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# Assessment of myocardial performance in preterm infants less than 29 weeks gestation during the transitional period

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ABSTRACT

*Background:* The transitional circulation and its effect on myocardial performance are poorly understood in preterm infants.
*Aims:* We assessed myocardial performance in infants less than 29 weeks gestation in the first 48 h of life using a comprehensive echocardiographic assessment.
*Design:* Infants <29 weeks gestation were prospectively enrolled. Small for gestation, infants on inotropes and/or inhaled nitric oxide and septic infants were excluded. Conventional echocardiography, left ventricular (LV), septal and right ventricular (RV) tissue Doppler imaging (TDI) and tissue Doppler-derived strain and strain rate (SR), tricuspid annular plane systolic excursion (TAPSE) and global RV fractional area change (FAC) were assessed at a median of 10 and 45 h post-delivery.
*Results:* Fifty-four infants with a median [IQR] gestation and birth weight of 26.5 weeks [25.8–28.0 weeks] and 915 g [758–1142 g] were included. There was no change in shortening or ejection fraction across the two time points. Systolic and diastolic TDI of the LV, septum and RV increased across the two time points (all p values $\leq 0.01$). There was an increase in septal peak systolic and early diastolic SR ($p = 0.002$). Septal systolic strain and late diastolic SR did not change. With the exception of RV strain and early diastolic SR, all RV functional parameters including SR, late diastolic SR, TAPSE, and FAC increased across the two time points (all p values $< 0.01$).
*Conclusion:* Describing the normal hemodynamic adaptations in stable preterm infants during the transitional period provides the necessary information for the assessment of those parameters in various disease states.


## 1. Introduction

Cardiovascular adaptation during the transitional period and its effect on myocardial performance is poorly described in preterm infants. During the early phase, preterm infants are particularly susceptible to morbidities such as intraventricular hemorrhage (IVH), hypotension, and ventilator dependency, which may be partially related to hemodynamic instability [1,2]. Monitoring the cardiovascular status of preterm infants remains a challenge due to the insensitivity of clinical indicators in defining systemic perfusion [3], and the limitations of conventional echocardiography functional parameters such as shortening fraction (SF) and ejection fraction (EF) in assessing left ventricular (LV) function [4]. Moreover, data on the assessment of right ventricular (RV) function in preterm infants are still limited.

Recent advances in echocardiography have led to the development of techniques that directly measure global and regional myocardial function, rather than depend on changes in cavity dimensions. Tissue Doppler imaging (TDI) and myocardial deformation measurements (myocardial strain rate and strain) may provide more accurate information on systolic and diastolic myocardial function [5–7]. Tissue Doppler imaging (TDI) and myocardial deformation based on

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tissue Doppler derived strain and strain rate (SR) are emergent techniques [8]. The most significant value of those techniques is the ability to detect subclinical local myocardial dysfunction before the appearance of clinically apparent ventricular impairment. Quantitative assessment of RV function can be obtained using TDI, strain and strain rate, in addition to RV specific markers of performance including tricuspid annular plane systolic excursion (TAPSE) and fractional area contraction (FAC). These modalities may possess better sensitivity in detecting changes in myocardial performance during the early preterm neonatal period, and provide more insight into the adaptations that occur during the transitional period.

In this study, we aimed to document changes in myocardial performance at two discrete time points over the first 48 h of life in stable preterm infants less than 29 weeks gestation using a comprehensive echocardiographic assessment.

## 2. Methods

### 2.1. Study population

This was a prospective observational study carried out in the neonatal intensive care unit (NICU) of the Rotunda Hospital Dublin, Ireland (a tertiary maternity unit which caters for over 9000 deliveries per annum). This was a nested study within a larger ongoing cohort study designed to define the natural history of patent ductus arteriosus (PDA) in preterm infants less than 29 weeks gestation. Infants were excluded if they: were small for gestational age (weight less than the 10th centile for given gestation); received inotropes or inhaled nitric oxide (iNO) in the first 48 h of life; died within the first 7 days of life; had a suspected or definite chromosomal abnormality; culture confirmed sepsis or congenital heart disease other than a PDA and patent foramen ovale (PFO) identified antenatally or on the initial echocardiogram.

Our unit currently adopts a conservative approach to PDA treatment. Prophylactic indomethacin is not used at this institution and medical treatment of the PDA with non-steroidal anti-inflammatory drugs is not provided in the first 7 days of life. High frequency oscillation (HFO) is only used as a rescue mode of ventilation. Hypotension is treated with inotropes if blood pressure is lower than the 3rd centile for any given gestation in addition to clinical and laboratory signs of hemodynamic compromise. The results of the two research scans were not communicated to the medical team caring for the infants unless they specifically requested a clinically indicated echocardiographic assessment or if congenital heart disease was identified. Written parental informed consent was obtained from all participants and ethical approval was obtained from the Hospital Ethics Committee prior to recruitment.

### 2.2. Clinical demographics

Antenatal, birth and neonatal characteristics were collected. In addition clinical cardio-respiratory characteristics during the two echocardiography assessments were collected and included: systolic, diastolic and mean blood pressure, heart rate, mean airway pressure, mode of ventilation, oxygen requirements, oxygen saturation, volume of fluid intake and pH.

### 2.3. Echocardiographic assessment

Echocardiography was performed on day 1 of life at a median of 10 h (echo 1) and at day 2 of life at a median of 45 h (echo 2) using the Vivid I echocardiography system and 10 MHz multi-frequency probe (GE Medical, Milwaukee, USA). All studies were conducted using a standardized functional protocol adapted from recently published guidelines [9]. All infants were in a supine position at the time of the scan. The scans were all stored as raw data in an archiving system (EchoPac, General Electric, version 112 revision 1.3) for later offline analysis. All offline analysis was carried out by a single investigator (ATJ).

We obtained the following echocardiography measurements in study infants using methods previously described [10]: diastolic septal wall thickness, LV internal diameter in diastole (LVID), LV posterior wall diameter in diastole (LVPWD) (LV dimension parameters all obtained using M-mode); left ventricular output (LVO); LV shortening fraction (SF) based on M-mode; ejection fraction measured by Simpson's biplane method [9]; PDA diameter in 2D measured at the pulmonary end; direction of flow and PDA shunt gradient, pulmonary artery acceleration time and RV ejection time. LV length was measured in diastole as the distance from the closed mitral valve to the apex in the four-chamber view. The presence of a patent foramen ovale and the shunting across it and the presence of tricuspid valve regurgitation (TR) were also noted. In addition, we calculated LV wall stress using the following formula: $[1.35 \times (\text{mean arterial pressure}) \times (\text{LVID})] / [4 \times (\text{LVPWD}) \times (1 + \text{LVPWD/LVID})]$ [11].

### 2.4. Tissue Doppler imaging (TDI)

Tissue Doppler velocities were obtained from the apical four-chamber view using a pulsed wave Doppler sample gate of 2 mm at the level of the annuli and the basal part of the intraventricular septum. We aligned the pulsed wave cursor with the longitudinal plane of motion at all times. On the tissue Doppler traces we measured peak systolic (s′), early diastolic (e′) and late diastolic (a′) velocities. If the e′ and a′ wave were fused, we measured the single wave as an a′ wave. The LV, septal and RV systolic velocities were normalized to LV and RV lengths accordingly using the following formula: normalized s′ = s′/ventricular length in cm. Isovolumic contraction (IVCT) and relaxation (IVRT) times and left ventricular systolic and diastolic times were also measured. The systolic to diastolic time ratio (SD ratio) was derived from the tissue Doppler traces. The myocardial performance index (MPI) was calculated from TDI as the sum of IVCT and IVRT divided by LV systolic time using the following formula: MPI = (IVCT + IVRT)/LV systolic time.

### 2.5. Tissue Doppler-derived strain and strain rate

The four-chamber view was used to acquire color-tissue Doppler images of the LV and RV free walls and the septum. Sector width was narrowed to maximally increase the frame rates. Offline analysis was performed to measure longitudinal peak systolic strain, peak systolic strain rate (SRS), early diastolic strain rate (SRE) and late diastolic strain rate (SRA) in the basal segments of the LV and RV free wall and the IVS. RV strain was obtained from the free wall following angling towards the RV to obtain a clearer image of the wall. Image quality was assessed visually prior to analysis and only images of sufficient 2D quality were used. A single elliptical region of interest (ROI) was determined with a width of 2 mm and length of 1 mm. Strain length (the computational distance) was set at 6 mm. Those settings have been demonstrated to be the most reliable in extremely premature infants [12–14]. Linear drift compensation and 40 ms Gaussian smoothing was used. Event timing, including aortic and mitral valve opening and closure, was determined using the electrocardiogram and pulsed wave Doppler of the flow across those valves. Strain, SR, SRE and SRA were manually determined by averaging the results of three cardiac cycles (Fig. 1). Two cardiac cycles were used if measurement artifact was present in one cycle. If two cycles contained measurement artifact then the study was excluded from analysis. If E and A wave fusion was present in diastole then the single wave was reported as an A wave.

### 2.6. RV functional and dimension measurements

Tricuspid annular plane systolic excursion (TASPE) is a measure of movement of the tricuspid annulus from base to apex during systole and reflects global RV function. TAPSE was measured based on