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**Title:** Insights into the mechanisms of left ventricular dysfunction through assessment of diastolic flow in patients with mitral stenosis using 3D echocardiography

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**Background & Aims:** The reduction of flow across the mitral valve characterizes the pathophysiology of mitral stenosis, which can subsequently impair left ventricular (LV) performance. Three-dimensional echocardiography provides the advantage of accurate left ventricular volume calculation, which reduces variability compared to two-dimensional imaging. By calculating the ratio of volume variation during diastole to the time interval, it becomes possible to estimate average diastolic flow. Our study aims to test the hypothesis that reduced average diastolic flow in patients with severe mitral stenosis contributes to LV impairment of contractility.

**Methods:** We conducted an analysis of left ventricular volume-time curves in two groups: group 1 consisted of 16 patients with mitral stenosis who underwent percutaneous mitral valvuloplasty, while group 2 comprised 15 healthy individuals with normal transthoracic echocardiography. Patients with atrial fibrillation were excluded from the study. A single experienced examiner conducted the three-dimensional echocardiographic study using commercially available machines (EPIQ7, Philips). Offline analysis using QLAB software, version 13, was performed to generate left ventricular volume curves (Figure 1). The software provided measurements of end-diastolic volume, end-systolic volume, stroke volume, diastolic volume variation, and diastolic time. A Student's t-test was employed to compare normally distributed variables between the groups, while the Mann-Whitney U test was used for non-normally distributed variables. Statistical significance was determined at  $p < 0.05$ .

**Results:** The age of patients with mitral stenosis was  $46 \pm 11$  years, and the majority of them (85%) were female. In comparison, the control group had an average age of  $41 \pm 12$  years, with 47% being female. The patients with mitral stenosis (group 1) exhibited a significantly lower left ventricular end-diastolic volume compared to the control group ( $64.3 \pm 13.6$  ml vs.  $93.0 \pm 32.6$  ml;  $p = 0.005$ ). Additionally, they exhibited a lower ejection volume and a tendency towards a lower left ventricular end-systolic volume. However, the ejection fraction was similar between the two groups. The median diastolic flow in patients with mitral stenosis was 76.3 ml/s (interquartile range [IQR]: 65.8 to 118.6). This value was found to be significantly lower than the median diastolic flow in the control group, which was 104.0 ml/s (IQR: 94.5 to 170.0), with a p-value of 0.027.

**Conclusions:** The measurement of flow, previously conducted invasively in the 1970s, has been replaced by the fractional assessment of its determinants with the introduction of two-dimensional echocardiography. In our study, we have successfully shown that the study of flow in mitral stenosis can be resumed non-invasively using three-dimensional echocardiography, which provides a similar and more accurate approach.

Our study contributes compelling evidence that three-dimensional echocardiography is capable of detecting reduced average diastolic flow in patients with mitral stenosis. The clinical utility and prognostic significance of these findings warrant further investigation in future studies.