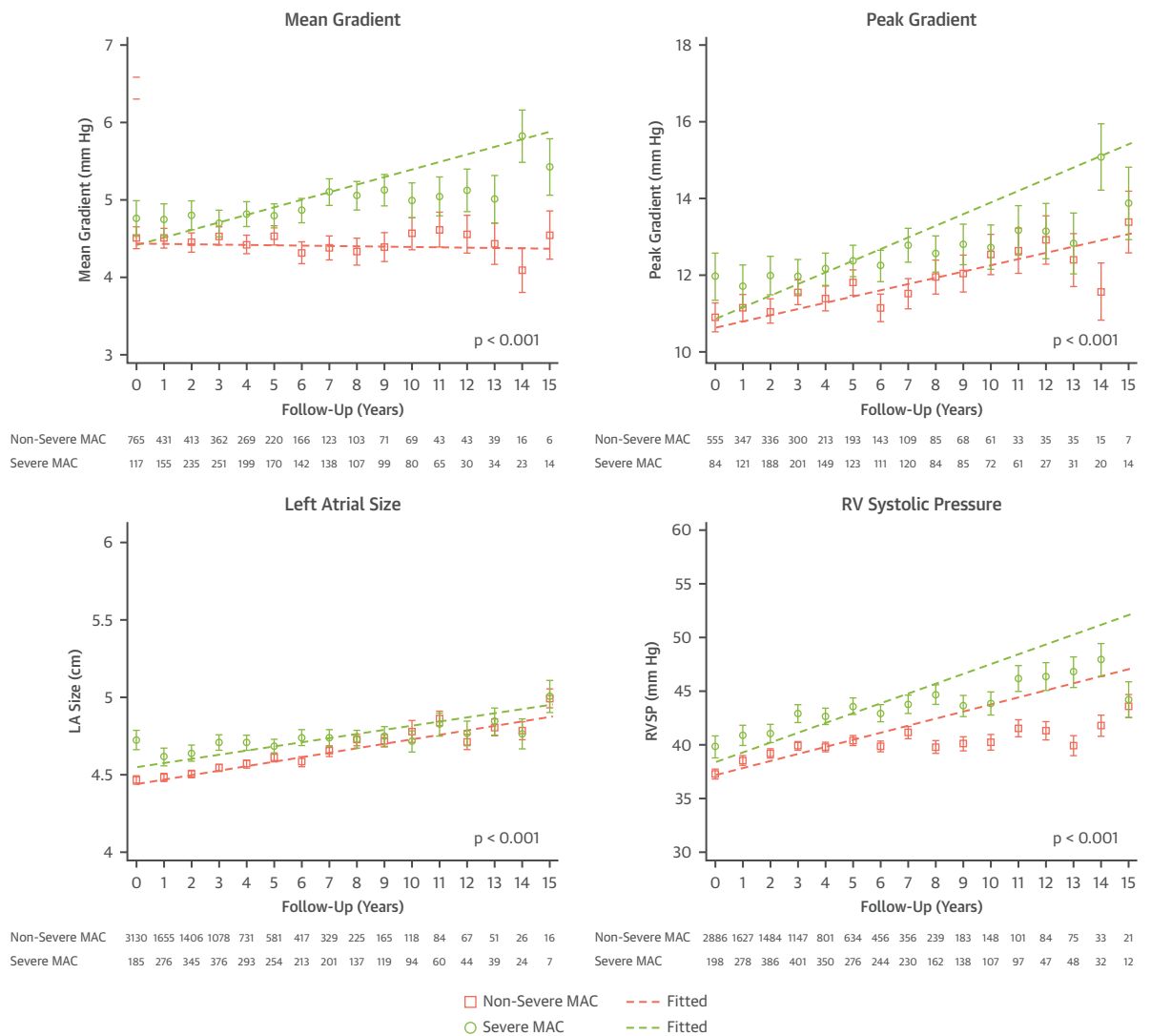
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FIGURE 1 MS Progression Rates With MAC

Annual progression rates of mean and peak MV gradients, LA size, and RVSP demonstrate faster progression in the group with severe MAC than in the nonsevere MAC group (p values reflect the differences in slopes). LA = left atrium; MAC = mitral annular calcification; MV = mitral valve; RV = right ventricle; RVSP = right ventricular systolic pressure.

Please note: Dr. Thomas is a consultant for GE Healthcare, Abbott, Edwards Life Science, and Bay Labs. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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