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Myocardial function in term and preterm infants. Influence of heart size, gestational age and postnatal maturation

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ABSTRACT

Background: Sparse knowledge exists on the differences in cardiac function between term and preterm infants. This study examines the impact of heart size, gestational age and postnatal maturation on myocardial function.
Aim: To assess and compare serial echocardiographic indices of myocardial function in term and moderately preterm infants.
Methods: Longitudinal, prospective, observational echocardiographic cohort study of 45 healthy term infants examined at day three and at 12–20 weeks postnatal age and 53 moderately preterm infants (gestational age 31–35 weeks) examined at day three and at term equivalent (4–10 weeks postnatal age).
Outcomes: Primary: Systolic mitral and tricuspid annular plane excursions and annular peak systolic pulsed wave tissue Doppler (pwTDI) velocities.
Secondary: Indices normalized for heart size.
Results: On day three, all indices were higher in the term than in the preterm infants whereas normalized systolic pwTDI velocities were lower in the term infants and normalized excursions showed no difference. All indices increased with advanced postnatal age. The indices in term infants on day three were lower than in preterm infants at term equivalent, with and without normalization. After postnatal maturation in both groups, all indices were higher in the term group (except left pwTDI), whereas normalized indices showed no consistent pattern.
Conclusions: Myocardial function indices increased with gestational age at birth and more profoundly with postnatal maturation. Serial examinations of non-normalized and normalized myocardial function indices showed no sustained differences between the preterm and the term infants.
Normalization by heart size may be of value when assessing myocardial function in infants.

1. Introduction

The myocardium in term infants is structurally more mature than that in premature infants and studies in preterm fetal lambs show that fetal myocytes are smaller, have fewer myofibrils per unit mass and a larger proportion of mononucleated cardiomyocytes compared to myocytes in lambs at term [1]. The mature and the immature myocardium may respond differently to the abrupt circulatory changes during fetal–neonatal transition [2].

Functional or targeted echocardiography provides bedside information on the central circulation and cardiac function and is increasingly incorporated into clinical practise in neonatal intensive care units [3]. The information obtained may be useful for the diagnosis and treatment of hemodynamic compromise. Several studies have assessed parameters reflecting postnatal hemodynamic adaption [4–7], but few studies have focused directly on the cardiac function by quantifiable measures. By applying conventional echocardiography, mitral annular plane systolic excursion (MAPSE) and tricuspid annular plane systolic excursion (TAPSE) can be assessed as parameters of left and right ventricular longitudinal systolic shortening [8–10]. Newer echocardiographic indices based on tissue Doppler imaging (TDI) are increasingly applied in the evaluation of myocardial function in adults [11] is feasible in children

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and infants [12–15]. A recently published review advocates its use in the pediatric age group [16]. Measures of myocardial wall velocities along the longitudinal axis of the left and right ventricles can be obtained by pulsed wave (pw) TDI, and peak annular systolic velocity is validated as a measure of ventricular longitudinal systolic function [17]. pwTDI indices are less load dependent than blood flow measurements [18] and the method provides assessment of myocardial function in case of poor endocardial definition or abnormal septal motion [11].

The size of cardiovascular structures increase during normal body growth and development [19,20]. Scaling or normalization to correct for size is therefore customary. However, linear correction by body size has shown to be inaccurate in children [21]. Recent studies in children have shown that atrioventricular excursions normalized for heart size are independent measures of systolic function [22,23]. Eidem et al. also found that pwTDI velocities strongly correlated to left ventricular end-diastolic length (LVEDL) [14]. Annular excursions and velocities normalized by LVEDL are indices of longitudinal myocardial function that might more readily be compared between hearts of different size [24,25].

We have recently shown that atrioventricular plane velocities by pwTDI and atrioventricular plane excursions by conventional echocardiography are related to heart size, gestational and postnatal age in moderately premature infants [26,27]. The aim of this study was to serially assess and compare selected indices of longitudinal systolic myocardial function in healthy term born infants and to study the relative impact of prematurity and postnatal maturation. Secondly, parameters adjusted for heart size, normalizing by LVEDL, were assessed and compared between the groups. Our hypothesis was that indices of myocardial function were dependent on both gestational age at birth and postnatal maturation.

2. Methods

2.1. Study design and study population

In this prospective, longitudinal, observational study, forty-five healthy term infants were enrolled from the Maternity Ward at Oslo University Hospital, Ullevål in 2005 [28]. They had been examined by echocardiography day three after birth and at three to four months of age. They were compared to 53 preterm infants (gestational age 31–35 weeks) recruited from the Neonatal Intensive Care Unit at Ålesund Hospital ($n = 40$) and the Department of Neonatal Intensive Care at Oslo University Hospital, Ullevål ($n = 13$) from March 2009 until December 2010 and examined on day three after birth and at the time of term equivalent (± 14 days). Infants with major congenital anomalies of any organ system were excluded. In the preterm group, infants requiring cardiovascular supportive treatment were excluded, whereas ventilator support was not an exclusion criterion. Results from the majority of the preterm group, on days one and two after birth, have been published earlier [26,27].

2.2. Ethical considerations

The studies were approved by the Scientific Committees in both hospitals and by the Regional Committees for Medical and Health Research Ethics (South-East and Mid-Norway). Written informed parental consent was obtained.

2.3. Image acquisition

Vivid 7 (term group) and Vivid I or Vivid S6 (preterm group) ultrasound machines (GE Vingmed, Horten, Norway) and standard phase array multi-frequency transducers (7S probe, 3.5–8 MHz and 5S probe; 2.0–5.0 MHz) were used to perform the echocardiographic examinations. Structural normality of the heart was established. Images for assessment of pwTDI velocities and MAPSE and TAPSE were recorded from the apical four-chamber view according to the methods described previously [26,27]. Default frame rate and tissue velocity range of ± 0.16 cm/s were applied.

2.4. Off-line analyses

All images in both groups were analyzed by the same observer (BHE) during a period of a few months in 2010/2011 using the manufacturer's software (EchoPac PC version 108.1.5, SW, GE Vingmed, Horten, Norway). Lateral and septal MAPSE and TAPSE were measured in B-mode by M-mode tracings (Fig. 1), and peak systolic (S′) atrioventricular plane Doppler velocities were measured in pwTDI as previously described [26,27] (Fig. 2). LVEDL was measured in B-mode four-chamber images as the distance from the apical epicardium to the level of the septal attachment of the mitral valve. Parameters adjusted for heart size were obtained by dividing the indices by LVEDL. Heart rate (HR) was obtained from the mitral Doppler flow signal. All variables were calculated using the average of three cardiac cycles.

2.5. Statistics

Demographic data are reported as median (range) or number (percentage). Normally distributed continuous echocardiographic variables are expressed as means (95% CI). Independent sample t-tests were used when comparing means between groups and paired sample t-tests when comparing measurements within groups. Multiple regression analysis was used to test the effect of HR on the echocardiographic parameters. Two sided p-values <0.05 were considered significant. Statistical analyses were performed using SPSS 19.0 for Windows (SPSS Inc., Chicago, IL, USA) or JMP 9.0 (SAS Institute).

3. Results

3.1. Study population and demographic data

Patient characteristics of the two groups are shown in Tables 1 and 2. Eight patients in the term group and five in the preterm group were lost to follow up. Images with inferior quality were not analyzed. One term and three preterm infants had an insignificant muscular ventricular septal defect. Otherwise, all the participants had structurally normal hearts.

There was no significant difference in postmenstrual age (PMA) in the term group day three and in the preterm group at term equivalent. The lowest HR was found for the term infants on day three ($p < 0.001$) (Table 2). LVEDL was larger in the term group day three than in the preterm group day three ($p < 0.001$), whereas LVEDL were similar between the term group day three and the preterm group at term equivalent. In the preterm group, two infants were treated with positive pressure ventilation and three with nasal continuous positive airway pressure (nCPAP) at day three.

3.2. Myocardial deformation indices

Table 3 shows all indices of myocardial function in both groups at the two different study points. All indices increased in the term group with growth and postnatal maturation from day three. Comparing both groups at day three, both S′ and excursions in all walls were higher in the term group ($p < 0.05$ and $<0{,}001$, respectively). All measurements were lower in the term group at day three compared to the preterm group at term equivalent ($p < 0.001$). After postnatal growth and maturation in both groups, all indices were higher in the term infants than in the preterm infants ($p < 0.001$ and $p < 0.05$ for left MAPSE), but not statistically significant for left S′. Multiple regression analyses, adjusting for term or preterm birth, showed a moderate negative effect of HR only on left and septal MAPSE day three (R^2 0.246 and 0.209, $p < 0.001$ and 0.019). Otherwise, no effect of HR on the myocardial