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Serial assessment of right ventricular function using tissue Doppler imaging in preterm infants within 7 days of life

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ABSTRACT

Background: We aimed to evaluate right ventricular (RV) function longitudinally using tissue Doppler imaging (TDI) echocardiography in preterm infants.
Methods: We selected 101 very-low-birth-weight (VLBW) infants for the study. Echocardiographic examinations including TDI were performed serially within 7 days of life. Pulsed-Doppler TDI waveforms were recorded at the tricuspid valve annulus, and peak systolic velocities (Sa), early diastolic velocities (Ea), and late diastolic velocities (Aa) were measured.
Results: Sa, Ea and Aa were all reduced significantly from 3 h to 12 h, and then increased gradually thereafter. These three velocities also increased with gestational age in the early neonatal period. The ratio of Ea to Aa (Ea/Aa) did not change significantly within the first week of life. The ratio of E to Ea (E/Ea) in VLBW infants also seemed to remain stable from birth to day 7. The values of Sa appeared to be associated with cardiac output in the early neonatal period. Both Sa and Aa in intubated infants were significantly higher than in non-intubated infants.
Conclusion: RV TDI velocities of preterm infants in the early neonatal period are influenced by gestational age, postnatal age, and respiratory status, although the RV E/Ea ratio appears to be almost stable throughout the neonatal period. Our findings may provide some basis for assessment of RV function in critically ill preterm infants.

1. Introduction

Left ventricular (LV) function plays a leading role in blood circulation in humans. Any deficit in LV performance impacts cardiopulmonary circulation and thus the status of the body as a whole. The right ventricle (RV) seems to play a secondary, supportive role in passive venous return and pulmonary circulation. In adults, RV function is more complex than LV function [1], and RV failure may not be prominent in various cardiac disorders in spite of its definitive prognostic impact in many patients with chronic heart disease [1,2]. In fetuses, on the other hand, the RV plays an important and leading role in circulatory dynamics [3]. Before the switch to respiration/pulmonary circulation in the womb, the left atrium (LA) and the LV receive relatively limited blood return, and RV output (RVO) is larger than LV output (LVO) [3]. Therefore, any deficit of RV function may lead to profound circulatory failure in fetuses and infants, especially those that are preterm. In tiny infants, however, precise assessment of RV function is much more difficult than in adults because of many clinical and methodological problems.

Tissue Doppler imaging (TDI) is a new echocardiographic technique that directly measures velocities in the myocardium and at the valve annulus [4,5]. This makes it possible to analyze both the systolic and diastolic function of the ventricles, and the data can be correlated with the findings of invasive catheterization, being also valuable in adult cardiology for long-term management of cardiac failure [4,5]. Recently, it has also been suggested that TDI might be applicable to the management of children with and without heart disease [6–8], healthy infants [6,7,9,10], critically ill infants [11–13], and fetuses [14,15]. TDI enables the assessment of RV myocardial performance, separately from LV performance, non-invasively and quickly [7–10,16–18]. In very preterm infants, few authors have reported the clinical use of TDI for early management of circulatory dysfunction [17–19]. In our previous article, we described serial assessment of LV function using TDI in very-low-birth-weight (VLBW) infants for the first time [20]. Here we report longitudinal assessment of RV function using TDI in the same VLBW patients as those assessed in our former study from birth to day 7 of life.

2. Methods

2.1. Patients

One hundred seventy-three VLBW infants weighing less than 1500 g, who were admitted to the neonatal intensive care unit at Kakogawa Municipal Hospital between September 2004 and August

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2007, were enrolled. Among these infants, 72 were excluded because of intrauterine growth retardation, congenital anomalies, congenital heart disease, or death within 48 h of birth, leaving 101 infants for final analysis. The infants were divided into four groups according to gestational age: group 1, 21–25 weeks; group 2, 26–27 weeks; group 3, 28–29 weeks; and group 4, 30–33 weeks. The clinical characteristics of these four groups are presented in Table 1. Written informed parental consent was obtained in all cases upon admission. The study was approved by the local ethics committee at Kakogawa Municipal Hospital.

2.2. Echocardiography

A Hewlett–Packard SONOS 5500 with a 5.5/7.5-MHz transducer was used. The 7.5-MHz transducer was used for two-dimensional studies, while the 5.5-MHz transducer was employed for color-Doppler flow recordings. Serial echocardiographic examinations of VLBW infants were started at 3 h after birth, with subsequent measurements at 12, 24, 36, 48, 72 and 96 h, and on days 5, 6, and 7. Each echocardiographic estimate was expressed as the mean value of 3–5 measurements. Pulsed-wave TDI measurements were performed at the lateral annulus of the tricuspid valve using an apical four-chamber view. The sample volume was set at 1 mm, and filters were set to exclude high-frequency signals. Angle corrections were not used, and gains were minimized to yield a clear tissue signal with minimal background noise. From the consecutive recordings, peak systolic velocities (Sa), early diastolic velocities (Ea), and late diastolic velocities (Aa) were measured online. Pulsed Doppler waveforms of ventricular inflow in the right ventricle were also recorded, maximum velocities of the early diastole (E) and late diastole (A) waves were measured, and then left ventricular E/Ea (E/E′) was calculated [4,5]. Although pulsed-Doppler waveforms of E-waves were fused to a degree with those of A-waves in most of the patients, peak velocity for both waves was measurable in most cases (97–100%). As for TDI-waveforms, peak velocity for both Ea and Aa waves was also measurable in 94–100% of patients, although partially fused waveforms were seen in almost all VLBW infants. Pulsed-wave TDI measurements were also performed at the lateral annulus of the mitral valve to analyze left ventricular TDI, as reported previously [20]. Left ventricular ejection fraction (LVEF) and fractional shortening (LVFS) were assessed by M-mode echocardiography from the parasternal long axis view according to the standardized method. Doppler measurements of LVO and right ventricular output (RVO) were assessed by the method of Alverson et al. [21]. The ductal shunt was visualized using color-Doppler, and assessed with pulsed or continuous wave Doppler, the sample volume being set in the pulmonary end of the duct. All measurements were performed by one of the authors (MM). Intraobserver variability was assessed using Bland–Altman plots, as reported previously [16]. Clinical information on each VLBW infant was obtained from our nursery records.

2.3. Statistical analysis

Statistical analysis was performed using a statistical software package, JMP 10.0.2 (SAS Institute Inc., Japan). Longitudinal changes in measured TDI velocities and their differences among the four gestational age groups were subjected to one-way analysis of variance (ANOVA), followed by post-hoc analysis. Longitudinal changes in the values for the two groups were assessed by two-way repeated-measures ANOVA. Correlations between two different echo indices were assessed by simple regression analysis and Spearman's ρ coefficient. Differences at $p < 0.05$ were considered significant.

3. Results

As was seen for mitral TDI velocities, tricuspid Sa velocities were reduced significantly from 3 h to 12 h, then increased gradually after 24 h of life (Fig. 1A, B). At most points of assessment, there were no significant differences between the four different gestational age groups, except at 3 h of life (Fig. 1B). Longitudinal changes in tricuspid Ea values were the same as those of tricuspid Sa values, while the Ea values in mature groups were significantly higher than those in preterm groups, especially before 36 h of life (Fig. 1C, D). Serial changes in tricuspid Aa values in the patients as a whole were precisely the same as those of both Sa and Ea, but differences in the mean values of Aa between the four groups at the same time point tended to be larger than those for the former two velocities (Fig. 2A, B). There were no significant changes in the mean value of the tricuspid Ea to Aa (Ea/Aa) ratio throughout the early neonatal period in the patients as a whole (Fig. 2C). Otherwise, the Ea/Aa ratio differed significantly among the four gestational age groups, infants in the mature groups showing higher values than those in the preterm groups at the same assessment points (Fig. 2D). No longitudinal changes in the RV E to Ea (E/Ea) ratio were evident throughout the early neonatal period, and there were no significant differences in RV E/Ea values among the four groups at the same assessment points, except at 24 h of life (Fig. 3A, B).

Fig. 4 shows the relationships between tricuspid Sa velocities and LVO at 12 h of life. The early tricuspid Sa velocity was positively correlated with LVO, but no other significant relationships were found among other conventional echo indices and tricuspid TDI velocities. In the 28–29-week gestational group (group 3), we examined differences in serial changes in tricuspid TDI values between intubated and non-intubated infants (Fig. 5). Both Sa and Aa were significantly higher in the former than in the latter. The longitudinal changes in Ea, the Ea/Aa ratio and the E/Ea ratio showed no significant differences between

Table 1
Clinical characteristics of four gestational age groups.

	Group 1 (n = 22): 21–25 weeks	Group 2 (n = 25): 26–27 weeks	Group 3 (n = 22): 28–29 weeks	Group 4 (n = 32): 30–33 weeks
Male/female	13/9	16/9	15/7	12/20
Gestational age (weeks)	24.5 (21 + 0–25 + 6)	27.0 (26 + 0–27 + 6)	28.9 (28 + 0–29 + 6)	31.2 (30 + 0–33 + 6)
Birthweight (g)	608 (360–850)	888 (694–1158)	1266 (942–1476)	1352 (1136–1496)
Apgar score, 1 min	4 (0–7)	6 (1–9)	7 (3–9)	8 (6–9)
Apgar score, 5 min	6 (1–10)	8 (4–10)	8 (7–10)	9 (7–10)
Outborn	0 (0%)	1 (4%)	2 (9.1%)	5 (15.6%)
Cesarean section	14 (63.6%)	24 (96%)	18 (81.8%)	31 (96.9%)
Multiple births	1 (4.5%)	6 (24%)	3 (13.6%)	12 (37.5%)
Mechanical ventilation	22 (100%)	23 (92%)	17 (77.3%)	14 (43.8%)
Times of ventilation (days)[a]	46 (3–65)	4.5 (3–45)	3 (0–11)	3 (0–14)
Oxygen duration (days)[a]	80 (38–135)	64 (40–96)	41 (9–75)	9 (2–39)
Surfactant	22 (100%)	23 (92%)	15 (68.2%)	13 (40.6%)
Volume expander	14 (63.6%)	17 (68%)	14 (63.6%)	11 (34.4%)
Alive at discharge	16 (72.7%)	24 (96%)	22 (100%)	32 (100%)

Values are median for continuous variables, and patient numbers for categorical variables.
[a] …Median values in infants who were successfully extubated and discharged.