# Influence of Sampling Site and Flow Area on Cardiac Output Measurements by Doppler Echocardiography

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In 40 patients cardiac output was simultaneously determined by pulsed Doppler echocardiography and thermodilution (range 4.0 to 10.2 liters/min). The sample volume was located in the center of the mitral anulus, at the tips of the mitral leaflets and in the center of the aortic anulus. Circular cross-sectional areas of the mitral anulus, aortic anulus and aortic bulbus were calculated from M-mode and two-dimensional echocardiographic diameters. The varying short axis of the elliptical mitral opening area was obtained from the diastolic leaflet separation in the M-mode, and the long axis was derived from the maximal mitral orifice area or mitral anulus diameter. Cardiac output was calculated by multiplying time-velocity integrals with the different areas and heart rate.

Doppler flow measurements correlated significantly with the thermodilution method (r = 0.79 to 0.93). Flow measurements at the aortic anulus were most accurate (r = 0.93, SEE = 0.589 liter/min) if the annular area was derived from the M-mode tracing. Measurement of the anulus in the apical five chamber view yielded a significant underestimation and the area of the aortic bulbus provided an overestimation of cardiac output. Left ventricular inflow was underestimated at the mitral leaflet tips and overestimated at the mitral anulus.

The accuracy of pulsed Doppler cardiac output measurements strongly depends on the assumed flow area and sampling site. Both should be determined at the same level in the inflow or outflow tract of the left ventricle. Measurement of cardiac output in the center of the aortic anulus provided the highest accuracy.

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Theoretically, for cardiac output calculations using Doppler echocardiography a correct determination of the flow area, a laminar flow with a flat velocity profile at this area and exact measurement of the mean temporal velocity is necessary (1). A variety of methods have been described to measure cardiac output in the inflow or outflow tract of the left and right ventricles and in the great arteries (2–24).

Few data exist about the accuracy of the different methods using Doppler echocardiography in the left ventricular inflow and outflow tract compared with an accepted standard of cardiac output measurement, simultaneously determined in the same patient (7,13). Thus, the purpose of this study was to compare the accuracy of different Doppler methods of cardiac output calculation in the same individual. The influence of various sampling sites and the method of flow area calculation on the accuracy of the Doppler study was determined.

## Methods

**Study patients.** The study group consisted of 40 patients with high quality echocardiograms and excellent Doppler signals, who underwent a complete Doppler and echocardiographic examination 1 day before the cardiac output study. Patients with valvular heart disease or intracardiac shunts were excluded. The age of the 32 men and 8 women ranged from 14 to 64 years. Thirty-nine patients had sinus rhythm and only one patient had atrial fibrillation. Right and left heart catheterization, cineventriculography and selective coronary arteriography were performed in all patients. No patient had signs of aortic, mitral or tricuspid regurgitation by angiography and echocardiography. Nineteen patients had coronary artery disease, 5 had dilated cardiomyopathy and 16 had no organic heart disease.

**Thermodilution method.** After routine right and left heart catheterization, a 7F Swan-Ganz thermodilution catheter was placed in the pulmonary artery. Cardiac output was simultaneously determined by the thermodilution technique (25) and Doppler echocardiography under steady state conditions with a constant heart rate throughout the measurements. The thermodilution measurements were performed

during the Doppler flow velocity measurements. Because the optimal probe position was known from the prior examination, the time for acquisition of flow velocity was considerably reduced and the study time shortened. The thermodilution cardiac output was obtained with an Edward cardiac output instrument model 9520-A by injecting rapidly 10 ml of 0.9% cold sodium chloride solution through the proximal part of the Swan-Ganz thermodilution catheter. Cardiac output was computed as the average of three values with a difference of <10%. If the difference between the lowest and highest value of the first three measurements was >10%, two additional cardiac output measurements were performed and the extremes were discarded before averaging.

**Echocardiography.** The study was performed using a 90° phased array sector scanner with a single transducer for the M-mode, two-dimensional and Doppler echocardiographic examination (Toshiba SSH-40A, Toshiba SDS-21A). The ultrasound frequency of the probe was 2.4 MHz and the pulse repetition frequency of the Doppler unit was 4 or 6 kHz, depending on the depth of the sampling site. The axial length of the sample volume was 3 mm. The Doppler frequency shifts were processed through a fast Fourier transform spectral analyzer. Cross-sectional echocardiograms were documented on videotapes (Panasonic 6200, VHS). The M-mode echocardiograms and Doppler frequency spectra were recorded at a paper speed of 100 mm/s on a hard copy unit (Line Scan Recorder 20B, Toshiba).

**Flow area recording.** Each patient was examined in the left lateral recumbent position. With the transducer in the left parasternal position, M-mode echocardiography was performed, controlled by the two-dimensional image. In the left ventricular outflow tract M-mode tracings were obtained at the aortic anulus, directly proximal to the insertion of the aortic leaflets and at the maximal diameter of the bulbus aortae. Two-dimensional images of the mitral valve orifice were recorded in a standard short-axis view. Both leaflet tips were visualized at a level just proximal to the point at which the circumference was incomplete. At the same level the M-mode echocardiogram of the maximal leaflet separation was obtained. It was used to correct for diastolic variations in mitral valve orifice size (5). The transducer was then positioned near the apex to obtain the four and five chamber views. After visualizing the mitral and aortic anulus in the apical views, the Doppler study was performed.

**Flow velocity measurement.** The sample volume was placed parallel to the left ventricular diastolic flow in the center of the mitral valve anulus and just apical to the tips of the mitral valve leaflets. In the left ventricular outflow tract, flow velocity was recorded in the center of the aortic anulus, just proximal to the aortic valve leaflets. The sequence of the Doppler measurements was nonrandomized and individually variable. In every sampling position the

angle between the assumed blood flow and the cursor line of the sample volume was kept less than 20°.

**Echocardiographic data analysis.** All measurements were made with an off-line digitizing computer system (Cardio 200, Kontron). This system allowed measurements to be taken directly from the video screen by an electronic cursor. The recorded two-dimensional images were played back through a video system with a search and stop frame module (Panasonic 6200, VHS). Hardcopies were analyzed using the digitizing pad of the computer system. All area and distance measurements were done in triplicate and during three different heart cycles before averaging. In the one patient with atrial fibrillation only cardiac cycles of medium length and a difference in cycle length of less than 5% were analyzed. Two-dimensional echocardiograms (26) and the M-mode tracing of the aortic anulus and aortic bulbus were digitized at the inner edge of the endocardial echoes. For the M-mode echocardiogram of the mitral valve the leading edge standard was used (27). Only those Doppler recordings were chosen that showed maximal flow velocities and a narrow frequency bandwidth representative of undisturbed flow. These profiles were traced through their darkest portion at their modal velocity (5). The area under the curve was the time-velocity integral of a cardiac cycle.

**Cardiac output calculation.** Cardiac output was calculated as the product of the Doppler time-velocity integral, cross-sectional area and heart rate. In the left ventricular outflow tract the time-velocity integral, recorded in the center of the aortic anulus, was matched with different cross-sectional areas. The areas were assumed to be circular and calculated from the mid-systolic diameter of the aortic anulus and aortic bulbus in the M-mode echocardiogram or from the mid-systolic diameter of the aortic anulus in the apical five chamber view (28) (Table 1).

In the left ventricular inflow tract flow, volume was calculated at the mitral anulus and at the tips of the mitral leaflets. The cross-sectional area of the mitral anulus was assumed to be circular and derived from the mid-diastolic diameter of the mitral ring, seen in the apical four chamber view (29). The orifice area at the mitral valve leaflet tips was assumed to be elliptical with a varying short axis and a constant long axis. The mean diastolic length of the short axis was derived from the mitral valve M-mode tracing and was used to correct for diastolic variations of the mitral orifice area according to Fisher et al. (5). In a second flow area calculation, the elliptical mitral valve area was derived from the mean diastolic leaflet separation in the M-mode and the mid-diastolic diameter of the mitral anulus in the apical four chamber view (21).

**Reproducibility.** In 10 randomly chosen patients the reproducibility of the time-velocity integral measurements for one observer and between two observers was determined.

**Table 1.** Cardiac Output Calculation by Different Doppler Methods

| | Flow Area | | Sampling Site |
|---|---|---|---|
| | Shape | Variable | |
| Aortic anulus (M mode) | Circular | Diameter, M mode | Aortic anulus |
| Aortic anulus (2DE) | Circular | Diameter, five-chamber view | Aortic anulus |
| Aortic bulbus (M mode) | Circular | Diameter, M mode | Aortic anulus |
| Mitral anulus | Circular | Diameter, four-chamber view | Mitral anulus |
| Mitral leaflets I | Elliptical | Mitral orifice area, M mode | Mitral leaflets |
| Mitral leaflets II | Elliptical | Mitral anulus diameter, M mode | Mitral leaflets |

For every method the assumed shape of the flow area and the echocardiographic variable for flow area calculation are described. M-mode = M-mode echocardiogram; 2DE = two-dimensional echocardiogram.

**Statistics.** Invasive and noninvasive data were compared by paired $t$ test and linear regression analysis. The 95% confidence limits for the correlation coefficients (r) and SEE were calculated. Variability was expressed as a percent error of each measurement and was determined as the difference between the two observations divided by the mean value of the two observations. A probability (p) value $<0.05$ was considered statistically significant (30).

## Results

The cardiac output by the thermodilution method ranged from 4.0 to 10.2 liters/min (mean 6.99). All cardiac output measurements by the different Doppler methods correlated significantly with the thermodilution derived values (Table 2).

**Left ventricular outflow.** For the left ventricular out-flow volume the correlation coefficients ranged from 0.79 to 0.93 and the SEE from 0.589 to 1.516 liters/min, depending on the assumed flow area (Fig. 1). Only if the diameter of the aortic anulus, measured in the M-mode echocardiogram, was used for flow area calculation, were Doppler-derived cardiac outputs not statistically different from the thermodilution outputs (Table 2). This method yielded a correlation coefficient of 0.93 and an SEE of 0.589 liter/min. Flow volumes were underestimated if the aortic anulus was measured in the apical five chamber view and

were overestimated if the cross-sectional area of the aortic bulbus was used.

**Left ventricular inflow.** In the left ventricular inflow tract the accuracy of Doppler flow measurements was dependent on the site of velocity measurements and the calculated flow area (Fig. 2). For flow measurements in the center of the mitral anulus the correlation was 0.86 with an SEE of 0.800 liter/min (Table 2). At this site flow was overestimated by the Doppler technique. In contrast, at the mitral leaflet tips Doppler measurements underestimated cardiac output significantly. At the mitral valve leaflet tips flow was dependent on the method of calculation of the mean diastolic opening area. The maximal mitral valve area corrected for the mean diastolic M-mode leaflet separation yielded a correlation coefficient of 0.91 and an SEE of 0.532 liter/min. If the elliptical area was calculated from the mean diastolic leaflet separation in the M-mode tracing and the mitral anulus diameter, the correlation was 0.81 and the SEE was 0.731 liter/min.

The 95% confidence limits for the correlation coefficients and the SEE are listed in Table 2. There was statistically no difference in the strength of the correlations, but flow measurements using the area of the aortic bulbus provided the greatest SEE.

**Reproducibility of data.** In 10 patients the mean percent intraobserver variability for the time-velocity integrals was 5.3% at the mitral leaflet tips and 3.8% at the aortic anulus.

**Table 2.** Correlations Between the Thermodilution Method and Different Doppler Techniques for Measuring Cardiac Output

| | r | y = ax + b (liters/min) | SEE (liters/min) | $r_{95\%}$ | $SEE_{95\%}$ (liters/min) | $\overline{D}$ |
|---|---|---|---|---|---|---|
| Aortic anulus (M-mode) | 0.93 | 0.94x + 0.44 | 0.589 | 0.87 to 0.96 | 0.497 to 0.759 | NS |
| Aortic anulus (2DE) | 0.89 | 0.92x − 0.18 | 0.695 | 0.80 to 0.94 | 0.586 to 0.896 | PDE < Th* |
| Aortic bulbus (M-mode) | 0.79 | 1.28x + 0.47 | 1.516 | 0.64 to 0.88 | 1.279 to 1.955 | PDE > Th† |
| Mitral anulus | 0.86 | 0.88x + 1.75 | 0.800 | 0.75 to 0.93 | 0.675 to 1.031 | PDE > Th† |
| Mitral leaflets I | 0.91 | 0.79x + 0.63 | 0.532 | 0.84 to 0.95 | 0.449 to 0.685 | PDE < Th† |
| Mitral leaflets II | 0.81 | 0.67x + 1.29 | 0.731 | 0.67 to 0.90 | 0.617 to 0.941 | PDE < Th† |

*p $< 10^{-7}$; †p $< 10^{-8}$. a and b = slope and intercept, respectively, of the regression line; $\overline{D}$ = difference between thermodilution (Th) and pulsed Doppler echocardiogram (PDE) in paired $t$ test; $r_{95\%}$ and $SEE_{95\%}$ = 95% confidence limits of the correlation and standard error of the estimate, respectively.
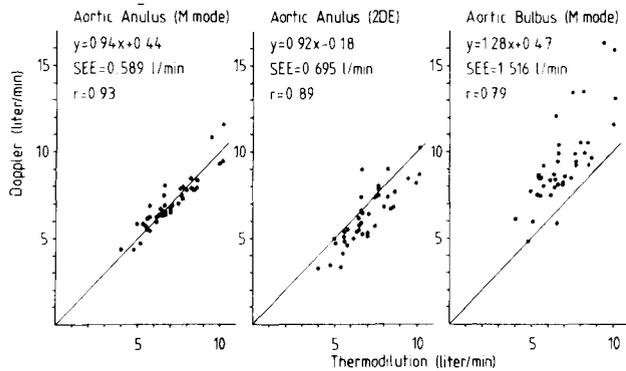
**Figure 1.** Cardiac output measurements in the left ventricular outflow tract (aortic anulus and bulbus). The correlations between the Doppler echocardiographic estimated cardiac outputs and the thermodilution method were dependent on the assumed flow area. The cross sections were calculated from the mid-systolic diameter in the M-mode or two-dimensional (2DE) echocardiogram.

The correlation between the two readings was 0.99 at the mitral valve and 0.98 at the aortic anulus. The interobserver variability was 6.2% at the mitral valve tips and 4.5% at the aortic anulus. For each site the correlation coefficient between the measurements was 0.96. Mean differences in the paired $t$ test were not significant.

## Discussion

In the present study Doppler flow measurements in the left ventricular inflow and outflow tract correlated significantly with the thermodilution cardiac output. The accuracy of the Doppler measurements by means of systematic overestimation or underestimation was considerably influenced by the site of velocity measurement and the method of flow area calculation.

**Flow measurement in the left ventricular outflow tract.** Cardiac output measurement was most accurate in the center of the aortic anulus, if at the site of flow velocity measure-

**Figure 2.** Cardiac output measurements at the mitral anulus and at the mitral leaflet tips. The opening area of the mitral leaflets was calculated from the maximal orifice area (I) or from the mid-diastolic mitral anulus diameter (II) and corrected for the mean diastolic M-mode leaflet separation.
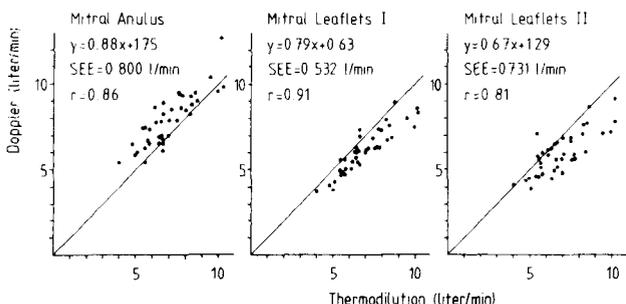


ment the cross-sectional area of the vessel was derived from the two-dimensional guided M-mode record (Table 2). Calculation of the aortic anulus area from its diameter in the five chamber view resulted in a systematic underestimation of cardiac output and a slightly but not significantly decreased correlation. This might be the effect of the lower lateral resolution of the two-dimensional echocardiogram compared with the better axial resolution of the M-mode record (31).

Blood flow is laminar with a flat velocity profile in the left ventricular outflow tract at the aortic anulus and in the first part of the ascending aorta (1,32,33). In patients with a normal aortic valve and outflow tract, blood flow velocity in this region is determined by the smallest flow area at the aortic anulus (1,11). Therefore, in the present study the generally larger cross-sectional area of the aortic bulbus produced a significant overestimation of cardiac output. This result is substantiated by the work of Ihlen et al. (11), who overestimated flow volumes if the measurements of blood velocities and cross-sectional areas were performed in the first part of the ascending aorta.

In the majority of previous studies cardiac output measurements by Doppler echocardiography have been performed in the ascending aorta from the suprasternal notch (2-4,6,9-12,14,17-19,22). In contrast to flow measurements proximal to the aortic leaflets, coronary blood flow is neglected (2,6). The results of the study of Labovitz et al. (12) indicated the superiority of flow determinations in the left ventricular outflow tract from the apical window to flow measurements in the ascending or descending aorta.

**Flow measurement in the left ventricular inflow tract.** In our study quantification of left ventricular inflow by Doppler echocardiography was performed at the mitral valve anulus and at the tips of the mitral leaflets. Experiments on normal mitral valves (34) have shown a fairly flat velocity profile at the mitral anulus and a slightly peaked profile at the valve orifice. At these sites Doppler measurements therefore estimate the mean spatial velocity with reasonable accuracy, provided that they are made in alignment with the flow direction. For cardiac output measurements the accurate determination of flow areas at the anulus and at the leaflet tips is crucial (35).

**Flow at the mitral anulus.** For measurements at the mitral anulus the correlation coefficient of 0.86 and the SEE of 0.800 liter/min in the present investigation were comparable with the results of previous clinical and experimental studies (7,13,23). The Doppler measurements at the mitral anulus, however, overestimated cardiac output systematically. This may be a result of the method of the cross-sectional area calculation. The shape of the mitral anulus is elliptical rather than circular (8,29). In the four chamber view the long axis of the elliptical anulus area was determined and used for calculation of a circular flow area. This resulted in an overestimation of the real size of the anulus.

Similarly, Goldberg et al. (8) determined cardiac output more accurately if they used an elliptical annular area instead of a circular cross section. They matched the annular areas with the flow velocity integrals obtained at the mitral valve tips. Despite the greater flow velocity integrals at the mitral valve tips compared with the mitral anulus (24), they avoided a significant overestimation of cardiac output. In our study, as in the report of Zhang et al. (24), the velocity integrals were significantly larger at the mitral leaflet tips than in the center of the mitral anulus (mean 16.8 versus 12.9 cm, p $< 0.0001$).

**Flow at the mitral leaflet tips.** Doppler ultrasound quantification of left ventricular inflow at the mitral leaflet tips was first validated by Fisher et al. (5) in an open chest animal model. The flow velocity was sampled at the tips of the mitral valve leaflets and the maximal opening area of the mitral valve was corrected for diastolic variation with the M-mode tracing of the leaflets. Our data, with a correlation of 0.91 and an SEE of 0.532 liter/min, confirm the strong correlation between invasive and noninvasive flow measurements reported by Fisher et al. In our study we attribute the underestimation of cardiac output by the method of Fisher et al. to the different method of maximal mitral valve opening area measurement. We traced the maximal mitral valve opening area at the inner edge (26) of the leaflets, whereas Fisher et al. (5) measured through the middle of the leaflets.

In a second flow area calculation for the mitral valve leaflets we used a modification of a mitral valve ellipse method proposed by Touche et al. (21). The mitral anulus diameter was used for the long axis of the ellipse and the short axis was estimated from the mean diastolic leaflet separation in the M-mode record. In our modification, however, we did not integrate the changing orifice with the changing velocities instantaneously. This may be the reason for the slightly decreased correlation in our study in comparison with the method of Fisher et al. (5).

**Reproducibility.** In previous studies (13,36), the intraobserver and interobserver variability of velocity measurements was greater at the mitral valve than in the left ventricular outflow tract. Lewis et al. (13) reported an interobserver variability for cardiac output measurements of 6.8% at the aortic anulus and 16.4% at the mitral anulus. Nicolosi et al. (37) found an intraobserver variability of 5.8% and an intraobserver variability of 6.1% for Doppler flow calculation at the mitral leaflet tips.

**Conclusions.** The accuracy of cardiac output measurements by Doppler echocardiography in the inflow or outflow tract of the left ventricle is influenced by the site of flow velocity measurement and especially by the method of flow area calculation. Both variables should be determined at the same level. Systematic errors in noninvasive cardiac output determinations refer to different modalities of estimating relevant flow areas. Flow measurement is most accurate in

the center of the aortic anulus, if the circular area of the anulus is derived from the two-dimensional guided M-mode record.

Thus, Doppler echocardiographic determination of cardiac output in the center of the aortic anulus has become a routinely used clinical method in our laboratory and it seems to be especially useful for hemodynamic monitoring in the cardiac care unit.

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