Effective Mitral Regurgitant Orifice Area: Clinical Use and Pitfalls of the Proximal Isovelocity Surface Area Method

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Objectives. We attempted to determine the accuracy and pitfalls of calculating the mitral regurgitant orifice area with the proximal isovelocity surface area method in a clinical series that included patients with valvular prolapse and eccentric jets.

Background. The effective regurgitant orifice area, a measure of lesion severity of mitral regurgitation, can be calculated by the proximal isovelocity surface area method, the accuracy and pitfalls of which have not been established.

Methods. In 119 consecutive patients with isolated mitral regurgitation, effective regurgitant orifice area was measured by the proximal isovelocity surface area method and compared with measurements simultaneously obtained by quantitative Doppler and quantitative two-dimensional echocardiography.

Results. The effective mitral regurgitant orifice area measured by the proximal isovelocity surface area method tended to be overestimated compared with that measured by quantitative

Doppler and quantitative two-dimensional echocardiography (38 ± 39 vs. 36 ± 33 mm^2 [p = 0.09] and 34 ± 32 mm^2 [p = 0.02], respectively). Overestimation was limited to patients with prolapse (61 ± 43 vs. 56 ± 35 mm^2 [p = 0.05] and 54 ± 34 mm^2 [p = 0.014]) and was restricted to patients with nonoptimal flow convergence (n = 7; 137 ± 35 vs. 84 ± 34 mm^2 [p = 0.002] and 79 ± 33 mm^2 [p = 0.002]). In patients with optimal flow convergence (n = 112), excellent correlations with both reference methods were obtained (r = 0.97, SEE 6 mm^2 and r = 0.97, SEE 7 mm^2, p < 0.0001).

Conclusions. In calculating the mitral effective regurgitant orifice area with the proximal isovelocity surface area method, the observed pitfall (overestimation due to nonoptimal flow convergence) is rare. Otherwise, the method is reliable and can be used clinically in large numbers of patients.

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Semiquantitative grading of mitral regurgitation is used frequently but is hindered by important limitations, for both angiography (1) and color flow Doppler imaging (2,3), which leads to frequent and significant clinical discrepancies (4). Consequently, ongoing research is directed toward quantitation of the regurgitation (5,6). Recently, new developments in the hemodynamic concept (7) of effective regurgitant orifice area measurement (8,9) have allowed the severity of the regurgitant lesion to be quantitated noninvasively. The effective regurgitant orifice area is a major determinant of the effect of valve regurgitation on the left ventricle and left atrium and provides information in addition to that furnished by a classic variable such as regurgitant fraction (8). To allow calculation of the effective regurgitant orifice area in all clinical circumstances, it is essential that several methods of measurement be available.

The recently described flow convergence, or proximal isovelocity surface area (PISA), method (10,11) has been validated

in vitro (12,13) and used to measure the effective orifice area of mitral stenosis (14) or regurgitation (9) in preliminary clinical series. However, in vitro studies demonstrated that the shape (15) and radius (16) of the flow convergence zone vary with the selected aliasing velocity and produce potential variations in the calculated flow rate that can result in significant error. Similarly, clinical studies suggested that overestimation of flow rate may occur with severe regurgitations (11,17). Eccentric jets due to mitral prolapse are also a potential source of error (18).

The available clinical series in which the PISA method was used to calculate the effective regurgitant orifice area included a limited number of patients with severe mitral regurgitation (9), and the accuracy in patients with eccentric jets and mitral valve prolapse could not be analyzed. Thus, the reliability and potential pitfalls of the method in all types and degrees of regurgitation have not been established.

The hypothesis examined was that appropriate measurement of the flow convergence region allows reliable calculation of the effective regurgitant orifice area and can be obtained in most patients and in any type and degree of mitral regurgitation. To prove this hypothesis, this method was prospectively compared with simultaneously performed quantitative Doppler and echocardiography in a large number of patients with mitral regurgitation.

Methods

Patients. The patients were included in the study prospectively in 1992 and 1993. Inclusion criteria were 1) presence of pure isolated mitral regurgitation of at least mild degree, as determined by standard Doppler color flow imaging; 2) complete two-dimensional echocardiographic and Doppler measurement, allowing quantitation of mitral regurgitation and measurement of the effective regurgitant orifice area; and 3) measurement of the effective regurgitant orifice area by the PISA method. During the period, 125 patients who met criterion 1 were screened. Three patients did not meet criterion 2 and were excluded. Measurement of the effective regurgitant orifice area with the PISA method could not be achieved in 3 patients, leaving a study group of 119 (mean [±SD] 68 ± 13 years; 83 men, 36 women). Of the 119 patients, 92 were in sinus rhythm and 27 in atrial fibrillation. The mechanism of regurgitation was mitral valve prolapse in 60 patients, ischemic or functional regurgitation (or both) in 45 and miscellaneous causes in 14. The jet was central in 72 patients and eccentric in 47. In 16 patients, PISA measurements of the effective regurgitant orifice area were repeated by a second observer during the same examination for the purpose of determining interobserver variability.

Theoretic basis. The theoretic basis for calculating the effective regurgitant orifice (ERO) area has been described previously (8,9,19). For any given orifice,

$$\text{Flow} = \text{Area} \times \text{Velocity.} \qquad [1]$$

For a regurgitant orifice,

$$\text{Regurgitant flow} = \text{ERO area} \times \text{Regurgitant velocity.} \qquad [2]$$

Thus,

$$\text{ERO area} = \frac{\text{Regurgitant flow}}{\text{Regurgitant velocity}}. \qquad [3]$$

Integrated over the cardiac cycle,

$$\text{ERO area} = \frac{\text{Regurgitant volume}}{\text{Regurgitant time velocity integral}}. \qquad [4]$$

Doppler echocardiographic analysis. All patients had a complete two-dimensional and Doppler echocardiographic study using multiple windows, as described previously (20,21). Data collection for quantitative Doppler echocardiography, quantitative two-dimensional Doppler echocardiography and the PISA method was performed during the same examination.

Proximal isovelocity surface area method. The theoretic basis for the PISA method, reviewed elsewhere (10,13), is based on analysis of the flow convergence proximal to the regurgitant orifice. Blood flow entering the regurgitant orifice accelerates progressively and concentrically to produce a series of shells of identical velocity that converge toward the regurgitant orifice. Because the blood flow in the flow convergence region enters the regurgitant orifice exclusively, the principle of conservation of mass can be applied. Thus, the flow rate through the proximal isovelocity surfaces is equal to the

regurgitant flow rate and can be measured as the product of the area of the shell multiplied by the velocity at the same level. Assuming a hemispheric shape of the proximal isovelocity surface,

$$\text{Regurgitant flow} = 2 \times \pi \times r^2 \times Vr, \qquad [5]$$

where r = radius of the measured shell; and Vr = velocity of the shell. Practically, the isovelocity surface area is made visible by shifting the baseline of the color flow scale, and r is measured in the centerline of the flow convergence region. The position of the transducer was modified to minimize the angle between the centerline of the flow convergence and the ultrasound beam. Because within the hemisphere lateral flows at an angle close to 90° to the ultrasound beam are not visible, the optimal visible shape of the flow convergence region is a portion of a sphere (Fig. 1) (13). The baseline shift was adjusted to obtain such a shape, which was noted prospectively and achieved in all but six patients (Fig. 2). The optimal timing of the flow convergence measured in the cardiac cycle was midsystole, which was achieved in all but one patient. Thus, optimal measurements of the flow convergence region could be achieved in 112 patients and suboptimal measurements in 7, all with valve prolapse and eccentric jet.

The effective regurgitant orifice (ERO) area by the PISA method was calculated with equation 3 as follows:

$$\text{ERO area (PISA)} = \frac{\text{Regurgitant flow}}{\text{Regurgitant velocity}}, \qquad [6]$$

where regurgitant velocity was the maximal velocity of the mitral regurgitant jet as obtained with continuous wave Doppler (Fig. 1).

Quantitative Doppler and two-dimensional echocardiography. The effective regurgitant orifice area was calculated with equation 4, as previously described (8), using the regurgitant time velocity integral obtained by tracing the contour of the mitral regurgitant jet obtained by continuous wave Doppler.

Quantitative Doppler. With quantitative Doppler, the mitral and aortic stroke volumes were calculated, as described previously (5,22), as the product of the pulsed wave Doppler time velocity integral and the area of the annuli of the mitral and aortic valves. The regurgitant volume was calculated as follows:
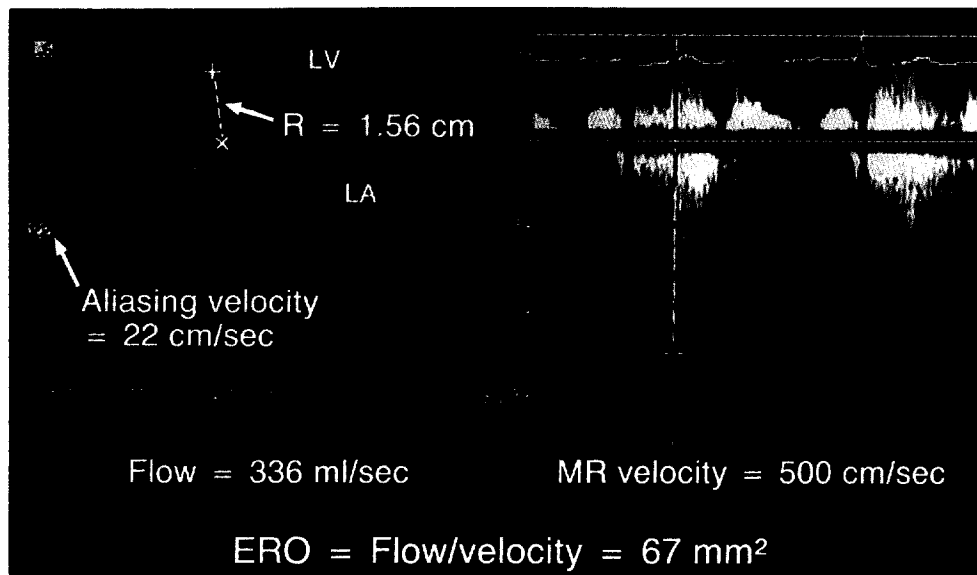
Regurgitant volume (Doppler)

$$= (\text{Mitral} - \text{Aortic}) \text{ Stroke volume.} \qquad [7]$$

The effective regurgitant orifice area was calculated as follows:

$$\text{ERO area (Doppler)} = \frac{\text{Regurgitant volume (Doppler)}}{\text{Regurgitant time velocity integral}}. \qquad [8]$$

Quantitative two-dimensional echocardiography. Quantitative two-dimensional echocardiography (2-DE) was applied as described previously (6). Left ventricular volumes were measured at end-diastole and at end-systole by using the biapical Simpson's rule (method of disks) (23), as recommended by the American Society of Echocardiography.

Figure 1. Example of calculation of effective regurgitant orifice using the proximal isovelocity surface area method. **Left,** Color flow imaging of the flow convergence region. **Right,** Continuous wave Doppler echocardiography of the mitral regurgitant (MR) jet. ERO = effective regurgitant orifice area; LA = left atrium; LV = left ventricle; R = radius of flow convergence region.

The total left ventricular stroke volume was calculated as the difference between the end-diastolic and end-systolic volumes. The regurgitant volume was calculated as follows:

Regurgitant volume (2-DE)

$$= (\text{Left ventricular} - \text{Aortic}) \text{ Stroke volume.} \quad [9]$$

The effective regurgitant orifice area was calculated as follows:

$$\text{ERO area (2-DE)} = \frac{\text{Regurgitant volume (2-DE)}}{\text{Regurgitant time velocity integral}}. \quad [10]$$

Statistical analysis. Descriptive results were expressed as mean value ± SD. The calculated effective regurgitant orifice area obtained by the three methods was compared by analysis of variance for repeated measures and paired t test in the

entire study group and in subgroups defined according to the presence of mitral valve prolapse or an eccentric jet of mitral regurgitation and the ability to obtain optimal flow convergence measurements. The relation between the PISA method and the quantitative Doppler and quantitative two-dimensional echocardiographic methods of measuring the effective regurgitant orifice area was analyzed with linear regression and the Bland and Altman method (24), plotting and regressing the method difference against the method mean value. To determine the independent predictors of overestimation, or underestimation, the method difference was also used as the dependent variable in a multiple linear regression analysis in which the value of the effective regurgitant orifice (measured with reference methods) and the presence of prolapse, eccentric jet and appropriate flow convergence were used as independent variables; $p < 0.05$ was considered significant.

Figure 2. Examples of suboptimal flow convergences with nonhemispheric shape: oblong (high flow) **(left)**; curvilinear (interaction wall-flow convergence) **(right)**.

Table 1. Variables Used to Calculate Effective Regurgitant Orifice Area

Variable	Mean ± SD
PISA	
Vr	25 ± 9 cm/s
r	0.99 ± 0.40 cm
Regurgitant flow	191 ± 198 cm³/s
Q Doppler	
Regurgitant volume	52 ± 43 ml/beat
Regurgitant fraction	39% ± 18%
Q-2DE	
Regurgitant volume	50 ± 42 ml/beat
Regurgitant fraction	38% ± 18%
Regurgitant velocity	504 ± 62 cm/s
Regurgitant TVI	156 ± 31 cm

PISA = proximal isovelocity surface area; Q Doppler = quantitative Doppler echocardiography; Q-2DE = quantitative two-dimensional Doppler echocardiography; r = radius of flow convergence region; Vr = selected aliasing velocity; TVI = time velocity integral.

Results

The feasibility of measuring the mitral effective regurgitant orifice area with the PISA method was excellent: overall, 98% (119 of 122) and optimal measurement in 92% (112 of 122).

Correlation between the Doppler and the two-dimensional methods of calculation of the effective regurgitant orifice was excellent ($r = 0.98$, $p < 0.0001$, SEE 5.4 mm²), and the absolute value of the difference between the two methods was 3.9 ± 3.9 mm².

The variables used to calculate the effective regurgitant orifice area by the three methods are presented in Table 1. The effective regurgitant orifice area calculated by the three methods in the overall study group and in subgroups of patients is presented in Table 2. It should be noted that overall the PISA method tended to overestimate the effective regurgitant orifice area. This was of borderline significance compared with quantitative Doppler and of statistical significance compared with quantitative two-dimensional echocardiography. The overestimation was restricted to the groups of patients with mitral valve prolapse and with eccentric jets. This overestimation

occurred only for patients with nonoptimal proximal flow convergence measurements. Multivariate analysis of the difference between the PISA method and the reference methods (i.e., quantitative Doppler and quantitative two-dimensional echocardiography) showed that the independent determinants of overestimation were the area of effective regurgitant orifice ($p = 0.04$ and $p = 0.02$, respectively, for quantitative Doppler echocardiography and quantitative two-dimensional echocardiography) but, most significantly, a nonoptimal flow convergence measurement ($p = 0.0001$ for both reference methods). Thus, a valvular prolapse or an eccentric jet is not independently associated with overestimation if the flow convergence is optimal.

Good correlations were found between the effective regurgitant orifice area as measured by the PISA method and the quantitative Doppler echocardiographic method ($r = 0.92$, $p < 0.0001$) and the quantitative two-dimensional echocardiographic method ($r = 0.91$, $p < 0.0001$). However, the standard error of the estimate was large, 15 and 16 mm², respectively, using quantitative Doppler and quantitative two-dimensional echocardiography as reference methods. When restricted to the 112 patients with optimal flow convergence measurements, excellent correlations were found between the PISA method and quantitative Doppler echocardiography ($r = 0.97$, $p < 0.0001$, SEE 6 mm²) and quantitative two-dimensional echocardiography ($r = 0.97$, $p < 0.0001$, SEE 7 mm²) (Fig. 3).

Quality control plots using the Bland and Altman method in patients with optimal flow convergence showed that there was no overall overestimation and no specific trend for overestimation or underestimation according to the level of the effective regurgitant orifice area (Fig. 4). Also, in patients with optimal flow convergence, the absolute values of the differences (PISA − Quantitative Doppler echocardiography) and (PISA − Quantitative two-dimensional echocardiography) were 4.7 ± 4.3 and 5.0 ± 4.3 mm², respectively. However, the superposition of suboptimal cases on the graphs clearly demonstrated the overestimation of the effective regurgitant orifice area in these patients.

For the 16 patients in whom the PISA measurements were repeated by a second observer, interobserver variability was

Table 2. Effective Regurgitant Orifice Area Calculated With Proximal Isovelocity Surface Area Method and Quantitative Doppler and Quantitative Two-Dimensional Echocardiography

Study Group	No. of Pts	ERO (mm²)				
		PISA	Q Doppler	p Value*	Q-2DE	p Value*
Overall	119	38 ± 39	36 ± 33	0.09	34 ± 32	0.02
Prolapse	60	61 ± 43	56 ± 35	0.05	54 ± 34	0.014
No prolapse	59	15 ± 9	15 ± 10	NS	15 ± 11	NS
Eccentric jet	47	66 ± 41	61 ± 34	0.07	58 ± 34	0.013
Noneccentric jet	72	20 ± 23	19 ± 19	NS	19 ± 19	NS
Optimal	112	32 ± 30	33 ± 30	NS	32 ± 30	NS
Nonoptimal	7	137 ± 35	84 ± 34	0.002	79 ± 33	0.002

*Applies to comparison with the proximal isovelocity surface area (PISA) method. ERO = effective regurgitant orifice; Pts = patients; other abbreviations as in Table 1.
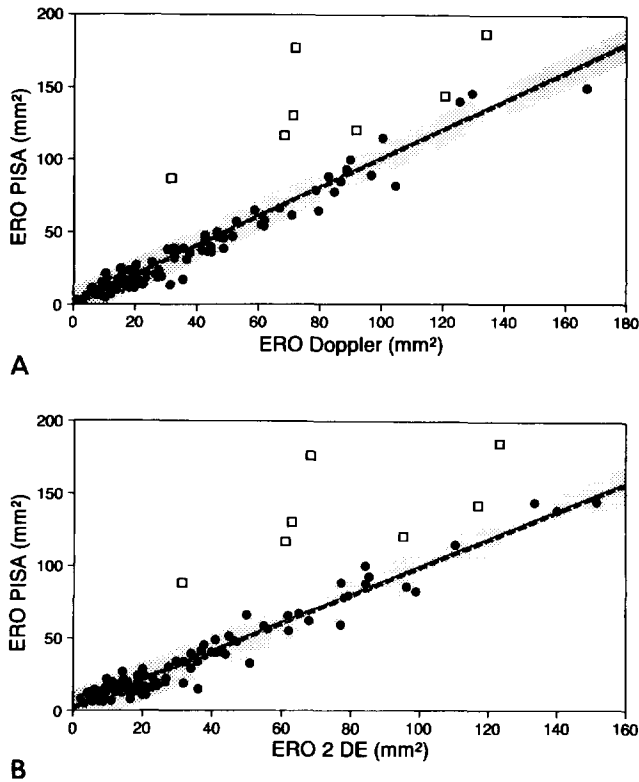
Figure 3. Correlations between the effective regurgitant orifice (ERO) area obtained by the proximal isovelocity surface area (PISA) method and by quantitative Doppler echocardiography (A) and quantitative two-dimensional echocardiography (2 DE) (B). **Dashed line** = identity line; **circles** = patients with optimal flow convergence; **solid line** and **gray zone** = respectively, regression line and 95% confidence interval in patients with optimal flow convergence; **squares** = patients with nonoptimal flow convergence.

Figure 4. Scatter plot of the method differences (proximal isovelocity surface area [PISA] minus the reference method [Doppler]) compared with the method mean (proximal isovelocity surface area plus reference method divided by 2) using for reference the calculation of effective regurgitant orifice (ERO) area by quantitative Doppler echocardiography (A) and quantitative two-dimensional (2 DE) echocardiography (B). Symbols as in Figure 3.

low, with a standard error of the estimate of the effective regurgitant orifice area of 4 mm².

Discussion

Present study. The present study shows that the PISA method of measurement of the effective regurgitant orifice area can be performed in a large number of unselected patients with mitral regurgitation of various causes. The pitfall of the method is overestimation of the mitral effective regurgitant orifice area observed only in patients with mitral valve prolapse and eccentric jets but restricted to patients with a nonoptimal flow convergence region. Thus, with optimal timing and shape of the flow convergence region, the PISA method can be used to obtain highly reliable measurements of the effective regurgitant orifice area, including that in patients with severe regurgitation, valve prolapse or eccentric jets.

Effective regurgitant orifice area. The concept of measuring the effective regurgitant orifice area was described >40 years ago (7), but the measurement has remained elusive in clinical practice because of the many assumptions and indirect calculations introduced in the invasive hemodynamic formula.
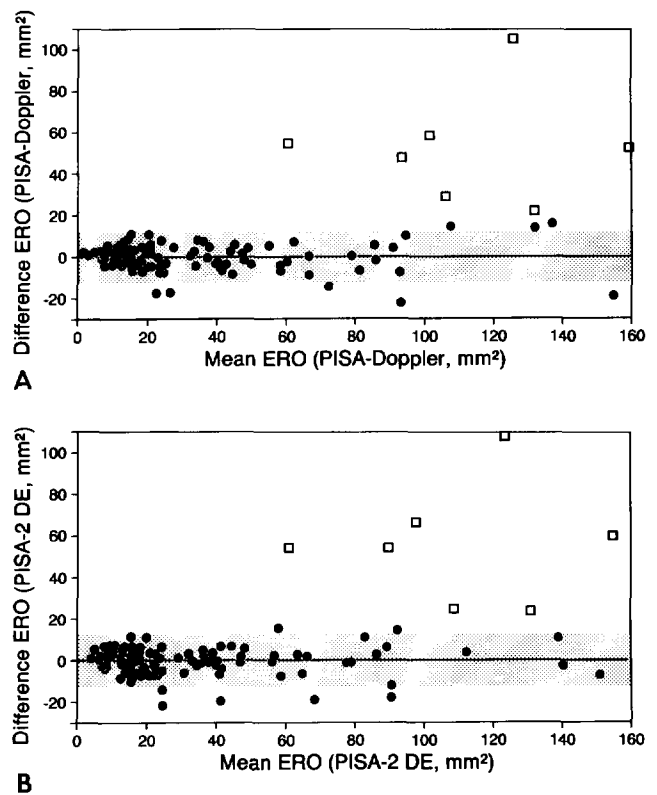
However, this concept has been the basis of the experimental analysis of the influences of loading conditions and contractility on the degree of mitral regurgitation. These studies suggested that the effective regurgitant orifice is less sensitive to hemodynamic manipulation than are the regurgitant volume and fraction (25–27). With the development of Doppler techniques, there is renewed interest in this concept and in its clinical application in patients with mitral and aortic regurgitation (8,9,28,29). The effective regurgitant orifice area is a measure of the severity of the regurgitant lesion. It is also a major determinant of the enlargement of the left ventricle and left atrium in mitral regurgitation and provides additional information compared with regurgitant volume and regurgitant fraction (8). Thus, effective regurgitant orifice area is a fundamental quantitative measure of mitral regurgitation. However, it represents a new variable that has not been available in clinical practice, and future longitudinal studies are necessary to determine its prognostic implications in different types of mitral regurgitation. Thus, validation of various methods, applicable in clinical practice, for the calculation of effective regurgitant orifice area in all possible clinical circumstances is essential.

Proximal isovelocity surface area method. Flow acceleration toward the regurgitant mitral valve has been observed by pulsed wave Doppler (29), but color flow imaging in combination with a baseline shift for the analysis of the flow convergence region was the key factor in the development of the PISA method of quantitating mitral regurgitation. On the basis of the principle of the conservation of mass, this method is attractive because of the simplicity of its clinical application for measuring flow through restrictive orifices (10). It has been used not only in mitral regurgitation (11,17,30,31), but also in mitral stenosis (14), periprosthetic regurgitation (32,33) and in shunts through restrictive orifices (34). However, for the calculation of the effective regurgitant orifice area, the experience with this method is still preliminary (9), and the pitfalls of the technique in clinical practice have not been analyzed fully. The finite nature of the regurgitant orifice in mitral regurgitation is not an impediment to the technique (13), but the user-defined aliasing velocity of the color flow mapping is an essential determinant of the shape of the visualized acceleration shell and can be a source of overestimation or underestimation of flow (15), which represents an important limitation of the use of M-mode color (35). On this basis, the technique used in the present study was two-dimensional color flow imaging to allow visual assessment of the shape of the flow convergence region, which was prospectively noted as optimal or suboptimal. In the present study, overestimation of regurgitant flow and the effective regurgitant orifice area occurred for two reasons: 1) In six patients, the shape of the flow convergence region was not optimal, being either hemielliptic (due to high flow and an inappropriate aliasing velocity selection) (35) or asymmetric (due to compression of the flow convergence zone) (18); 2) in one case, flow convergence was not measured in midsystole but at end-systole in a patient with mitral valve prolapse, leading to overestimation of the mean effective regurgitant orifice area (but underestimation of the maximal orifice), because the timing of the flow measurement and the maximal velocity were not appropriately coincident. As demonstrated in Figure 4, the degree of overestimation of the inappropriate measurements could be considerable. However, with experience, these cases are easily identified, and a proper course of action can be taken, such as modifying the aliasing velocity or using an algorithm of correction for the degree of compression (14) or deciding not to use the technique if a proper flow convergence region cannot be visualized.

Limitations of the study. In the present study, no invasive measurement of the effective regurgitant orifice area was performed. For all practical purposes, such a method does not exist, mainly because of the inaccuracies of measurements of flow by invasive methods (36).

The two reference methods used for calculation of regurgitant orifice have their own limitations. The use of quantitative Doppler echocardiography to measure the regurgitant volume has been a point of controversy (5,37), but with consistent use it has proved to be a very reliable method (22). Also, ventricular volumes as measured by two-dimensional echocardiography have been suggested as underestimating the

angiographic volumes (38). However, this underestimation was not confirmed with the use of other techniques (39,40), and current high resolution imaging technology allows accurate measurement of left ventricular volumes (41).

Furthermore, the measurement of the effective regurgitant orifice area has been validated previously in our laboratory (8), and the consistency of the results obtained by quantitative Doppler and quantitative echocardiography further confirms the appropriateness of the reference methods used.

Clinical implications. The present study demonstrated the following:

1. The PISA method of measuring the effective regurgitant orifice area in patients with mitral regurgitation can be performed in a clinical laboratory in a large number of patients, including those with mitral valve prolapse and eccentric jets.

2. The usual pitfall is overestimation of the regurgitant flow and the effective regurgitant orifice area. However, this type of error is rare and can be identified on the basis of an inappropriate flow convergence region.

3. Optimal flow convergence can be obtained in most cases, allowing the effective regurgitant orifice area of mitral regurgitation to be calculated reliably. Therefore, combined methods can now be used during a single Doppler examination to provide consistent and reliable measurements of the effective regurgitant orifice area of mitral regurgitation.

References

1. Croft CH, Lipscomb K, Mathis K, et al. Limitations of qualitative angiographic grading in aortic or mitral regurgitation. Am J Cardiol 1984;53: 1593-8.
2. Chen C, Thomas JD, Anconina J, et al. Impact of impinging wall jet on color Doppler quantification of mitral regurgitation. Circulation 1991;84:712-20.
3. Enriquez-Sarano M, Tajik AJ, Bailey KR, Seward JB. 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.
4. Slater J, Gindea AJ, Freedberg RS, 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.
5. Rokey R, Sterling LL, Zoghbi WA, et al. Determination of regurgitant fraction in isolated mitral or aortic regurgitation by pulsed Doppler two-dimensional echocardiography. J Am Coll Cardiol 1986;7:1273-8.
6. Blumlein S, Bouchard A, Schiller NB, et al. Quantitation of mitral regurgitation by Doppler echocardiography. Circulation 1986;74:306-14.
7. Gorlin R, Dexter L. Hydraulic formula for the calculation of the cross-sectional area of the mitral valve during regurgitation. Am Heart J 1952;43: 188-205.
8. Enriquez-Sarano M, Seward JB, Bailey KR, Tajik AJ. Effective regurgitant orifice area: a noninvasive Doppler development of an old hemodynamic concept. J Am Coll Cardiol 1994;23:443-51.
9. Vandervoort PM, Rivera M, Mele D, et al. Application of color Doppler flow mapping to calculate effective regurgitant orifice area: an in vitro study and initial clinical observations. Circulation 1993;88:1150-6.
10. Recusani F, Bargiggia GS, Yoganathan AP, 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. Circulation 1991;83:594-604.
11. Bargiggia GS, Tronconi L, Sahn DJ, et al. A new method for quantitation of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. Circulation 1991;84:1481-9.
12. Utsunomiya T, Doshi F, Patel D, et al. Calculation of volume flow rate by the proximal isovelocity surface area method: simplified approach using color Doppler zero baseline shift. J Am Coll Cardiol 1993;22:277-82.

13. Rodriquez L, Anconina J, Flachskampf FA, Weyman AE, Levine RA, Thomas JD. Impact of finite orifice size on proximal flow convergence: implications for Doppler quantification of valvular regurgitation. Circ Res 1992;70:923-30.

14. Rodriquez L, Thomas JD, Monterroso V, et al. Validation of the proximal flow convergence method: calculation of orifice area in patients with mitral stenosis. Circulation 1993;88:1157-65.

15. Deng Y-B, Shiota T, Shandas R, Zhang J, Sahn DJ. Determination of the most appropriate velocity threshold for applying hemispheric flow convergence equations to calculate flow rate: selected according to the transorifice pressure gradient. Circulation 1993;88:1699-708.

16. Giesler MO, Stauch M. Color Doppler determination of regurgitant flow: from proximal isovelocity surface areas to proximal velocity profiles: an in vitro study. Echocardiography 1992;9:51-62.

17. Chen C, Koschyk D, Brockhoff C, et al. Noninvasive estimation of regurgitant flow rate and volume in patients with mitral regurgitation by Doppler color mapping of accelerating flow field. J Am Coll Cardiol 1993;21:374-83.

18. Thomas JD, Powell KA, Greenberg N, Vandervoort PM, Stewart WJ. Use of the proximal flow convergence method to quantitate mitral regurgitation in patients with a flail leaflet: lessons from fluid dynamical modelling [abstract]. J Am Coll Cardiol 1993;21:485A.

19. Vandervoort PM, Thoreau DH, Rivera JM, Levine RA, Weyman AE, Thomas JD. Automated flow rate calculations based on digital analysis of flow convergence proximal to regurgitant orifices. J Am Coll Cardiol 1993;22:535-41.

20. Tajik AJ, Seward JB, Hagler DJ, Mair DD, Lie JT. Two-dimensional real-time ultrasonic imaging of the heart and great vessels: technique, image orientation, structure identification, and validation. Mayo Clin Proc 1978; 53:271-303.

21. Nishimura RA, Miller FA Jr, Callahan MJ, Benassi RC, Seward JB, Tajik AJ. Doppler echocardiography: theory, instrumentation, technique, and application. Mayo Clin Proc 1985;60:321-43.

22. Enriquez-Sarano M, Bailey KR, Seward JB, Tajik AJ, Krohn MJ, Mays JM. Quantitative Doppler assessment of valvular regurgitation. Circulation 1993; 87:841-8.

23. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989;2:358-67.

24. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-10.

25. Yoran C, Yellin EL, Becker RM, Gabbay S, Frater RWM, Sonnenblick EH. Dynamic aspects of acute mitral regurgitation: effects of ventricular volume, pressure and contractility on the effective regurgitant orifice area. Circulation 1979;60:170-6.

26. Yoran C, Yellin EL, Becker RM, Gabbay S, Frater RWM, Sonnenblick EH. Mechanism of reduction of mitral regurgitation with vasodilator therapy. Am J Cardiol 1979;43:773-7.

27. Yoran C, Yellin EL, Hori M, et al. Effects of heart rate on experimentally produced mitral regurgitation in dogs. Am J Cardiol 1983;52:1345-9.

28. Reimold SC, Ganz P, Bittl JA, et al. Effective aortic regurgitant orifice area: description of a method based on the conservation of mass. J Am Coll Cardiol 1991;18:761-8.

29. Yeung AC, Plappert T, St John Sutton MG. Calculation of aortic regurgitation orifice area by Doppler echocardiography: an application of the continuity equation. Br Heart J 1992;68:236-40.

30. Rivera JM, Vandervoort PM, Thoreau DH, Levine RA, Weyman AE, Thomas JD. Quantification of mitral regurgitation with the proximal flow convergence method: a clinical study. Am Heart J 1992;124:1289-96.

31. Giesler M, Grossmann G, Schmidt A, et al. Color Doppler echocardiographic determination of mitral regurgitant flow from the proximal velocity profile of the flow convergence region. Am J Cardiol 1993;71:217-24.

32. Yoshida K, Yoshikawa J, Akasaka T, Nishigami K, Minagoe S. Value of acceleration flow signals proximal to the leaking orifice in assessing the severity of prosthetic mitral valve regurgitation. J Am Coll Cardiol 1992;19: 333-8.

33. Bargiggia GS, Tronconi L, Raisaro A, et al. Color Doppler diagnosis of mechanical prosthetic mitral regurgitation: usefulness of the flow convergence region proximal to the regurgitant orifice. Am Heart J 1990;120:1137-42.

34. Rittoo D, Sutherland GR, Shaw TRD. Quantification of left-to-right atrial shunting and defect size after balloon mitral commissurotomy using biplane transesophageal echocardiography, color flow Doppler mapping, and the principle of proximal flow convergence. Circulation 1993;87:1591-603.

35. Zhang J, Jones M, Shandas R, et al. Accuracy of flow convergence estimates of mitral regurgitant flow rates obtained by use of multiple color flow Doppler M-mode aliasing boundaries: an experimental animal study. Am Heart J 1993;125:449-58.

36. Lopez JF, Hanson S, Orchard RC, Tan L. Quantification of mitral valvular incompetence. Cathet Cardiovasc Diagn 1985;11:139-52.

37. Iliceto S, D'Ambrosio G, Amico A, et al. Errors in measurements of stroke volume for invasive and echo-Doppler evaluations of valvular regurgitant fractions: clinical evaluation and computer simulation. Eur Heart J 1990;11: 355-60.

38. Erbel R, Schweizer P, Lambertz H, et al. Echoventriculography—a simultaneous analysis of two-dimensional echocardiography and cineventriculography. Circulation 1983;67:205-15.

39. Weiss JL, Eaton LW, Kallman CH, Maughan WL. Accuracy of volume determination by two-dimensional echocardiography: defining requirements under controlled conditions in the ejecting canine left ventricle. Circulation 1983;67:889-95.

40. Buser PT, Auffermann W, Holt WW, et al. Noninvasive evaluation of global left ventricular function with use of cine nuclear magnetic resonance. J Am Coll Cardiol 1989;13:1294-300.

41. Görge G, Erbel R, Brennecke R, Rupprecht HJ, Todt M, Meyer J. High-resolution two-dimensional echocardiography improves the quantification of left ventricular function. J Am Soc Echocardiogr 1992;5:125-34.