

Echocardiographic assessment of cardiac function in shocked very low birthweight infants

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Abstract

The contribution of abnormal cardiac function to hypotension and metabolic acidosis, which affect approximately 40% of ventilated very low birthweight infants in the first 24 hours after birth was assessed using M mode, two dimensional, and Doppler echocardiography in 75 very low birthweight infants during the first few hours after birth. Thirty four infants whose blood pressure was less than the 10th centile or who had a metabolic acidosis in the first 24 hours were compared with 41 who showed neither feature. The median shortening fraction was significantly lower in the hypotensive/acidotic (shocked) group than in the controls. In 16 of 34 (47%) shocked infants left ventricular contractility and output were significantly worse than in the control subjects. One and five minute Apgar scores were also significantly lower in the shock group when compared with controls.

Cardiac dysfunction was an important feature in the shocked very low birthweight infants. It is speculated that volume expansion may not always be the most appropriate first line treatment for such infants.

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Hypotension and metabolic acidosis occur in approximately 40% of ventilated very low birthweight infants, particularly in the first 24 hours after birth.^{1,2} There is a strong body of evidence to suggest that both these problems are associated with increased morbidity and mortality.¹⁻⁶ Volume expansion is considered by many to be the appropriate first line treatment. Failure to respond is followed by treatment with cardiac inotropes, such as dopamine or dobutamine, or both. A pilot study undertaken in this neonatal intensive care unit, before the study described here, showed that dopamine was given to as many as 50% of very low birthweight infants who were hypotensive or acidotic, or both. This requirement for cardiac inotropes suggested that cardiac dysfunction might be a feature.

Echocardiography has become an important diagnostic aid in the management of the preterm infant. It has been extensively used to assess cardiac function non-invasively in the structurally normal heart, particularly in older preterm and term infants.⁷⁻¹⁵ The assessment may include evaluation of left ventricular con-

tractility and output, but previous research has focused on very low birthweight infants in whom the ductus arteriosus has closed and has only assessed either contractility or output, not both.¹³⁻¹⁵ The effects of the ductus arteriosus do not become apparent until the pulmonary arterial pressure has decreased below systemic levels, an event that normally takes at least 24 hours to occur in the ventilated very low birthweight infant.^{16,17} Any assessment must be performed before treatment as this is likely to influence the results dramatically.¹⁸

The purpose of this study was to assess myocardial contractility and output in the first 24 hours after birth in very low birthweight infants, firstly to define a normal range and secondly to determine if cardiac dysfunction occurred in those infants who were hypotensive or acidotic, or both.

Patients and methods

Cardiac function was assessed in 75 infants admitted to the neonatal intensive care unit with a birth weight less than 1500 g, less than 24 hours after birth, and who had an indwelling arterial line for the measurement of systemic blood pressure. Cardiac function was assessed by M mode, two dimensional and Doppler echocardiography. If, in the view of the doctor responsible for resuscitation, the infant was clinically shocked, cardiovascular stabilisation was first achieved by the infusion of colloid. After admission to the neonatal unit and insertion of an arterial catheter for measuring systemic blood pressure, cardiac measurements were made with an ATL Ultramark 4 scanner (Advanced Technology Laboratories). This machine had a 5, 7.5, and 10 MHz sector/linear scan head with two dimensional and M mode facilities. It had a range gated 5 MHz pulsed wave Doppler crystal with a velocity limit of 480 cm/s and a 2.25 MHz Pedof continuous wave Doppler with a maximum velocity of 1300 cm/s. A simultaneous electrocardiogram recording with a sweep speed of 100 mm/s and a filter of 400 Hz were used. Images were recorded onto the system computer module and video recorder for analysis.

At 24 hours of age, two groups of infants were identified and their cardiac function compared.

Group 1 consisted of shocked infants who had been: (a) hypotensive (defined as mean systemic blood pressure less than the 10th centile for birth weight and postnatal age⁵;

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and/or (b) identified as having a metabolic acidosis (defined as an arterial pH less than 7.25 and base deficit greater than 6).

Group 2 consisted of control infants who had not had either of these two problems.

Resuscitation plasma has been given to 40% of infants in the two groups before insertion of the arterial catheter. No infant was acidotic (pH <7.25), hypotensive, or receiving cardiovascular support at the time the cardiac function measurements were made. Infants were excluded if there was evidence of congenital heart disease or if an infant had received treatment for hypotension before admission to the unit.

Cardiac function was assessed in two forms. Firstly, by considering left ventricular contractility, using the shortening fraction and the pre-ejection to ejection time ratio (PEP:ET).⁷⁻¹⁰ Secondly, by considering left ventricular output, using the peak aortic velocity, cardiac output, and stroke volume.¹¹⁻¹⁵ In each instance the mean of five consecutive cardiac cycles was taken. All diameter measurements were using the trailing edge-leading edge method¹⁹ and all echocardiography was performed by one investigator (ABG). Using standardised techniques, the measurements were made as follows.

SHORTENING FRACTION

In the parasternal long axis view of the left ventricle at the junction of the mitral valve leaflets and the papillary muscles, using M mode, the shortening fraction of the left ventricle was calculated by

$$\frac{\text{LVDD}-\text{LVDS}}{\text{LVDD}}$$

(LVDD=left ventricle diastolic diameter; LVDS=left ventricle systolic diameter.)

The LVDD was measured at the point of maximum diameter of the left ventricle. The LVDS was measured at the point of peak downward deflection of the interventricular septum. Expressing the resulting figure as a percentage gave the shortening function.

PEP:ET RATIO

Using the continuous wave Doppler from the suprasternal notch, the aortic Doppler trace was recorded. From the Doppler trace, the pre-ejection time was measured from the onset of the Q wave of the electrocardiogram to the onset of ejection of blood. The ejection period was measured from the onset to the end of ejection. The resultant PEP:ET ratio was recorded.

CARDIAC OUTPUT

In the long axis view of the left ventricular outflow tract, using the M mode, the aortic diameter (AoD) was measured at the end diastole, taken at the R wave of the electrocardiogram.

From the aortic Doppler trace, using spectral analysis, the peak and mean aortic velocity (MVEL) were measured in cm/s.

Cardiac output (ml/kg/min) was calculated by

$$\pi \times \text{MVEL} \times (\text{AoD})^2 / 4 \times 60 / \text{birth weight}$$

STROKE VOLUME

Heart rate was calculated from the R-R interval of the electrocardiogram and stroke volume (ml/kg) as cardiac output/heart rate.

Ductal patency was assessed using a short axis view of the right ventricular outflow tract.^{16 17} The direction of ductal flow and haemodynamic significance was assessed using pulsed wave Doppler.

STATISTICS

The reproducibility of all the echocardiographic measurements was assessed in a group of normal preterm infants before the study. Five measurements of each parameter were made on five consecutive days. All the measurements had, beat to beat and day to day, coefficients of variation between 5 and 10%.

Results are expressed as medians and interquartile range. Statistical analysis of medians was carried out using the Mann-Whitney U test. The influence of birth weight and gestational age on the cardiac function measurements was assessed using Spearman's non-parametric correlation. Only cardiac output significantly correlated with birth weight ($r=-0.37$, $p<0.05$). To control for birth weight, the cardiac output values obtained were divided into blocks of 10 ml/kg and each block was assigned a different numerical constant. Logistic regression analysis was then used to compare the cardiac output between the groups after controlling for birth weight. Statistical significance was taken at the 5% level. The study was approved by the Liverpool area ethics committee.

Results

There were 34 infants in the shocked group (24 were hypotensive, eight were acidotic, and two both) and 41 in the control group. Infants in the shocked group developed periods of hypotension/acidosis at a median postnatal age of nine hours (interquartile range 6-14 hours). Seventy three of the 75 infants were receiving positive pressure ventilation at the time of the scan.

Table 1 showed the demographic and clinical data in the two groups. Infants in the shocked group were of significantly lower gestational age ($p=0.004$), but the birth weight was not significantly different between the groups ($p=0.07$). The birthweight ratio, which was calculated as each patient's birth weight divided by the mean birthweight for their gestational age, was significantly lower in the control group ($p=0.044$).

One and five minute Apgar scores were significantly lower in the shocked group (see table 1) ($p=0.013$ and $p=0.005$ respectively). Initial haemoglobin was significantly lower in the shocked group ($p=0.007$). There was no difference in the first pH value between the two groups. When the cardiac scans were performed there were no significant differences in the alveolar to arterial oxygen ratio (a marker of the severity of hyaline membrane disease), arterial pH, peak inspiratory pressure, concentration of inspired oxygen, ventilator rate, or

Table 1 Demographic and clinical data by group. Values are medians (interquartile range)

	Control group (n=41)		Shocked group (n=34)	
Birth weight (g)	1058	(832-1298)	868	(723-1180)
Gestation (weeks)	28	(27-29)	26	(24-28)**
Birthweight ratio	0.93	(0.8-1.08)	1.0	(0.86-1.2)*
Apgar score				
One minute	5	(3-6)	3.5	(2-5)*
Five minutes	8	(7-9)	7	(6-8)**
First pH value	7.34	(7.26-7.4)	7.33	(7.26-7.39)
First haemoglobin concentration (g/l)	160	(150-177)	143	(129-161)*
Echocardiographic data				
Alveolar arterial oxygen difference ratio	0.21	(0.12-0.42)	0.16	(0.10-0.25)
Peak inspiratory pressure (cm/H ₂ O)	18	(18-21.5)	20	(18-24)
Ventilator rate (breaths/min)	40	(30-60)	60	(40-69)
FIO ₂ (%)	45	(26-74)	62	(46-93)

*p<0.05; **p<0.01.

FIO₂=fractional inspired oxygen expressed as a percentage.

Table 2 Echocardiographic data by group. Values are medians (interquartile range)

	Control group (n=41)		Shocked group (n=34)	
Echo (hours after birth)	3	(2-5)	3	(2-5)
Shortening fraction (%)	38	(36-40)	34	(28-38)*
Peak aortic velocity (cm/s)	76	(66-85)	71	(65-84)
Mean aortic velocity (cm/s)	48	(40-53)	44	(38-53)
Aortic diameter (mm)	5.6	(5.3-6.2)	5.5	(5.3-6.0)
Cardiac (output ml/kg/min)	218	(190-245)	219	(192-270))
Heart rate (beats/min)	166	(152-176)	160	(152-170)
Stroke volume (ml/kg)	1.36	(1.16-1.59)	1.39	(1.18-1.79)
PEP:ET	0.30	(0.27-0.375)	0.32	(0.27-0.42)

*p=0.001.

blood glucose estimation between the two groups.

Table 2 gives the cardiac function data in the two groups. The two groups of infants were scanned at a median of 3 hours of age. The shortening fraction was significantly lower in the shocked group (p=0.001). There was no significant difference in the PEP:ET, peak aortic velocity, mean aortic velocity, cardiac output, or stroke volume between the shocked and control groups.

The figure shows the individual shortening fraction for the two groups of infants. Infants in the control group had a median shortening fraction of 38% (solid line) with a 10th centile of 31%. The shortening fraction of infants in the shocked group formed two distinct populations. Fifty three per cent (18/34) of infants

had a distribution similar to the control group, with a median of 38% (group 2). The other 47% (16/34) of infants had a shortening fraction less than or equal to 30% (that is, less than the 10th centile for our control infants), with a median of 28%.

Dividing the shortening fraction results into three groups (group 1, the control infants; group 2, shocked infants with a shortening fraction greater than the 10th centile for the controls (shortening fraction greater than 30%); and group 3, shocked infants with a shortening fraction less than the 10th centile for the controls (shortening fraction less than or equal to 30%)), we compared the other cardiac function measurements between the three groups (table 3).

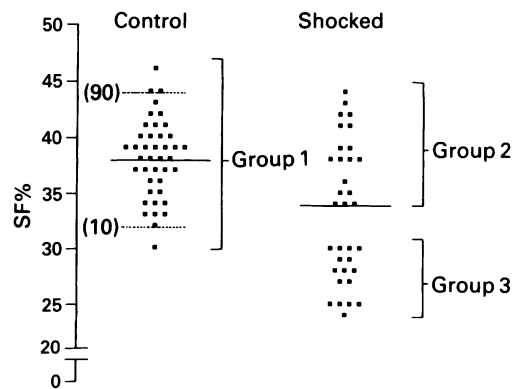
The indicators of left ventricular output, peak aortic velocity, mean aortic velocity, and stroke volume, were all significantly lower in group 3 infants compared with groups 1 and 2 (p values as shown). After controlling for birth weight using logistic regression (see under methods), the cardiac output was significantly lower in group 3 (p=0.04). Aortic diameter and heart rate were not significantly different between group 3 and groups 1 and 2 (p=0.95 and p=0.27 respectively). LVDS was significantly greater in group 3 compared with groups 1 and 2 (p=0.001). There was no significant difference in the LVDD between the groups (p=0.14). The left ventricular pre-ejection time and PEP:ET ratio were significantly greater in group 3 compared with the other two groups (p=0.04 and p=0.03 respectively). There was no significant difference in the ejection time between the three groups (p=0.14).

Ductal flow was present in all the infants: 50% were left to right, 45% were bidirectional, and 5% were right to left. In no infant was the flow considered to be haemodynamically significant as it was in diastole only, of low velocity, and there was no left atrial or ventricular enlargement.

Discussion

Hypotension and metabolic acidosis may be caused by hypovolaemia or cardiac dysfunction, or both. Although volume expansion by the administration of colloid is often currently used as a first line treatment in most patients, Barr *et al* found that preterm infants who were hypotensive had similar circulating plasma and blood volumes compared with normotensive infants.²⁰ They also found no significant improvement in mean blood pressure after infusions of 10 ml/kg albumin. They concluded that hypovolaemia was not the cause of hypotension or metabolic acidosis in the hypotensive infants that they studied.

From a clinical viewpoint, the lower Apgar scores in the shocked group compared with the controls suggested that birth asphyxia may have been responsible for the myocardial dysfunction. This is in accord with the observations of Walther *et al* who found that asphyxiated term infants who were hypotensive or acidotic, or both, commonly had clinical and



Individual shortening fractions for shocked and control groups of very low birthweight infants. Solid lines represent median values. Broken lines represent the 10th and 90th centiles for the control group 1. SF%=shortening fraction expressed as a percentage; group 1=SF% for control group; group 2=SF% in shocked group greater than or equal to the 10th centile for the control group; group 3=SF% in shocked group less than the 10th centile for the control group (see text).

Table 3 Echocardiographic data by shortening fraction; group 1, control; group 2, treatment plus shortening fraction greater than or equal to 31; and group 3, treatment plus shortening fraction less than or equal to 30. Values are means. Only the comparison of cardiac output values was adjusted for birth weight (see text)

	Group 1 (n=41)	Group 2 (n=18)	Group 3 (n=16)
LVDD (mm)	12.6	12.2	11.6
LVDS (mm)	7.8	7.5	8.3*
Aortic diameter (mm)	5.6	5.4	5.6
Peak aortic velocity (cm/s)	76	79	65*
Mean aortic velocity (cm/s)	48	52	39**
Cardiac output (ml/kg/min)	218	232	196**
Heart rate (beats/min)	161	152	162
Stroke volume (ml/kg)	1.35	1.49	1.23*
Pre-ejection period (ms)	0.050	0.049	0.057*
Ejection time (ms)	0.160	0.172	0.151
PEP:ET	0.30	0.31	0.34*

*p<0.05; **p<0.01.

echocardiographic evidence of abnormal cardiac function.¹⁸ Abnormal cardiac function was even present in infants with transient tachypnoea, hypoglycaemia, and septic shock. Not only did they have poor contractility, but also reduced cardiac output. After treatment with cardiac inotropes the echocardiographic findings returned to normal. Cabal *et al* published four case reports of asphyxiated preterm infants who had increased central venous pressure and serum lactate in the first few hours after birth.²¹ After cardiac inotropes and diuretics, the symptoms improved dramatically and it was suggested that they had had myocardial ischaemia following in-partum asphyxia. There were no echocardiographic measurements to confirm this.

Alverson *et al*¹³ and Walther *et al*¹⁴ assessed cardiac output in a group that was older than the infants described in this series. The mean age of these two small groups of very low birthweight infants was 5 days. They produced a range of 200–320 ml/kg/min as encompassing 95% of their observations. Walther *et al*¹⁵ measured M mode diameters of the left ventricle in a different group of very low birthweight infants and calculated the shortening fraction. The cardiac measurements were not performed if there was a ductus arteriosus but the cardiac output, LVDD, LVDS, and shortening fraction values obtained in these three studies are similar to our control group. Therefore, we feel that the cardiac function of our control group probably represents the normal for this selected group of infants and that a shortening factor of less than or equal to 30% and a cardiac output of less than 200 ml/kg/min appears to represent reduced left ventricular function in the very low birthweight infant.

Our results show that, of 34 infants who were shocked, 16 had evidence of cardiac dysfunction (table 3, group 3) in that there was reduced left ventricular contractility and output. The difference in the shortening fraction in group 3 infants compared with groups 1 and 2 was accounted for by the greater systolic diameter in this group and not by a smaller diastolic diameter. The diastolic diameter is influenced more by the preload—that is, filling pressure of the left ventricle, than by

myocardial dysfunction unless the latter becomes severe. The left ventricular PEP:ET is altered in states of poor contractility and altered loading conditions on the heart.^{9–22} Increased afterload, as might occur in aortic stenosis, shortens the pre-ejection time and prolongs the ejection time. Myocardial dysfunction and hypovolaemia lengthen the pre-ejection time and shorten the ejection time, precisely the findings in our group 3 infants. The fact that the LVDD is similar in all the groups makes it likely that the poor contractility represented abnormal myocardial muscle function and not hypovolaemia.

The echocardiographic assessment of cardiac output has been shown to closely correlate with catheter derived values, mainly in older children and adults.^{11–12} The estimates of cardiac output, stroke volume, and peak aortic velocity were significantly lower in group 3 infants compared with the other two groups. Hypovolaemia and poor myocardial muscle function will have a similar effect on these measurements but the evidence of poor contractility suggests that poor myocardial muscle function is the prominent cause in group 3 infants. The absence of heart rate differences probably reflects the similar birth weights in the groups.

Echocardiography will only assess cardiac function at the time the scan is performed. All 75 infants were assessed in the first few hours after birth and only divided into the shocked and control groups once they had reached 24 hours of age. Electrolyte abnormalities, particularly hypocalcaemia and hypokalaemia, will affect ventricular performance. Serum calcium and potassium concentrations were not routinely measured in the first few hours after birth as they invariably reflect maternal levels. Subsequent measurements of calcium and potassium after 12 hours of age did not show any difference between the groups. Metabolic acidosis will have deleterious effects on myocardial function. Those infants who developed acidosis did so about six hours after the scans were performed and it seems reasonable to assume that this did not influence the myocardial function at the time of assessment. The subsequent metabolic acidosis is more likely to have been a consequence of poor myocardial function rather than the reverse.

We only identified cardiac dysfunction in 47% of the shocked group, but in some of the shocked infants with normal cardiac function at the time of scan there was a time delay of more than 12 hours before hypotension/acidosis occurred. The workload of the left ventricle increases in the first 24 hours after birth as part of the normal physiological adaptation to extrauterine life.^{23–24} If myocardial function is not an optimum, then further deterioration may occur as the workload increases.

The influence of the ductus arteriosus on the results can probably be ignored. Evans *et al*¹⁶ and Skinner *et al*¹⁷ have shown that pulmonary artery pressure remained increased for at least 24 hours after birth in preterm infants and considerable shunting was unlikely to

occur until after this time. In the three groups of infants that we studied, there was no clinical or echocardiographic evidence that the degree of ductal shunting was significant and likely to alter the results.

It is important that we provide the most appropriate treatment for the hypotensive or acidotic very low birthweight infant. The cardiac function measurements used were relatively easy to perform using a standard ultrasound machine. Most ultrasound machines have cardiac analysis modules built in and the skills required to assess cardiac function are easily acquired. It may be beneficial to assess cardiac function in all very low birthweight infants during the first few hours after birth as part of the initial management. Should the infants then require treatment for shock, the echocardiographic findings may well influence the choice of treatment. Our results suggests that myocardial dysfunction does occur in the shocked very low birthweight infant and we speculate that volume expansion may not always be the most appropriate first line treatment for such infants.

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