JACC Vol. 31, No. 6
May 1998:1383–90

Quantitation of Mitral Regurgitation Using the Systolic/Diastolic Pulmonary Venous Flow Velocity Ratio

CHRISTIAN SEILER, MD, FACC, BEAT C. AESCHBACHER, MD,
BERNHARD MEIER, MD, FESC, FACC

Bern, Switzerland

Objectives. **The purpose of this study was to test the hypothesis that pulmonary venous flow velocity ratios during systole and diastole in patients with mitral regurgitation (MR) correctly predict the quantitative degree of MR.**

Background. **Pulmonary venous flow velocity measurements have thus far been used only for the qualitative assessment of MR. Recent studies have evaluated this method using transesophageal echocardiography against semiquantitative references.**

Methods. **In 100 patients without aortic regurgitation or atrial fibrillation and with left ventricular (LV) ejection fraction >45%, MR was assessed by quantitative echocardiographic Doppler and color Doppler, providing forward and total LV stroke volume for the calculation of the mitral regurgitant fraction ($RF_{standard}$), the reference parameter, and also supplying mitral regurgitant orifice area (ROA) values and the RF by the flow convergence method (RF_{PISA} [proximal isovelocity surface area]). Measurements of pulmonary venous flow velocity time integral values during systole to diastole (VTI_s/VTI_d) were obtained and tested for their predictibility of ROA, $RF_{standard}$ and RF_{PISA}.**

Results. **There was an inverse and significant correlation between VTI_s/VTI_d and ROA, RF_{PISA} and $RF_{standard}$, respectively: $RF_{standard} = 49 - 20\ VTI_s/VTI_d$, r = 0.77, p = 0.0001. A principal source of variability in the relation between VTI_s/VTI_d and $RF_{standard}$ was the presence of mitral valve prolapse as the cause of MR. Pulmonary venous flow reversal (VTI_s/VTI_d <0) correctly identified severe MR with 52% sensitivity, 96% specificity and 80% positive and 87% negative predictive accuracy.**

Conclusions. **The VTI_s/VTI_d ratio allows a moderately accurate assessment of the severity of MR.**

(J Am Coll Cardiol 1998;31:1383–90)

Quantitation of mitral regurgitation (MR) is a prerequisite to surgical decision making in patients with MR (1,2), but a recent study has shown that the best method of quantitative characterization remains uncertain (3). This is also reflected by the wide variety of methods used for the determination of MR, including the invasive left ventricular (LV) angiography/thermodilution technique (4), noninvasive Doppler flow methods such as color Doppler flow mapping of the regurgitant jet (5,6), vena contracta analysis of the regurgitant jet (7), analysis of the flow convergence zone proximal to the regurgitant orifice (8), examination of the power or amplitude of the received regurgitant jet flow velocity signal (9,10) and analysis of the momentum of the regurgitant jet (11). It has even been declared that there is no single effective method for the calculation of MR in an individual patient using echocardiographic Doppler (12). This notion may be challenged because the so-called quantitative Doppler method of total and forward (across the LV outflow tract) LV stroke volume (SV_{tot} and SV_{fw}) calculation has been demonstrated to be accurate compared with invasive methods, although it is tedious and time-consuming to perform (13).

Pulmonary venous flow velocity patterns have been used for the qualitative or semiquantitative estimation of MR (14). Systolic flow reversal in the pulmonary veins indicates severe MR with high diagnostic accuracy (Fig. 1). However, there are a number of other variables influencing either the systolic or diastolic part of pulmonary vein flow such as atrial compliance (changing with age), the presence of systolic dysfunction (with increased atrial pressure), atrial fibrillation and diastolic dysfunction (15–17). So far, pulmonary venous flow velocity spectra for the qualitative characterization of MR have been obtained exclusively by transesophageal Doppler echocardiography (TEE) (14,18,19). Yet in our experience, at least one of the pulmonary veins (usually the upper right) can be interrogated through the transthoracic approach in >90% of cases.

Consequently and because of the lack of an ideal, easy to apply gold standard for the quantitation of MR, the goal of this prospective study was to test the hypothesis that the ratio of pulmonary venous flow velocity during systole and diastole (Fig. 2) accurately predicts the regurgitant fraction (RF) in patients with pure MR.

From the Department of Cardiology, University Hospital, Bern, Switzerland.
Manuscript received July 25, 1997; revised manuscript received January 21, 1998, accepted January 28, 1998.
Address for correspondence: Dr. Christian Seiler, University Hospital, Cardiology, Inselspital, Freiburgstrasse, Bern, Switzerland. E-mail: christian.seiler@insel.ch.

Published by Elsevier Science Inc.

0735-1097/98/$19.00
PII S0735-1097(98)00090-4

Abbreviations and Acronyms

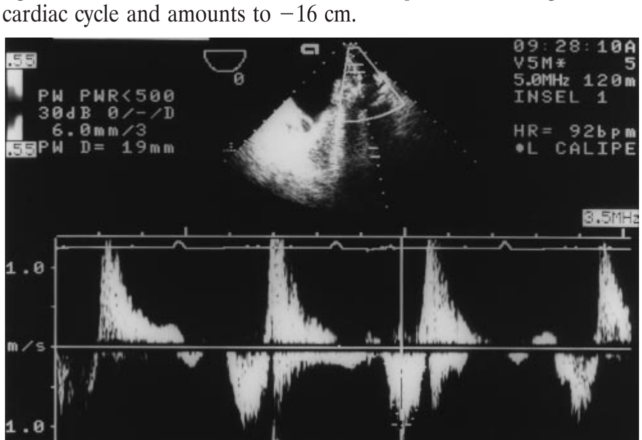
LV	= left ventricular
MR	= mitral regurgitation
PISA	= proximal isovelocity surface area
RF	= regurgitant fraction
ROA	= regurgitant orifice area
RV	= regurgitant volume
SV_{fw} and SV_{tot}	= forward and total stroke volume
TEE	= transesophageal echocardiography (echocardiographic)
TTE	= transthoracic echocardiography (echocardiographic)
VTI_s/VTI_d	= systolic/diastolic flow velocity time integral ratio

Methods

Patients. One hundred patients (age 62 ± 14 years, range 30 to 88; 58 men, 42 women) with pure MR ranging from minimal to severe were included in this prospective study. All of them underwent transthoracic Doppler echocardiography (TTE) (n = 80) or TTE and TEE (n = 20) depending on the clinical indication. The patients gave informed consent to participate in this study.

The inclusion criteria were 1) the presence of pure, isolated, at least mild MR or no regurgitation as determined by standard two-dimensional Doppler echocardiography, 2) an adequate measurement of the LV outflow tract in the parasternal long axis view, 3) the satisfactory determination of end-diastolic and end-systolic LV volumes in the apical four-chamber and two-chamber view, 4) the ability to measure flow convergence zone data at the regurgitant orifice in order to calculate the regurgitant orifice area (ROA) and the regurgitant volume (RV) according to the proximal isovelocity surface area (PISA) method (8), and 5) adequate pulmonary flow velocity signals obtained by TTE or TEE from one or more pulmonary veins. The exclusion criteria were 1) age <30 years, 2) an LV ejection fraction $<45\%$, 3) the presence of atrial fibrillation or flutter, and 4) the presence of aortic regurgitation.

Figure 1. TEE in a patient with severe MR depicting a spectral pulsed Doppler recording of the upper left pulmonary vein. There is a flow velocity reversal during systole and a diastolic forward flow velocity signal directed into the left atrium. The VTI_s is traced during the third cardiac cycle and amounts to −16 cm.



The study cohort was divided into four groups according to the mitral RF determined by echocardiographic LV planimetry (providing the SV_{tot}) and by the echocardiographic Doppler–derived calculation of SV_{fw} across the LV outflow tract. This method is subsequently called the *quantitative echocardiographic Doppler (standard) method*. The four study groups were "mild MR" (RF $\leq 20\%$; n = 31), "moderate MR" (RF $>20\%$ to 35%; n = 28), "moderately severe MR" (RF $>35\%$ to 50%; n = 18), and "severe MR" (RF $>50\%$; n = 23).

Two-dimensional Doppler echocardiography. Patients underwent conventional two-dimensional echocardiography and Doppler examination using an Acuson XP-128 phased array system equipped with a 2.0-, 2.5- or 3.5-MHz transducer. LV measurements were obtained at end-systole and end-diastole and were performed according to the recommendations of the American Society of Echocardiography (leading edge method [20]). LV volume measurements were performed as recommended by the American Society of Echocardiography (21). Apical two- and four-chamber views were acquired. The LV volumes were calculated on-line. Trabeculations and papillary muscles were excluded from the endocardial border. LV end-diastolic and end-systolic volumes were computed using the biapical Simpson rule (summed disk method) (21). LV SV_{tot} was calculated as the difference between end-diastolic and end-systolic LV volume. LV SV_{fw} across the LV outflow tract was computed as the LV outflow tract cross-sectional area (from the parasternal long axis view) times the velocity time integral of the systolic outflow signal obtained by pulsed Doppler, with the sample volume positioned in the LV outflow tract. The RF determined by this quantitative echocardiographic Doppler standard method, that is, $RF_{standard}$, was determined as follows:

$$RF_{standard} = \frac{(SV_{tot} - SV_{fw})}{SV_{tot}}.$$

In all patients, MR was also quantitated using the flow convergence method (PISA method [8]), whereby the radius of the flow convergence zone at the regurgitant orifice was measured several times during systole. Determination of the aliasing velocity of the flow convergence zone, the maximum velocity within the regurgitant orifice and the flow velocity time integral of the regurgitant continuous wave Doppler spectrum allowed calculation of the mitral ROA and RV (8). RF_{PISA} was then determined as follows:

$$RF_{PISA} = RV/SV_{tot}.$$

Arterial blood pressure was recorded at the time when the flow convergence measurements were made.

Color Doppler imaging of MR. Qualitative assessment of MR was performed using color Doppler imaging through an apical window, as described previously (22). Visual estimates of four degrees of MR (mild, moderate, moderately severe and severe) were acquired on-line, and comprised factors such as

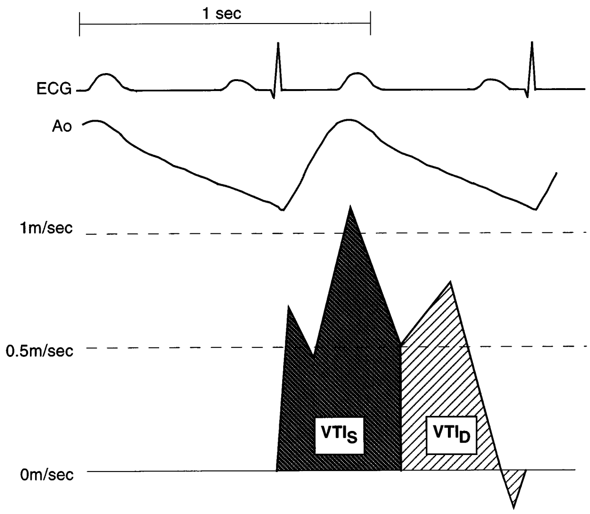


Figure 2. Schematic drawing from a normal patient illustrating the calculation of VTI_s/VTI_d. The systolic pulmonary venous flow velocity signal comprises two peaks, one related to the early and a second to the late systolic atrial filling. VTI_s/VTI_d in centimeters per second times second (i.e., cm) is determined by planimetry of VTI_s, the **dark hatched** signal, divided by the planimetry derived VTI_d, the **light hatched** signal (including a short pulmonary venous flow reversal after atrial contraction). Planimetry includes positive and negative flow velocity signals (i.e., a predominantly negative VTI during systole translates into $VTI_s < 0$ or $VTI_s/VTI_d < 0$; a predominantly positive VTI during systole results in $VTI_s > 0$ or $VTI_s/VTI_d > 0$). Ao = aortic pressure signal; ECG = electrocardiogram.

the width of the MR jet at its origin, the length of the jet, the area of the color Doppler jet and its size relative to the atrial cavity size.

Spectral Doppler examination of pulmonary vein flow. Doppler examination of the pulmonary vein(s) was performed using pulsed Doppler with the patient in the left supine position, with the sample volume positioned ~1 cm within the right upper pulmonary vein in all patients undergoing TTE and with the sample volume located 1 cm within the right upper and left upper pulmonary veins in all patients undergoing TEE. Measurements included systolic and diastolic maximal velocity as well as the VTI_s and VTI_d of the pulmonary vein signal. Measurements in both upper pulmonary veins were averaged. The VTI_s/VTI_d ratio was computed as the predictor for the severity of MR (Fig. 2). Negative ratios resulted from predominantly negative velocity time integrals during systole, as determined by planimetry.

Statistical analysis. Between group comparison of continuous demographic, echocardiographic and Doppler flow velocity data were performed by an analysis of variance test. Between group comparison of categorial data were analyzed using a chi-square test. Linear or polynomial regression analysis was applied for analysis of an association between pulmonary vein velocity ratios and ROA values or RF values, respectively. Linear regression analysis and a Bland Altman analysis (23) were used to test the agreement between the two methods (echocardiographic Doppler and PISA method) used to determine the severity of MR. Test accuracies of normal ($VTI_s/VTI_d > 1$), mildly blunted ($VTI_s/VTI_d > 0.5$ to 1), blunted ($VTI_s/VTI_d = 0$ to 0.5) and reversed ($VTI_s/VTI_d < 0$) pulmonary venous flow velocity ratios for different degrees of MR according to $RF_{standard}$ were determined. Statistical significance was defined as a p value < 0.05.

Results

Patient characteristics. There were no statistically significant differences among the four groups regarding the age of the patients, gender, body size, blood pressure, heart rate and the presence of LV diastolic dysfunction (Table 1). The cause of MR was ischemia in 30, dilated cardiomyopathy in 12, endocarditis in 5, mitral annular calcification in 5, rheumatic disease in 14, mitral valve prolapse in 20 and uncertain in 14 patients. The occurrence of mitral valve prolapse as the cause of MR increased with the severity of MR. Patients with severe MR were examined more often by TEE than those of the other groups.

Table 1. Patient Characteristics

	Mild MR (RF >0–20%) (n = 31)	Moderate MR (RF >20–35%) (n = 28)	Moderately Severe MR (RF >35–50%) (n = 18)	Severe MR (RF >50%) (n = 23)	p Value
Age (yr)	63 ± 16	62 ± 13	62 ± 18	61 ± 12	NS
Male gender (%)	18 (58%)	14 (50%)	9 (50%)	16 (70%)	NS
Body surface area (m^2)	1.76 ± 0.2	1.84 ± 0.2	1.72 ± 0.2	1.82 ± 0.2	NS
Systolic blood pressure (mm Hg)	132 ± 25	123 ± 20	133 ± 21	122 ± 15	NS
Diastolic blood pressure (mm Hg)	77 ± 11	73 ± 12	76 ± 12	70 ± 11	NS
Heart rate (beats/min)	71 ± 18	70 ± 21	84 ± 20	74 ± 17	NS
Mitral valve prolapse	2 (6%)	2 (7%)	6 (33%)*	10 (43%)*	0.0006
LV diastolic dysfunction	14 (45%)	11 (39%)	5 (28%)	6 (26%)	NS
TEE	6 (19%)	3 (11%)	3 (18%)	10 (34%)	NS

*$p < 0.01$ versus mild and moderate mitral regurgitation (MR). Data presented are mean value ± SD or number (%) of patients. LV = left ventricular; RF = regurgitant fraction; TEE = transesophageal echocardiography.

Table 2. Echocardiographic Data

	Mild MR (RF >0–20%) (n = 31)	Moderate MR (RF >20–35%) (n = 28)	Moderately Severe MR (RF >35–50%) (n = 18)	Severe MR (RF >50%) (n = 23)	p Value
End-diastolic LV diameter (mm)	49 ± 8	51 ± 9	56 ± 8	57 ± 5*	0.0005
End-systolic LV diameter (mm)	32 ± 8	35 ± 9	39 ± 9	37 ± 7	NS
Septal wall thickness, ED (mm)	13 ± 3	12 ± 3	12 ± 2	13 ± 3	NS
Posterior wall thickness, ED (mm)	11 ± 2	11 ± 3	11 ± 2	12 ± 3	NS
Left atrium (mm)	40 ± 7	43 ± 5	46 ± 9	52 ± 8†	0.0001
LV ejection fraction (%)	63 ± 10	59 ± 14	59 ± 15	63 ± 13	NS
LV mass index (g/m^2)	135 ± 49	124 ± 40	141 ± 37	162 ± 39	0.04
Systolic ΔP_{max} RA–RV (mm Hg)	30 ± 8 (n = 10)	38 ± 11 (n = 14)	35 ± 13 (n = 18)	36 ± 13 (n = 23)	NS

*p < 0.05 versus mild mitral regurgitation (MR). †p < 0.05 versus mild and moderate mitral regurgitation. Data presented are mean value ± SD. ΔP_{max} = maximal pressure gradient; ED = end-diastolic; RA = right atrium; RV = right ventricle; other abbreviations as in Table 1.

Echocardiographic data. Table 2 shows that there was a tendency to larger end-diastolic LV cavity sizes with increasing severity of MR, although the respective differences were statistically different only between patients with severe and those with mild MR. The same trend to larger cavity sizes with more severe MR was found for the left atrium. The LV mass index tended to be larger in patients with severe MR than in those with mild and moderate MR (Table 2), a finding related to the larger cavity sizes in patients with more severe MR and not to different LV wall thicknesses. There was no significant difference in maximal systolic pressure gradients across an insufficient tricuspid valve among the study groups.

Doppler echocardiographic data for the assessment of MR. The comparison between the two quantitative methods for the assessment of MR used in this study, the quantitative echocardiographic Doppler standard method and the PISA method, revealed a good and statistically significant agreement (Fig. 3), although the $RF_{standard}$ values were slightly underestimated by the PISA method (SEE = 10.6%). The data presented in Table 3 indicate that mild to moderate degrees of MR were overestimated by color Doppler imaging in most cases, whereas the more severe MR was most often assessed correctly. All values of PISA-derived RVs and ROAs differed significantly among the study groups.

Association between pulmonary venous flow velocity measurements and MR. VTI_s/VTI_d ratios differed significantly among all study groups (Table 3). Figure 4 illustrates that there was an inverse curvilinear, significant relation between the VTI_s/VTI_d ratio and the ROA of the mitral valve. This relation was improved by normalizing ROA for body surface area: $ROA/m^2 = 0.48 - 0.52\ VTI_s/VTI_d + 0.1(VTI_s/VTI_d)^2$; r = 0.70, p = 0.0001. An inverse, linear relation was observed between the VTI_s/VTI_d ratio and the RF (i.e., RF_{PISA}; Fig. 5). There was a slight tendency toward a closer correlation between those parameters if the pulmonary venous flow velocity signals were obtained using TEE instead of TTE (Fig. 5, filled symbols; TEE-derived $RF_{PISA} = 59 - 26\ VTI_s/VTI_d$, r = 0.82). The linear regression equation for the correlation be-

Figure 3. A, Comparison between mitral RF determined by the flow convergence method (PISA method, RF_{PISA}; horizontal axis) and RF calculated by quantitative echocardiographic Doppler ($RF_{standard}$, vertical axis). There was a significant correlation between those parameters. **B,** Analysis of the average between the RF_{PISA} and $RF_{standard}$ values (horizontal axis) and the deviation of RF_{PISA} from the average (vertical axis).

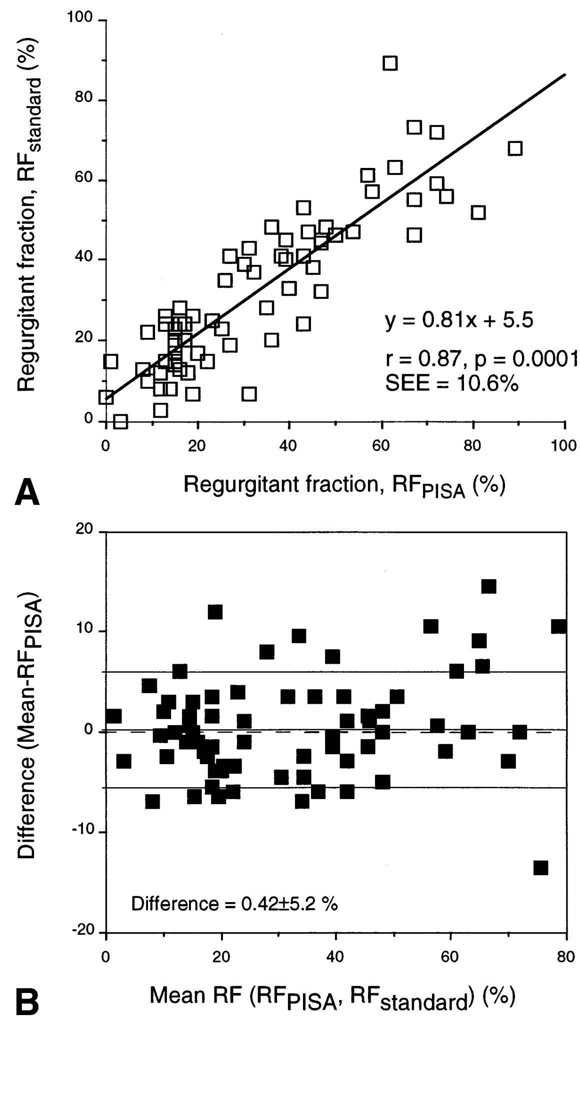


Table 3. Echocardiographic Doppler Assessment of Mitral Regurgitation

	Mild MR (RF >0–20%) (n = 31)	Moderate MR (RF >20–35%) (n = 28)	Moderately Severe MR (RF >35–50%) (n = 18)	Severe MR (RF >50%) (n = 23)	p Value
Color Doppler assessment of MR					
Exact agreement	8 (26%)	4 (14%)	12 (67%)	23 (100%)	0.0001
Exact agreement or agreement with next higher MR category	28 (90%)	28 (100%)	18 (100%)	23 (100%)	NS
$RF_{standard}$ (%)	16 ± 8	30 ± 13	42 ± 11	63 ± 13	0.0001*
RF_{PISA} (%)	12 ± 6†	30 ± 6†	47 ± 9†	74 ± 12	0.0001*
RV_{PISA} (ml)	10 ± 6	24 ± 10	41 ± 17	91 ± 47	0.0001*
ROA_{PISA} (cm^2)	0.07 ± 0.05	0.16 ± 0.07	0.28 ± 0.12	0.76 ± 0.61	0.0001*
Pulmonary vein VTI_s/VTI_d (cm)	1.44 ± 0.47	0.86 ± 0.40	0.36 ± 0.49	−0.21 ± 0.41	0.0001*

*$p < 0.05$ among all groups. †p = NS versus regurgitant fraction (RF) by standard echocardiographic Doppler method. d = diastole; LV = left ventricular; MR = mitral regurgitation; PISA = proximal isovelocity surface area method; ROA = regurgitant orifice area; RV = regurgitant volume; standard = quantitative echocardiographic Doppler standard method (i.e., calculation of total LV stroke volume by LV planimetry and forward stroke volume by Doppler); s = systole; VTI = velocity time integral.

tween TEE-derived and TTE-derived VTI_s/VTI_d (n = 20) was as follows: TEE-derived $VTI_s/VTI_d = 0.93$ TTE-derived $VTI_s/VTI_d + 0.03$; r = 0.91, p = 0.0001. The regression equation for the calculation of echocardiographic Doppler–derived RF values was $RF_{standard} = 49 - 20\ VTI_s/VTI_d$; r = 0.77, p = 0.0001.

The test accuracies of normal (VTI_s/VTI_d >1), mildly blunted (VTI_s/VTI_d >0.5 to 1), blunted (VTI_s/VTI_d = 0 to 0.5) and reversed (VTI_s/VTI_d <0) pulmonary venous flow velocity ratios for different degrees of MR according to $RF_{standard}$ are shown in Table 4. The test accuracy of any systolic pulmonary venous flow reversal (i.e., not only net flow reversal during the entire systole) for severe MR was 56% sensitivity, 91% specificity, 65% positive predictive accuracy and 88% negative predictive accuracy.

Discussion

This prospective study of 100 patients with pure MR found that the quantitative characterization of pulmonary venous flow patterns using TEE or TTE, or both, allows the prediction of echocardiographic Doppler–derived mitral RF with moderate accuracy.

Methods for the quantitation of MR. Although angiography is a clinically useful and well accepted semiquantitative

Figure 4. Correlation between VTI_s/VTI_d (horizontal axis) and mitral ROA determined by the flow convergence method (vertical axis). The **thick vertical line** indicates the limit between systolic anterograde (>0) and retrograde pulmonary vein flow.

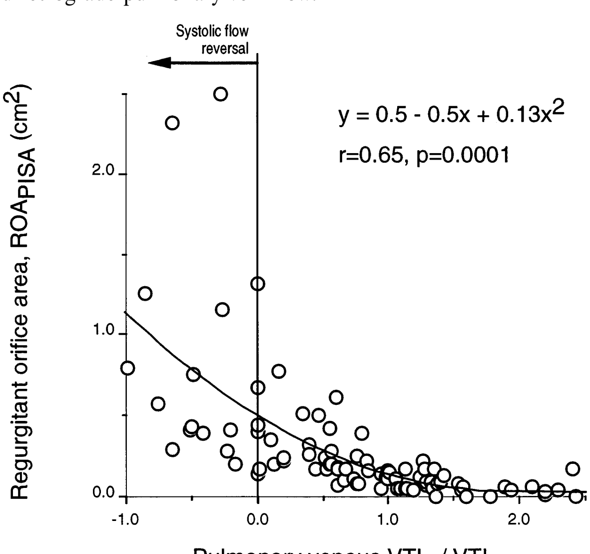


Figure 5. Correlation between VTI_s/VTI_d (horizontal axis) and mitral RF determined by the flow convergence method (vertical axis). The **thick vertical line** indicates the limit between systolic antegrade (>0) and retrograde pulmonary vein flow. **Open triangles** indicate patients who underwent TTE, **solid triangles** those who underwent TEE. **Upright triangles** indicate patients without mitral valve prolapse (MVP), **reversed triangles** those with MVP.

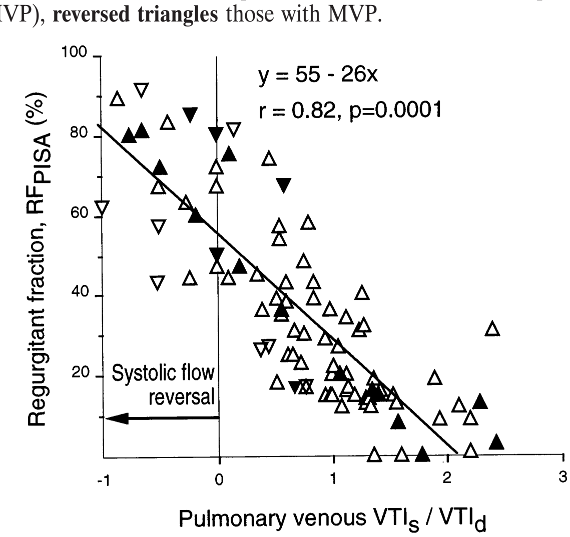


Table 4. Test Accuracy of Pulmonary Venous Flow Velocity Ratios for Different Degrees of Mitral Regurgitation

	Normal PV Ratio (VTI_s/VTI_d >1 predicts RF >0–20%)	Mildly Blunted PV Ratio (VTI_s/VTI_d >0.5–1 predicts RF >20–35%)	Blunted PV Ratio (VTI_s/VTI_d = 0–0.5 predicts RF >35–50%)	Reversed PV Ratio (VTI_s/VTI_d <0 predicts RF >50%)
Sensitivity	84%	57%	33%	52%
Specificity	84%	81%	85%	96%
Positive predictive accuracy	70%	53%	33%	80%
Negative predictive accuracy	92%	83%	85%	87%
Total accuracy	84%	74%	76%	86%

PV = pulmonary vein; RF = mitral regurgitant fraction; VTI_d = pulmonary venous flow velocity time integral during diastole (cm); VTI_s = pulmonary venous flow velocity time integral during systole (cm).

approach in the assessment of MR, it cannot be considered a reference method. Qualitative angiographic grading of MR has been demonstrated to very often be at variance with the quantitative indexes of MR (24). Studies using "quantitative" angiography have reported up to 40% of RF computed in normal subjects (25) and 0% RF in patients with documented significant MR (24,25). Similarly, there are numerous problems and pitfalls inherent in the noninvasive, echocardiographic Doppler–based methods for the assessment of MR, such as the reported underestimation of RF using color Doppler in patients with eccentric MR jets or MR jets due to ischemic heart disease (5). The sound theory behind the flow convergence (PISA) method, a procedure widely used for the quantitation of MR, is affected by several error-producing discrepancies, namely the noncircular orifice of the regurgitant hole; the nonhemispheric, often blunted, proximal flow convergence region; the nonflat surface of the mitral valve plane; and eccentric MR jet directions (26). The theoretically very elegant method of the jet momentum analysis (11) is actually almost unemployable because the receiving chamber of the MR jet is not unlimited in space but has discrete, often narrow, boundaries that render the analysis of the color Doppler jet impractical. The amplitude-weighted mean MR jet velocity method, a nonvolumetric spectral Doppler method, mandates a special, not widely available, data processing software; it is not applicable in the presence of turbulent MR jets; the correct calculation of RF values is dependent on maintaining the Doppler gain constant; and ultrasound coverage of the entire valvular orifice under investigation is mandatory (9,10).

In the light of these problems affecting the quantitation of MR, we sought to test a simple, so far qualitative method (i.e., the pulmonary vein characterization) for the quantitative assessment of MR. We performed the test using an approved and widely applicable quantitative echocardiographic Doppler method as the reference (i.e., LV planimetry and echocardiographic Doppler–derived SV_{fw} calculation) (13) and one of the above described procedures, the PISA method. Comparison of these two reference methods revealed good agreement but overestimation of the standard by the PISA method, a finding in agreement with one, recently published, comparable study (27) that determined the ROA as the Doppler-derived RV divided by the mitral regurgitant jet velocity time integral. RF values in patients with mild to moderate MR tended to be overestimated using the color Doppler assessment (Table 3).

Studies of pulmonary vein flow assessment for the characterization of MR. Qualitatively the results of the present study agree with those published recently, in that all of them identified a blunted systolic pulmonary venous flow as an indicator for moderate MR and systolic pulmonary vein flow reversal as characteristic for severe MR (14,18,19). At variance with those studies, our investigation did not use just one qualitative grading reference method (i.e., 1+ to 4+ angiographic degrees of MR) but rather two quantitative references. From our perspective, it is methodologically problematic to use a qualitative reference to evaluate a quantitative method. The study of a larger number of patients than in previous reports to determine the validity of pulmonary vein flow patterns for the estimation of MR is overdue because the influence of other variables on the dependence of pulmonary vein flow and MR can be estimated only in this way. In addition to the earlier mentioned qualitative association of the previous studies, the present study reveals a continuous, inverse relation between an index of the systolic to diastolic pulmonary vein flow and the RF. However, this association is not strong because of the covarying effect of factors other than MR altering pulmonary venous flow patterns (see later).

The ROA of the mitral valve, the parameter regarded as the most fundamental measure for the severity of the regurgitation, showed a curvilinear relation to pulmonary venous flow patterns that was weaker than the RF to pulmonary vein flow velocity association. Most likely, body size is a covariable that influences the ROA in addition to the degree of MR.

Covariables influencing pulmonary venous flow. The earlier mentioned association holds true even when more crude means are used to obtain pulmonary vein flow velocity spectra (i.e., TTE). It is also correct in patients with conditions presumably influencing the systolic/diastolic pulmonary venous flow velocity ratios such as a younger age (between 30 and 40 years; probably with increased atrial compliance) and LV diastolic as well as mild systolic dysfunction. Figure 5 illustrates that most of the deviation from the *exact* association among pulmonary vein flow ratios and MR is related to the presence of mitral valve prolapse. The excentricity of the MR jet in the presence of posterior (medial-anterior direction) or anterior leaflet (lateral-posterior direction) mitral valve prolapse likely caused an over- or underestimation, respectively, with regard to the right upper pulmonary vein, (i.e., the prevalent measurement site used in this study). Unexpectedly, the use of TEE for pulmonary venous flow assessment did not improve the association between the RF and systolic/diastolic flow velocity ratio, suggesting that the application of TTE was not a limitation to our study. Young age and systolic or diastolic dysfunction did not appear to be associated with the scattering of the relation between pulmonary vein flow velocity ratios and mitral RF (data not shown), most likely because they did not occur often in the entire study group.

In the case of the PISA reference method, an additional factor causing variation in the predictability of mitral RF by pulmonary vein flow characterization is the increasing overestimation of RF in higher degrees of MR by the PISA method (Fig. 3), which may be related to factors such as underestimation of the peak regurgitant flow velocity in cases of excentric jet directions. Problems with the correct detection of MR flow velocity spectra using the PISA method can be circumvented by the use of an empirically determined constant that reflects the maximal/time integrated velocity ratio of the MR jet (28).

Clinical implications. In patients without atrial fibrillation and with an LV ejection fraction >45%, assessment of pulmonary vein flow velocities should be used more often for the characterization of MR. Measurement of pulmonary vein flow velocities can also be readily performed using TTE, which provides semiquantitative 1+ to 4+ degrees of MR, whereby a VTI_s/VTI_d ratio >1 corresponds to 1+; >1:2 corresponds to 2+; <1:2 corresponds to 3+; and flow reversal corresponds to 4+ degrees of MR. The positive and negative predictive accuracies of normal and reversed pulmonary vein flow ratios for the detection of mild and severe MR, respectively, are moderately good to high. That, in this study, pulmonary vein flow reversal did not predict severe MR with absolute accuracy cannot be explained by the use of a velocity integral–derived *net* flow reversal during the entire systole (Fig. 2), because the "traditional" flow reversal (i.e., *any* systolic reversal) predicted severe MR even less accurately. Most (4 of 5) of the patients whose pulmonary venous flow velocity class changed because of the use of the alternative definition of flow reversal were patients with mitral valve prolapse. In addition, the test accuracy of flow reversal did not change further when patients with asymmetric flow reversal in the right pulmonary vein were included as having reversal without averaging it with left upper pulmonary vein signals. As the data on Table 4 indicate, the test accuracy of mildly blunted and blunted pulmonary venous flow ratios to determine mild and moderate MR is poor. By merging the two "blunted" categories (i.e., $VTI_s/VTI_d = 0$ to 1), newly defined "moderate" MR (i.e., RF >20% to 50%) can be predicted with 67% sensitivity, 73% specificity and 70% positive and 73% negative predictive accuracy.

Conclusions. The VTI_s/VTI_d ratio allows a moderately accurate assessment of the severity of MR. However, it cannot replace the quantification of MR using quantitative Doppler echocardiographic methods.

References

1. Scott W, Miller D, Haverich A, et al. Operative risk of mitral valve replacement: discriminant analysis of 1329 procedures. Circulation 1985;72 Suppl II:II-108–19.
2. Thomas J. How leaky is that mitral valve? Simplified Doppler methods to measure regurgitant orifice area. Circulation 1997;95:548–50.
3. Slater J, Gindea A, Freedberg R, et al. Comparison of cardiac catheterization and Doppler echocardiography in the decision to operate in aortic and mitral valve disease. J Am Coll Cardiol 1991;17:1026–36.
4. Baim D, Rothman M, Harrison D. Simultaneous measurement of coronary venous flow and oxygen saturation during transient alterations in myocardial oxygen supply and demand. Am J Cardiol 1982;49:743–50.
5. Enriquez-Sarano M, Tajik A, Bailey K, Seward J. Color flow imaging compared with quantitative Doppler assessment of severity of mitral regurgitation: influence of eccentricity of jet and mechanism of regurgitation. J Am Coll Cardiol 1993;21:1211–9.
6. Smith M, Grayburn P, Spain M, De Maria A. Observer variability in the quantitation of Doppler color flow jet areas for mitral and aortic regurgitation. J Am Coll Cardiol 1988;11:579–84.
7. Hall SA, Brickner ME, Willett DL, Irani WN, Afridi I, Grayburn PA. Assessment of mitral regurgitation severity by Doppler color flow mapping of the vena contracta [see comments]. Circulation 1997;95:636–42.
8. Recusani F, Bargiggia G, Yoganathan A, et al. A new method for quantification of regurgitant flow rate using color Doppler flow imaging of the flow convergence region proximal to a discrete orifice: an in vitro study. J Am Coll Cardiol 1991;83:594–604.
9. Jenni R, Ritter M, Eberli F, Grimm J, Krayenbühl H. Quantification of mitral regurgitation with amplitude-weighted mean velocity from continuous wave Doppler spectra. Circulation 1989;79:1294–9.
10. Enriquez-Sarano M, Kaneshige A, Tajik A, Bailey K, Seward J. Amplitude-weighted mean velocity: clinical utilization for quantitation of mitral regurgitation. J Am Coll Cardiol 1993;22:1684–90.
11. Thomas J, Liu C, Flachskampf F, O'Shea J, Davidoff R, Weyman A. Quantification of jet flow by momentum analysis: an in vitro color Doppler flow study. Circulation 1990;81:247–59.
12. Simpson I, De Belder M, Kenny A, Martin M, Nihoyannopoulos P. How to quantitate valve regurgitation by echo Doppler techniques. Br Heart J 1995;73 Suppl 2:1–9.
13. Enriquez-Sarano M, Bailey K, Seward J, Tajik A, Krohn M, Mays J. Quantitative Doppler assessment of valvular regurgitation. Circulation 1993; 87:841–8.
14. Klein A, Obarski T, Stewart W, et al. Transesophageal Doppler echocardiography of pulmonary venous flow: a new marker of mitral regurgitation severity. J Am Coll Cardiol 1991;18:518–26.
15. Rossvoll O, Hatle L. Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: relation to left ventricular diastolic pressures. J Am Coll Cardiol 1993;21:1686–96.
16. Appleton C. Doppler assessment of left ventricular diastolic function: the refinements continue. J Am Coll Cardiol 1993;21:1697–700.
17. Pasierski T, Alton M, Pearson A. Transesophageal echocardiographic characterization of pulmonary vein flow not due to atrial contraction or mitral regurgitation. Am J Cardiol 1991;68:415–8.
18. Castello R, Pearson A, Lenzen P, Labovitz A. Effect of mitral regurgitation on pulmonary venous velocities derived from transesophageal echocardiography color-guided pulsed Doppler imaging. J Am Coll Cardiol 1991;17: 1499–506.
19. Klein A, Stewart W, Bartlett J, et al. Effects of mitral regurgitation on pulmonary venous flow and left atrial pressure: an intraoperative transesophageal echocardiographic study. J Am Coll Cardiol 1992;1992:1345–52.
20. Sahn D, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantification in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.
21. Schiller N, Shah P, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989;2:358–67.
22. Smith M, Grayburn P, Spain M, DeMaria A. Observer variability in the quantitation of Doppler color flow jet areas for mitral and aortic regurgitation. J Am Coll Cardiol 1988;11:579–84.
23. Bland J, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.

24. Croft C, Lipscomb K, Mathis K, et al. Limitations of qualitative angiographic grading in aortic or mitral regurgitation. Am J Cardiol 1984;53:1593–8.
25. Lopez J, Hanson S, Orchard R, Tan L. Quantification of mitral valvular incompetence. Cathet Cardiovasc Diagn 1985;11:139–52.
26. Simpson I. Quantitative color Doppler flow mapping: is flow convergence at the end of the rainbow? Circulation 1993;87:1762–4.
27. Enriquez-Sarano M, Seward J, Bailey K, Tajik A. Effective regurgitant orifice area: a noninvasive Doppler development of an old hemodynamic concept. J Am Coll Cardiol 1994;23:443–51.
28. Seiler C, Aeschbacher B, Meier B. Assessment of mitral regurgitation by the flow convergence (PISA-) method: can the spectral Doppler measurement of the regurgitant jet be avoided [abstract]? Eur Heart J 1997;19 Suppl:327.