CONGENITAL HEART DISEASE

Non-invasive automated assessment of the ratio of pulmonary to systemic flow in patients with atrial septal defects by the colour Doppler velocity profile integration method

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Background: The recent introduction of the automated cardiac flow measurement (ACM) method, using spatiotemporal integration of the Doppler velocity profile, provides a quick and accurate automated calculation of cardiac output.

Objective: To evaluate the ACM method against oximetry during cardiac catheterisation for estimating the Qp/Qs (pulmonary to systemic flow) ratio in patients with an atrial septal defect.

Methods: Left and right ventricular stroke volume (LVS, RVS) were calculated by ACM in 22 patients with an atrial septal defect who underwent cardiac catheterisation and in 11 patients without heart disease (control group). With ACM, the Qp/Qs ratio was estimated from RVS divided by LVS. In the patients with an atrial septal defect, the Qp/Qs ratio was assessed by oximetry at the time of cardiac catheterisation.

Results: There was a good correlation between LVS and RVS obtained by ACM in the control group ($r = 0.98$, $y = 0.97x + 0.25$, $SEE = 2.9$ ml). The mean difference between LVS and RVS by ACM was -1.25 (2.76) ml. The Qp/Qs ratio obtained by ACM in the control group was 0.98 (0.06). The Qp/Qs ratio in patients with an atrial septal defect was significantly higher than in the control group (3.11 (1.20), $p < 0.001$). ACM determination of the Qp/Qs ratio correlated well with oximetry determination ($r = 0.86$, $y = 0.75x + 0.55$, $SEE = 0.64$). The mean difference between ACM and oximetry for the measurement of the Qp/Qs ratio was -0.28 (0.69).

Conclusions: The newly developed ACM method is clinically useful for non-invasive automated estimations of the Qp/Qs ratio in patients with an atrial septal defect.

Pulsed Doppler echocardiography provides non-invasive quantitation of the ratio of pulmonary to systemic flow (Qp/Qs) in patients with an atrial septal defect.^{1–3} However, this established method requires calculation of aortic and pulmonary orifice areas and integrals of the Doppler velocity waveform by manual procedures. The newly developed automated cardiac flow measurement (ACM) method, using spatial and temporal integration of colour Doppler velocity profiles, provides an accurate and quick automated flow volume measurement without the limitations inherent in pulsed Doppler echocardiography.^{4–9} This new method has recently been validated for the calculation of the Qp/Qs ratio by measurement of both left and right ventricular stroke volumes in an animal study.¹⁰ To our knowledge, however, there have been no reports of the application of ACM for determining the Qp/Qs ratio in patients with atrial septal defects. Our aim in this study was to evaluate the new ACM method against oximetry during cardiac catheterisation for estimation of the Qp/Qs ratio in patients with atrial septal defects.

METHODS

Study population

The study patients, who had an atrial septal defect detected by transthoracic or transoesophageal Doppler echocardiography, were recruited prospectively. Inclusion criteria were an atrial septal defect confirmed at the time of cardiac catheterisation and the presence of normal sinus rhythm. Of 25 patients who met the criteria, three patients were excluded because of difficulty in obtaining complete two dimensional images and colour Doppler images of adequate quality to permit measure-

ments of left ventricular stroke volume (LVS) and right ventricular stroke volume (RVS) using the ACM method. The study population consisted of 22 patients with an atrial septal defect (six men and 16 women, age range 20–68 years, mean 44 years). The defect was secondary in 20 patients and primary in two. The interval between colour Doppler echocardiography and cardiac catheterisation was within one week in all the study patients.

The control group consisted of 11 subjects without organic heart disease (eight male, three female, mean age 43 years). They underwent echocardiographic examination for the measurement of left and right ventricular stroke volume (LVS, RVS) by the ACM method.

Automated cardiac flow measurement

In both the study patients and the normal control subjects, colour Doppler echocardiographic examinations were undertaken with a Toshiba SSA-380A ultrasound system (Toshiba, Thochigi, Japan), equipped with software for ACM and a 2.5 MHz transducer. The principle of ACM has been described in previously reported experimental and clinical studies^{4–10} and is outlined in fig 1. The velocity profile in a region of interest set on the flow tract is detected in each frame of the colour imaged recorded on the image memory. The rectangular

Abbreviations: ACM, automated cardiac flow measurement; LVS, left ventricular stroke volume; Qp/Qs, pulmonary to systemic flow; RVS, right ventricular stroke volume

Figure 1 Schematic representations of the calculation of flow volume rate by automated cardiac flow measurement (ACM) using spatiotemporal integration of Doppler velocity profile. (A) When the area S perpendicular to the velocity component of the absolute velocity (V_d) measured by Doppler method is obtained, the flow volume rate can be calculated by the product of S and V_d without compensating for the Doppler angle because $V_0 = V_d / \cos \theta$, $S_0 = S \cos \theta$, and $\cos \theta$ is cancelled. (B) Flow volume rate can be calculated by integrating the product of the V_{di} and the ring area dS_i at each sample point i along a circular arch, which is perpendicular to ultrasound beams. As area dS_i becomes oval in shape, note that angle compensation is required to obtain the area from only the single long axis plane.

region of interest included five sampling lines to detect the velocity profile, and calculates the averaged flow volume rate for each frame. The spatial integration is made by rotational integration of the velocity profile to obtain the flow volume rate. Finally, the stroke volume is calculated by temporal integration of flow volume rate in each frame throughout the systolic period.

In the present study, frame rate was set at 27 frames a second with a 30° colour sector in both LVSV and RVSV measurements. The pulse repetition frequency was 4.5 kHz. Aliasing was prohibited by shifting the colour baseline (Doppler zero shift) velocity up to approximately 1.4 m/s. The cut off frequency of the wall filter was set high enough to eliminate the clutter signals from the moving tissue (cut off frequency 900 Hz). An optimal gain setting was obtained without random colour noise in the non-flow areas by maximising the gain level.

For left ventricular and right ventricular stroke volume (LVSV, RVSV) measurements, colour Doppler image acquisition was obtained from the apical long axis view and the parasternal short axis view, respectively. Several frames of colour

Figure 2 An example of measurement of left ventricular stroke volume in the apical long axis view (A) and right ventricular stroke volume in the parasternal short axis view (B) by automated cardiac flow measurement. A region of interest is set on the aortic and pulmonary annulus on the display to obtain the velocity profile. Flow volume is measured by the temporal integration of the flow volume rate obtained by spatial integration of the velocity profile throughout the systolic period. Ao, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RVOT, right ventricular outflow tract.

images were recorded sequentially on the image memory. On a selected beat, the systolic period for both LVSV and RVSV measurements was manually defined by a trigger mark based on the ECG. A region of interest was set on the aortic annulus for LVSV and the pulmonary annulus for RVSV in the displays to obtain the velocity profile (fig 2). Angle compensation was performed in each case. For each frame of the colour images, the flow volume rate was automatically calculated by rotational integration of the velocity profile in the region of interest. Stroke volume was then automatically measured by the temporal integration of the flow volume rate throughout the systolic period for both LVSV and RVSV measurements. Three measurements of each variable were averaged to determine both LVSV and RVSV. The Qp/Qs ratio was defined as the ratio RVSV/LVSV. This examination was performed by one investigator blinded to the results from the cardiac catheterisation.

Cardiac catheterisation

All 22 patients with atrial septal defects underwent cardiac catheterisation. Oxygen saturation in the blood was measured in pulmonary arterial (Spa), pulmonary venous (Spv), systemic arterial (Ssa), and mixed venous (Smv) samples. In the mixed venous sample, the inferior vena cava sample was weighed 3:1 in combination with superior vena cava sample. The Qp/Qs ratio was calculated from the oxygen saturation in blood using the equation:

$$Qp/Qs = (Ssa - Smv) / (Spv - Spa).$$

Figure 3 (A) Automated cardiac flow measurement (ACM) of left and right ventricular stroke volume (LVSV, RSVS) in the control group. (B) Agreement plots between LVSV and RSVS determined by ACM. Values are mean difference (solid line) $\pm$ 2 SD (dashed lines).

Figure 4 (A) Scatterplots showing relations between automated cardiac flow measurement (ACM) derived Qp/Qs ratio and Qp/Qs determined by oximetry. (B) Agreement plots between ACM derived Qp/Qs ratio and Qp/Qs determined by oximetry. Values are mean difference (solid line) $\pm$ 2 SD (dashed lines).

Data analysis

Data are expressed as mean (SD). Linear regression analysis was used to compare ACM derived LVSV with ACM derived RSVS in the control group. Agreement between ACM derived LVSV and RSVS was evaluated using the Bland-Altman method.¹¹ Comparison between Qp/Qs in atrial septal defect and Qp/Qs in normal control was made with an unpaired *t* test. A probability value of $p < 0.01$ was considered significant. The ACM derived Qp/Qs was compared with Qp/Qs by oximetry using linear regression analysis. Agreement

between ACM derived Qp/Qs and Qp/Qs obtained by oximetry was evaluated by the Bland-Altman method.¹¹

To test the reproducibility of the measurements by the ACM method, we randomly selected eight study subjects and submitted them to two independent examiners for evaluation of LVSV and RSVS using the ACM method. Reproducibility was calculated as the standard deviation of the differences between the measurements obtained by the two examiners, and was expressed as a percentage of the average value.

In the eight randomly selected patients, we measured the time required for estimating the Qp/Qs ratio in one cardiac cycle by the ACM method, including optimising the image, selecting the systolic period from the stored image memory, positioning a desired region of interest, and performing the automated calculation of LVSV and RSVS in one recorded cardiac cycle.

RESULTS

LVSV, RSVS, and the Qp/Qs ratio measured by ACM

There was a good correlation between LVSV and RSVS obtained from ACM in the control group ($r = 0.98$, $y = 0.97x + 0.25$, $SEE = 2.9$ ml; fig 3A). The mean difference between LVSV and RSVS values obtained by ACM was -1.25 (2.76) ml (fig 3B). The mean (SD) Qp/Qs ratio obtained from ACM in normal subjects was 0.98 (0.06). The Qp/Qs ratio in patients with atrial septal defects was significantly higher than in the control group, at 3.11 (1.20) ($p < 0.001$).

Comparison of the Qp/Qs ratio by ACM and oximetry

Table 1 shows ACM and cardiac catheterisation measurements in patients with atrial septal defects. The ACM determined Qp/Qs ratio correlated well with the Qp/Qs ratio determined by oximetry ($r = 0.86$, $y = 0.75x + 0.55$, $SEE = 0.64$; fig 4A). The mean difference between ACM and oximetry was -0.28 (0.69) for the measurement of the Qp/Qs ratio (fig 4B).

Reproducibility

The reproducibility of the ACM method was 3.9% and 4.7% for the measurement of LVSV and RSVS, respectively.

Time required for estimation of the Qp/Qs ratio

The mean (SD) time required for estimation of the Qp/Qs ratio in one cardiac cycle by the ACM method was 123 (26) seconds.

DISCUSSION

In this study, we applied a newly developed ACM method in order to estimate the Qp/Qs ratio in patients with atrial septal defects by automated measurement of LVSV and RSVS. The results showed that the Qp/Qs ratio obtained using this new technique correlated well with that determined by oximetry. The technique was also shown to be feasible in 22 of 25 patients with an atrial septal defect who were in sinus rhythm (88%). This suggests that a significant atrial septal defect can be diagnosed easily by non-invasive echocardiography without cardiac catheterisation.

Estimation of the Qp/Qs ratio by ACM method

The ACM method applied in our study was developed for the automated measurement of flow volume using spatial and temporal integration of the Doppler velocity profile.⁴⁻¹⁰ It has been reported that flow volume determined by the ACM algorithm shows good agreement with that measured by flowmeter in experimental studies.⁴ Recent reports have shown good correlations between ACM and clinically accepted techniques such as the thermodilution method for estimating aortic outflow volume in the clinical situation.⁵⁻⁹ This new method has recently been validated in animals with atrial septal defects for the calculation of the Qp/Qs ratio by measuring LVSV and RSVS.¹⁰ To our knowledge, this is the first report evaluating the ACM method against oximetry during

Table 1 Comparison of automated cardiac flow measurement (ACM) and catheter measurements in patients with atrial septal defects

Patient number	Age (years)	Sex	ACM measurements		Catheter measurements	
			RVSV (ml)	LVSV (ml)	Qp/Qs	Qp/Qs
1	23	F	70	37	1.9	2.5
2	68	M	167	45	3.7	2.7
3	25	F	118	29	4.1	3.8
4	71	F	102	34	3.0	4.8
5	40	F	100	40	2.5	2.3
6	60	M	148	33	4.6	6.1
7	53	F	157	24	6.5	7.4
8	20	M	55	45	1.2	1.4
9	57	F	72	42	1.7	2.7
10	27	F	85	35	2.4	3.2
11	37	F	84	38	2.1	1.7
12	47	F	121	42	2.9	2.6
13	55	F	87	34	2.4	3.0
14	40	F	116	40	2.9	3.6
15	52	M	88	36	2.4	2.9
16	37	M	128	45	2.8	3.5
17	61	F	218	58	3.8	3.4
18	40	F	186	37	5.0	4.6
19	23	F	114	36	3.1	3.7
20	34	M	172	40	4.3	3.9
21	26	F	99	41	2.4	2.7
22	63	F	113	43	2.6	2.0

F, female; LVSV, left ventricular stroke volume; M, male; RVSV, right ventricular stroke volume.

cardiac catheterisation for estimating the Qp/Qs ratio in patients with an atrial septal defect.

Advantages of the ACM method

There are several advantages of the ACM method in comparison with conventional pulsed Doppler method for evaluating the Qp/Qs ratio.

Firstly, quick and simple calculation of LVSV and RVSV can be achieved with the ACM because the method requires only two manual procedures—the selection of the systolic period in the stored image memory, and positioning a region of interest on the aortic or pulmonary annulus in the Doppler colour flow images. LVSV and RVSV calculations can be performed by ACM without tracing the Doppler waveform to measure the time-velocity integral which is necessary with the pulsed Doppler method. In addition, we do not need to measure the area of the flow tract, which is a major source of error in the pulsed Doppler method,^{12–14} because the edge of the colour profile is detected as the width of the flow tract in each frame. Recent studies validating the accuracy of ACM for measurement of cardiac output have reaffirmed that this automated method is much simpler and faster than pulsed Doppler.^{5,9} Thus this new technique can easily be applied to the estimation of the Qp/Qs ratio in patients with atrial septal defects.

Secondly, ACM uses the velocity profile across the flow tract diameter in the calculation of the flow volume rate, while in conventional pulsed Doppler methods the spectral velocity from a centrally placed sample point is measured. In addition, the flow rate at each frame is temporally integrated for stroke volume calculation in the ACM method. Thus this automated method requires fewer assumptions than the pulsed Doppler method.

Study limitations

There were several limitations to our study that must be considered.

Firstly, the Qp/Qs ratio measured by ACM was not simultaneously compared with Qp/Qs measured by oximetry, although cardiac catheterisation was done within one week after the ACM study. Although estimation of Qp/Qs by oximetry has already been accepted in the clinical setting, this might not necessarily be true in certain individual cases.

Secondly, the velocity profile of the aortic and pulmonary flow may be skewed,^{15–18} while ACM assumes an axisymmetric flow to calculate the flow rate. However, as discussed in the experimental study, averaging over the entire axial flow velocity field cancels out the overestimation from one radius and the underestimation from another, for both LVSV and RVSV.¹⁰

Finally, machine settings including frame rate, colour gain, and colour filter can affect on the accuracy of the ACM method for flow volume calculation¹⁹ because flow volume is integrated from time-sequential colour flow images.⁴ In addition, Sun and colleagues reported that cardiac output estimation is influenced by the colour gain using the same method, although reliable cardiac output values can be obtained by optimising the colour gain.⁵ Adequate setting of colour gain, colour filter, and frame rate is necessary to obtain accurate flow volume measurement by this method.^{9,19}

Conclusions

The new simplified ACM method is clinically useful in the non-invasive automated estimation of the Qp/Qs ratio in patients with atrial septal defects.

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REFERENCES

- Sanders SP, Yeager S, Williams. Measurement of systemic and pulmonary blood flow and Qp/Qs ratio using Doppler and two-dimensional Doppler echocardiography. *Am J Cardiol* 1983;51:652–6.
- Kitabatake A, Inoue M, Asao M, et al. Noninvasive evaluation of the ratio of pulmonary to systemic flow in atrial septal defect by duplex Doppler echocardiography. *Circulation* 1984;69:73–9.

- 3 **Dittman H**, Jackson R, Voelker W, *et al.* Accuracy of Doppler echocardiography in quantitation of left to right shunts in adult patients with atrial septal defect. *J Am Coll Cardiol* 1988;**11**:338–42.
- 4 **Tsujino H**, Shiki E, Hiram M, *et al.* Quantitative measurement of volume flow rate (cardiac output) by the multibeam Doppler method. *J Am Soc Echocardiogr* 1995;**8**:621–30.
- 5 **Sun JP**, Pu M, Fouad FM, *et al.* Automated cardiac output measurement by spatiotemporal integration of color Doppler data: in vitro and clinical validation. *Circulation* 1997;**95**:932–9.
- 6 **Shiota T**, Jones M, Aida S, *et al.* Calculation of aortic regurgitant volume by a new digital Doppler color flow mapping method: an animal study with quantified chronic aortic regurgitation. *J Am Coll Cardiol* 1997;**30**:834–42.
- 7 **Hozumi T**, Yoshida K, Akasaka T, *et al.* Automated assessment of mitral regurgitant volume and regurgitant fraction by a newly developed digital color Doppler velocity profile integration method. *Am J Cardiol* 1997;**80**:1325–30.
- 8 **Sun JP**, Yang XS, Qin JX, *et al.* Quantitation of mitral regurgitation by automated cardiac output measurement: experimental and clinical validation. *J Am Coll Cardiol* 1998;**32**:1074–82.
- 9 **Hozumi T**, Yoshida K, Mori I, *et al.* Noninvasive assessment of hemodynamic subsets in patients with acute myocardial infarction using digital color Doppler velocity profile integration and pulmonary venous flow analysis. *Am J Cardiol* 1999;**83**:1027–32.
- 10 **Shiota T**, Jones M, Aida S, *et al.* Validation of the accuracy of both right and left ventricular outflow volume determinations and semiautomated calculation of shunt volumes through atrial septal defects by digital color Doppler flow mapping in a chronic animal model. *J Am Coll Cardiol* 1999;**34**:587–93.
- 11 **Bland JM**, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;*ii*:307–10.
- 12 **Lewis JF**, Kuo LC, Nelson JC, *et al.* 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.
- 13 **Meijboom EJ**, Rijsterborgh H, Bot H, *et al.* Limits of reproducibility of blood flow measurements by Doppler echocardiography. *Am J Cardiol* 1987;**59**:133–7.
- 14 **Crabson S**, Murray A, Peart I, *et al.* Reproducibility of cardiac output measurement by cross sectional and Doppler echocardiography. *Br Heart J* 1988;**59**:680–4.
- 15 **Zhou YQ**, Faerstrand S, Matre K, *et al.* Velocity distributions in the left ventricular outflow tract and the aortic annulus measured with Doppler colour flow mapping in normal subjects. *Eur Heart J* 1993;**14**:1179–88.
- 16 **Sloth E**, Houliand K, Oyre S. Three-dimensional visualization of velocity profile in the human main pulmonary artery using magnetic resonance phase velocity mapping. *Am Heart J* 1994;**128**:1130–8.
- 17 **Sun Y**, Ask P, Sjoberg BJ, *et al.* Estimation of volume flow rate by surface integration of velocity vectors from color Doppler images. *J Am Soc Echocardiogr* 1995;**8**:904–14.
- 18 **Kim WY**, Poulsen JK, Tepp K, *et al.* A new Doppler method for quantification of volumetric flow: a two-dimensional color Doppler study. *J Am Coll Cardiol* 1996;**27**:182–92.
- 19 **Hozumi T**, Yoshida K, Akasaka T, *et al.* Effect of frame rate, colour gain, and filter setting on automated cardiac output measurement by spatio-temporal integration of Doppler velocity profile in vivo [abstract]. *J Am Coll Cardiol* 1998;**31**:43A.

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