Left Ventricular Systolic and Diastolic Function During Early Neonatal Period Using Transthoracic Echocardiography

Terukazu Shiota, Kenji Harada and Goro Takada

Department of Pediatrics, Akita University School of Medicine, Akita 010-8543

Shiota, T., Harada, K. and Takada, G. Left Ventricular Systolic and Diastolic Function During Early Neonatal Period Using Transthoracic Echocardiography. Tohoku J. Exp. Med., 197 (3), 151–158 —— To examine the effects of ductal closure on left ventricular (LV) systolic and diastolic function during the early neonatal periods, 45 normal term neonates delivered after uncomplicated pregnancies (mean 39 weeks) were studied using two-dimensional and Doppler echocardiography. We measured ductus arteriosus size, arterial blood pressures, ascending aortic size, LV dimensions, and transmitral flow velocity patterns and calculated LV output and rate-corrected fiber shortening fraction (mVefe) at 2, 12, 24, and 120 hours after birth. The inner diameter of the ductus arteriosus was 4.3±0.7 mm at 2 hours, 2.1±0.6 mm at 12 hours, and had closed in 42 of 45 neonates at 24 hours. LV output and LV end-diastolic dimension showed the highest level at 2 hours of age. However, the mVefe did not change from 2 to 120 hours of age. The peak velocity during early diastole (peak E) was significantly greater at 2 hours than at 12 hours. The peak velocity during atrial contraction (peak A) remained unchanged during this period. The normalized peak filling rate at isovolumic relaxation time did not change over 120 hours. The present study demonstrated changes in LV systolic function and LV diastolic filling during the early neonatal period. LV systolic and diastolic function was preserved under the hemodynamic changes associated with the early neonatal period.

Neonate; echocardiography; ductus arteriosus; left ventricular function

© 2002 Tohoku University Medical Press

Cardiovascular system in fetuses and neonates is immature compared with that in adults. Invasive animal studies have demonstrated that the myocardium of the neonatal heart is more sensitive to an increase in afterload and less compliant than that of adults (Friedman 1972; Berman and Musselman 1979; Romero and Friedman 1979; Reimenschneider et al. 1981; Van Hare et al. 1990), supporting the findings of several clinical studies (Areias et al.)

Received October 26, 2001; revision accepted for publication June 25, 2002.
Address for reprints: Terukazu Shiota, Department of Pediatrics, Akita University School of Medicine, 1-1-1 Hondo, Akita 010-8543, Japan.
e-mail: kharada@doc.med.akita-u.ac.jp
1990; Kimball et al. 1991; Colan et al. 1992; Harada et al. 1995a, 1999, 2000; Rowland and Gutgesell 1995; Toyono et al. 1998; Yasuoka et al. 1999, 2001). Maturational changes in both systolic function and diastolic properties may occur in infants and in young children. Pulmonary blood flow, which is the preload for the LV, is increased during the early neonatal period by left-to-right shunting through the ductus arteriosus. Studies of newborn lambs have demonstrated a lowered LV response to increased preload (Klopfenstein and Rodolph 1978), whereas, others have shown that the LV handles increased volume overload through ductus arteriosus shunting (Clyman et al. 1987). Although an increase of LV preload during early neonatal period should influence LV systolic and diastolic function, the LV systolic and diastolic filling state during ductus arteriosus patency in neonates has not been fully evaluated. The purpose of the present study is to examine serial changes in LV systolic and diastolic function obtained by echocardiography during the early neonatal periods.

METHODS

Protocol

The study population consisted of 45 normal term neonates delivered after uncomplicated pregnancies with no evidence of toxemia, diabetes mellitus, or pregnancy-induced hypertension. None of the infants were acutely ill or had any evidence of congenital malformations. The gestational age at birth ranged from 36 to 40 weeks (mean 39 weeks), and the birth weight ranged from 2516 to 3934 g (mean 3063 ± 261 g). The first feedings consisted of 10 ml of 5% dextrose in water within 4 hours of birth. Twenty-four hours later, the infants were fed with breast milk on demand, usually at a rate of 8–12 feedings per day. The mothers gave written informed consent to participate in the study.

Echocardiography

M-mode, two-dimensional, pulsed-Doppler, and color Doppler echocardiography were serially applied to the neonates at 2, 12, 24, and 120 hours after birth. All neonates were examined while lying quietly in the supine position and breathing room air. By means of high-speed (100 mm/sec.) hard-copy, two-dimensional echocardiography and M-mode recordings of the left ventricular minor axis were obtained using an Aloka SSD 2200 ultrasonoscope (Aloka Inc., Tokyo) with a 5.0 MHz transducer. Simultaneous electrocardiograms, indirect axillary or carotid pulse traces and phonocardiograms were obtained. Peripheral blood pressure was also simultaneously obtained using an automatched blood pressure recorder (BP-103N, Colin Medical Instruments, Tokyo). All subsequent measurements proceeded according to the American Society of Echocardiography (Sahn et al. 1978), and the following variables were obtained: LV end-diastolic diameter, LV end-systolic diameter, and aortic root diameter. LV ejection time was derived from the pulse trace and was rate-corrected by dividing by the square root of the R-R interval (ETc).

Ascending aortic and transmitral flow was recorded using pulsed Doppler echocardiography. The size of the Doppler sample volume was set at an axial length of 1–2 mm, and the wall filter setting was 200–400 Hz. The transducer beam was kept as close as possible to the Doppler beam at <20 degrees in selected planes. The angle of the Doppler signal was not corrected. Using a computer-interfaced digitizer pad (Cardio 500, Kontron Medical System), Doppler flow measurements were calculated. Seven consecutive cardiac cycles were averaged.

Ductus arteriosus

The patency, size, and shunt pattern of the ductus arteriosus were serially investigated from the high left parasternal position along with other hemodynamic parameters using two-
dimensional color Doppler echocardiographic images. The minimal ductal diameter of the color jet at the site of maximum constriction was used as a measurement parameter. The ductus arteriosus was considered to be closed when a color image no longer detected shunt flow.

**Indexes of LV systolic function**

LV performance was assessed by calculating the left ventricular cardiac output and rate-corrected mean velocity of fiber shortening (mVcfe) as reported previously (Colan et al. 1992). The systolic flow velocity-time integral was determined from the ascending aortic flow tracings obtained from the suprasternal notch view. The aortic root area was then calculated by assuming that the valve orifice was circular. LV output was calculated as follow: (ascending aortic flow velocity-time integral) \times (heart rate) \times (aortic cross sectional area). The mVcfe was calculated as SF/ETc.

**Index of LV preload**

LV preload was estimated from the LV end-diastolic dimension.

**Indexes of LV afterload**

LV afterload was assessed from the following indexes: systolic blood pressure, diastolic pressure, mean blood pressure, and systemic vascular resistance. Total peripheral vascular resistance was calculated as mean blood pressure/LV output.

**LV diastolic filling**

To record the transmitral flow velocity profile, a standard apical two-chamber view was visualized, and the Doppler sample volume was placed at the tips of the mitral valve leaflets. Doppler velocity tracings were digitized using the contour of the following computer-generated parameters as we reported previously (Harada et al. 1999): peak velocities during early diastole (E wave) and during atrial contraction (A wave), total diastolic filling flow velocity time integral during diastole, flow velocity time integrals of E wave (E area) and A wave (A area). When the E and A waves overlapped, these flow velocity-time integrals were calculated by dropping a vertical line to the baseline from the intersection of the two waves. Doppler velocity and flow velocity-time integrals were measured by tracing the outermost border of the spectral recordings. The following values were obtained from each Doppler profile analyzed: ratio of peak velocities of E to A waves (peak E/A); ratio of flow velocity-time integrals of E to A waves (E/A-area), and normalized peak filling rate (NPPFR). NPPFR was calculated as peak E wave/total diastolic filling velocity-time integral (Bowman et al. 1988). Isovolumic relaxation time was measured from the onset of the second heart sound to the beginning of E wave.

**Statistical analysis**

Results are expressed as means ± s.d. The Tukey-Kramer multiple comparison procedure evaluated differences in the sets of measurements obtained from 2 to 120 hours after birth. A value of \( p < 0.05 \) were considered statistically significant.

**RESULTS**

**Ductus arteriosus**

The inner diameter of the ductus arteriosus was 4.3 ± 0.7 mm at 2 hours, 2.1 ± 0.6 mm at 12 hours, and had closed in 42 of 45 neonates at 24 hours. Table 1 shows systolic performance indexes during 5 days after birth.

**Heart rate**

The mean heart rate did not significantly change between 2 and 120 hours.

**LV systolic performance**

LV output was high at 2 hours and decreased significantly at 12 hours (882 ± 125 vs. 705 ± 91 ml/min., \( p < 0.01 \)). Changes in LV
output were not statistically significant between 12 and 120 hours. LV mVcfe remained constant during the entire investigation.

LV preload: LV end-diastolic diameter did not change between 2 and 12 hours, but decreased significantly at 24 hours (1.72±0.13 cm, \( p<0.01 \)) compared values at 2 hours (1.79±0.11 cm). Changes between 24 and 120 hours were not significant. LV end-systolic diameter was constant within 120 hours.

LV afterload: Systolic and diastolic blood pressures increased significantly from 2 to 12 hours (57±8 to 64±6 mmHg during systole, and 33±4 to 39±4 mmHg during diastole, \( p<0.01 \), respectively) and between 12 to 120 hours (64±6 to 73±7 mmHg during systole, and 39±4 to 45±6 mmHg during diastole, \( p<0.01 \), respectively). No changes were significant between 12 and 24 hours and between 24 and 120 hours. The total peripheral resistance changed in a manner similar to that of blood pressure: significantly increasing from 2 to 12 hours (48±9 to 69±12 mmHg×min/liter, \( p<0.01 \)) and from 12 to 120 hours (69±12 to 80±16 mmHg×min/liter, \( p<0.01 \)). However, no difference was observed between 12 and 24 hours and between 24 and 120 hours.

**LV diastolic filling**

Table 2 shows diastolic filling indexes during 5 days after birth. The total diastolic filling flow velocity-time integral, E area, and peak E at 2 hours were significantly greater than at 12 hours (7.9±1.1 vs. 7.1±1.6 cm, 4.9±0.9 vs. 4.2±1.2 cm, 60±10 vs. 51±10 cm/sec, \( p<0.01 \), respectively), but these parameters did not significantly change between 12 to 120 hours. The A area and peak A remained unchanged from 2 to 120 hours. The E/A area and peak E/A were significantly higher at 2 hours than at 12 hours (1.70±0.40 vs. 1.42±0.27 and 1.30±0.22 vs. 1.13±0.15, \( p<0.01 \), respectively) and these parameters did not significantly change between 12 to 120 hours. The NPFR and isovolumic relaxation time did not change over 120 hours.

**DISCUSSION**

The present study demonstrated the effects of patent ductus arteriosus on LV systolic function and LV diastolic filling during the early neonatal period. The present study found that high LV output, increased LV preload, and decreased LV afterload were characteristic features of neonates. Although ductal closure
### Table 2. Left ventricular diastolic filling data in neonates during 5 days after birth

<table>
<thead>
<tr>
<th></th>
<th>2 hours</th>
<th>12 hours</th>
<th>24 hours</th>
<th>120 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-area (cm)</td>
<td>7.9±1.1</td>
<td>7.1±1.6*</td>
<td>7.1±1.2*</td>
<td>6.8±1.1*</td>
</tr>
<tr>
<td>E-area (cm)</td>
<td>4.9±0.9</td>
<td>4.2±1.2*</td>
<td>4.2±0.9*</td>
<td>3.9±0.7*</td>
</tr>
<tr>
<td>A-area (cm)</td>
<td>3.0±0.5</td>
<td>3.0±0.5</td>
<td>3.0±0.5</td>
<td>2.9±0.5</td>
</tr>
<tr>
<td>E/A-area</td>
<td>1.70±0.40</td>
<td>1.42±0.27*</td>
<td>1.41±0.24*</td>
<td>1.4±0.18*</td>
</tr>
<tr>
<td>Peak E wave (cm/sec)</td>
<td>60±10</td>
<td>51±10*</td>
<td>55±9*</td>
<td>50±5*</td>
</tr>
<tr>
<td>Peak A wave (cm/sec)</td>
<td>47±5</td>
<td>44±5</td>
<td>44±5</td>
<td>43±6</td>
</tr>
<tr>
<td>Peak E/A wave</td>
<td>1.30±0.22</td>
<td>1.13±0.15*</td>
<td>1.19±0.15*</td>
<td>1.16±0.12*</td>
</tr>
<tr>
<td>NPFR (/sec)</td>
<td>7.6±0.8</td>
<td>7.2±0.7</td>
<td>7.5±0.6</td>
<td>7.4±0.7</td>
</tr>
<tr>
<td>IVRT (msec)</td>
<td>52±3</td>
<td>56±5</td>
<td>53±4</td>
<td>55±6</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>132±16</td>
<td>126±13</td>
<td>123±18</td>
<td>125±11</td>
</tr>
</tbody>
</table>

T-area, total flow velocity-time integral during diastole; E, early diastolic filling; A, atrial filling; NPFR, normalized peak filling rate; IVRT, isovolumic relaxation time.

*p < 0.01 vs. 2 hours.

Increased systolic and diastolic blood pressure and total peripheral resistance; LV systolic performance and diastolic function were generally maintained. This observation indicates that the neonatal LV is malleable and can adapt more rapidly than what has been believed to the hemodynamic burden imposed by ductal closure.

**LV systolic function**

The foramen ovale functionally closes at birth and the left-to-right ductus arteriosus shunt may directly act as a volume load to the left ventricle. Our study found that the LV end-diastolic diameter and LV output were significantly higher when the ductus arteriosus was wide open, which is consistent with the findings of previous reports. However, the mVcfc as an index of contractility was constant without significant changes during this period of our investigation. We demonstrated the role of the Frank-Starling mechanism in the preterm infants with an open ductus arteriosus (Takahashi et al. 1994). Likewise, the increased LV output observed in the present study under open ductus arteriosus was not achieved by increasing contractility, but by the Frank-Starling effect.

Some studies have shown that LV systolic function is more sensitive to changes in afterload in the newborn infants than in older child (Kimball et al. 1991; Colan et al. 1992; Rowland and Gutgesell 1995; Toyono et al. 1998). We demonstrated that the relationship between mVcfc and end-systolic wall stress in newborn has a steeper slope and a higher y intercept than that in older children, which supports the data from lambs showing that LV pump function in the newborn is highly dependent on afterload (Toyono et al. 1998). The present study found that systolic and diastolic pressures and total peripheral vascular resistance were low in neonates shortly after birth, suggesting low afterload. Maintenance of LV contractility may be achieved by low afterload. Clyman et al. (1987) postulated that an associated reduction in the LV afterload plays a significant role in the increase of LV output in newborn lambs with ductus arteriosus after birth, and our present results support his hypothesis. Thus those results and present findings indicate that the neonatal LV works at a maximum level of contractility and may possess only a limited capacity to further increase its contractile state in the presence of LV volume load.
Although LV systolic performance is affected by LV afterload, the noninvasively estimating LV afterload is difficult in neonates soon after birth. End-systolic wall stress is the most sensitive echocardiographic index of afterload (Grossman et al. 1975), but this method may be unreliable for measurements of the distorted LV chamber soon after birth (Rein et al. 1987; Harada et al. 1995b). In accordance with a previous study (Winberg et al. 1990), we measured total peripheral vascular resistance as a criterion of afterload evaluation. We found that total peripheral vascular resistance was significantly lower at 2 hours; when maximally patent ductus arteriosus coincides with high LV end-diastolic volume and ejection fraction. Our findings are consistent with the data of Winberg and Lundell (1990), who showed that systemic vascular resistance reached the lowest level within 2 hours after birth. Consequently, low peripheral vascular resistance shortly after birth (an index of afterload evaluation) may help maintain LV systolic performance under a patent ductus arteriosus.

**Diastolic filling**

An experimental study demonstrated less active tension and higher passive stiffness in neonatal lambs than in adult sheep, suggesting that the neonatal myocardium is less compliant than that of the adult animal. Significant ultrastructural differences between neonate and adult myocardium may explain these age-related changes in ventricular diastolic properties (Marijanowski et al. 1994). Previous echocardiographic studies in human neonates detected a profile of mitral velocities showing a lower peak E wave without changes in the peak A wave, which disclosed less early left ventricular filling in neonates that could be related to diminished relaxation (Areias et al. 1990; Harada et al. 1995a). In the present study, the total diastolic filling flow velocity-time integral, the E area and peak E were highest level at 2 hours. These indexes at 12 hours significantly declined, with no change in the A area and peak A, causing significant reductions in the E/A area and peak E/A. The decline in the total diastolic filling flow velocity-time integral, E area and peak E at 12 hours may reflect the decreased LV preload caused by a reduction in left-to-right shunt flow volume through a patent ductus arteriosus. After birth, the left atrial pressure increased in accordance with the increase in pulmonary venous return caused by a patent ductus arteriosus. Among the hemodynamic factors affecting LV diastolic filling, preload appears to play an important role (Ishida et al. 1986; Choong et al. 1987). Therefore, the major determinant of the reduced Doppler flow velocity during rapid filling at 12 hours may be attributable to the diminished atrial pressure caused by decreased preload due to the closure of the ductus arteriosus. The NPFR is supposedly unaffected by sample volume position, heart rate or ventricular size, allowing comparisons of the filling rates of ventricles of different sizes (Bowman et al. 1988). Our study demonstrated that NPFR remained unchanged during the first 120 hours after delivery. LV stroke volume increases with a widely patent ductus arteriosus; greater changes in LV systolic volume produce greater restoring forces, which may reduce resistance to the flow at the beginning of the following diastole with a consequently higher peak filling velocity. The mitral velocity-time integral also increases, concomitant with an increase in peak E maintaining a constant ratio to the velocity time integral during the early neonatal period. Our NPFR findings suggest that the changes in peak E and E/A are related to the changes in loading conditions other than sequential changes in myocardial properties.

**Conclusions**

The present study demonstrated changes in LV systolic function and LV diastolic filling during the early neonatal period. LV systolic
and diastolic function were preserved under the hemodynamic changes associated with the early neonatal period.

References


Sahn, D.J., DeMaria, A., Kistler, J. & Weyman, A. (1978) The committee on M-mode standardization of the American Society of Echocardi-


