Application of the Proximal Flow Convergence Method to Calculate the Effective Regurgitant Orifice Area in Aortic Regurgitation

CHRISTOPHE M. TRIBOUILLOY, MD, PhD, MAURICE ENRIQUEZ-SARANO, MD,
SARA L. FETT, BS,* KENT R. BAILEY, PhD,* JAMES B. SEWARD, MD, A. JAMIL TAJIK, MD

Rochester, Minnesota

Objectives. We sought to determine the reliability of the proximal isovelocity surface area (PISA) method for calculation of effective regurgitant orifice (ERO) of aortic regurgitation (AR).

Background. The ERO area can be calculated by the PISA method, but this method has not been validated in AR.

Methods. ERO calculation by the PISA method was undertaken prospectively in 71 consecutive patients with isolated AR and achieved in 64 and compared with two simultaneous reference methods (quantitative Doppler and quantitative two-dimensional echocardiography). In addition, this method was compared with angiography in 12 patients, with surgical assessment in 18 patients and with ventricular volumes in all patients.

Results. Good correlations between PISA and reference methods were obtained (both r = 0.90, both p < 0.0001), but a trend toward underestimation of the ERO by the PISA method was noted (24 ± 19 vs. 26 ± 22 mm^2 and 27 ± 23 mm^2, respectively, both p = 0.04). However, this trend was confined to five patients

with an obtuse flow convergence angle ($>220°$), and on multivariate analysis this variable was the only independent determinant of underestimation of the ERO. In contrast, in 59 patients with a flat flow convergence ($\leq220°$), the PISA method, in comparison with reference methods, showed excellent correlations, with a narrow standard error of the estimate (r = 0.95, SEE 5.4 mm^2, and r = 0.95, SEE 5.8 mm^2; all p < 0.0001) and no trend toward underestimation (22 ± 18 vs. 23 ± 16 mm^2, p = 0.44, and vs. 23 ± 18 mm^2, p = 0.34).

Conclusions. In patients with AR, the PISA method can be used to measure the ERO with reasonable feasibility. Underestimation of the ERO by PISA may occur in patients with an obtuse flow convergence angle. However, in most patients with appropriate flow convergence, PISA provides reliable measurement of the ERO of AR.

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Assessment of the degree of regurgitation is paramount to clinical decision-making in patients with aortic regurgitation (AR), because patients with severe AR most often require surgical treatment. Semiquantitative grading of AR with color and spectral Doppler echocardiography (1–3) or with angiography (4) is widely used, but both techniques are hindered by important limitations (5–8). Noninvasive and invasive quantitative estimations of regurgitant volume and regurgitant fraction are available (8,9), but regurgitant volume and fraction depend on loading conditions (10,11). Recently, noninvasive calculation of aortic effective regurgitant orifice (ERO), a measure of lesion severity in AR, was proposed (12). The ERO area is a fundamental descriptor of AR (13), determines the effect of AR on the left ventricle and provides information additional to the volume overload measurements such as

regurgitant fraction (12). However, measurement of the ERO area by quantitative Doppler echocardiography is not always feasible, and to obtain a high degree of reliability, a combination of methods is desirable (14).

There has been considerable interest in the proximal isovelocity surface area (PISA) method to assess the severity of valvular and congenital heart diseases (14–21). Based on the conservation of mass, the PISA method has been validated experimentally and clinically for calculating the effective orifice area in mitral stenosis (19) and mitral (14,16,21) and tricuspid (20) regurgitation. In AR, the importance of the concept of ERO has been underscored (12,13), and the PISA method has been pioneered in animal models (22), but the applicability of this method in patients with AR has not been documented (18).

Therefore, we hypothesized that the proximal flow convergence (FC) method allows a reliable determination of the ERO area of AR with great feasibility. To verify this hypothesis, the calculation of the ERO of AR by the PISA method was prospectively performed in patients with isolated AR, and the results were compared with those simultaneously obtained by two reference methods—quantitative Doppler echocardiography and quantitative two-dimensional echocardiography (12,14).

Methods

Patients. Patients were screened prospectively in the echocardiographic laboratory by one of the investigators. Inclusion criteria included 1) isolated and pure AR of at least mild degree, as determined by standard Doppler color flow imaging; 2) complete two-dimensional echocardiographic and Doppler measurements, allowing calculation of the ERO area of AR; and 3) assessment of the AR by the PISA method. Exclusion criteria included 1) associated mitral valve disease, particularly more than a trace of mitral regurgitation; 2) inability to obtain the continuous wave Doppler signal of AR; and 3) inability to acquire both quantitative reference methods.

In addition, 80 patients (46 men, age 57 ± 15 years) without regurgitation had the Doppler echocardiographic measurements prospectively performed to assess the accuracy of stroke volume measurements.

PISA method. The PISA method, derived from analysis of the FC region proximal to the regurgitant orifice and from the conservation of mass, has been previously described (14–16,20,23). Doppler color flow images of the proximal FC of the AR were obtained from an apical long-axis view. The position of the transducer was modified to minimize the angle between the centerline of the FC and the ultrasound beam. The frame rate was maximized by reducing the depth of imaging and by using the narrowest color sector window possible. A zoom view of the region of interest was obtained. The color flow velocity scale was maximized and its baseline shifted upward to reduce

the aliasing velocity until the FC region was clearly visualized of optimal shape and measurable. Because only the axial component of velocity was visualized with color flow imaging, the optimal visible shape of the FC region was close to a portion of a sphere, with the base of the truncated sphere located at the level of the regurgitant orifice, as previously demonstrated (14,23) (Fig. 1). The radial distance, r (radius), between the first aliasing contour (red–blue interface) of the FC region and the regurgitant aortic orifice was measured along the centerline of the FC region in early diastole, simultaneously with the maximal aortic regurgitant velocity.

Assuming a hemispheric shape of the PISA, the diastolic aortic regurgitant flow, R_{Flow}, was calculated as

$$R_{Flow} = 2\pi \times r^2 \times V_r$$

where r was the radius of the FC measured in early diastole, and V_r was the corresponding aliasing velocity (15). The aortic regurgitant ERO area was then calculated (14,16) as

$$ERO\ (PISA) = R_{Flow}/R_{Vel}$$

where R_{Vel} was the maximal velocity of the aortic regurgitant jet in early diastole recorded with continuous wave Doppler echocardiography from the apical, para-apical or right parasternal transducer position. In 12 patients, PISA measurements of the ERO area were repeated by a second observer during the same examination to determine the interobserver variability.

To assess the interaction of AR characteristics with the accuracy of the PISA method, four variables were analyzed: nonplanar FC, valvular prolapse, eccentricity of the AR jet and confinement by the aortic wall. The valvular coaptation zone was imaged at a high frame rate and with high contrast in the parasternal long-axis view. To assess whether nonplanar FC was present, the angle of the aortic leaflets forming the FC region (19–21), corresponding to the inverted aortic valvular funnel (Fig. 2), was measured on a printout of the specific

Figure 1. Example of calculation of the ERO area with the PISA method. **Left,** Color flow Doppler imaging of the proximal FC recorded from the apical view. **Right,** Aortic regurgitant jet recorded by continuous wave Doppler echocardiography. R = radius of FC in early diastole.
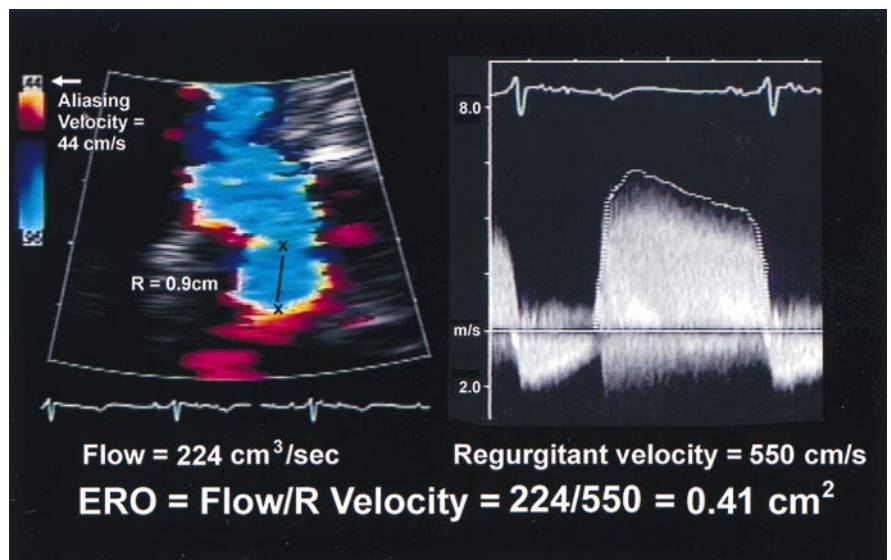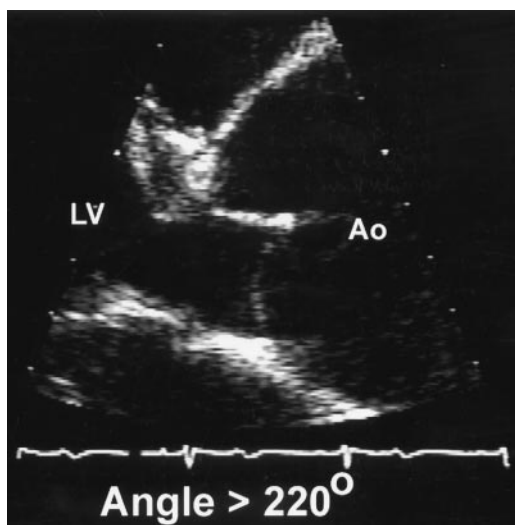
Figure 2. Flow convergence with an obtuse angle in a patient with aneurysm of the ascending aorta. The position of the aortic leaflets is associated with an obtuse angle of the FC region proximal to the regurgitant orifice (>220°). Ao = aorta; LV = left ventricle.

image with use of a protractor. Because of the potential limitations of such measurement, the patients were classified as having an obtuse angle (>220°) (corresponding to a change in ERO of at least 20%, depending on the shape of the FC region) (24) or a flat angle (≤220°) of FC. The angle classification was confirmed in all patients by multiple-view imaging of the aortic valve in diastole. The diagnosis of valvular prolapse was based on movement of the body of the cusps beyond the plane of the aortic annulus in diastole. An eccentric AR jet was determined by the direction of the jet immediately below the regurgitant orifice. Confinement of the FC was analyzed by measuring the size of the aorta at the sinuses and by observing possible compression of the FC by the aortic walls.

Doppler echocardiographic reference methods. All patients had complete two-dimensional and Doppler echocardiographic studies (25,26). Data for quantitative Doppler echocardiography and quantitative two-dimensional Doppler echocardiographic ERO area measurements (12,14) were collected simultaneously with the PISA method during the same examination. The aortic ERO area with quantitative Doppler echocardiography (ERO [Dop]) and with quantitative two-dimensional echocardiography (ERO [2D]) methods was calculated as

$$ERO = R_{Vol}/R_{TVI}$$

where R_{Vol} was the aortic regurgitant volume and R_{TVI} was the regurgitant time–velocity integral of the aortic regurgitant jet obtained by continuous wave Doppler echocardiography.

For *quantitative Doppler echocardiography*, the aortic regurgitant volume was calculated as the difference between the mitral and the aortic stroke volumes measured with pulsed wave Doppler echocardiography (9,27). Calculation of the mitral annulus area used diameters measured along multiple axes to account for the noncircular shape of the annulus. The Doppler sample was repeatedly positioned at the mitral annulus level to avoid interaction with the AR flow. For *quantitative two-dimensional echocardiography*, the total left ventricular stroke volume was calculated as the difference between the end-diastolic and end-systolic volumes measured at end-diastole and end-systole by use of Simpson's rule (method of disks), as recommended by the American Society of Echocardiography (28). The regurgitant volume was calculated as the difference between the left ventricular stroke volume (9) and the pulsed wave Doppler mitral stroke volume (27).

Other methods. During the same episode of care, 12 patients underwent invasive aortography in which the degree of AR was graded 1 to 4, and 18 patients underwent surgical examination of the aortic valve during which the lesion was classified as severe or not severe by the surgeon.

Statistical analysis. Descriptive results were expressed as the mean value ± SD for continuous variables and as percentages for categorical variables. The calculated ERO area obtained by the three methods was compared by analysis of variance for repeated measurements and by the paired *t* test in the entire study group and in subgroups defined according to the presence or absence of a valve prolapse, an eccentric jet and a nonplanar angle of FC. The association between the PISA and reference methods of measuring the ERO area was analyzed with linear regression and the Bland and Altman method (29). Then, the differences between the ERO area by the PISA method and the reference methods were used as dependent variables in multivariate analyses in which jet eccentricity, valve prolapse and nonplanar FC angle were independent variables. Also, the association of ERO [PISA] to left ventricular volumes was based on linear correlations and to angiographic and surgical evaluations was based on nonparametric correlations and the Fisher exact test. A p value <0.05 was considered significant.

Results

Seventy-one patients were prospectively examined for study inclusion. The proximal FC region was not adequately visualized by color flow imaging in 7 of the 71 patients. Thus, the feasibility of measuring the aortic ERO area with the PISA method was 90% (64 of 71 patients). These 64 patients comprised the final study group (age 53 ± 18 years, 44 men); 63 were in sinus rhythm and 1 had atrial fibrillation. The mechanism of AR was degenerative valve disease in 21 patients, bicuspid or congenitally abnormal aortic valve in 16, aortic root dilation in 12, valve prolapse in 6, rheumatic in 5 and unclear in 4. The jet was central in 25 patients and eccentric in 39. The FC angle was flat in 59 patients and obtuse in 5. An obtuse angle was associated in all cases with aneurysmal dilation of the ascending aorta. The aortic root diameter was overall 4.1 ± 1.0 cm and was ≥5 cm in all 5 patients with an obtuse angle, but was ≥5.0 cm in only 2 of 59 patients with a flat angle (p < 0.001). No confinement of the FC, in particular by the walls of the aorta, was observed. There was a

Table 1. Quantitative Measures of Regurgitant Volume Overload

Variable	Mean ± SD	Range
PISA		
V_r (cm/s)	29 ± 9	12–61
r (cm)	0.7 ± 0.2	0.2–1.3
Regurgitant flow rate (cm³/s)	112 ± 89	8–414
Quantitative Doppler echocardiography		
Regurgitant volume (cm³)	58 ± 41	6–209
Regurgitant fraction (%)	38 ± 16	5–72
Quantitative two-dimensional echocardiography		
Regurgitant volume (cm³)	58 ± 43	4–216
Regurgitant fraction (%)	37 ± 17	6–73
Regurgitant velocity (cm/s)	461 ± 45	381 ± 554
RTVI (cm)	233 ± 56	105 ± 370

PISA = proximal isovelocity surface area; r = radius of flow convergence region; RTVI = regurgitant time–velocity integral; V_r = selected aliasing velocity.

significant correlation between the aortic diameter and the ERO [Dop] (r = 0.65, p < 0.0001) and the ERO [2D] (r = 0.63, p < 0.0001), demonstrating that the aortic size increased with the degree of AR.

The mean values of the variables used to calculate the ERO area by the three methods are listed in Table 1. Good correlations were found between the ERO [PISA] and the ERO [Dop] (r = 0.90, p < 0.0001, SEE 8.2 mm²) and ERO [2D] (r = 0.90, p < 0.0001, SEE 8.0 mm²). The ERO area calculated by the three methods in the study group and in the subgroups are presented in Table 2. Overall, the ERO [PISA] tended to slightly underestimate (p = 0.019) the ERO [Dop] (p = 0.04) and ERO [2D] (p = 0.04) (Table 2). Multivariate analysis of the predictor of the difference between the ERO [PISA] and the ERO by reference methods identified obtuse FC as the independent determinant of underestimation with both reference methods (both p = 0.0001). Valvular prolapse and eccentric jet were not significantly associated with underestimation on multivariate analysis. Marked underestimation of the ERO [PISA] compared with both reference methods (Fig. 3 and 4) was noted only in the five patients with an FC
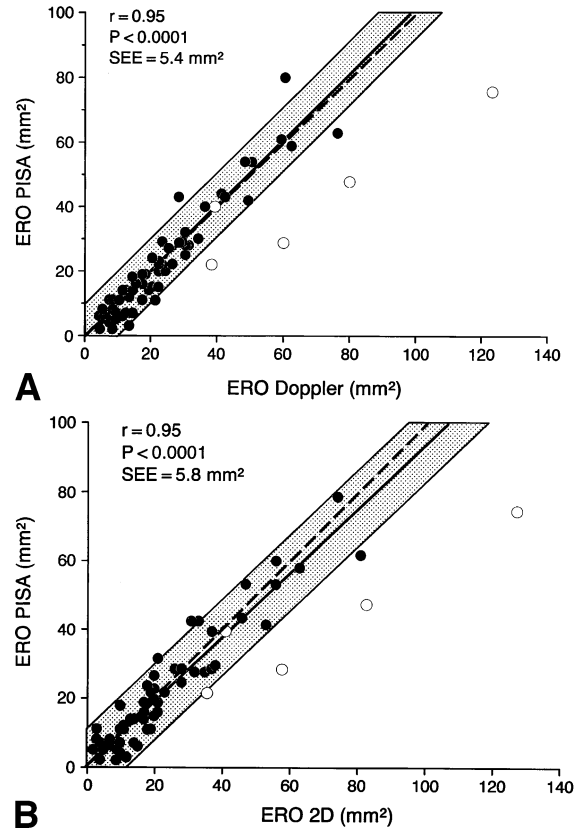

Figure 3. Correlations between the PISA method and **(A)** quantitative Doppler echocardiography and **(B)** two-dimensional echocardiography for calculation of the ERO area. **Solid line** regression line; **gray zone** = 95% confidence interval for 59 patients with a flat angle (220°) of the FC region **(solid dots)**. **Dashed line** = identity line. **Open dots** superimposed represent the five patients with an obtuse angle of the proximal FC region (>220°).

with obtuse angle and not in the 59 patients with a flat FC angle (Table 2).

When comparisons were restricted to the 59 patients with optimal measurements (i.e., flat FC angle), excellent correlations were found between ERO [PISA] and ERO [Dop] (r =

Table 2. Value of the Aortic Effective Regurgitant Orifice Area Calculated With the Proximal Isovelocity Surface Area Method and Quantitative Doppler and Two-Dimensional Echocardiographic Methods in the Overall Study Group and in Subgroups of Patients

Group	n	ERO (mm²)				
		PISA	Doppler	p Value*	2D	p Value†
Overall	64	24 ± 19	26 ± 22	0.04	27 ± 23	0.04
Prolapse	6	43 ± 12	44 ± 12	0.40	46 ± 13	0.35
No prolapse	58	22 ± 18	25 ± 22	0.06	25 ± 23	0.06
Eccentric jet	39	27 ± 21	30 ± 25	0.15	30 ± 26	0.06
Noneccentric jet	25	19 ± 14	21 ± 15	0.13	21 ± 15	0.38
Obtuse flow convergence	5	43 ± 21	68 ± 35	0.04	69 ± 37	0.04
Flat flow convergence	59	22 ± 18	23 ± 16	0.44	23 ± 18	0.34

*Comparison between PISA method and quantitative Doppler echocardiographic method. †Comparison between PISA method and quantitative two-dimensional echocardiographic method. 2D = two-dimensional; ERO = effective regurgitant orifice; PISA = proximal isovelocity surface area. Data are presented as mean value ± SD.
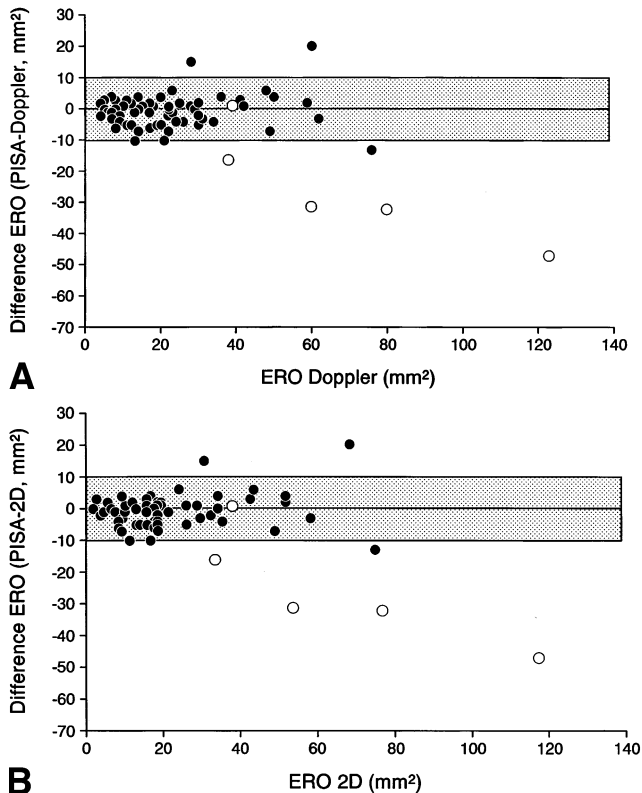
Figure 4. Scatterplots of the difference (PISA minus reference methods, y-axis) to the reference methods (x-axis) for calculation of ERO using the Doppler echocardiographic method (**A**) or two-dimensional method (**B**) as a reference. The patients with appropriate FC are represented by **solid dots,** and their 95% confidence interval is represented by the **gray zone.** The differences were not statistically different from zero. The **open dots** superimposed represent the five patients with an obtuse angle of the proximal FC region (>220°).

0.95, p < 0.0001, SEE 5.4 mm^2) and ERO [2D] (r = 0.95, p < 0.0001, SEE 5.8 mm^2) (Fig. 3), with no significant differences (overall p = 0.53) between the calculated values (p = 0.44 and 0.34, respectively, compared with the reference methods). The absolute values of the differences between the PISA method and the reference methods were 3.8 ± 3.7 mm^2 and 4.6 ± 3.6 mm^2, respectively. Quality control plots using the Bland and Altman method in patients with an optimal (flat) FC indicated that there was no trend toward underestimation (Fig. 4). The superposition of the five patients with nonplanar FC illustrated the marked underestimation of the ERO area observed in four of the five patients with an obtuse FC angle.

In comparison with other methods, the correlation with angiographic grade was good (r = 0.81, p = 0.0014). Five of six patients with an AR grade ≤3 had an ERO [PISA] <30 mm^2, and five of six patients with an AR grade 4 had an ERO [PISA] ≥30 mm^2 (p = 0.04). In comparison with surgical assessment, 13 of 14 patients with a severe lesion had an ERO ≥30 mm^2, whereas 4 of 4 patients with a less severe lesion had an ERO [PISA] <30 mm^2. There were good correlations of the ERO [PISA] with left ventricular end-systolic (r = 0.74, p < 0.0001)

and end-diastolic (r = 0.83, p < 0.0001) volumes indexed to body surface area.

For the 12 patients in whom the PISA measurements were repeated by a second observer, interobserver variability was low, with an absolute value of the difference of ERO of 3.0 ± 2.5 mm^2. For the 80 patients without regurgitation, the absolute value of the difference between aortic and mitral stroke volumes was 4.1 ± 3.1 ml, and between the left ventricular and mitral stroke volumes it was 3.8 ± 3.6 ml.

Discussion

This study showed that for measurement of the ERO of AR, 1) the proximal FC could be analyzed in a high proportion of patients with various degrees and causes of AR; 2) there was a trend toward overall underestimation of the ERO by PISA, observed only in a minority of patients with an obtuse FC angle due to aneurysmal dilation of the ascending aorta; and 3) the PISA method could obtain a reliable measurement of the ERO area in patients with an appropriate flat FC, including those with an eccentric jet or valve prolapse.

Effective regurgitant orifice: concept and previous determinations. The concept of ERO area was originally described for mitral regurgitation (30). The ERO corresponds to the area of the vena contracta, which is smaller than the anatomic regurgitant area (31). Experimental (10,32–34) and clinical (35–37) studies have suggested that the ERO area yields unique information on the severity of regurgitation, is less dependent on hemodynamic variables than is regurgitant volume and fraction (10,32,34) and is not dependent on heart rate (38). Recently, the aortic ERO area in AR was determined by Doppler echocardiography invasively (13) and noninvasively (12). These studies showed that the ERO area is an important and clinically significant index of AR severity that provides additional information to the regurgitant fraction (12). Thus, development of other clinically reliable noninvasive methods is essential so that the ERO area can be obtained in all circumstances with a combination of methods during the same Doppler echocardiographic examination, to reach a high degree of reliability in the evaluation of severity of the AR (14).

PISA method. Recently, the PISA method, based on the conservation of mass, was validated clinically to measure the ERO area in mitral (14,16) and tricuspid (20) regurgitation. It has been used also in mitral stenosis (19), ventricular septal defect (17) and prosthetic regurgitation (39). The PISA method is particularly attractive because of its simplicity (14). Experimental studies have suggested that the PISA method may be of value in the quantitation of AR (22,40). The proximal FC region is considered technically difficult to access in AR (41), but in this study it was measurable in 90% of patients and adequate for calculation of the ERO in 83% of patients. This feasibility is slightly lower than that found in mitral regurgitation (14,16), because, in contrast to its mitral counterpart, the aortic FC may be shadowed by thickened valvular tissue.

The present study is, to our knowledge, the first to apply the

PISA method in a large number of patients with AR. The ERO area calculated by the PISA method correlated well with that obtained by Doppler and two-dimensional echocardiographic methods. However, there was an overall trend toward underestimation of the aortic ERO area by the PISA method. In fact, marked underestimations were found in a minority of patients with an obtuse FC angle (Figs. 3 and 4). This complex nonplanar geometry of the aortic valve was observed only in patients with aneurysmal dilation of the ascending aorta (Fig. 2). The significant association between dilation of the aortic root and valvular morphology suggests that the aortic deformation imposes tension on the attachment of the aortic cusps, with secondary tenting of the valvular apparatus. Such cases invalidate the geometric assumptions of the PISA method, but can easily be identified with echographic examination of valvular morphology. When the ERO was measured in patients with appropriate planar FC, excellent correlation with no trend toward underestimation, in comparison with the reference methods, was observed. Recent pioneering animal studies demonstrated the accuracy of appropriate ERO measurements in AR in comparison with the definitive standard of electromagnetic flow measurement (22). Therefore, both animal and clinical studies confirm that in AR, the PISA method is highly feasible and provides an accurate measurement of the ERO area.

With nonplanar FC, angle corrections have been used (19–21,24). However, the exact geometry of aortic regurgitant valves with obtuse FC, and therefore the most appropriate correction formula, have not been established. In most machines, angle measurements are not possible on-line or on-screen and have a relatively high variability (21). Therefore, we did not attempt angular correction and currently consider obtuse FC angles inappropriate for measurement. This approach, which makes the present results applicable to most patients and most centers, may be reconsidered after further human studies in which three-dimensional reconstruction of valve geometry and velocity field is used (42).

Another important consideration with quantitation of AR is the calculation of the mean ERO over the regurgitant phase of the cardiac cycle as a measure of lesion severity (12). The PISA method provides instantaneous measurements of flow and ERO. Because the regurgitant flow rate by the PISA method and the regurgitant velocity were measured simultaneously in early diastole, the calculated aortic ERO area is the early diastolic ERO. In AR the potentially dynamic nature of the regurgitant orifice area during diastole remains controversial (22,43). Despite these conjectural considerations, an important result of the present study is that in patients with AR and appropriate FC, early diastolic measurements concomitant to peak regurgitant velocity provide a calculated ERO that correlates closely with the mean ERO measured by the reference methods, without a significant trend toward overestimation or underestimation. Such a result is consistent with previous observations in mitral regurgitation showing that even in patients with highly variable EROs, measurements by PISA at peak velocity correlated well with the mean ERO (44).

Therefore, despite the instantaneous nature of the PISA method, measurement of the ERO at peak regurgitant velocity of AR provides an appropriate estimate of the mean aortic regurgitant ERO. The mean ERO is a strong determinant of the consequences of the regurgitation and is a clinically relevant measure of lesion severity (12); consequently, the PISA method, which is reasonably feasible and highly accurate with appropriate FC, can be used in clinical practice for the quantitation of AR.

Importantly, the ERO by the PISA method correlates well with other methods of assessment of the degree of AR using left ventricular volumes, angiographic grade or surgical assessment of lesion severity, further supporting the relevance of this measure in patients with AR.

Study limitations. Although the accuracy of Doppler echocardiographic methods for quantitation of regurgitation and measurement of left ventricular volumes has been questioned (27,45,46), reliability has been confirmed through high resolution imaging and consistent use (9,47,48). Importantly, the analysis of the patients without regurgitation confirms the reliability of stroke volume measurements, even on the mitral valve, with the present methods. Furthermore, the reference methods used allowed all measurements to be made simultaneously, avoiding changes of loading conditions, and showed similar results, confirming that their utilization is not a limitation (14).

Possible limitations of the PISA method, related to assumption of a hemispheric shape of the proximal FC, have been discussed (23,24,42,49–52), but clinical series have demonstrated that in most cases the hemispheric assumption provides appropriate measurement of the flow rate and ERO (14,16,20). Confined FC was not observed in the current study. This is easily understandable in light of the enlarged aortic root of patients with AR, which tends to be larger in patients with more severe AR, avoiding interference of aortic walls with the FC. Furthermore, examination of the FC region allows identification of the cases in which the geometry of this region may invalidate the hemispheric assumption (14,21), so that they can be either corrected or classified as inappropriate. The shape of the observed proximal FC, and therefore the reliability of the ERO calculation, depends on the radius value (52), which is determined by the selected aliasing velocity (22,23). The appropriate and individualized selection of the aliasing velocity, as performed in the present study, avoids overestimation or underestimation of the flow rate (16,23). Because the angle between the centerline of the FC and the ultrasound beam may affect imaging by the Doppler color flow technique (41), apical or para-apical views were used in the present study to align the regurgitant flow direction and the ultrasound beam.

Conclusions. The current study shows that for the measurement of the ERO of AR, the PISA method has a reasonable feasibility and high accuracy with appropriate FC and can be used clinically, including in patients with an eccentric jet and valve prolapse. The major pitfall is an obtuse angle of the FC region due to the geometry of the aortic cusps. However, this morphology of the aortic valve can be easily recognized as

inappropriate for the PISA method. In most patients, the FC angle is flat and determination of the aortic ERO area is reliable. Thus, multiple noninvasive Doppler echocardiographic methods can be combined during the same examination to obtain an accurate measurement of the ERO area in AR in most circumstances. The development of these methods should foster understanding of the clinical importance of the regurgitant orifice area on the natural history of AR and on the development of left ventricular dilation and dysfunction.

References

1. Perry GJ, Helmcke F, Nanda NC, Byard C, Soto B. Evaluation of aortic insufficiency by Doppler color flow mapping. J Am Coll Cardiol 1987;9:952–9.

2. Tribouilloy C, Avinee P, Shen WF, Rey JL, Slama M, Lesbre JP. End diastolic flow velocity just beneath the aortic isthmus assessed by pulsed Doppler echocardiography: a new predictor of the aortic regurgitant fraction. Br Heart J 1991;65:37–40.

3. Labovitz AJ, Ferrara RP, Kern MJ, Bryg RJ, Mrosek DG, Williams GA. Quantitative evaluation of aortic insufficiency by continuous wave Doppler echocardiography. J Am Coll Cardiol 1986;8:1341–7.

4. Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease: technic, indications and interpretations in 700 cases. Am J Cardiol 1964;14:437–47.

5. 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.

6. Tribouilloy C, Shen WF, Leborgne L, Trojette F, Rey JL, Lesbre JP. Comparative value of Doppler echocardiography and cardiac catheterization for management decision-making in patients with left-sided valvular regurgitation. Eur Heart J 1996;17:272–80.

7. Baron MG. Angiocardiographic evaluation of valvular insufficiency. Circulation 1971;43:599–605.

8. 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.

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

10. Reimold SC, Byrne JG, Caguioa ES, et al. Load dependence of the effective regurgitant orifice area in a sheep model of aortic regurgitation. J Am Coll Cardiol 1991;18:1085–90.

11. Bolen JL, Alderman EL. Hemodynamic consequences of afterload reduction in patients with chronic aortic regurgitation. Circulation 1976;53:879–83.

12. 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.

13. 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.

14. Enriquez-Sarano M, Miller FA Jr, Hayes SN, Bailey KR, Tajik AJ, Seward JB. Effective mitral regurgitant orifice area: clinical use and pitfalls of the proximal isovelocity surface area method. J Am Coll Cardiol 1995;25:703–9.

15. 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.

16. Vandervoort PM, Rivera JM, 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.

17. Moises VA, Maciel BC, Hornberger LK, et al. A new method for noninvasive estimation of ventricular septal defect shunt flow by Doppler color flow mapping: imaging of the laminar flow convergence region on the left septal surface. J Am Coll Cardiol 1991;18:824–32.

18. Simpson IA, Shiota T, Gharib M, Sahn DJ. Current status of flow convergence for clinical applications: is it a leaning tower of "PISA"? J Am Coll Cardiol 1996;27:504–9.

19. Rodriguez 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.

20. Rivera JM, Vandervoort PM, Mele D, et al. Quantification of tricuspid regurgitation by means of the proximal flow convergence method: a clinical study. Am Heart J 1994;127:1354–62.

21. Pu M, Vandervoort PM, Griffin BP, et al. Quantification of mitral regurgitation by the proximal convergence method using transesophageal echocardiography: clinical validation of a geometric correction for proximal flow constraint. Circulation 1995;92:2169–77.

22. Shiota T, Jones M, Yamada I, et al. Effective regurgitant orifice area by the color Doppler flow convergence method for evaluating the severity of chronic aortic regurgitation: an animal study. Circulation 1996;93:594–602.

23. Rodriguez 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.

24. 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.

25. 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.

26. 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.

27. Lewis JF, Kuo LC, Nelson JG, Limacher MC, Quinones MA. Pulsed Doppler echocardiographic determination of stroke volume and cardiac output: clinical validation of two new methods using the apical window. Circulation 1984;70:425–31.

28. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography: American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358–67.

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

30. 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.

31. Yoganathan AP, Cape EG, Sung HW, Williams FP, Jimoh A. Review of hydrodynamic principles for the cardiologist: applications to the study of blood flow and jets by imaging techniques. J Am Coll Cardiol 1988;12:1344–53.

32. Yoran C, Yellin EL, Becker RM, Gabbay S, Frater RW, 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.

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

34. Caguioa ES, Reimold SC, Velez S, Lee RT. Influence of aortic pressure on effective regurgitant orifice area in aortic regurgitation. Circulation 1992;85:1565–71.

35. Keren G, Bier A, Strom JA, Laniado S, Sonnenblick EH, LeJemtel TH. Dynamics of mitral regurgitation during nitroglycerin therapy: a Doppler echocardiographic study. Am Heart J 1986;112:517–25.

36. Keren G, Laniado S, Sonnenblick EH, LeJemtel TH. Dynamics of functional mitral regurgitation during dobutamine therapy in patients with severe congestive heart failure: a Doppler echocardiographic study. Am Heart J 1989;118:748–54.

37. Keren G, Katz S, Gage J, Strom J, Sonnenblick EH, LeJemtel TH. Effect of isometric exercise on cardiac performance and mitral regurgitation in patients with severe congestive heart failure. Am Heart J 1989;118:973–9.

38. 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.

39. 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.

40. Shiota T, Jones M, Yamada I, et al. Evaluation of aortic regurgitation with digitally determined color Doppler-imaged flow convergence acceleration: a quantitative study in sheep. J Am Coll Cardiol 1996;27:203–10.

41. Yamachika S, Reid CL, Savani D, et al. Usefulness of color Doppler proximal isovelocity surface area method IRM quantitating valvular regurgitation. J Am Soc Echocardiogr 1997;10:159–68.

42. Shiota T, Sinclair B, Ishii M, et al. Three-dimensional reconstruction of color Doppler flow convergence regions and regurgitant jets: an in vitro quantitative study. J Am Coll Cardiol 1996;27:1511–8.

43. Reimold SC, Maier SE, Fleischmann KE, et al. Dynamic nature of the aortic regurgitant orifice area during diastole in patients with chronic aortic regurgitation. Circulation 1994;89:2085–92.

44. Enriquez-Sarano M, Sinak LJ, Tajik AJ, Bailey KR, Seward JB. Changes in effective regurgitant orifice throughout systole in patients with mitral valve prolapse: a clinical study using the proximal isovelocity surface area method. Circulation 1995;92:2951–8.

45. 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.

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

47. Gorge 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.

48. 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;13:1294–1300.

49. Deng YB, 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: digital computer analysis of the Doppler color flow convergence region. Circulation 1993;88:1699–1708.

50. Shiota T, Jones M, Teien DE, et al. Evaluation of mitral regurgitation using a digitally determined color Doppler flow convergence "centerline" acceleration method: studies in an animal model with quantified mitral regurgitation. Circulation 1994;89:2879–87.

51. Utsunomiya T, Doshi R, 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.

52. Nozaki S, Shandas R, DeMaria AN. Requirement for accurate measurement of regurgitant stroke volume by the combined continuous-wave Doppler and color Doppler flow convergence method. Am Heart J 1997;133:19–28.