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Serial changes in myocardial function in preterm infants over a four week period: the effect of gestational age at birth ☆

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ABSTRACT

Background: Myocardial performance is impaired in the first days of life in preterm infants but improves by day 5. Tissue Doppler imaging (TDI) is a novel and reliable means of assessing myocardial performance.
Objective: To investigate myocardial performance using TDI and shortening fraction (SF) in preterm infants of different gestational age groups and serial changes in these parameters in first four weeks of life.
Study design
Infants less than 36 weeks of gestation were divided into group 1 (24–27 weeks, n = 8), group 2 (28–31 weeks, n = 12) and group 3 (32–35 weeks, n = 13). Infants with severe congenital malformations, a hypoxic insult at birth, and those on inotropic support were excluded. Echocardiograms were performed at 36–48 hours, 2 weeks and 4 weeks of life. Left ventricular (LV) SF, systolic (S′), early diastolic (E′) and late diastolic (A′) TDI velocities were assessed. We analyzed the data using a repeated-measures ANOVA.
Results: Thirty three infants underwent serial TDI and SF measurements. There was an increase in LV S′ ($p = .02$) and E′ (.01) velocities in group 2 , and in group 3 ($p = .03$ for S′ and $p = .04$ for E′), but no significant increase in group 1 ($p = .48$ for S′ and .32 for E′). At each study point, there was significant difference in myocardial performance between group 1 and 3 for each of the parameters ($p < .05$). There was no significant increase in SF over time in any of the groups.
Conclusion: We describe a serial increase in myocardial performance in infants of 28 weeks gestation and above. While there was no change in myocardial performance among the most extremely preterm infants, this may have been the result of small sample size of the group.

1. Introduction

The preterm myocardium is characterized by reduced diastolic function and intolerance to increased afterload, due to the inefficient contractile mechanism and lack of adequate elastic recoil[1]. The impact of these inherent structural differences, and of premature delivery on myocardial function in the first few weeks of life, warrants further study.

Tissue Doppler imaging (TDI) is an emerging tool for the assessment of myocardial performance in preterm infants [2,3]. TDI directly measures myocardial velocities allowing quantitative assessment of systolic and diastolic function of both ventricles [4,5]. TDI measures muscle movement velocity by assessing the high amplitude, low velocity ultrasound signals reflected from muscle wall movement while suppressing high velocity, low amplitude signals reflected from moving fluid [6]. The high temporal resolution of TDI is suited for the fast heart rates of preterm infants [5]. Several studies have demonstrated that assessment of myocardial velocity using TDI is feasible in the preterm population with acceptable reproducibility [2,5,7,8].

Assessment of myocardial function using TDI may be more accurate than conventional measures of myocardial performance which rely on the change in the dimensions of the ventricular cavity, namely shortening (SF) and ejection (EF) fraction [9–11]. In addition to being less sensitive, those conventional markers are very heavily load dependent and may not accurately reflect myocardial function. Recent studies have demonstrated the superiority of TDI in detecting myocardial dysfunction when compared to SF and EF [4,12]. Following patent ductus arteriosus (PDA) ligation, TDI can identify myocardial dysfunction in the subset of infants who develop clinical hypotension [13]. In addition, TDI can demonstrate significant improvement in myocardial performance following blood transfusion in anemic infants. SF fails to demonstrate those changes [4].

In this study, we investigated myocardial performance values for left ventricular peak myocardial systolic (S′), early diastolic (E′) and late diastolic (A′) TDI velocities and shortening fraction (SF), in preterm

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infants of different gestations at delivery and assessed the change in these velocities over a 4 week period.

2. Methods

This prospective observational study was conducted at the neonatal intensive care unit of the Rotunda Hospital in Dublin, Ireland. The local institutional ethical committee approved the study and informed consent was obtained from all parents. We included stable preterm infants beyond the first 36 hours of life between 24 and 35 weeks gestation. Stable infants were defined as those who were over 36 hours old; without inotropic support; receiving less than 30% oxygen on CPAP or conventional ventilation, or in less than 30% ambient oxygen. We excluded infants less than 24 weeks gestation, those with congenital malformations, those with evidence of an hypoxic insult at birth (defined as an Apgar score less than 6 at 5 min or a cord pH of less than 7.25), those with clinical or confirmed sepsis or necrotising enterocolitis (NEC) and those receiving either high frequency ventilation or nitric oxide. The haematocrit (Hct) was above 35% in all ventilated infants, >30% for infants on NCPAP, and >20% if on room air as per our hospital guidelines.

2.1. Study cohort and patient demographics

Our cohort was divided into three groups based on their gestation at birth: Group 1 (24–27 weeks gestation); Group 2 (28–31 weeks gestation) and Group 3 (32–35 weeks gestation). Each group underwent three echocardiography assessments of myocardial performance at 36 to 48 hours of life, and at two and four weeks of life.

2.2. Echocardiography assessment

Echocardiograms were performed by one observer (MSS), when all neonates were in a quiet state, using a Vivid I echocardiography machine (General Electrical, Haifa, Israel). A 10S-RS probe was used for groups 1 and 2 and a 7S-RS probe was used for group 3. Concurrent electrocardiography tracing was recorded to time the cardiac events. The first scan of each infant included a formal structural study and offline images were subsequently assessed by a consultant cardiologist (OF) for image quality and to rule out congenital heart disease. An apical four chamber view was obtained for assessment of tissue Doppler velocities. A pulsed waved Doppler gate of 0.35 cm was positioned at the lateral mitral annulus to acquire peak myocardial systolic (S′), early diastolic (E′) and late diastolic velocities (A′) of the left ventricle. An angle of less than 20 degrees was maintained and angle correction software was not used. The images were assigned a unique identity and functional parameters were measured offline following completion of study by a single observer who was unaware of the timing of study. The average velocities of peak S′, E′ and A′ in three cardiac cycles were obtained during offline analysis. Parasternal transthoracic M-mode echocardiography was used to measure LV end systolic diameter (LVESD), LV end diastolic diameter (LVEDD) and to calculate shortening fraction (SF) as described elsewhere [4]. At least three consecutive waveforms were recorded to obtain mean LV SF. The presence of a PDA was also noted. Two dimensional echocardiography (2D) was used to visualize PDA and the ductal diameter was measured at the pulmonary end from a high parasternal view. The PDA flow was assessed by color Doppler echocardiography. In our study, we defined PDA as haemodynamically significant if the diameter was >1.5 mm.

We have previously studied the inter- and intra-observer variability (gestational age and birth weight matched) in the similar cohort of patients [4]. The mean standard deviation (SD) of inter- and intra-observer difference of peak S′ velocity was 0.043 (0.375) cm/sec and 0.046 (0.323) cm/sec respectively. The intra-class correlation coefficient was 0.845 for inter-observer (95% CI 0.776–0.892) and 0.857 (95% CI 0.752–0.918) for intra-observer values [4].

2.3. Statistics

Values were presented as means (standard deviations) unless stated otherwise. Differences between each group over time were assessed using one way ANOVA. Pairwise comparisons (between Echo 2 and baseline and Echo 3 and baseline) within the groups were conducted using the Bonferroni adjustment. A two way repeated measures ANOVA was used to assess the differences between groups across time. A p value less than .05 was considered significant. We used SPSS version 21 to conduct the analysis.

3. Results

Forty-one infants consented for the study. Eight infants were excluded after consent: three due to suspected sepsis, one for culture proven sepsis and one for clinical and radiological evidence of NEC. Three further infants did not complete the study as they were transferred back to the local referring hospital. The remaining 33 infants underwent serial TDI and SF measurements over a 4 week period.

Table 1, describes the demographic data, respiratory support and presence of PDA for the study population. At 48 hours of age, all infants required either respiratory support or supplemental oxygen. The mean PDA diameter and SD values for each of the groups are also shown in Table 1. None of the infants had a PDA in subsequent studies.

Table 2 describes the effect of gestational and postnatal ages on myocardial performance in the study population (Fig. 1).The change in left ventricular systolic (LV S′) velocities in each group over the three time points is illustrated in Fig. 2.

The TDI velocities for infants with or without PDA were also analyzed within group 2 and 3. The S′ velocities for PDA vs. non PDA infants within each of the group 2 and 3 were [4.15 (0.98) cm/sec vs. 4.04 (0.77) cm/sec, p = .82] and [4.56 (1.69) cm/sec vs. 4.83 (0.99) cm/sec, p = .71] respectively.

4. Discussion

In this study, we demonstrated that myocardial systolic and diastolic function, measured by TDI, shows differing progression patterns over the first four weeks of life in infants of varying gestations at birth. At baseline, extremely premature infants born at a mean gestation of 25 weeks have lower TDI velocities when compared to those born at a mean of 29 and 33 weeks respectively. In addition, systolic and diastolic function in infants born between 24 and 27 weeks does not increase

Table 1
Demographic data and respiratory support.

	Group 1 (n = 8) 24–27 weeks	Group 2 (n = 12) 28–31 weeks	Group 3 (n = 13) 32–35 weeks	p value
Gestational age	25 (1.1)	29.1 (1.2)	32.8 (1.0)	<.001*
Birth weight	600 (72)	1146 (186)	1956 (262)	<.001*
Female	5 (63)	5 (42)	7 (54)	.644**
PDA at the first scan	8 (100)	8 (67)	4 (31)	.006**
PDA diameter (mm)	1.12 (0.16)	1.01 (0.24)	1.04 (0.11)	.504*
Mechanical ventilation				
48 hours	6 (75)	6 (50)	3 (23)	
2 weeks	3 (37.5)	2 (16.6)	0	
4 weeks	1 (12.5)	0	0	
NCPAP				
48 hours	2 (25)	5 (42)	8 (62)	
2 weeks	4 (50)	7 (58)	5 (39)	
4 weeks	5 (63)	4 (33)	1 (8)	
Supplemental oxygen or room air				
48 hours	0	1 (8)	2 (15)	
2 weeks	1 (13)	3 (25)	8 (62)	
4 weeks	2 (25)	8 (67)	12 (92)	

Values are presented as mean (SD) or absolute value (%). One way ANOVA* and chi square** were used to compare means between groups.