Noninvasive assessment of left-to-right shunting in ventricular septal defects by the proximal isovelocity surface area method on Doppler colour flow mapping

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BACKGROUND AND AIM: The proximal isovelocity surface area (PISA), which is the zone of flow convergence appearing on the left ventricular septal surface where flow approaching the defect accelerates, allows quantitative estimation of ventricular septal defect (VSD) flow and defect area on colour Doppler imaging. In the present study, the clinical applicability and reliability of the PISA method in assessing the amount of left-to-right shunting in patients with VSDs were evaluated.

PATIENTS AND METHODS: Fifty-eight patients aged 0.25 to 15 years (mean age 4.3 ± 4.4 years) with VSDs were prospectively studied. Maximum PISA radius in peak systole (r), peak velocity ($V_{\max}$) and velocity time integral (VTI_{VSD}) of flow through the VSD were measured. In addition, peak VSD flow ($2\pi r^2 \times \text{Nyquist limit [NL]}$), amount of left-to-right shunting ($Qp-Qs = \text{heart rate} \times [2\pi r^2 \times NL \times VTI_{VSD}] / V_{\max}$) and defect area ($[2\pi r^2 \times NL] / V_{\max}$) were calculated.

RESULTS: There were significant positive correlations between Qp-Qs values calculated by PISA and other spectral Doppler methods using the cross-sectional area, as well as the VTI of pulmonary-aortic ($r=0.73$, $P<0.001$) or mitral-tricuspid ($r=0.58$, $P<0.001$) flows and cardiac catheterization (20 patients, $r=0.82$, $P<0.001$). PISA-derived left-to-right-shunting discriminated moderate to large defects from small defects, which were classified according to the catheter-derived Qp/Qs ratio (2 or greater versus less than 2; $P=0.001$) or clinical evaluation ($P<0.001$).

CONCLUSIONS: The present study demonstrated that the PISA method is a reliable semiquantitative method to determine the amount of left-to-right shunting of VSDs and to discriminate moderate to large defects from small defects. Consequently, this method may serve as a simple and useful adjunct to conventional spectral Doppler methods in the noninvasive assessment of patients with VSDs.

Key Words: Congenital heart disease; Proximal isovelocity surface area; Ventricular septal defect

The amount of left-to-right shunting is an important hemodynamic parameter in the clinical evaluation of patients with ventricular septal defects (VSDs) (1,2). Various Doppler echocardiographic methods have been used for measuring the left-to-right shunt noninvasively, but their accuracy and reliability are still disputable. On colour Doppler imaging of a VSD, the proximal

L'évaluation non effractive du shunt gauche-droite en cas de communication interventriculaire par la surface d'isovélocité proximale à la cartographie Doppler couleur

HISTORIQUE ET OBJECTIF : La surface d'isovélocité proximale (SIP), soit la zone de convergence du débit qui paraît à la surface interventriculaire gauche où le débit accélère à l'approche de la communication, permet une évaluation quantitative du débit de la communication interventriculaire (CIV) et de la zone de cette communication à l'imagerie Doppler couleur. Dans le cadre de la présente étude, les auteurs évaluent l'applicabilité et la fiabilité cliniques de la SIP pour établir l'importance du shunt gauche-droite chez les patients présentant une CIV.

PATIENTS ET MÉTHODOLOGIE : Cinquante-huit patients de 0,25 à 15 ans (moyenne de $4,3 \pm 4,4$ ans) ayant une CIV ont fait l'objet d'une étude prospective. Les auteurs ont mesuré le rayon maximal de la SIP pendant la systole de pointe (r), la vélocité de pointe ($V_{\max}$) et le débit intégré de vélocité en fonction du temps (IVT_{CIV}) par la CIV. Ils ont également calculé le débit de pointe de la CIV ($2\pi r^2 \times \text{limite de Nyquist [LN]}$), le shunt gauche-droite ($Qp-Qs = \text{rythme cardiaque} \times [2\pi r^2 \times LN \times IVT_{CIV}] / V_{\max}$) et le foyer de la communication ($[2\pi r^2 \times LN] / V_{\max}$).

RÉSULTATS : On remarque des corrélations positives importantes entre les valeurs Qp-Qs calculées au moyen de la SIP et d'autres méthodes Doppler spectrales, à l'aide de la zone transversale, ainsi que l'IVT des débits pulmonaire-aortique ($r=0,73$, $p < 0,001$) ou mitral-tricuspid ($r=0,58$, $p < 0,001$) et le cathétérisme cardiaque (20 patients, $r=0,82$, $p < 0,001$). Le shunt gauche-droite dérivé de la SIP permettait de distinguer les communications modérées à grandes des communications mineures, classées d'après le ratio Qp/Qs dérivé du cathéter (2 ou plus par rapport à moins de 2, $P=0,001$) ou l'évaluation clinique ($p < 0,001$).

CONCLUSIONS : La présente étude démontre que la SIP est une méthode semi-quantitative fiable pour déterminer l'importance du shunt gauche-droite des CIV et distinguer les communications modérées à importantes des communications mineures. Par conséquent, cette méthode peut constituer un ajout simple et utile aux méthodes Doppler spectrales classiques dans l'évaluation non effractive des patients présentant une CIV.

isovelocity surface area (PISA) – the flow convergence zone appearing proximal to the left ventricular septal surface where flow approaching the defect accelerates – allows for quantitative estimation of VSD flow and area (3,4). In patients with VSDs, calculation of the left-to-right shunt by this method can be accomplished with relative ease, and can be promptly compared with

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Figure 1) Proximal isovelocity surface area (PISA) image of ventricular septal defect flow on colour Doppler echocardiography from the parasternal long-axis view. AO Aorta; IVS Interventricular septum; LA Left atrium; LV Left ventricle; RV Right ventricle

other conventional spectral Doppler methods. Previous studies using the PISA method, although limited in number, have documented results concordant with the findings of cardiac catheterization (CC) (5-7). However, more studies are needed to evaluate the reliability of this method.

In the present study, we aimed to evaluate the clinical applicability of the PISA method in the assessment of the amount of left-to-right shunting in patients with VSD and to compare the findings with those of conventional spectral Doppler methods, CC and clinical findings.

PATIENTS AND METHODS

Patients

Fifty-eight patients with VSDs were prospectively studied between February 2002 and May 2003. Their symptoms, physical findings, chest x-ray results, and electrocardiographic and echocardiographic findings were evaluated. Later, a PISA imaging study was performed using colour Doppler. Patients with an additional cardiac anomaly (affecting the amount of left-to-right shunting), multiple defects and an insufficient PISA image were not included in the study. CC was performed only for indications other than for this study.

Echocardiographic studies

An Acuson 128XP/10 echocardiography instrument (Acuson Corporation, USA) with a 3.5 MHz to 4 MHz transducer was used in the present study. Midazolam (0.4 mg/kg, rectal administration) was given to patients who required sedation. Images were recorded on videotape to allow a frame-by-frame review. During a usual echocardiographic evaluation, which was performed using the segmental analysis method, the localization and size of defect, right ventricular pressure and interventricular pressure gradient through defect were determined (3). Defect area (DA) was also calculated from the VSD diameter measured by two-dimensional (2-D) echocardiography by assuming a circular defect shape ($DA_{2-D} = \pi [\text{VSD diameter}]^2/4$) (8).

Pulmonary flow (Q_p) and systemic flow (Q_s) were obtained by conventional spectral Doppler methods using the cross-sectional area and the velocity time integral (VTI) of pulmonary-aortic (PA-AO) or mitral-tricuspid (MV-TV) flows, and the amount of left-to-right shunting (Q_p-Q_s) was calculated (9). The aortic

valve annulus diameter (D_{AO}) from the parasternal long-axis view, the pulmonary valve annulus diameter (D_{PA}) from the parasternal short-axis view, and the tricuspid and mitral valve annulus diameters (D_T and D_M , respectively) from the apical four-chamber view were measured. The VTI at the levels of the aortic, mitral and tricuspid annuli (VTI_{AO} , VTI_M and VTI_T , respectively) in the apical five-chamber view, as well as the pulmonary annulus (VTI_{PA}) in the parasternal short-axis view, were obtained by placing the sample volume of pulsed-wave Doppler. All calculations were performed using the following formulas (9-11):

$$Q_{pPA-AO} = (\pi D_{PA}^2/4) \times VTI_{PA} \times \text{heart rate}$$

$$Q_{sPA-AO} = (\pi D_{AO}^2/4) \times VTI_{AO} \times \text{heart rate}$$

$$Q_{pMV-TV} = (\pi D_M^2/4) \times VTI_M \times \text{heart rate}$$

$$Q_{sMV-TV} = (\pi D_T^2/4) \times VTI_T \times \text{heart rate}$$

PISA imaging study

PISA images were obtained by colour Doppler echocardiography in the parasternal long-axis view in all patients. The wall filter was kept at minimum, and the colour gain level was kept just below the point at which static noise was visible in the colour signal. The aliasing velocity determined by the device ranged from 44 cm/s to 96 cm/s. PISA was visualized as a hemispheric aliasing zone proximal to the VSD on the left ventricular septal surface and was composed of a series of isovelocity rings, with colour flow changes from red to blue. The radius of the PISA hemisphere was measured from the first alias (the outermost boundary of the PISA), coinciding with the T wave on the electrocardiogram, thereby implicating peak systole (Figure 1). The maximum PISA radius in one cycle (r) from the first aliasing line to the left ventricular side of the defect, peak velocity (V_{max}) and the VTI of flow through the defect were measured. According to the 'continuity equation', the flow passing through this area should be equal to the flow passing through the VSD into the right ventricle (3,4). Consequently, peak VSD flow (Q_{VSD}), left-to-right shunt (Q_p-Q_{sPISA}) and defect area (DA_{PISA}) were calculated using the following formulas:

$$Q_{VSD} = 2\pi r^2 \times NL$$

$$Q_p-Q_{sPISA} = ((2\pi r^2 \times NL \times VTI_{VSD}/V_{max}) \times \text{heart rate})$$

$$DA_{PISA} = (2\pi r^2 \times NL)/V_{max}$$

The abbreviations used in the above formulas include: r – the maximal PISA in one cycle; NL – the Nyquist limit velocity; VTI – the velocity time integral recorded by continuous-wave Doppler ultrasound at the defect; and V_{max} is the peak velocity recorded by the continuous-wave Doppler of flow through the defect.

CC

Because of indications other than those for the present study, 20 patients underwent CC and angiography under general anesthesia during the subsequent days. Blood samples were obtained from all chambers for oxygen saturation. It was shown that there was no extra shunt by oximetry and angiography. Q_p and Q_s were calculated by Fick's rule, based on estimated oxygen consumption (12,13). Consequently, Q_p-Q_s derived by CC (Q_p-Q_{sCC}) and the pulmonary to systemic flow (Q_p/Q_s) ratio were obtained.

All data were standardized according to body surface area. Q_p-Q_{sPISA} values were compared with those obtained by conventional spectral Doppler methods and by CC.

Patient classification

According to the clinical evaluation (symptoms, physical findings, electrocardiogram, chest x-ray and echocardiographically derived

pulmonary artery pressure), patients were classified as having small, moderate or large VSDs (14-16).

Statistical analysis

Statistical analysis was performed using the SPSS version 10.0 program (SPSS Inc, USA). Numerical values are given as mean $\pm$ SD. Student's *t* test was performed to compare numerical values. Pearson linear regression analysis was performed to correlate between the variables. Specificity and sensitivity values of the PISA findings for moderate to large defects were calculated and receiver operating characteristic curves were drawn. $P < 0.05$ was considered to be statistically significant.

RESULTS

The present study included 58 patients with VSDs (23 female and 35 male patients) 0.25 to 15 years of age (mean age 4.3 ± 4.4 years). The VSD was perimembranous in 54 patients (93.1%), muscular in one (1.7%) and doubly committed juxta-arterial in three patients (5.2%). In 36 patients (62.1%), the VSD was small; 11 patients (19%) had moderate defects and 11 patients (19.0%) had large defects. Thirty-five patients (60.3%) had been taking digoxin or digoxin plus a diuretic. After evaluation, 21 patients (36.2%) had surgical repair and 37 patients (63.8%) had clinical follow-up. Of the patients who underwent surgical repair, 20 had moderate to large defects and only one had a small defect. There were no patients with a large defect and a Qp/Qs ratio of less than 2.

Patient echocardiographic and CC findings are provided in Table 1. There was a significant correlation between DA_{PISA} and DA_{2-D} ($r = 0.86$, $P < 0.001$) (Figure 2A), although the mean DA_{PISA} was higher than the mean DA_{2-D} (difference of 0.69 ± 1.28 cm²/m², $P < 0.001$).

There were significant positive correlations between Qp-Qs_{PISA} and Qp-Qs_{PA-AO} ($r = 0.73$, $P < 0.001$), Qp-Qs_{MV-TV} ($r = 0.58$, $P < 0.001$) and Qp-Qs_{CC} ($r = 0.82$, $P < 0.001$) (Figures 2B, 2C and 2D, respectively). The mean Qp-Qs_{PISA} was higher than Qp-Qs calculated by conventional spectral Doppler methods ($P < 0.001$) and lower than Qp-Qs_{CC} (difference of 7.1 ± 12.1 L/min/m², $P = 0.014$).

Qp-Qs_{PISA} and DA_{PISA} discriminated moderate to large defects from small defects classified according to clinical evaluation (small versus moderate to large defects, $P < 0.001$) and the catheter-derived Qp/Qs ratio (2 or greater versus less than 2, $P = 0.001$) (Figures 3A and 3B).

The reliability of Qp-Qs_{PISA} and DA_{PISA} in discriminating moderate to large defects from small defects, as classified by the clinical evaluation, was high (0.95 for both) (Figure 4A). With 95% sensitivity, the cut-off values for Qp-Qs_{PISA} and DA_{PISA} , which described the moderate to large defects, were 3.9 L/min/m² (78% specificity) and 0.34 cm²/m² (81% specificity), respectively.

In 14 of 20 patients who underwent CC, the catheter-derived Qp/Qs ratio was 2/1 or greater. According to this classification, Qp-Qs_{PISA} and DA_{PISA} reliably separated large defects (Qp/Qs ratio of 2 or greater) from small defects (Qp/Qs ratio of less than 2) (0.98 and 0.99, respectively) (Figure 4B). With 93% sensitivity and 100% specificity, the cut-off values for Qp-Qs_{PISA} and DA_{PISA} , which described large defects, were 6.1 L/min/m² and 0.43 cm²/m², respectively.

DISCUSSION

The PISA method is based on the principle of conservation of mass and the continuity equation in hydrodynamics (3,17). While the laminar stream passes through the constricted area, it constitutes an accelerated flow zone hemispherically shaped (half-moon)

TABLE 1
Echocardiography and cardiac catheterization (CC) findings

Variable	Mean $\pm$ SD
Heart rate (beats/min)	112 $\pm$ 25
Peak ventricular septal defect flow rate (cm/s)	400.5 $\pm$ 100.7
Interventricular peak pressure gradient (mmHg)	67.8 $\pm$ 29.4
Velocity time integral (cm)	79.8 $\pm$ 28.1
Right ventricular pressure (mmHg)	34.1 $\pm$ 20.1
Ventricular septal defect diameter (cm/m ²)	1.12 $\pm$ 0.92
2-D-derived defect area (cm ² /m ²)	0.56 $\pm$ 0.69
Qp-Qs _{PA-AO} (L/min/m ²)	5.2 $\pm$ 4.9
Qp-Qs _{MV-TV} (L/min/m ²)	4.5 $\pm$ 4.4
PISA-derived defect area (cm ² /m ²)	1.26 $\pm$ 1.85
Qp-Qs _{PISA} (L/min/m ²)	8.0 $\pm$ 8.8
Qp-Qs _{CC} (L/min/m ²)	20.5 $\pm$ 17.3
Qp/Qs _{CC}	2.5 $\pm$ 1.1

2-D Two-dimensional echocardiography; MV-TV Mitral-tricuspid; PA-AO Pulmonary-aortic; PISA Proximal isovelocity surface area; Qp-Qs Left-to-right shunting; Qp/Qs Pulmonary to systemic flow

proximal to the orifice. According to the principle of the conservation of mass, a constant amount of fluid that passes through a restrictive orifice generates flow with a higher velocity. Consequently, the flow (Q) proximal to a restrictive orifice becomes equal to the flow passing through the narrowed area. A region where a laminar stream narrows and gains momentum progressively proximal to the defect is defined as the flow convergence region. The instantaneous flow at this region (Q) is calculated by multiplying the cross-sectional area of the hemisphere (PISA) and aliasing velocity (NL) anywhere in this region (4-7).

In this method, PISA is assumed to be hemispheric (18). However, when the flow comes close to the restrictive orifice, the hemispheric shape of the flow convergence zone becomes smooth in clinical applications (19). Moreover, Chen et al (20) have shown that the PISA shape changes during systole. Therefore, hemispheric formulas may cause underestimation when the PISA is close to the orifice and overestimation when it is far from the orifice. In all the studies performed to date, the hemispheric model has been used (5-7). Moises et al (5) and Kurotobi et al (6) showed that the amount of left-to-right shunting calculated by the PISA method was in concordance with Qp-Qs_{CC}, but the mean Qp-Qs_{PISA} was higher than Qp-Qs_{CC}. Eren et al (7) also found that the Qp-Qs_{PISA} was lower than the spectral Doppler and Qp-Qs_{CC}, and this matter was explained with the measurement of 'r' diameter close to the orifice due to high aliasing velocity.

In the present study, hemispheric formulas were used, as in the previous studies (5-7), and the amount of Qp-Qs_{PISA} correlated significantly with that obtained by CC and other spectral Doppler methods; however, PISA overestimated Qp-Qs compared with the other echocardiographic methods and underestimated it compared with CC. The lower Qp-Qs_{PISA} than Qp-Qs_{CC} might have been due to the measurement of 'r' diameter close to the orifice secondary to high aliasing velocity. However, in the studies in which Qp-Qs_{PISA} was found to be higher than Qp-Qs_{CC}, it was calculated by assuming that the flow rate into the defect was constant during the cardiac cycle (5,6). In the present study, as in the report by Eren et al (7), Qp-Qs_{PISA} was calculated by assuming that Qp-Qs through the defect was only during systole. This might have been the other cause of the lower Qp-Qs_{PISA} than Qp-Qs_{CC}.

Figure 2) Linear regression curves between defect areas (DAs) calculated by proximal isovelocity surface area (PISA) and two-dimensional echocardiography (2-D) (**A**), and between left-to-right shunting (Qp-Qs) derived by PISA (Qp-Qs_{PISA}) and Qp-Qs derived using the pulmonary-aortic flows (Qp-Qs_{PA-AO}) (**B**), Qp-Qs derived using the mitral-tricuspid flows (Qp-Qs_{MV-TV}) (**C**) and Qp-Qs derived by cardiac catheterization (Qp-Qs_{CC}) (**D**)

Figure 3) Left-to-right shunting (Qp-Qs) derived by proximal isovelocity surface area (PISA) and defect area (DA) derived by PISA discriminate moderate to large defects from small defects that were classified according to clinical evaluation (**A**) and catheter-derived pulmonary to systemic flow (Qp/Qs) ratio (**B**)

Utsunomiya et al (21) showed that the underestimation may be improved by using a hemielliptical PISA model in an in vitro study. However, because the diameter measurements should be obtained from two orthogonal planes, it appears that its application in vivo was difficult. For this reason, PISA should be obtained from three-dimensional echocardiographic images. Ishii et al (22) were the first to report that Qp-Qs_{PISA} calculated from

Figure 4) Receiver operating characteristic (ROC) curves of proximal isovelocity surface area-derived left-to-right shunting (Qp-Qs) and proximal isovelocity surface area-derived defect area (DA) for detection of moderate to large defects classified by clinical evaluation (**A**) and large defects (pulmonary to systemic flow ratio of 2 or greater) according to cardiac catheterization (**B**)

three-dimensional echocardiographic images was very close to Qp-Qs_{CC}, with a significant positive correlation between them.

Enriquez-Sarano et al (23) calculated effective mitral regurgitant orifice area by estimating regurgitant flow obtained from the PISA method and comparing that with the maximal velocity of a regurgitant jet. Eren et al (7) calculated the DA in patients with VSDs by the same method and found that mean DA_{PISA} was

higher than mean 2-D echocardiographically derived DA. In the present study, the DA was calculated by the same method and, similarly, DA_{PISA} was found to be higher than 2-D echocardiographically derived DA. Although there was a very close and positive correlation between the two DA values, the mean difference was statistically significant, and the difference was particularly higher in large defects. This finding may show that the defect was asymmetrical. While the defect diameter increases, the asymmetrical shape causes overestimation of the DA (7). However, this parameter may be used in discriminating the moderate to large defects from small defects as an index value.

In our study, the $Qp-Qs_{PISA}$ and DA_{PISA} values in patients with VSDs were significantly correlated with those obtained by other echocardiographic methods and CC. Furthermore, $Qp-Qs_{PISA}$ and DA_{PISA} discriminated moderate to large defects from small defects that are classified according to the catheter-derived

Qp/Qs ratio (2 or greater versus less than 2) or clinical evaluation. PISA-derived $Qp-Qs$ greater than 3.9 L/min/m² and DA greater than 0.34 cm²/m² can reliably distinguish, with 95% sensitivity, moderate to large VSDs from small defects that are classified according to clinical evaluation.

CONCLUSIONS

The PISA method is a reliable semiquantitative method to determine the amount of $Qp-Qs$ and to discriminate moderate to large defects from small defects. Therefore, it may serve as a simple and useful adjunct to conventional spectral Doppler methods in the noninvasive assessment of patients with VSDs.

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