Pediatrics and Neonatology (2019) 60, 523—529

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.pediatr-neonatol.com

Original Article

Cesarean section predominantly affects right ventricular diastolic function during the early transitional period☆,☆☆

Katsuo Tao [a,c], Yoshikazu Hara [b], Yasunori Ishihara [a], Yusei Ohshima [c,*]

[a] *Department of Pediatrics, Fukui Aiiku Hospital, Fukui, Japan*
[b] *Department of Pediatrics, Sugita Genpaku Memorial Obama Municipal Hospital, Fukui, Japan*
[c] *Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, Fukui, Japan*

Received Aug 8, 2018; received in revised form Dec 10, 2018; accepted Jan 15, 2019
Available online 19 January 2019

Key Words
cesarean section;
echocardiography;
ventricular function

Background: Although the mode of delivery is well known to affect pulmonary function, the effects of a cesarean delivery on postnatal changes in cardiac mechanics have not been clearly defined.
Methods: To evaluate whether delivery mode influences cardiac function in the early transitional period, 42 infants delivered by cesarean section (CS) and 110 by vaginal delivery (VD) were enrolled, and they underwent serial echocardiography at 0, 1, 2, and 5 days of age. Longitudinal changes in ejection fraction (EF), fractional area change (FAC), mitral annular plane systolic excursion (MAPSE), tricuspid annular plane systolic excursion (TAPSE), Tei index, ratio of peak early diastolic flow velocity (E) to peak early diastolic annular velocity (e') (E/e'), and deceleration time (DcT) were compared between the two groups.
Results: FAC and DcT of both ventricles increased during the first week, whereas Tei index of each chamber decreased irrespective of delivery mode. E/e's of both ventricles were significantly higher and MAPSE was significantly lower in the CS than VD group throughout the observation period. After adjustment for the effects of birth weight, gestational age, and oxygen administration by multivariate analysis, right ventricular E/e', which reflects diastolic function of the right ventricle, was most affected by delivery mode.

Abbreviations: CS, cesarean section; DcT, deceleration time; E/e', ratio of peak early diastolic flow velocity (E) to peak early diastolic annular velocity (e'); EF, ejection fraction; FAC, fractional area change; LV, left ventricular; MAPSE, mitral annular plane systolic excursion; PDA, patent ductus arteriosus; RV, right ventricular; TAPSE, tricuspid annular plane systolic excursion; VD, vaginal delivery.
☆ http://www.fab.or.jp/.
☆☆ http://www.obamahp-wakasa.jp/hospital/index.html.

* Corresponding author. Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, 23-3 Shimoaizuki, Matsuoka, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan. Fax: +81 776 61 8129.
E-mail addresses: katsuo1203@yahoo.co.jp (K. Tao), hara-yo@obamahp-wakasa.jp (Y. Hara), ishiyasu@fab.or.jp (Y. Ishihara), yohshima@u-fukui.ac.jp (Y. Ohshima).

https://doi.org/10.1016/j.pedneo.2019.01.004

Conclusion: CS affected diastolic function of the right ventricle in the 2nd day after giving birth and did not persist. Delayed adaptation of the neonatal myocardium and/or persistence of pulmonary hypertension might explain the hemodynamic changes in neonates born by CS.

1. Introduction

After birth, the initiation of respiration with lung expansion and the cessation of the placental circulation caused by cutting the umbilical cord produce drastic changes in hemodynamics. The increased oxygen tension of the blood that occurs with breathing induces functional closure of the ductus arteriosus and facilitates a decrease in pulmonary vascular resistance, resulting in an increase in pulmonary blood flow. Thus, the increased blood return to the left atrium increases the preload of the left ventricle. The increased systemic arterial blood pressure caused by cessation of the placental circulation increases the afterload of the left ventricle. In the right ventricle (RV), as pulmonary vascular resistance gradually decreases, afterload decreases. These changes in preload and afterload affect the contractility of the ventricles.[1]

It has been shown that caesarean section (CS) is associated with lower levels of epinephrine, norepinephrine and cortisol in neonatal blood, compared with vaginal delivery (VD).[2] With parturition, increased levels of epinephrine, glucocorticoids, and other hormones effectively cause the lung epithelia to transition from a secretory to a resorptive phenotype, which may play an important role in fetal lung fluid absorption. Catecholamine release with labor pains and thoracic compression during VD could facilitate lung fluid clearance. Thus, because of less severe labor pains and the lack of thoracic compression, delivery by CS is considered a risk factor for transient tachypnea of the newborn.

Although delivery mode is well known to affect pulmonary function, the effects of CS on postnatal changes in cardiac mechanics have not been clearly defined. Coskun et al.[3] reported that one hour after delivery, a larger stroke volume was observed in infants born by CS. However, 24 h after delivery, there were no significant differences in stroke volume, mean arterial pressure, total systemic vascular resistance, ejection fraction, or ductus arteriosus diameter between infants born vaginally or by CS.

2. Methods

2.1. Subjects

Neonates ($n = 156$) born at Sugita Genpaku Memorial Obama public hospital from April 2016 to March 2017 were enrolled in the study. All patients with congenital heart disease, including three neonates with ventricular septal defect and one with coronary arteriovenous fistula, were excluded. Forty-two out of 152 neonates were delivered by CS. The reasons for CS were as follows: 26 women had a previous CS; five had malpresentation; two had arrested labor; five had maternal factors, including pregnancy-induced hypertension, spina bifida, postoperative uterine fibroids, and placenta accreta; and four fetuses had fetal distress. Six neonates were delivered by an urgent CS. The study was approved by the local ethics committee at Sugita Genpaku Memorial Obama public hospital. Written informed consent was obtained from the parents upon admission.

2.2. Echocardiographic measurement

Serial echocardiographic examinations were done in all neonates on day 0, 1, 2, and 5, when they were sleeping well. The examinations were performed using an Apron EUB-7000HV with a 5.5 MHz transducer. Left-ventricular ejection fraction (LV EF) was measured in the parasternal short-axis and apical four-chamber views, using the Teichholz, and modified Simpson methods. For the assessment of longitudinal myocardial movement, mitral annual plane systolic excursion (MAPSE) and tricuspid annual plane systolic excursion (TAPSE) were measured in the apical four-chamber view. Right ventricular fractional area change (RV FAC), defined as the difference in traced RV chamber area between end-diastole and end-systole, was assessed by the area-length method in the apical four-chamber view. To record mitral and tricuspid flow velocities with the pulsed Doppler method, the sample volume was placed at the tip of both valve leaflets in the apical four-chamber view. The peak atrial flow velocity (A), the peak early diastolic flow velocity (E) and the deceleration time (DcT) of the peak early diastolic flow were measured in both ventricles. Ventricular outflow patterns were visualized by pulsed-wave Doppler in the parasternal short-axis view (right ventricle), and apical or parasternal four-chamber views (left ventricle). The Tei index, defined as the sum of the isovolumetric contraction time and the isovolumetric relaxation time divided by the ejection time, was calculated for both ventricles using the method proposed by Tei et al.[4–6] Myocardial wall motion velocity was recorded by pulsed-wave tissue Doppler imaging. In the apical four-chamber view, the sample volume was placed in the lateral portion of the mitral or tricuspid valve annulus, to measure the peak early diastolic velocity (e'), with the angle between the estimated direction of wall motion and the Doppler beam $< 15°$. The ratio of peak early diastolic flow velocity to peak early diastolic annular velocity (E/e') was calculated for both chambers.[7]

The respiratory rate was recorded at the same time as the echocardiographic parameters. All measurements were performed by one author (K.T). A pediatric cardiologist certified by the Japanese Society of Pediatric Cardiology

Table 1 Demographics and perinatal factors.

	Vaginal delivery (N = 110)	Cesarean section (N = 42)	*P* value
Male/Female	66/44	22/20	0.463
Gestational age, weeks days	39w2d (35w2d-41w4d)	37w4d (36w4d-40w6d)	<0.001
Birth weight, g	2997 (2172—4374)	2700 (1792—3414)	<0.001
Birth height, cm	48.8 (43.5—54.5)	46.95 (43—50)	<0.001
Birth order, 1st/2nd or later	45/65	12/30	0.192
cord blood pH	7.305 (7.102—7.511)	7.315 (7.207—7.379)	0.492
Apgar score at 1 min	9 (5—10) [9.06 ± 0.94]	9 (4—9) [8.45 ± 0.94]	<0.001
Apgar score at 5 min	10 (9—10) [9.87 ± 0.34]	10 (9—10) [9.57 ± 0.50]	<0.001
Oxygen supplement	5 (4.55%)	3 (7.14%)	0.685
PDA closure time (day)	1 (0—2)	1 (0—2)	0.503

Values are expressed as median (range), [mean ± SD], or number (%).
PDA = patent ductus arteriosus.
A Mann—Whitney U test or Fisher's exact probability test were used to compare variables between the two groups.

and Cardiac Surgery confirmed the validity of these measurements. Clinical information on all neonates was obtained from nursery records. Gestational age was determined by either the last menstrual period or fetal ultrasound examination.

2.3. Statistical analysis

All statistical analyses were performed with R (The R Foundation for Statistical Computing, Vienna, Austria). A Mann—Whitney U test or Fisher's exact probability test were used to compare variables between the two groups. Longitudinal changes in the variables in both two groups were assessed by two-way repeated-measures analysis of variance (ANOVA).

Linear regression analysis and the Pearson correlation coefficient were used to assess the effects of gestational age and body weight on the changes in the echocardiographic parameters. Comparison of the two delivery modes at each time point was performed using a t-test, and comparisons between day 0 and the other time points in each group were performed using one-way analysis of variance (Dunnet method). The data are presented as the median and range. A *P* value < 0.05 was considered to indicate a statistically significant difference.

3. Results

Because most of the deliveries by CS were scheduled before the predicted birth date, gestational ages, birth weights, heights, and Apgar scores were lower in the CS group than the VD group (Table 1). There was no significant difference in the cord blood pH between the two groups. Three neonates in the CS group and five in the VD group required oxygen for short periods after birth. No neonate required either mechanical ventilation support or oxygen therapy with an inspiratory oxygen fraction >0.3.

There was no significant difference in patent ductus arteriosus (PDA) closure time, size, and peak flow velocity between the two groups (Table 1 and Fig. 1). Twenty-four infants had PDA on day 1, only three on day 2, and none on day 5.

More prolonged tachypnea was observed in the CS group until day 2 (Fig. 2). LV EF and MAPSE were relatively stable during the first 5 postnatal days, whereas RV FAC and TAPSE increased gradually and on day 5. The Tei index of both ventricles consistently decreased, suggesting postnatal

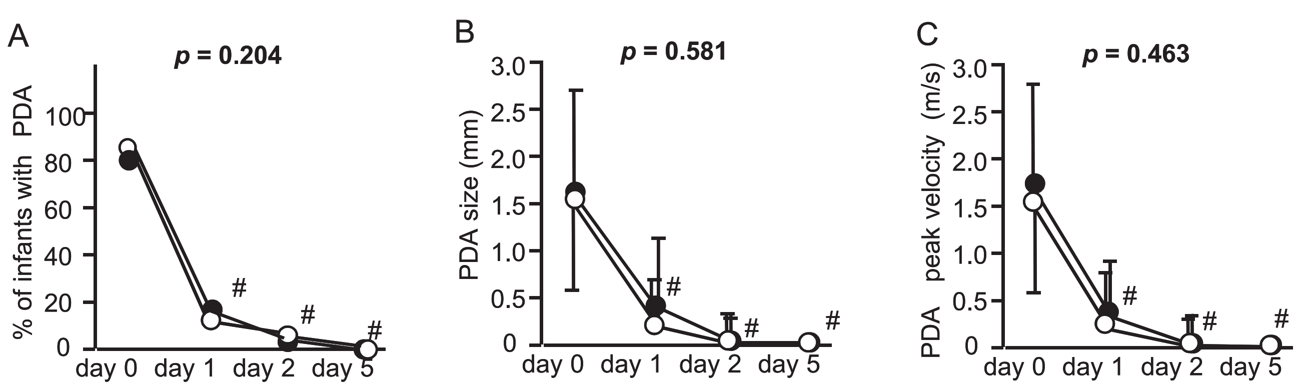

Figure 1 Longitudinal changes of patent ductus arteriosus (PDA). A: The proportion of infants with PDA, B: The size of PDA, C: The peak flow velocity of PDA. Values in the cesarean section group (open circles) and the vaginal delivery group (closed circles) are presented as means ± SDs. *P* values were calculated by two-way repeated-measures ANOVA to compare the two groups. *Significant difference between the two groups at the indicated time points. #Significant difference between day 0 and the indicated time points.

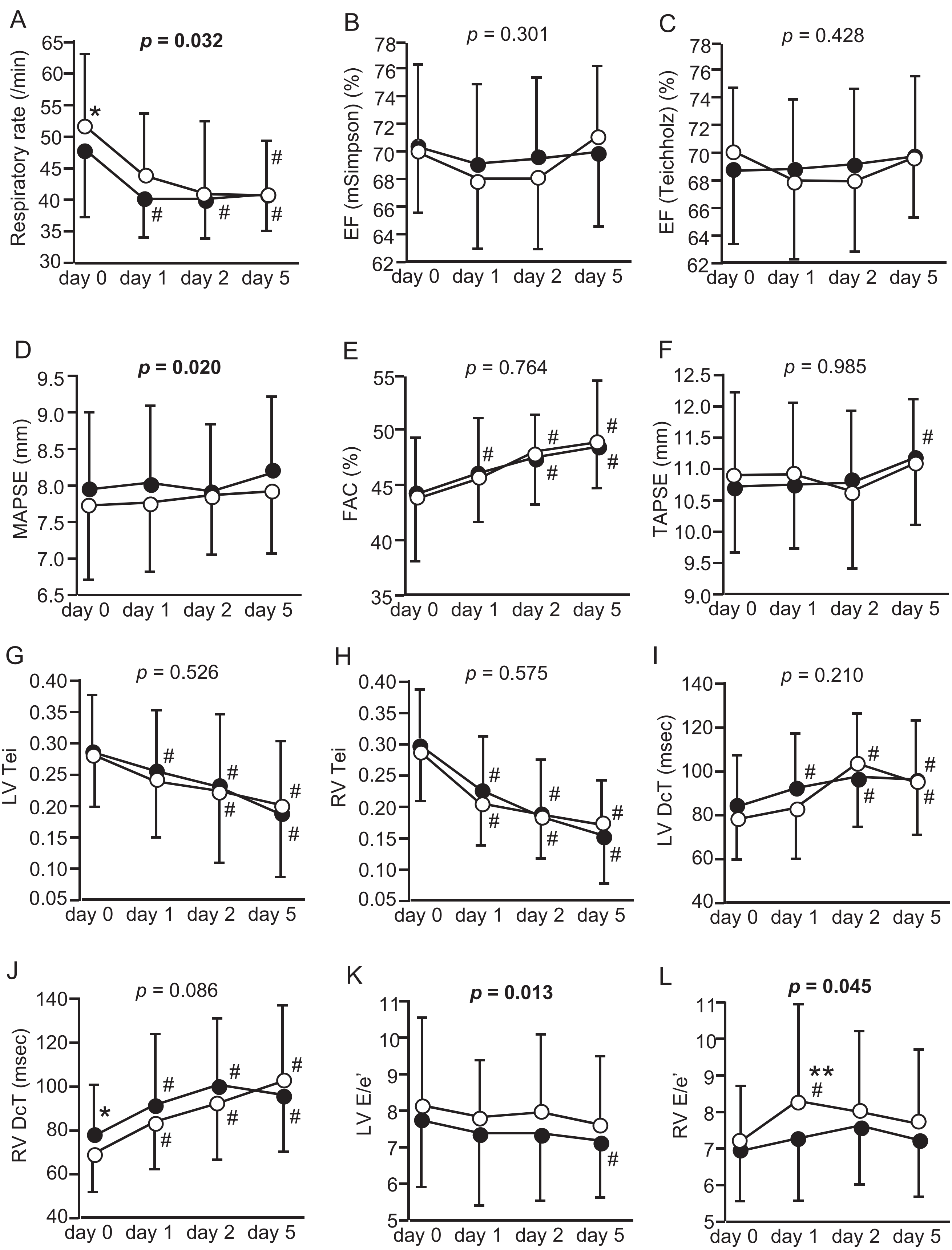
A
p = 0.032
Respiratory rate (/min)
30 35 40 45 50 55 60 65
day 0 day 1 day 2 day 5
*
#
B
p = 0.301
EF (mSimpson) (%)
62 64 66 68 70 72 74 76 78
day 0 day 1 day 2 day 5
C
p = 0.428
EF (Teichholz) (%)
62 64 66 68 70 72 74 76 78
day 0 day 1 day 2 day 5
D
p = 0.020
MAPSE (mm)
6.5 7.0 7.5 8.0 8.5 9.0 9.5
day 0 day 1 day 2 day 5
E
p = 0.764
FAC (%)
35 40 45 50 55
day 0 day 1 day 2 day 5
F
p = 0.985
TAPSE (mm)
9.0 9.5 10.0 10.5 11.0 11.5 12.0 12.5
day 0 day 1 day 2 day 5
G
p = 0.526
LV Tei
0.05 0.10 0.15 0.20 0.25 0.30 0.35 0.40
day 0 day 1 day 2 day 5
H
p = 0.575
RV Tei
0.05 0.10 0.15 0.20 0.25 0.30 0.35 0.40
day 0 day 1 day 2 day 5
I
p = 0.210
LV DcT (msec)
40 60 80 100 120 140
day 0 day 1 day 2 day 5
J
p = 0.086
RV DcT (msec)
40 60 80 100 120 140
day 0 day 1 day 2 day 5
K
p = 0.013
LV E/e'
5 6 7 8 9 10 11
day 0 day 1 day 2 day 5
L
p = 0.045
RV E/e'
5 6 7 8 9 10 11
day 0 day 1 day 2 day 5
**

Table 2 Correlation between echocardiographic parameters and gestational age or birth weight.

	Vaginal delivery		Cesarean section	
	gestational age	birth weight	gestational age	birth weight
MAPSE	0.085 (−0.104−0.269)	0.215 (0.028−0.387)	0.117 (−0.194−0.406)	0.268 (−0.039−0.529)
TAPSE	−0.004 (−0.192−0.185)	**0.531** (0.383−0.653)	0.160 (−0.151−0.442)	**0.351** (0.053−0.592)
LV E/e’	−0.003 (−0.195−0.187)	0.135 (−0.057−0.318)	**0.320** (0.179−0.569)	**0.360** (0.063−0.599)
RV E/e’	−0.131 (−0.314−0.061)	−0.013 (−0.203−0.178)	0.127 (−0.184−0.415)	0.227 (−0.083−0.496)
LV DcT	0.164 (−0.024−0.34)	0.149 (−0.040−0.327)	0.267 (−0.040−0.528)	0.158 (−0.157−0.444)
RV DcT	0.140 (−0.048−0.319)	0.040 (−0.015−0.226)	0.227 (−0.087−0.499)	0.193 (−0.118−0.469)

Pearson correlation coefficient between each echocardiographic parameter and gestational age or birth weight (95% confidence interval). Bold figures mean that the absolute value of coefficient is larger than 0.3.
DcT = deceleration time; E/e’ = ratio of peak early diastolic flow velocity to peak early diastolic annular velocity; LV = left ventricular; MAPSE = mitral annular plane systolic excursion; RV = right ventricular; TAPSE = tricuspid annular plane systolic excursion.

Table 3 Multivariate linear regression models for E/e’ and MAPSE on postnatal day 1.

	Regression coefficient	Standard deviation	Standardized coefficient	t value	*p* value
RV E/e’					
Mode of delivery	1.110	0.448	0.235	2.570	**0.011**
Gestational age	−0.056	1.348	−0.440	1.143	0.731
Birth weight	0.001	389.72	0.111	1.140	0.256
Oxygen	0.871	0.223	0.919	1.305	0.255
LV E/e’					
Mode of delivery	0.670	0.449	0.162	1.746	0.083
Gestational age	−0.038	1.340	−0.277	−0.265	0.792
Birth weight	0.001	392.52	0.119	1.928	0.056
Oxygen	0.456	0.2240	0.552	0.673	0.502
MAPSE					
Mode of delivery	0.165	0.449	0.049	0.565	0.573
Gestational age	0.000	315.45	−0.002	−0.025	0.980
Birth weight	0.001	459.07	0.224	2.424	**0.017**
Oxygen	0.597	0.224	0.887	1.100	0.273

LV E/e’, RV E/e’ and MAPSE were set as dependent variables, and oxygen administration, gestational age, birth weight, and delivery mode were included as independent variables.
E/e’ = ratio of peak early diastolic flow velocity to peak early diastolic annular velocity; LV = left ventricular; MAPSE = mitral annular plane systolic excursion; RV = right ventricular.

improvement or maturation of myocardial performance. The DcT of both ventricles increased during the first 2 postnatal days and then reached a plateau. The E/e’s of both ventricles decreased on day 5 (Fig. 2K). The RV E/e’ in the CS and VD groups reached peak levels on day 1 and day 2, respectively. Although there were no significant differences in most echocardiographic parameters between the CS and VD groups, MAPSE was lower, and both RV and LV E/e’s were higher in the CS than the VD group.

Because of differences in the gestational age and birth weight between the CS and VD groups, we analyzed the effects of these 3 variables on each echocardiographic

Figure 2 Effects of delivery mode on longitudinal changes of the echocardiographic parameters. A: respiratory rate, B: left-ventricular ejection fraction (LV EF) by the modified Simpson method, C: LV EF by the Teichholz method, D: mitral annual plane systolic excursion (MAPSE), E: right ventricular fractional area change (RV FAC), F: tricuspid annular plane systolic excursion (TAPSE), G: LV Tei index, H: RV Tei index, I: LV deceleration time (DcT), J: RV DcT, K: LV ratio of peak early diastolic flow velocity to peak early diastolic annular velocity (E/e’), L: RV E/e’. Values in the cesarean section group (open circles) and the vaginal delivery group (closed circles) are presented as means ± SDs. *P* values were calculated by two-way repeated-measures ANOVA, to compare the two groups. *Significant difference between the two groups at the indicated time points. #Significant difference between day 0 and the indicated time points. #, *$p < 0.05$, **$p < 0.01$.

parameter. TAPSE showed moderate and mild correlations (Pearson correlation coefficient) with birth weight in the VD and CS groups, respectively (Table 2). LV E/e' showed mild correlations with gestational age and birth weight in the CS but not in the VD group.

To clarify the effects of delivery mode, we used multivariate linear regression models for E/e' and MAPSE on postnatal day 1, in which delivery mode, gestational age, birth weight, and oxygen administration were included as independent variables. The regression models revealed that RV E/e' was significantly dependent on delivery mode, but that delivery mode had little, if any, effects on LV E/e' (Table 3). MAPSE was dependent on birth weight but not delivery mode. When the 24 infants who had PDA on day 1 were excluded from the analysis, similar regression models were obtained (data not shown).

4. Discussion

In this prospective observational study, we analyzed postnatal changes in cardiac mechanics of neonates born by CS or VD. We demonstrated that RV E/e' was significantly higher and peaked earlier after delivery by CS compared with vaginal delivery. Although MAPSE was consistently lower in the CS than VD group, multiple regression analysis suggested that MAPSE was dependent on body weight rather than delivery mode.

RV E/e' has been shown to be relatively stable and lower than LV E/e' during the early neonatal period,[1] suggesting relatively high RV filling pressure and delayed adaptation of the RV myocardium to the postnatal circulation compared with the LV myocardium. The RV E wave of term neonates is augmented as RV preload increases and afterload decreases.[8] Neonates with pulmonary hypertension have a smaller tricuspid e' wave than control infants, indicating impaired early diastolic relaxation associated with pulmonary hypertension.[8–10] Given that RV E/e' is positively correlated with mean right atrial pressure,[11] a tentative increase in RV E/e' in the CS group suggests a relatively higher and more prolonged RV filling pressure caused by delayed adaptation of the neonatal myocardium and/or persistence of pulmonary hypertension, compared with the VD group.

Mori et al.[1] reported that in term neonates, LV E/e' showed a significant decrease during the first 24 h after birth and no change during the following 6 days, and presumed that a higher LV E/e' during the first 24 h caused a relatively higher LV filling pressure due to PDA or immature diastolic function of the myocardium. Murase et al.[12] demonstrated that LV E/e' in premature infants, appeared to depend on PDA but not on gestational age. In our study, there was no significant difference in the time of PDA closure between the CS and VD groups, and a higher LV E/e' after CS might be due to delayed maturation of diastolic function of the myocardium rather than a younger gestational age.

MAPSE is a surrogate marker for LV long-axis contraction, whereas EF reflects LV short-axis contraction.[13] The longitudinal changes in MAPSE and EF suggest that changes in LV contractility could be reflected in the long-axis rather than short-axis during the first week of life, and LV contractility was lower in the CS than VD group. Lower blood levels of catecholamines and cortisol might partially explain the lower contractility observed after CS.[2] On the other hand, MAPSE has been shown to be correlated with body weight in preterm and term infants.[13] The correlation coefficient between MAPSE and birth weight was similar in both groups; therefore, MAPSE seems to depend on birth weight rather delivery mode.

Kukulski et al.[14] argued that because of immaturity of the right ventricle, long-axis RV contractility was more susceptible to afterload changes than LV contractility. TAPSE indexed to body surface area is lower in newborns with pulmonary hypertension compared with controls.[9] The increased TAPSE on postnatal day 5 indicates a decrease in afterload, which is comprised of pulmonary artery pressure and vascular resistance.

Murase et al.[15] demonstrated that the Tei indexes of both ventricles rose rapidly from 3 to 12 h after birth and then gradually fell in preterm infants, and that RV and LV Tei indexes were inversely correlated with RV and LV outputs, respectively. In this context, the changes in the Tei indexes indicate a gradual maturation of systolic and diastolic function of both ventricles after birth by either VD or CS.

This study has several limitations. First, it was an observational cohort study performed at a single center. Second, technical errors due to certain conditions, such as tachycardia, lack of rest, and a narrow echo window could not be ignored. Third, postnatal changes of pulmonary arterial pressure might have a great impact on RV and LV function as well as PDA. Because of technical reasons, we could not measure pulmonary artery pressure. Fourth, since we compared many echocardiographic parameters, some of them might have been significantly different between the VD and CS groups by chance. Further studies using validation set of infants are required to confirm our findings.

In conclusion, we demonstrated that postnatal longitudinal changes of several echocardiographic parameters and found that CS affected diastolic function of the right ventricle in the 2nd day after giving birth but did not persist. Our results are useful for understanding postnatal hemodynamic changes in neonates born by CS, in which delayed adaptation of the neonatal myocardium and/or persistence of pulmonary hypertension might play pivotal roles.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Acknowledgements

This research was not supported by any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Mori K, Nakagawa R, Nii M, Edagawa T, Takehara Y, Inoue M, et al. Pulsed wave Doppler tissue echocardiography assessment of the long axis function of the right and left ventricles during the early neonatal period. *Heart* 2004;**90**:175–80.
2. Vogl SE, Worda C, Egarter C, Bieglmayer C, Szekeres T, Huber J, et al. Mode of delivery is associated with maternal and fetal endocrine stress response. *BJOG* 2006;**113**:441–5.

3. Coskun S, Yüksel H, Bilgi Y, Lacin S, Tansug N, Onag A. Non-invasive evaluation of the adaptations of cardiac function in the neonatal period: a comparison of healthy infants delivered by vaginal route and caesarean section. *Acta Med Okayama* 2001;**55**:213—8.
4. Tei C, Ling LH, Hodge DO, Bailey KR, Oh JK, Rodeheffer RJ, et al. New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function—a study in normals and dilated cardiomyopathy. *J Cardiol* 1995;**26**:357—66.
5. Tei C, Dujardin KS, Hodge DO, Bailey KR, McGoon MD, Tajik AJ, et al. Doppler echocardiographic index for assessment of global right ventricular function. *J Am Soc Echocardiogr* 1996;**9**:838—47.
6. Tei C, Nishimura RA, Seward JB, Tajik AJ. Noninvasive Doppler-derived myocardial performance index: correlation with simultaneous measurements of cardiac catheterization measurements. *J Am Soc Echocardiogr* 1997;**10**:169—78.
7. Ichihashi K, Sato A, Shiraishi H, Momoi M. Tissue Doppler combined with pulsed-wave Doppler echocardiography for evaluating ventricular diastolic function in normal children. *Echocardiography* 2011;**28**:93—6.
8. Harada K, Shiota T, Takahashi Y, Suzuki T, Tamura M, Takada G. Right ventricular diastolic filling in the first day of life. *Tohoku J Exp Med* 1994;**172**:227—35.
9. Patel N, Mills JF, Cheung MM. Assessment of right ventricular function using tissue Doppler imaging in infants with pulmonary hypertension. *Neonatology* 2009;**96**:193—9.
10. Richardson C, Amirtharaj C, Gruber D, Hayes DA. Assessing myocardial function in infants with pulmonary hypertension: the role of tissue Doppler imaging and tricuspid annular plane systolic excursion. *Pediatr Cardiol* 2017;**38**:558—65.
11. Sundereswaran L, Nagueh SF, Vardan S, Middleton KJ, Zoghbi WA, Quiñones MA, et al. Estimation of left and right ventricular filling pressures after heart transplantation by tissue Doppler imaging. *Am J Cardiol* 1998;**82**:352—7.
12. Murase M, Morisawa T, Ishida A. Serial assessment of left-ventricular function using tissue Doppler imaging in premature infants within 7 days of life. *Pediatr Cardiol* 2013;**34**:1491—8.
13. Koestenberger M, Nagel B, Ravekes W, Gamillscheg A, Binder C, Avian A, et al. Longitudinal systolic left ventricular function in preterm and term neonates: reference values of the mitral annular plane systolic excursion (MAPSE) and calculation of z-scores. *Pediatr Cardiol* 2015;**36**:20—6.
14. Kukulski T, Hübbert L, Arnold M, Wranne B, Hatle L, Sutherland GR. Normal regional right ventricular function and its change with age: a Doppler myocardial imaging study. *J Am Soc Echocardiogr* 2000;**13**:194—204.
15. Murase M, Ishida A, Morisawa T. Left and right ventricular myocardial performance index (Tei index) in very-low-birth-weight infants. *Pediatr Cardiol* 2009;**30**:928—35.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pedneo.2019.01.004.