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Doppler Echocardiographic Evaluation of Left Ventricular Output and Left Ventricular Diastolic Filling Changes in the First Day of Life

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ABSTRACT. The aim of this study was to evaluate the changes in Doppler transmitral flow patterns during the 1st d of life. Doppler echocardiography of the ascending aorta and mitral valve was performed serially in 20 normal neonates at 2, 12, and 24 h of age. A computer-interfaced digitizer pad was used to measure the following: ascending aorta flow velocity–time integral, total diastolic filling flow velocity–time integral, flow velocity–time integral of early diastolic filling, and flow velocity–time integral of atrial contraction. The inner diameter of the ductus arteriosus was 4.2 ± 0.6 mm at 2 h of age, 2.3 ± 0.5 mm at 12 h of age, and had closed in 17 of 20 neonates (85%) by 24 h of age. The ascending aorta flow velocity–time integral and total diastolic filling flow velocity–time integral, which were high at 2 h of age, decreased significantly at 12 h of age [12.2 ± 2.1 cm *versus* 9.6 ± 1.7 cm ($p < 0.001$) and 8.0 ± 1.1 *versus* 7.1 ± 1.4 ($p < 0.01$), respectively] but remained constant thereafter. Although no significant changes in flow velocity–time integral of atrial contraction and peak velocity of atrial contraction were noted during the first 24 h of birth, the flow velocity–time integral of early diastolic filling and peak velocity of early diastolic filling that were high at 2 h of age were reduced significantly at 12 h of age [5.0 ± 0.9 cm *versus* 4.1 ± 1.1 cm ($p < 0.005$) and 60.9 ± 9.0 cm/s *versus* 50.3 ± 9.0 cm/s ($p < 0.001$), respectively], resulting in significant reductions in the ratio of flow velocity–time integral of early diastolic filling/flow velocity–time integral of atrial contraction and the ratio of peak velocity of early diastolic filling/peak velocity of atrial contraction at 12 h of age. The size of the ductus arteriosus was found to be correlated with the peak velocity of early diastolic filling ($r = 0.42$, $p < 0.05$). Our results clearly demonstrate that the pattern of early diastolic filling was dependent on preload, whereas that of late diastolic filling was independent of preload in the early neonatal period. (*Pediatr Res* 35: 506–509, 1994)

Abbreviations

AO, ascending aorta
E area, flow velocity–time integral of early diastolic filling
A area, flow velocity–time integral of atrial contraction
peak E, peak velocity of early diastolic filling
peak A, peak velocity of atrial contraction
E/A area, ratio of E area to A area
peak E/A, ratio of peak E to peak A

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The loading condition of the left ventricle changes markedly during the transition from fetal to neonatal circulation and continues to be unstable shortly after birth. During this period, pulmonary blood flow, which acts as preload to the left ventricle, increases because of left-to-right ductus arteriosus shunting (1, 2). Among the hemodynamic factors affecting left ventricular diastolic filling, preload appears to play an important role, as has been recently suggested (3, 4). Interest has more recently been directed toward the possibility of using Doppler echocardiography to assess left ventricular diastolic hemodynamics in the early neonatal period (5–8). However, the impact of changes in preload on the transmitral flow pattern in neonates is as yet unclear. The purpose of our study was to evaluate by Doppler echocardiography the serial changes of left ventricular filling patterns in normal neonates during their transition to postnatal circulation.

MATERIALS AND METHODS

Study population. The study population consisted of 20 normal term neonates. Their mothers had uncomplicated pregnancies with no evidence of toxemia, diabetes mellitus, or pregnancy-induced hypertension. None of the infants were acutely ill or showed any evidence of congenital malformations. The mean birth weight was 3068 ± 351 g (mean ± SD), and the mean gestational age was 39 ± 1 wk. Each mother received an explanation of the study and gave informed consent. Serial echocardiographic examinations were performed on each subject at 2, 12, and 24 h after birth.

Examination technique. A complete two-dimensional echocardiographic examination was performed on the subjects with an Aloka SSD 870 ultrasonoscope with a 5.0-MHz transducer. The size of the Doppler sample volume was set at an axial length of 2 mm, with a wall filter setting of 400 Hz. All neonates were examined while they were lying quietly in the supine position breathing room air. To record the transmitral flow velocity profile, a standard apical two-chamber view was visualized, and the Doppler sample volume was placed in the inflow area of the left ventricle just below the level of the mitral annulus, adjusted to record the maximal flow velocities. The ascending aortic flow was measured from the suprasternal long axis view. The sample volume was placed in the AO immediately distal to the aortic valve. Care was taken to carry out these studies with the transducer beam as close to parallel to the presumed blood flow direction as possible. Because the angle between the estimated direction of blood flow and the Doppler beam was 20 degrees or less in the selected planes, no angle correction of the Doppler signal was made. All examinations were recorded at a paper speed of 100 mm/s. The electrocardiogram and respiration of each subject (with a pressure transducer placed against the abdominal wall) were simultaneously recorded. With the aid of a computer-interfaced digitizer pad (Cardio 500, Kontron Medical System), the various Doppler flow indices were measured from the ascending aortic flow and transmitral flow and expressed in centimeters as the area under the flow velocity. These indices included the E area and A area, total diastolic filling flow velocity–time integral, peak E, and peak A (Fig. 1). When the early and late diastolic waveforms overlapped, the E and A areas were calculated by dropping a vertical line to the baseline from the intersection of both waves. From these measurements, the E/A area and the E/A were calculated.

Ductus arteriosus. The inner diameter and shunt pattern of the ductus arteriosus were serially obtained at the same time when the other hemodynamics were measured. The size of the ductus arteriosus was determined from the inner diameter on the two-dimensional color echocardiographic images. The inner diameter was measured at the narrowest portion of the ductal lumen in the parasternal long-axis plane. As suggested by Hiraishi *et al.* (9, 10), we also judged that the ductus arteriosus was closing when the narrowest diameter was less than 2 mm or nonphasic continuous low-velocity flow was recorded upstream of the narrowing portion of the ductus arteriosus. It was considered closed when the color image and shunt flow were no longer detectable.

Interobserver and intraobserver variability. To determine the interobserver and intraobserver variability of Doppler echocardiographic measurements, variables were analyzed in 10 randomly selected patients by two independent observers and by one observer on two different occasions. Both the variabilities were determined as the mean percent errors, derived from the absolute difference between two observations divided by the mean of the two observations and expressed in percentage. Data are presented as mean ± SD.

Statistical analysis. All Doppler measurements reported here were averaged over five cardiac cycles at expiration and are presented as the mean ± SD. The Tukey-Kramer multiple comparison procedure was used to evaluate the differences in a set of measurements from 2 to 24 h after birth. Spearman's correlation coefficients were calculated to relate the size of the ductus arteriosus and indices of left ventricular diastolic filling. Results with $p < 0.05$ were considered to be statistically significant.

RESULTS

Interobserver and intraobserver variability of Doppler flow measurements. Interobserver variabilities for AO flow velocity–time integral, total diastolic filling flow velocity–time integral, E area, A area, and E/A area were as follows (ranges in parentheses): 3.1 ± 1.4% (1.3–5.3%), 2.8 ± 2% (0.7–7.9%), 2.7 ± 1.9% (1.1–7.1%), 7.8 ± 7.4% (1.2–21.7%), and 8.0 ± 4.7% (0.4–19.8%), respectively. Intraobserver variabilities for these variables were 1.8 ± 1.4% (0.1–3.3%), 2.3 ± 2.0% (0–7.8%), 2.7 ± 2.4% (0–11.5%), 7.0 ± 4.7% (0–17.1%), and 8.0 ± 4.7% (0.6–18.2%), respectively.

The results of measurements of the Doppler flow indices in normal neonates are summarized in Table 1.

Heart rate. The mean heart rates of the AO and mitral valve did not show any statistically significant changes from 2 to 24 h of age.

Flow velocity–time integral and transmitral flow velocity. The AO flow velocity–time integral and total diastolic filling flow velocity–time integral decreased significantly at 12 h of age compared with the values at 2 h of age [9.6 ± 1.7 *versus* 12.2 ± 2.1 cm ($p < 0.001$) and 7.1 ± 1.5 *versus* 8.0 ± 1.1 cm ($p < 0.01$), respectively], with no significant differences between the values at 12 and 24 h. The E area and peak E at 12 h decreased significantly compared with the values at 2 h [4.1 ± 1.1 cm *versus* 5.0 ± 0.90 cm ($p < 0.005$), and 50.3 ± 9.0 cm/s ± 60.9 ± 9.0 cm/s ($p < 0.001$), respectively], but there were no significant differences between the two values at 12 and 24 h after birth. The A area and peak A remained virtually unchanged from 2 to 24 h and thus resulted in significant reductions in the E/A area and peak E/A at 12 h compared with the values at 2 h [1.40 ± 0.26 *versus* 1.67 ± 0.41 ($p < 0.005$) and 1.14 ± 0.14 *versus* 1.28 ± 0.25 ($p < 0.05$), respectively].

Size of ductus arteriosus. The inner diameter of the ductus arteriosus was 4.2 ± 0.6 mm at 2 h, 2.3 ± 0.5 mm at 12 h, and was closing in three neonates and had closed in 17 of 20 neonates (85%) by 24 h of age.

Relationship between size of ductus arteriosus and indices of left ventricular diastolic filling. Weak correlations were seen with peak E ($r = 0.42$, $p < 0.05$) and peak E/A ($r = 0.32$, $p < 0.05$).

DISCUSSION

Among the hemodynamic factors affecting left ventricular diastolic filling, preload appears to play an important role, as disclosed by recent experimental studies (11, 12). Few studies, however, have shown the effects of preload reduction on Doppler transmitral velocity patterns in human beings (3, 4). By using nonpharmacologic intervention to decrease preload in normal subjects, Triulzi *et al.* (3) observed decreases in the peak velocity and velocity-time integral of the E wave without changes in the same values of the A wave. Similar results were obtained by others using nitroglycerin for preload reduction (13, 14). Experimental studies (11, 12) have demonstrated that the instanta-

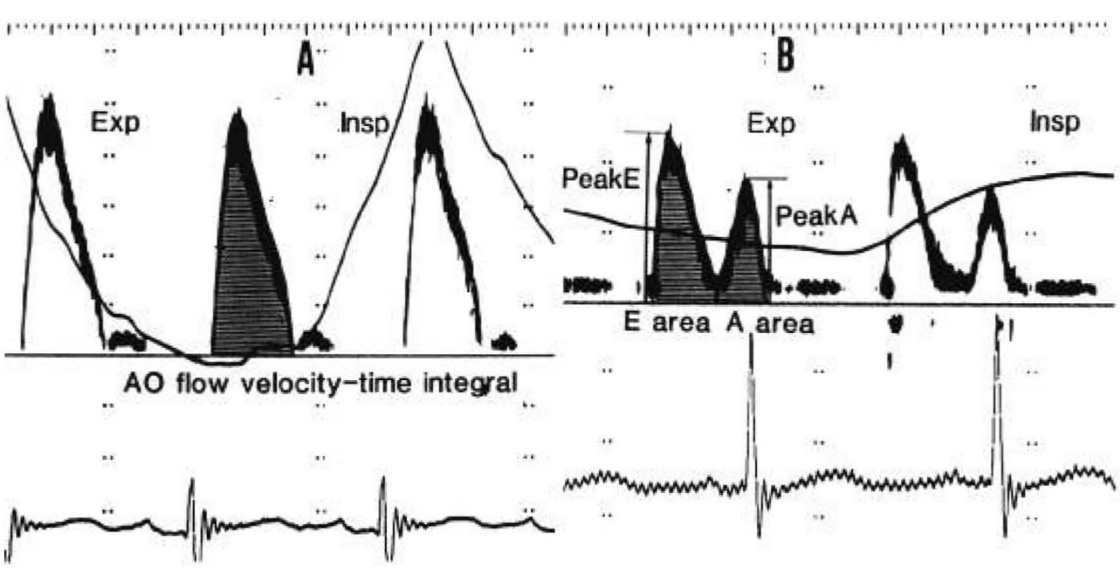

Fig. 1. Doppler flow velocity measurements. *A*, Ascending aortic flow velocity profile. *B*, Transmitral flow velocity profile. *Exp*, expiration; *Insp*, inspiration.

Table 1. *Echocardiographic measurements**

	Age (h)		
	2	12	24
AO HR (beats/min)	130 ± 16	126 ± 13	123 ± 18
AO flow velocity–time integral (cm)	12.16 ± 2.11	9.61 ± 1.74†	9.89 ± 1.48†
MV HR (beats/min)	125 ± 9	121 ± 7	121 ± 10
Total transmitral flow velocity–time integral (cm)	8.02 ± 1.07	7.09 ± 1.43‡	7.22 ± 1.10§
E area (cm)	4.97 ± 0.85	4.13 ± 1.12‖	4.24 ± 0.83‡
A area (cm)	3.05 ± 0.56	2.96 ± 0.46	2.97 ± 0.43
E/A area	1.68 ± 0.41	1.40 ± 0.26‖	1.44 ± 0.24‡
Peak E (cm/s)	60.9 ± 9.0	50.3 ± 9.0†	53.4 ± 8.4‖
Peak A (cm/s)	46.2 ± 5.2	43.9 ± 5.2	44.8 ± 4.7
Peak E/A	1.28 ± 0.25	1.14 ± 0.14‡	1.19 ± 0.14§

* HR, heart rate; MV, mitral valve.
† $p < 0.001$ compared with 2 h of age.
‡ $p < 0.01$ compared with 2 h of age.
§ $p < 0.05$ compared with 2 h of age.
‖ $p < 0.005$ compared with 2 h of age.

neous peak velocities of transmitral flow depend strictly on the atrioventricular pressure gradients and therefore on the left atrial pressure, which in turn is affected mainly by preload. However, to our knowledge, our report is the first serial evaluation of the relationship between left ventricular output changes and left ventricular diastolic filling changes in normal human subjects within the 1st d of life.

Serial left ventricular output changes. In our study, as in a previous study (15), the AO flow velocity–time integral was calculated as an indicator of left ventricular output. Volumetric flow in a great artery is equal to the product of the flow velocity integral and the cross-sectional area of the artery. However, because of technical limitations and inherent errors in measuring the diameter of such arteries (16), we assumed that the cross-sectional area of each artery remained constant between 2 and 24 h after birth so that any measured changes in the AO flow velocity–time integral would be reflective of changes in stroke volume. The AO flow velocity–time integral has been shown to correlate closely with invasively measured stroke volume in animals (17, 18) and in adult patients (19). In our study, and in that of Agata *et al.* (2), the AO flow velocity–time integral was at the highest level at 2 h of age. As previously documented (9, 20), our study has shown that the ductus arteriosus remained widely patent shortly after birth with a predominant left-to-right shunting. This shunt is likely to play a major role in the increased AO flow velocity–time integral at 2 h of age. At 12 h of age, the AO flow velocity–time integral declined markedly to 80% of that at 2 h. Most of our subjects had a small ductus arteriosus, either with a mean inner diameter of 2.3 mm or in the process of closing at 12 h of age. Although it is difficult to quantitate the amount of left-to-right shunt flow volume from the size of the ductus arteriosus, the present sequential data suggest that the left-to-right shunt was reduced markedly by 12 h of age. Our result of serial changes in the AO flow velocity–time integral is firmly supported by the data of Drayton and Skidmore (1), in which a left-to-right shunt of 62 mL/kg/min shortly after birth declined rapidly to 14 mL/kg/min during the first 12 h of age. The AO flow velocity–time integral dropped to 75% of the 2-h value by 24 h of age and did not show significant changes between 12 and 24 h of age. Therefore, from our study, we consider that the decline in preload on the left ventricle occurred during the first 12 h after birth.

Serial left ventricular diastolic filling changes. Only a few reports have been published on serial left ventricular diastolic filling changes in the early neonatal period. In addition, little is known about the impact of changes in preload on the transmitral flow pattern in neonates. In our study, the total diastolic filling flow velocity–time integral, peak E, and E area were at the highest level at 2 h of age, as was the AO flow velocity–time integral. These indices at 12 h of age declined significantly, with no change in the peak A and A area, causing significant reductions in the E/A velocity and E/A area. It is likely that the decline in the total diastolic filling flow velocity–time integral, peak E, and E area at 12 h of age may reflect the decreased left ventricular preload caused by a reduction in left-to-right shunt flow volume through a patent ductus arteriosus. Additionally, we have demonstrated that the size of the ductus arteriosus correlated well with peak E and peak E/A, suggesting that early diastolic filling is dependent on preload, whereas atrial filling is independent of preload in the early neonatal period.

After birth, the left atrial pressure increased in accordance with the increase in pulmonary venous return caused by a patent ductus arteriosus. Therefore, the major determinant of the reduced Doppler flow velocity during rapid filling at 12 h of age is attributable to the diminished atrial pressure caused by a decreased preload by the closing process of the ductus arteriosus. Triulzi *et al.* (3) speculated that the peak velocity and the integral of the A wave did not change because, despite a reduction in preload, the atrioventricular pressure gradient and the amount of ventricular filling in late diastole were kept constant by a parallel afterload reduction to atrial contraction. We can therefore conclude that any interpretation of the transmitral velocity pattern in terms of diastolic function should take into account the redistribution in transmitral flow induced by preload conditions.

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