

## Peak Mitral Inflow Velocity Predicts Mitral Regurgitation Severity

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**Objectives.** Mitral regurgitation (MR) is a common echocardiographic finding; however, there is no simple accurate method for quantification. The aim of this study was to develop an easily measured screening variable for hemodynamically significant MR.

**Background.** The added regurgitant volume in MR increases the left atrial to left ventricular gradient, which then increases the peak mitral inflow or the peak E wave velocity. Our hypothesis was that peak E wave velocity and the E/A ratio increase in proportion to MR severity.

**Methods.** We performed a retrospective analysis of 102 consecutive patients with varying grades of MR seen in the Adult Echocardiography Laboratory at the University of California, San Francisco. Peak E wave velocity, peak A wave velocity, E/A ratio and E wave deceleration time were measured in all patients. The reference standard for MR was qualitative echocardiographic evaluation by an expert and quantitation of regurgitant fraction using two-dimensional and Doppler echocardiography.

**Results.** Peak E wave velocity was seen to increase in proportion to MR severity, with a significant difference between the different groups ( $F = 37, p < 0.0001$ ). Peak E wave velocity correlated with regurgitant fraction ( $r = 0.52, p < 0.001$ ). Furthermore, an E wave velocity  $>1.2$  m/s identified 24 of 27 patients with severe MR (sensitivity 86%, specificity 86%, positive predictive value 75%). An A wave dominant pattern excluded the presence of severe MR. The E/A ratio also increased in proportion to MR severity. Peak A wave velocity and E wave deceleration time showed no correlation with MR severity.

**Conclusions.** Peak E wave velocity is easy to obtain and is therefore widely applicable in clinical practice as a screening tool for evaluating MR severity.

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The echocardiographic finding of mitral regurgitation (MR) is extremely common in the adult population, but in most patients it is hemodynamically insignificant. Although numerous strategies have been proposed (1), accurate quantitation of MR by echocardiography remains a continuing clinical challenge. Several qualitative echocardiographic measures have been described, including jet morphology (width, area and entrainment), continuous wave (CW) Doppler jet signal density, pulmonary venous flow patterns and left atrial (LA) dynamics (2). Quantitative echocardiographic methods include measurement of the regurgitant volume, fraction and orifice area (3-6). Although these methods are accurate, most laboratories find them too cumbersome and technically demanding for routine clinical application. Therefore, it would be useful to find a simple variable to screen for hemodynamically significant MR and to identify those patients in whom it might be appropriate to use more time intensive methods of analysis.

Early diastolic mitral inflow velocity relates directly to the instantaneous pressure gradient between the LA and the left ventricle (LV). The added regurgitant volume increases the LA to LV pressure gradient, which in turn increases the early mitral inflow velocity (E wave). Although increased E wave velocity in MR has been previously noted (2,7,8), its relation to the grade of MR severity has not been studied.

In this study we tested the hypotheses that 1) early mitral inflow velocity (peak E wave velocity) increases in direct proportion to the severity of MR; and 2) MR severity is proportional to the E/A ratio and inversely proportional to the peak A wave velocity and to the E wave deceleration time.

### Methods

**Study patients.** We retrospectively studied 102 consecutive patients (25 to 89 years old) with echocardiographically diagnosed native valve MR, from the University of California at San Francisco's Adult Echocardiography Data Base between January 1994 and December 1996. Inclusion criteria were 1) "isolated MR"; 2) sinus rhythm; and 3) heart rate (HR)  $<110$  beats/min. Patients with no more than trivial or mild aortic regurgitation (AR) and concurrent tricuspid regurgitation,

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#### Abbreviations and Acronyms

AR	=	aortic regurgitation
CW	=	continuous wave
EF	=	ejection fraction
HR	=	heart rate
LA	=	left atrium, left atrial
LV	=	left ventricle, left ventricular
MR	=	mitral regurgitation
PISA	=	proximal isovelocity surface area
PW	=	pulsed wave
RF	=	regurgitant fraction

regardless of severity, were also included. Exclusion criteria were 1) trace MR; 2) associated mitral or aortic stenosis (n = 6); 3) moderate or severe AR (n = 4); 4) atrial fibrillation or sinus tachycardia >110 beats/min (n = 3); 5) previous mitral valve repair surgery (n = 1); and 6) high cardiac output (LV outflow tract velocity time integral >40 cm) (n = 1). In addition, 10 age-matched normal subjects from the same data base were also analyzed.

In our laboratory, the routine evaluation and assignment of a qualitative grade of MR are reported using standard descriptions from a dictionary data base as mild, mild to moderate, moderate, moderate to severe and severe. Patients were classified into three categories on the basis of the expert's grading of MR severity: mild MR = patients graded as having mild MR; moderate MR = patients graded as having mild to moderate and moderate MR; and severe MR = patients graded as having moderate to severe and severe MR. As a quantitative expression of MR, regurgitant fraction (RF) was calculated in all patients by two-dimensional and Doppler echocardiography as described below.

The LV ejection fraction (EF) was remeasured at the time of the present study from the end-diastolic volume and the end-systolic volume using the biplane method of discs from the orthogonal four- and two-chamber apical views as described later. Subgroup analysis by EF was used to compare patients with normal or near normal EF (>50%) with those with moderate or severely decreased EF (<50%).

**Observer agreement.** In 30 randomly selected studies, two experts independently quantitated the degree of MR as mild, moderate and severe. The same studies were also reexamined by one observer at a separate time to determine intraobserver agreement.

**Echocardiographic study.** Doppler, M-mode and two-dimensional echocardiographic studies were performed according to the established clinical laboratory practice using commercially available instruments routinely used in the Echocardiography Laboratory (Hewlett-Packard Sonos 1500 and 2500 and the Acuson XP 128) with 2.5- or 3.5-MHz phased array transducers. Patients were positioned in the left lateral decubitus position with apical access gained at a cutout section of the mattress (9). Mitral inflow velocity was obtained by pulsed wave (PW) Doppler echocardiography at a sweep speed

of 100 mm/s from the apical four-chamber view by placing the sample volume at the tips of mitral leaflets. The inflow variables analyzed were 1) peak E wave velocity; 2) peak A wave velocity; 3) E to A wave ratio (E/A); and 4) E wave deceleration time. All variables had been measured at the time of clinical examination but were remeasured for the purpose of this study using the single best trace of mitral inflow with the highest E wave and A wave velocities. Three patients were excluded from the 87 cases for technical reasons: no mitral inflow recorded (n = 1) and incorrect placement of sample volume (n = 2).

**Assessment of MR severity.** The qualitative assessment of MR severity was a composite of several variables, including regurgitant jet characteristics such as jet width, entrainment and eccentricity (10-12); proximal isovelocity surface area (PISA) (13-17); CW Doppler characteristics and intensity of the regurgitant jet (3,18); pulmonary venous flow pattern (19-22); and LA size. In addition to this qualitative grading, measured RF provided an independent measure of the severity of MR. Of note is the fact that 9 of 28 patients grouped in the severe MR category went on to have valve repair or replacement in the next 2 years, although none in the categories of mild and moderate MR required an operation.

**Measurement of RF.** Left ventricular stroke volume was measured according to the recommendations of the American Society of Echocardiography (9). Left ventricular end-diastolic volume and LV end-systolic volume were obtained by applying the biplane method of discs to the orthogonal four- and two-chamber views using a standard off-line analysis system. Their difference (End-diastolic volume - End-systolic volume) was the LV stroke volume.

Forward stroke volume in patients with MR was calculated as the product of the LV outflow tract velocity time integral and the LV outflow tract area:

$$\text{Regurgitant volume} = \text{LV stroke volume} - \text{Forward stroke volume.}$$

$$\text{Regurgitant fraction} = \text{Regurgitant volume/LV stroke volume.}$$

**Analysis.** All data are expressed as the mean value  $\pm$  SD. Sensitivity, specificity and positive predictive values were calculated in accordance with methods described in Bailar J, Mosteller F, editors, *Medical Uses of Statistics*, 2nd ed, Waltham (MA): New England Journal of Medicine, 1992. The differences between groups were examined by analysis of variance. Simple and multiple regression analyses were used to examine the relation between peak mitral inflow velocity and RF, HR and age. The Student *t* test was used to study differences between unpaired groups. Data were analyzed using the Statview Student package and Statview 4.02 (Abacus Concepts).

## Results

We studied four groups: normal (n = 10), mild MR (n = 27), moderate MR (n = 29) and severe MR (n = 28). The mean values for the clinical and Doppler echocardiographic variables measured are listed (Table 1).

**Table 1.** Clinical, Doppler and Echocardiographic Variables in Normal Subjects and Those With the Three Grades of Mitral Regurgitation

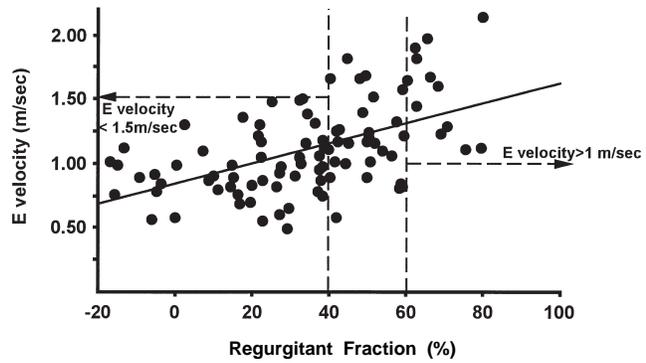
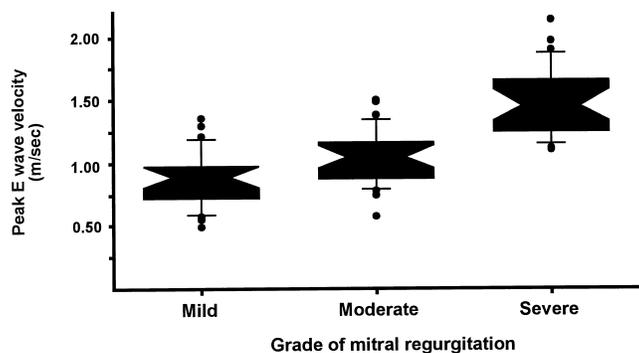
	Normal (n = 10)	Mild MR (n = 28)	Moderate MR (n = 29)	Severe MR (n = 28)
Age (yr)	57 ± 17	65 ± 14	60 ± 16	60 ± 15
E wave velocity (m/s)	0.89 ± 0.15*	0.87 ± 0.22*	1.05 ± 0.22†	1.48 ± 0.29
A wave velocity (m/s)	0.78 ± 0.26‡	0.77 ± 0.3‡	0.58 ± 0.24	0.69 ± 0.25
E/A ratio	1.3 ± 0.57*	1.5 ± 1.2*	2.1 ± 0.86	2.5 ± 1.2
E wave deceleration time (s)	220 ± 52	193 ± 59	176 ± 70	187 ± 61
RF	-1.6 ± 12.4§	18.5 ± 14.9*	40 ± 11†	57 ± 13

\*p < 0.05 compared with moderate and severe groups. †p < 0.05 compared with severe group. ‡p < 0.05 compared with moderate group. §p < 0.05 compared with mild, moderate and severe groups. Data are presented as mean value ± SD. RF = regurgitant fraction; MR = mitral regurgitation.

**Peak E wave velocity.** The peak E wave velocity was observed to increase in proportion to MR severity (Fig. 1), with a significant difference between the four groups (F = 36.7, p < 0.0001). A mitral inflow peak E wave velocity >1.2 m/s identified 24 of 27 patients with severe MR (sensitivity 86%, specificity 86%, positive predictive value 75%, negative predictive value 92%). Furthermore, no patient with severe MR had a peak E wave velocity <1 m/s, none with mild MR had a peak inflow velocity >1.4 m/s and none with moderate MR had a peak E wave velocity >1.5 m/s.

An A wave dominant pattern was not seen in any patient with severe MR. On univariate analysis there was good correlation between RF and peak E wave velocity (r = 0.52, p < 0.001) (Fig. 2).

**Figure 1.** Box plot of relation between peak E wave velocity and normal subjects and those with varying grades of MR determined echocardiographically (n = 94). The upper border of the box represents the 75th percentile, the middle border the 50th percentile and the lower border the 25th percentile. The upper bar represents the 90th percentile and the lower bar represents the 10th percentile. The remaining scatter points represent the outliers. The peak E wave velocity is seen to increase with increasing grades of MR. There was a significant difference between the four groups; post hoc tests revealed a significant difference in peak E wave velocity between normal subjects and those with moderate and severe MR, between mild MR and moderate and severe MR and between moderate MR and severe MR (p < 0.05 for all).



**Figure 2.** Regression plot of correlation between peak E wave velocity and RF in 84 patients with varying grades of MR (r = 0.52, p < 0.001). In patients with an RF <40%, the peak E wave velocity did not exceed 1.5 m/s. In patients with an RF >60%, the E wave always exceeded 1.0 m/s.

**Subgroup analysis in patients with a low EF (<50%) with MR.** There was a significant difference in the peak E wave velocity between the three MR groups in both categories (EF >50%: F = 27.5, p = 0.0001; EF <50%: F = 19.3, p = 0.0001). In the subgroup with an EF <50%, a peak E wave velocity >1.2 m/s identified patients with severe MR with a sensitivity of 90%, specificity of 87% and positive predictive value of 75% (Table 2).

**Effect of age and HR on E wave velocity.** We tested the relation of age and HR to peak mitral inflow velocity and found no significant correlation (p > 0.05); this was noted even in the subgroup of patients >50 years old. However, peak E wave velocity correlated significantly with RF (r = 0.52; p < 0.001). These three factors—age, HR and RF—were then entered into a multiple regression model, and once again only RF was seen to correlate significantly with peak E wave velocity (r = 0.5, p < 0.0001).

**E/A ratio.** There was a significant difference in the E/A ratio between the three groups (F = 5.55, p < 0.0015), with an increase in the ratio proportional to the severity of MR. On univariate analysis there was fair correlation between RF and the E/A ratio (r = 0.32, p < 0.05). No patient with severe MR had an E/A ratio <1.4.

**Peak A wave velocity and E wave deceleration time.** No significant difference in peak A wave velocity or E wave deceleration time was observed between the groups (p > 0.05).

The unpaired Student t test was used to compare patients

**Table 2.** Sensitivity, Specificity and Positive Predictive Value of Peak E Wave Velocity >1.2 m/s for Identifying Severe Mitral Regurgitation in Normal and Low Ejection Fraction Groups

Group	EF >50% (n = 51)	EF <50% (n = 33)
Sensitivity	86%	90%
Specificity	85%	87%
Positive predictive value	75%	75%

EF = ejection fraction.

with an E wave deceleration time <150 ms with those with an E wave deceleration time >150 ms, and no significant difference was noted between the two groups ( $p > 0.05$ ). Subgroup analysis of mild, moderate and severe MR also showed no significant difference between the two groups ( $p > 0.05$ ).

Forty-three of the 84 patients had chronic congestive heart failure. The unpaired Student *t* test showed no significant difference in peak E wave velocity between the two groups ( $p > 0.05$ ).

**Observer agreement.** Both the interobserver and intraobserver evaluation of the qualitative grade of MR showed a concordance of 1.

## Discussion

Doppler echocardiography, although largely qualitative, is used as the primary clinical tool to identify and approximate MR severity. Researchers have attempted to develop a more precise quantitative tool for measuring MR severity by calculation of regurgitant volume and fraction (3-6) and by the two-dimensional Doppler flow imaging technique (23). However, most cardiologists rely on a qualitative approach based largely on color flow appearance of the regurgitant jet. In this study we have demonstrated that in patients with isolated MR, the peak mitral inflow velocity is a simple and clinically useful correlate of MR severity. A peak mitral inflow velocity >1.2 m/s identified patients with severe MR (mean RF  $57 \pm 13$ ) with a sensitivity of 85%, specificity of 86%, positive predictive value of 75% and negative predictive value of 92%. Using an E wave velocity >1.2 m/s as a single variable to identify patients with severe MR has a modest positive predictive value. However, this variable may be used in conjunction with other variables to establish a diagnosis of severe MR. The peak E wave velocity normally ranges from 0.6 to 1.3 m/s (24,25) compared with a peak E wave velocity of  $1.5 \pm 0.3$  m/s in our patients with severe MR.

The dynamic nature of this relation was demonstrated in a canine model by Yellin et al. (26), when experimental rupture of the anterior papillary muscle, resulting in massive MR, caused a simultaneous increase in the peak mitral flow velocity. This has also been previously observed with native and prosthetic valves in patients with severe MR (2,7,8). Fujita et al. (27) used peak E wave velocity as a variable for grading MR severity. In all of these studies, however, the number of patients studied was small (3 to 19 patients), the E wave velocity not quantitated and no comparisons between the grades of MR were performed.

The position of the sampling site from the annulus to the leaflet tips alters the E wave velocity (28), and the highest velocity is recorded with the sample volume placed midway between the two leaflets in diastole (29). Further, because the leaflet separation varies with flow, whereas the annulus does not, measurement at the leaflet tips removes the variable of annular anatomy. Hence, in this study we used the peak E wave velocity recorded at the leaflet tips.

**Clinical application of evaluation of MR.** Mitral regurgitation is difficult to quantitate; the main echocardiographic variables used are jet penetration and width by color Doppler and CW Doppler of the regurgitant jet. These factors can often underestimate the severity of MR in patients with an eccentric jet (30). Quantitative estimation (regurgitant volume and fraction, PISA method) is laborious and not commonly used clinically. In comparison, the mitral inflow velocity is easy to obtain and is of particular assistance in patients with an eccentric jet where jet entrainment is inadequately assessed, CW Doppler echocardiography of the regurgitant jet is difficult to obtain and the PISA technique inapplicable.

In a recent study Hall et al. (31) used measurement of the jet width as an indicator of MR severity. The editorial comment by Thomas (32) with regard to this study emphasized the relative ease of measurement and applicability in routine clinical practice. Likewise, the peak mitral inflow velocity is relatively easy to obtain and, similar to jet width, can be easily applied in daily clinical practice.

**Effect of HR and age on E wave velocity.** The E wave velocity is known to be inversely related to age and HR. From our observations in this study, age and HR did not appear to influence the peak E wave velocity in patients with MR, possibly because the hemodynamic effects of MR dominate those of age and HR.

**Restrictive LV function and E wave velocity.** Left ventricular diastolic function affects the mitral inflow pattern (33,34); the E wave velocity is increased with a decrease in deceleration time. Comparison between patients with an E wave deceleration time <150 ms and those with a time >150 ms showed no significant difference between the two groups. Further, comparison between the two groups with and without congestive heart failure showed no significant difference in peak E wave velocity. Thus, it would appear that in the presence of isolated MR, the peak E wave velocity is increased despite the presence or absence of chronic congestive heart failure.

**Other variables.** No significant differences in peak A wave velocity and E wave deceleration time were noted between the groups. No patient with severe MR had an A wave dominant mitral inflow pattern. Intuitively, in MR it appears that the majority of the regurgitant volume enters the LV in early diastole. This would restore a normal atrial volume (i.e., preload) before atrial contraction, resulting in a normal peak A wave velocity. The increase in the E/A ratio with increasing MR severity is thus only a reflection of the increase in early diastolic filling with a relatively normal atrial contribution. Similar to our findings, in a recent study Tahirkheli and Sarano (35) found that E wave deceleration time and peak A wave velocity are not significantly related to MR, whereas peak E wave velocity and the E/A ratio were increased.

**Study limitations.** 1) There is no single method to quantify MR; we used qualitative echocardiographic grading by an expert reader and quantitation of RF as reference standards. However, these estimations have their inherent limitations. 2) This study was retrospective; therefore, we were unable to

control all the variables measured. Thus, two patients had to be excluded because of improper positioning of the sample volume and one had to be excluded for the lack of mitral inflow tracing. 3) The peak E wave velocity is increased in cases with restrictive physiologic findings. Our analysis showed no significant differences in the peak E wave velocity between two groups. However, the sample sizes studied were relatively small. 4) An increase in diastolic LV flow velocity and altered flow dynamics are well recognized phenomena in patients with severe AR (36-39). As the presence of more than mild AR was an exclusion criterion for this study, use of peak E wave velocity in patients with concomitant lesions has not been tested. 5) Only patients with chronic MR were studied. The hemodynamic variables of acute MR may lead to different results; further study is required. 6) Finally, the E wave velocity should not be used as a single method of judging MR severity, but as a useful simple screening tool that can assist in the initial grading of MR.

**Conclusions.** There is no single precise method for evaluation of MR. In patients with severe MR, particularly those with an eccentric jet, the commonly used variables are difficult to obtain. Mitral inflow by PW Doppler echocardiography is easy to obtain and is therefore widely applicable in clinical practice as a simple technique for screening patients with hemodynamically significant MR. An increase in peak inflow velocity and absence of an A wave dominant pattern were noted in severe MR. This may prove to be a useful additional semiquantitative tool in the evaluation of MR, including MR in those patients with an eccentric jet.

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