Reproducibility of measurements of cardiac output in newborn infants by Doppler ultrasound

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Abstract

Interobserver reproducibility in deriving cardiac output by measuring aortic blood flow velocity and diameter with imaging and Doppler ultrasound was investigated in 20 healthy infants born at full term. Aortic diameter was measured in three ways. Mean blood flow velocity was measured at three sites with both continuous wave and pulsed Doppler. Two observers carried out each study independently. Intraobserver reproducibility was investigated in 12 infants using the suprasternal site for measuring blood flow velocity. The most reproducible determination of cardiac output was found when the suprasternal site with continuous wave Doppler was used for measurement of blood flow velocity and M mode trailing edge to leading edge echocardiography was used for diameter. Normal mean (2 SD) cardiac output is 231 (77) ml/kg/min.

Technical difficulties in measuring aortic diameter accurately limit direct comparison between infants.

Reliable measurement of cardiac output in newborn infants would be useful in various ways. Non-invasive methods such as impedance cardiography,[1 2] or selected M mode echocardiographic indices,[3] have been available for over 10 years but have not become widely accepted. Doppler ultrasound has more recently been introduced. Theoretically this should be ideal, being both non-invasive and repeatable.

Measurement of cardiac output with Doppler ultrasound requires measurement of aortic cross sectional area and blood flow velocity. Alverson *et al*,[4–7] Mellander *et al*,[8] and Walther *et al*[9] have pointed out the limitations in measurement of diameter and there is no universally accepted method. Walther used M mode leading edge to leading edge echocardiography (fig 1),[9] and Alverson *et al* used M mode trailing edge to leading edge echocardiography.[4–7] Mellander *et al*, who used both the cross sectional image for internal aortic diameter and M mode trailing edge to leading edge method, found the M mode more satisfactory.[8] As the area is derived from the square of the radius, any error in the measurement of the diameter will be magnified.

Accurate assessment of blood flow velocity requires the Doppler beam to be aligned with the long axis of the aorta, and any deviation will result in an underestimation that is related to the cosine of the angle. In practice, providing the angle is less than 15°, the error will be less than 3% (fig 2). The suprasternal site has generally been used but this may not be ideal, especially in infants who are being ventilated and in whom this site may be inaccessible; either the apical window or the subcostal site may be preferable and geometrically better aligned.

Velocity can be measured by two different techniques; pulsed Doppler obtains information about flow at a predetermined depth and has usually been used, and the alternative, continuous wave, has no depth resolution but may be easier to use and be more reproducible.

Zero crossing detectors[4–7 9] or mean velocity estimators have been used in previous studies, but these have definite limitations.[10] Thus although discrete Fourier transformation is used in all modern Doppler systems, the results of measuring cardiac output in the newborn have not been fully investigated. In addition the advent of coloured Doppler enables a more accurate diagnosis of an arterial duct, allowing such patients to be excluded from the study.

We know of no other study in newborn infants that directly compares reproducibility in measurement of cardiac output at the three standard sites using both pulsed and continuous wave Doppler, and using the three different quoted methods for measuring aortic diameter. We therefore report the results of a study using Doppler spectral analysis.

Methods

The first part of the study determined interobserver differences in the measurement of cardiac output. We studied 20 healthy infants, whose gestational age range was 37 to 41 weeks, who were between 2 and 7 days old at the time of the study, and whose weights ranged from 2380 to 4020 g. They were all quiet at the time of the study.

Measurements were made using a Vingmed CFM 700 Duplex ultrasound scanner with a 5 MHz probe, which uses discrete Fourier transformation. Spectral signals were recorded at the time of study and the audio signals were later analysed by a Doptek spectrum analyser, which can edit and calculate mean blood flow velocity and analyse a sequence of cardiac cycles. For this study at least 10 cycles were analysed for each measurement of mean blood flow velocity. A ductus arteriosus was excluded using colour Doppler.

Observations were made either by a physiological measurement technician who was experienced in imaging and Doppler ultrasound, or by

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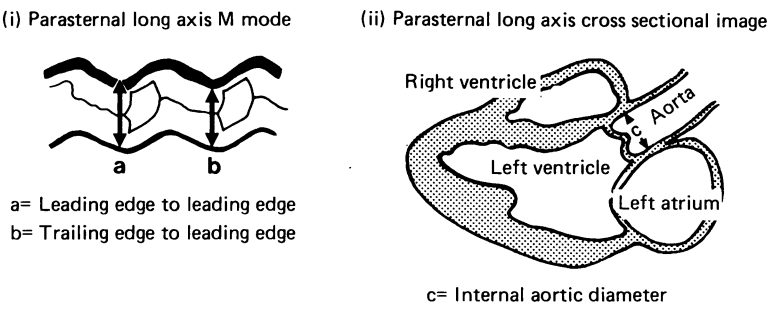

Figure 1 Methods of measuring aortic diameter.

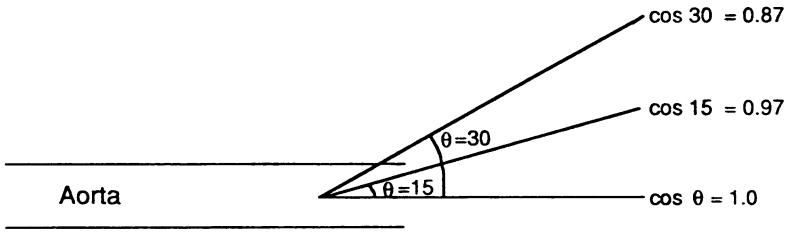

Figure 2 Effect of alignment of beam on underestimation of blood flow velocity. Velocity is calculated from Doppler equation ft– fr=2 ft Vcosθ/c: where ft is transmitted frequency, fr is received frequency, c is ultrasound propagation velocity, V is blood flow velocity, and θ is angle between ultrasound beam and direction of flow. Angle θ cannot be measured accurately and is assumed to be zero. Increasing angle θ causes progressive underestimation of velocity.

a neonatologist trained in the technique by cardiologists. The technique was acquired over several months.

Aortic diameter was determined at end diastole from a parasternal long axis view in three ways: firstly, using the M mode leading edge to leading edge technique; secondly, from the M mode trailing edge to leading edge method; and, thirdly, direct from the cross sectional image measuring the internal aortic diameter (fig 1). Measurement was taken as the average of three cycles from a hard copy. The measurement of the diameter was then repeated independently by a second observer.

Aortic Doppler signals were recorded for later analysis from three sites: suprasternal, apical, and subcostal, using both continuous wave and pulsed Doppler. The operator used imaging ultrasound to align the beam roughly in the correct anatomical site, then adjusted the beam and the depth to give the best possible signals independent of the image. Measurements were then repeated independently by a second observer. For each infant cardiac output was calculated from these signals at each of the three sites using both types of Doppler.

The second part of the study assessed intraobserver differences in the measurement of cardiac output. Twelve infants weighing between 1000 and 3900 g had both pulsed and continuous wave Doppler measurements of mean blood flow velocity made at the suprasternal site. Diameter was measured using the M mode trailing edge to leading edge method. Two independent measurements of cardiac output were made by the same observer 30 minutes apart.

STATISTICAL METHODS

Each observation of a particular patient should be thought of as arising in the following manner: an overall population mean, plus a patient component (relative to the mean), plus a between observer 'measurement error', plus a within observer 'measurement error' component. A measurement where the last two components are small compared to the first component (that is, the 'between patient' variability) is a reproducible measurement.

In the analysis of the data from two observers the first step in the investigation is to find out whether there is a significant degree of bias between observers and, if there is, the measurement is considered unsuitable for general use. If there is little or no bias between observers, all the above components of variability are estimated and the percentage of the total variability (that is, the 'sum' of all three components) that is constituted by the between/within observer components is reported.

Also reported are the standard deviations of a single measurement based on the 'sum' of all three components—that is, an estimate of the variability likely to be seen in an observation from a randomly chosen patient measured once by a single observer.

In the analysis of replicate measurements by the same observer one can estimate the 'within observer' variability only, and then report what percentage of the total variability this is.

All comparisons of sites, methods, or interobserver biases are made on repeated measures of analyses of variance and, where applicable, paired *t* tests.

Results

DETERMINATION OF INTEROBSERVER REPRODUCIBILITY

Aortic diameter

None of the three measurements of aortic diameter showed any significant interobserver bias (table 1). Clearly the best measurement was M mode trailing edge to leading edge echocardiography, which showed roughly half the between/within observer variability of the other two measurements—that is, only 25% of the total variability in a single measurement of aortic diameter taken from the M mode trailing edge to leading edge can be attributed to between observer or within observer error (table 1).

An overall summary of the means and estimated standard deviations from a single obser-

Table 1 Interobserver variability in measuring aortic diameter

Measurement	*Mean (SEM) interobserver difference (mm)*	*Estimated SD caused by observers (% of total variance) (mm)*
Cross sectional inner aortic diameter	0·04 (0·15)	0·47 (51)
M mode trailing edge to leading edge	0·00 (0·11)	0·35 (25)
M mode leading edge to leading edge	0·07 (0·16)	0·51 (46)

None of these measurements shows significant interobserver bias.

vation for the three measurements is shown in table 2. M mode trailing edge to leading edge echocardiography is the most reproducible measurement and henceforth used to calculate cardiac output.

Cardiac output

Table 3 shows both Doppler measurements for the subcostal site and the pulsed Doppler for the apical site in which there are significant interobserver biases making them unsuitable for general use until some explanation of, and correction for, these biases is forthcoming. There is little to choose among the other three site/type combinations. Because of the problem of interobserver bias at the apical site for pulsed Doppler values, however, it seemed more sensible to use the suprasternal site as a more reliable site for measurements of cardiac output. The second part of the study, therefore, investigated within observer variability at this site.

An overall summary of all site/type combinations and the resulting repeated measures analysis of variance showed no significant site difference ($p<0.05$) but among sites (table 4), there was a significant difference between Doppler types in that continuous wave measurements were between 5 and 25 ml/kg/min lower than the corresponding pulsed measurements.

Table 2 Summary of measurements of aortic diameter in 20 infants

Measurement	*Estimated population mean (mm)*	*Estimated SD based on a single observation (mm)*
Cross sectional inner aortic diameter	7·77	0·65
M mode trailing edge to leading edge	8·14	0·70
M mode leading edge to leading edge	9·94	0·74

Table 3 Interobserver variability in measuring cardiac output given as ml/kg/min

Site/ Doppler type	*Mean (SEM) interobserver difference*	*Estimated SD caused by observers (% of total variance)*
Subcostal:		
Pulsed	28·5* (8·9)	Interobserver bias
Continuous	22·9* (9·7)	Interobserver bias
Apical:		
Pulsed	32·6* (13·4)	Interobserver bias
Continuous	13·9 (9·9)	32·8 (55·2)
Suprasternal:		
Pulsed	3·9 (11·3)	35·8 (56·43)
Continuous	10·6 (8·9)	29·0 (57·2)

*Significant interobserver bias ($p=0.05$).

Table 4 Summary of measurements of cardiac output in 20 infants (ml/kg/min)

Site/ Doppler type	*Estimated population mean*	*Estimated SD based on a single observation*
Subcostal:		
Pulsed	244·0	Interobserver bias
Continuous	230·8	Interobserver bias
Apical:		
Pulsed	252·9	Interobserver bias
Continuous	227·7	44·2
Suprasternal:		
Pulsed	241·4	47·6
Continuous	230·9	38·3

DETERMINATION OF INTRAOBSERVER VARIABILITY

Continuous wave Doppler measurements for this observer were more reproducible than pulsed Doppler (table 5); the within observer variability constituted only 18% of the total variability in a single measurement, which is considerably less than the 57% contribution from the combination of between observer and within observer variability reported in the first part of the study.

The overall summary of the two measurements for this part of the study is shown in table 6, and the sample of 12 infants seems to come from a population with mean cardiac outputs about 20 ml/kg/min lower than that of the 20 infants in the first part of the study. This may be attributable to lower gestational ages in this sample of 12. Again, however, there is a consistent difference of about 10 ml/kg/min between cardiac output measured by the two Doppler types.

In summary, therefore, when taking into account both experiments it seems reasonable to conclude that the continuous wave Doppler measurements taken at the suprasternal site are the most reproducible of all those considered, in that they show no significant interobserver bias, and are repeatable by a single observer.

MINIMAL DETECTABLE CHANGE IN CARDIAC OUTPUT

These results indicate that using continuous wave Doppler at the suprasternal site, and assuming the same diameter for each measure-

Table 5 Intraobserver variability in measuring cardiac output at suprasternal site (mg/kg/min)

Doppler type	*Estimated SD caused by intraobserver variability (% of total variance)*
Pulsed	19·1 (29·0)
Continuous	16·5 (18·4)

Table 6 Summary of measurements cardiac output at suprasternal site in 12 infants for one observer (mg/kg/min)

Doppler type	*Estimated population mean*	*Estimated SD based on a single observation*
Pulsed	220·9	35·5
Continuous	209·3	38·5

Table 7 Calculated effect of error in measurement of aortic diameter

Actual diameter (mm)	*Measured diameter (mm)*	*Error in cardiac output (%)*
11	10	17
9	10	23
9	8	21
6	7	35
5	6	43

ment, the minimum difference in cardiac output that could be regarded as significant would be 90 ml/kg/min if made by two independent observers, or 45 ml/kg/min if made by the same observer on two occasions.

Discussion

Although pulsed Doppler has been used principally to measure cardiac output, Hatle used continuous wave Doppler successfully in neonates and young children for assessing aortic blood flow velocities.[11] Nishmura *et al* used continuous wave Doppler in adults to measure cardiac output, and found it correlated well with invasive methods.[12] Our results indicate that continuous wave is more reproducible than pulsed wave Doppler in the measurement of cardiac output by two independent observers. This may be because of the different depths being chosen by the two observers in attempting to obtain the best signals each time. We also found that roughly half the observed variance within the population of infants studied when measured by independent observers was the result of 'observer error'.

In comparing values obtained by the same observer the variability in both types of Doppler is less pronounced, and may reflect the same depth being chosen each time. We confirm the finding of Isken *et al* (VHA Isken, A Leonhardt, O Lindenkamp. Pulsed Doppler determination of cardiac output during the early neonatal period: validation of method using apical window. Presented to Internationales Symposium in Munster, June 1988, Neve Aspekte des Blurkreis laufes urd Sau erstoff-transportes bei Fluhgeborenen) who obtained similar values when comparing the apical window and suprasternal sites. Our own results show similar values from the three sites, but greater variability in the subcostal and apical sites compared with the suprasternal site, as well as interobserver biases.

We found that continuous wave Doppler gave significantly lower values than pulsed Doppler at each site; this was presumably because more lower velocity signals are recorded by the continuous wave beam. In some infants it was technically difficult to obtain clear continuous wave signals because of interference from other high velocity signals, and in these infants pulsed Doppler should be used. For pulsed Doppler studies, the equipment must be a duplex system, with both imaging and Doppler combined; this is available in almost all modern ultrasound equipment. Free standing Doppler systems are available (Doptek, Vingmed), and although these are difficult to use with pulsed Doppler they should give satisfactory results with continuous wave Doppler. Colour Doppler has no advantage in aligning the beam and is not neccessary for measuring cardiac output.

Using the suprasternal site and continuous wave Doppler, and measuring the diameter using M mode trailing edge to leading edge echocardiography, our results confirm those of Alverson *et al*,[4–7] Mellander *et al*,[8] and Walther *et al*.[9] We are surprised that the results obtained by Walther *et al* are similar to ours, as well as to those of Mellander *et al* and Alverson *et al*, because they calculated aortic diameter using the leading edge to leading edge method; Mellander *et al* and Alverson *et al* used the trailing edge method, and we found a 2 mm difference in the leading edge compared with the trailing edge method for measuring diameter. The effect of errors in measuring diameter can be calculated (table 7).

Alverson *et al* and Walther *et al* used zero crossing detectors, which are now outdated; we used discrete Fourier transformation. This is much less gain dependent, more widely available, and used in all modern Doppler machines (which also contain the software for calculating cardiac output). This study also has the advantage of colour Doppler, which enabled more accurate exclusion of patent ductus arteriosus and thus eliminated any possible error related to the resulting increased aortic flow.

Our study was designed to determine the most reproducible method of measuring cardiac output. To determine the method that gives the most accurate result, direct comparison with invasive techniques would be neccessary. Unfortunately there seems to be no 'gold standard' for direct comparison. Powner and Snyder[13], in reviewing six thermodilution cardiac output systems, pointed out that these may be liable to errors of up to 20%. Despite this Alverson[7] and Mellander *et al*[8] both compared invasive methods for determination of cardiac output using the Fick principle with Doppler ultrasound in infants and older children, and found good correlation; our results with Doppler are similar.

The main limitation of the technique seems to be in accurate measurement of aortic diameter, and as can be seen from our calculations (table 7) a small error may produce a relatively large error in the calculation of cardiac output, especially in preterm infants with small aortic diameters. Although direct comparison among different infants may give rise to considerable error, serial measurements within the same infant made by the same observer will reduce this error and this must be the main use of the technique. The result may, however, be an underestimation because the technique does not measure coronary blood flow and this may account for between 5% and 10% of the total cardiac output. It also assumes that aortic diameter does not change throughout systole.

Others have found Doppler ultrasound useful in monitoring serial changes in infants with myocardial dysfunction,[14] various arrhythmias, and in those receiving treatment for ductus arteriosus.[7]

We conclude that Doppler ultrasound is a useful technique for serially measuring cardiac output in an individual infant. The most reproducible results are obtained using diameters measured by M mode trailing edge to leading edge echocardiography, mean blood and flow velocities measured by continuous wave Doppler at the suprasternal site; the measurements should be made by the same observer on each occasion. Results obtained using spectral analysis are similar to those obtained using zero crossing detectors.

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