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Clinical utility of right ventricular fractional area change in preterm infants

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ABSTRACT

Introduction: Right ventricular fractional area change (RV FAC) is a novel non-invasive quantitative measure of RV function. Reference values of RV FAC and RV end systolic and diastolic areas (RVEDA, RVESA) have recently been established in preterm infants, but their role as marker to assess the efficacy of patient management strategies in the first week of life is largely unknown. The aims of this study were to assess the relationship between RV FAC and gestational age/birthweight, assess the RV FAC on day one of age to predict the later evolution of peri/intraventricular haemorrhage (P/IVH), and assess the influence of a persistent patent ductus arteriosus (PDA) on RV FAC during the first week of age.
Methods: Preterm infants <29 weeks gestation underwent echocardiography assessments on days 1, 2 and 5–7. RVEDA and RVESA were traced in the RV-focused apical four-chamber view, and RV FAC was calculated using the formula [(RVEDA − RVESA) ÷ (RVEDA)] × 100. PDA treatment was not carried out during the study period. A cranial ultrasound was carried out on all infants on Days 5–7 of age. P/IVH was defined as IVH grades II to IV.
Results: One hundred and one infants with a mean gestation of 26.5 (1.4) weeks and a birthweight of 983 (240) grams were enrolled in the study. There was no relationship between RV FAC and birthweight ($r = -0.02$, $p = 0.86$) but there was a negative correlation between RV FAC and echo-measured SVR ($r = -0.57$, $p < 0.001$). On Day 1, RV FAC was lower in infants who developed P/IVH (24% [18–34] vs. 31% [25–40], $p = 0.04$). On Days 5–7 infants with a PDA had a lower RV FAC compared with those without [42 (7) vs. 49 (9) %, $p < 0.001$].
Conclusion: RV FAC may be a useful addition to the haemodynamic assessment of preterm infants during the first week of age.

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1. Introduction

Assessment of right ventricular (RV) performance in preterm infants is gaining considerable interest with an increasing realisation that RV function has important prognostic implications in various disease states and populations [1–3]. Several studies have recently emerged describing various methods of objective RV functional assessment in preterm infants using a variety of methods including tissue Doppler imaging, tricuspid area plane systolic excursion (TAPSE), RV deformation imaging and RV fractional area change [4–9]. However, the clinical relevance of those markers in the preterm population and how they relate to disease states warrants further study.

Right ventricular fractional area change (RV FAC) describes the change in the RV cavity area from diastole to systole in the four chamber view and provides the dominant contribution to RV ejection fraction [6]. There is a strong correlation between RV FAC and RV ejection fraction determined by magnetic resonance imaging (MRI) [10]. RV FAC appears to be uninfluenced by significant intra-atrial shunts in adults [11] and therefore may reflect blood returning from the upper and lower circulation. Recently, the feasibility, reproducibility and reference values of RV FAC in preterm infants have been established [5,6]. However no current data is available on the relationship between RV FAC measured during the first week of life and perinatal characteristics, peri/intraventricular haemorrhage (P/IVH), and patent ductus arteriosus (PDA). Evaluating the role of RV FAC in the first week of life in relationship to common morbidities to demonstrate the validity of this measure in premature infants is of paramount importance.

In this study, we hypothesise that RV FAC has important associations with perinatal factors, P/IVH and haemodynamically significant PDAs in preterm infants less than 29 weeks gestation. The aims of this study are to assess the relationship between RV FAC and gestational age/birthweight, assess the ability of a low RV FAC on day one of age to predict the later evolution of P/IVH, and the assess the influence of a persistent PDA on RV FAC during the first week of age.

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2. Methods

This was a prospective observational cohort study carried out over a two year period in the neonatal intensive care unit of the Rotunda Hospital, Dublin, Ireland, between January 2013 and December 2014. Infants born less than 29 weeks gestation were included in the study. Prior to enrolment, all infants underwent a cranial ultrasound examination on the first day of age to rule out early P/IVH. Infants were excluded if there was evidence of a congenital or chromosomal abnormality at birth, congenital heart disease (other than a PDA or a PFO) identified antenatally or during the first echocardiogram, a P/IVH (IVH grades 2 or higher) identified on day one of age based on the Papile system of classification [12], or death within the first week of age. We currently adopt 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. The echocardiography assessments conducted for this study were not revealed to the clinical team caring for the infant unless there was a clinical reason (other than a PDA) to do so. Written parental informed consent was obtained from all parents and ethical approval was obtained from the Hospital's local Research Ethics Committee.

2.1. Clinical demographics

Antenatal, birth, and clinical cardiorespiratory characteristics were obtained from the hospital records. The following clinical outcomes were also obtained: culture proven sepsis, necrotizing enterocolitis (NEC) with radiological evidence of pneumatosis; chronic lung disease (CLD) defined as the need for oxygen at 36 weeks corrected gestation; treated retinopathy of prematurity; length of hospital stay; P/IVH assessed on Day 7 of age and classified according to the Papile Classification [12]; and death before discharge.

2.2. Echocardiography

Echocardiography was carried out at a median [inter-quartile range] of 10 h [7–13] (Day 1), 43 h [38–46] (Day 2), and 143 h [125–161] (Days 5–7) using a Vivid I or a Vivid S6 echocardiography machine and a 10 or 12 MHz neonatal probe (GE Medical, Milwaukee, USA). Studies were conducted during a resting state in accordance to recent guidelines and congenital heart disease was excluded during the first scan [13]. Data were stored as raw DICOM images in an archiving system (EchoPac, General Electric, version 112 revision 1.3) and analysis of all the echocardiography parameters was carried out by a single investigator who was blinded to the results of the cranial ultrasounds (ATJ).

To measure RV FAC, two dimensional images were obtained from a RV-focussed apical four-chamber view (Fig. 1). During offline analysis RV cavity end diastolic area (RVEDA) was identified as the frame just after tricuspid valve closure and RV cavity end systolic area (RVESA) was identified as the frame just before tricuspid valve opening. The area of the cavity was manually traced during those two time-points within the cardiac cycle as illustrated in Fig. 1. RV trabeculations were included in the trace [5,6]. RV FAC was then calculated using the following formula: RV FAC (%) = [RVEDA(cm^2) − RVESA (cm^2)] ÷ RVEDA(cm^2).

The following echocardiography parameters were also measured using previously described methods [14]: LVO (ml/kg/min); PDA diameter (mm) measured in 2D at the pulmonary end; diastolic and systolic flow velocity across the PDA; the presence of a patent foramen ovale (PFO) and the velocity of the shunt across the PFO; left atrial to aortic root ratio (LA:Ao); celiac artery and descending aortic end diastolic velocity; tricuspid regurgitant jet velocity (TRv) if present and right ventricular systolic pressure (RVSp) measured using Bernoulli's equation as follows: RVSp = 4 × TRv^2. Peak systolic to diastolic flow velocity ratio across the PDA was calculated on Days 5–7 to determine the flow pattern across the duct [15]. Systemic vascular resistance (SVR) was

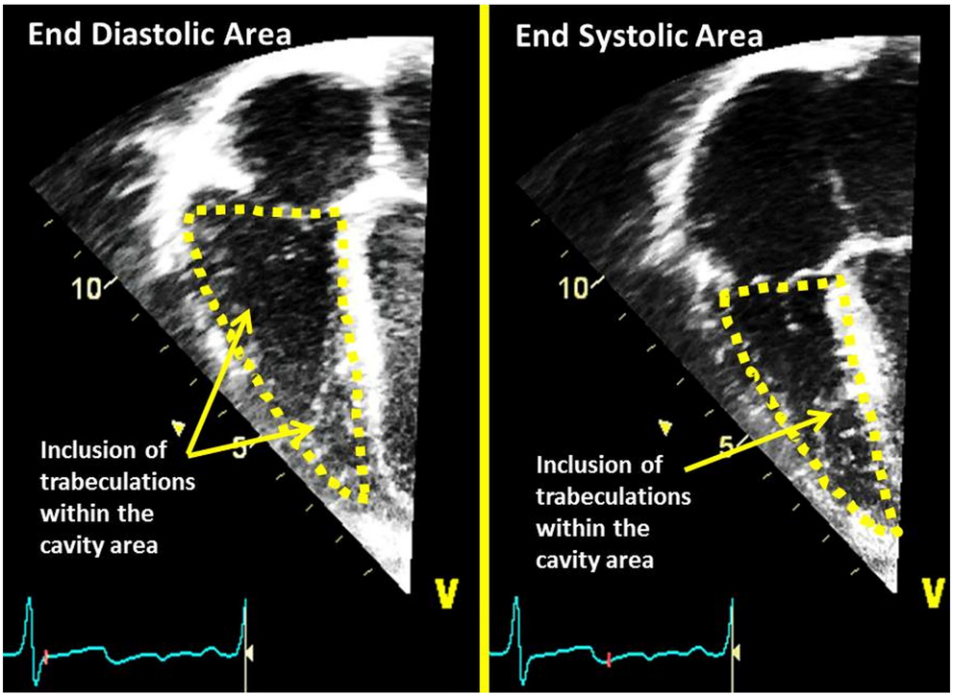

Fig. 1. Measurement of right ventricular fractional area change. During offline analysis RV cavity end diastolic area (RVEDA) was identified as the frame just after tricuspid valve closure and RV cavity end systolic area (RVESA) was identified as the frame just before tricuspid valve opening. The area of the cavity was manually traced during those two time-points within the cardiac cycle. RV trabeculations were included in the trace RV FAC was then calculated using the following formula: RV FAC (%) = [RVEDA(cm^2) − RVESA (cm^2)] ÷ RVEDA(cm^2).

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