Validation Study of the Accuracy of Echocardiographic Measurements of Systemic Blood Flow Volume in Newborn Infants

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Background: The echocardiographic assessment of circulatory function in sick newborn infants has the potential to improve patient care. However, measurements are prone to error and have not been sufficiently validated. Phase-contrast magnetic resonance imaging (MRI) provides highly validated measures of blood flow and has recently been applied to the newborn population. The aim of this study was to validate measures of left ventricular output and superior vena caval flow volume in newborn infants.

Methods: Echocardiographic and MRI assessments were performed within 1 working day of each other in a cohort of newborn infants.

Results: Examinations were performed in 49 infants with a median corrected gestational age at scan of 34.43 weeks (range, 27.43–40 weeks) and a median weight at scan of 1,880 g (range, 660–3,760 g). Echocardiographic assessment of left ventricular output showed a strong correlation with MRI assessment (R^2 = 0.83; mean bias, −9.6 mL/kg/min; limits of agreement, −79.6 to +60.0 mL/kg/min; repeatability index, 28.2%). Echocardiographic assessment of superior vena caval flow showed a poor correlation with MRI assessment (R^2 = 0.22; mean bias, −13.7 mL/kg/min; limits of agreement, −89.1 to +61.7 mL/kg/min; repeatability index, 68.0%). Calculating superior vena caval flow volume from an axial area measurement and applying a 50% reduction to stroke distance to compensate for overestimation gave a slightly improved correlation with MRI (R^2 = 0.29; mean bias, 2.6 mL/kg/min; limits of agreement, −53.4 to +58.6 mL/kg/min; repeatability index, 54.5%).

Conclusions: Echocardiographic assessment of left ventricular output appears relatively robust in newborn infant. Echocardiographic assessment of superior vena caval flow is of limited accuracy in this population, casting doubt on the utility of the measurement for diagnostic decision making. (J Am Soc Echocardiogr 2013;26:1365-71.)

Keywords: Echocardiography, Phase-contrast MRI, Preterm infants

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Echocardiographic assessments of circulatory function show significant potential to enhance the circulatory management of infants admitted to neonatal intensive care.[1-4] A consensus statement on targeted neonatal echocardiography was recently released by the American Society of Echocardiography to guide practice in this area.[5] The statement also highlights how prone to error quantitative measures are in newborns and reinforces the need for measurements of blood flow (left ventricular output [LVO] and superior vena caval [SVC] flow volume) to be standardized and validated.[5]

Phase-contrast (PC) magnetic resonance imaging (MRI) is a highly validated technique in adults[6] and children[7] and has recently been successfully applied to preterm infants.[8] Assessments can be performed during natural sleep without the need for anesthesia or sedation,[8] and scans can be performed on magnetic resonance systems located within neonatal intensive care units, allowing maintenance of cardiorespiratory and thermal stability even in the most preterm infants.[9] PC MRI can assess flow volume in any large vessel.[10] Critically, PC MRI is at least twice as repeatable as echocardiography in the preterm population,[8]

Abbreviations
LOA = Limits of agreement
LVO = Left ventricular output
MRI = Magnetic resonance imaging
PC = Phase-contrast
RI = Repeatability index
SVC = Superior vena caval
VTI = Velocity-time integral

and with improvements in imaging resolution, measures of flow volume can now be quantified to within ±11% to 13%.[11]

The aim of this study was to use PC MRI to validate measures of cardiac output and systemic blood flow in newborn preterm and term infants.

METHODS

All echocardiographic and PC MRI scans were carried out for research purposes only, with research ethics committee approval and signed parental consent. Infants were recruited from stable infants admitted to the neonatal intensive care unit or postnatal ward at Queen Charlotte's and Chelsea Hospital, London, at any time during admission.

Echocardiographic Measures

Echocardiographic images were acquired using a Vivid 7 ultrasound machine (GE Healthcare, Milwaukee, WI) with a 10-Mhz sector probe. Before the study of this cohort, image acquisition settings were optimized for preterm infants. All examinations were either performed by or directly supervised by a neonatologist with >10 years' experience in functional echocardiography (A.M.G.). All echocardiographic examinations were performed with infants asleep or quietly awake. No sedation was used. All subjects were screened for congenital heart disease, including the exclusion of bilateral superior venae cavae. In all cases, echocardiography was performed within 1 working day of MRI. Images were stored digitally and analyzed offline to minimize the duration of echocardiography. An additional cohort of infants was subsequently examined by echocardiography to investigate the repeatability of quantification of SVC flow volume. Examinations in these infants were all performed by a single investigator (B.F.) after standardization of approach between operators in 10 infants.

LVO

Aortic dimension was assessed from the parasternal long-axis view, with high-definition zoom to the aortic valve, and diameter was assessed at the valve hinge points at end-systole (Figure 1A, *dashed line*). Aortic flow velocity was assessed by pulsed-wave Doppler from an optimized apical five-chamber view, with the pulsed-wave Doppler gate placed at the level of the aortic valve (Figure 1B). Care was taken to minimize angulation between the Doppler beam and flow direction in the left ventricular outflow tract.

SVC Flow Volume

SVC dimension was assessed using two distinct techniques. First, diameter was assessed from a modified parasternal long-axis view as initial described by Kluckow and Evans,[12] hereafter described as the "sagittal" approach. High-definition zoom was used to focus on the superior vena cava as it begins to open up into the right atrium (Figure 2A, *dashed line*), with maximum and minimum diameters through the cardiac cycle taken from B-mode images. Because of concerns about the irregular shape of the Superior vena cava, we also measured vessel area directly from an axial view, again using high-definition zoom and tracing maximum and minimum cross-sectional area from the B-mode images (Figure 2B, *dashed line*). SVC flow velocity was assessed using pulsed-wave Doppler from a low subcostal view as described by Kluckow and Evans,[12] with the ultrasound probe moved caudally until a clear length of the superior vena cava could be seen entering the right atrium, where the pulsed-wave Doppler gate was placed (Figure 2C).

In all cases, three to five consecutive cycles were analyzed, except in the case of SVC flow velocity, for which eight to 10 cycles were used to reduce the impact of respiratory variability. Angle correction of flow velocity was not used. All flow quantification was performed offline using EchoPAC software (GE Healthcare, Milwaukee, WI) by investigators blind to the PC MRI results.

PC MRI Acquisition

PC MRI was performed using a 3-T scanner (Philips Medical Systems, Best, The Netherlands) using a specialized eight-channel pediatric body receive coil for infants weighing >2 kg or a small-extremity receive coil for infants weighing <2 kg. The methodology has previously been described,[8,11] but in summary, infants were allowed to fall into a natural sleep after a feeding, without the use of sedation or anesthesia. They had continuous monitoring of heart rate, oxygen saturation, and temperature. They received nasal continuous positive airway pressure or low-flow oxygen support as clinically indicated, and a specially trained pediatrician was in attendance at all times.

Single-slice PC MRI acquisition sequences with in-plane spatial resolution of 0.6 mm, slice thickness of 4 mm, repetition time of 5.9 ms, echo time of 3.1 ms, and 20 phases per cardiac cycle were used. Field of view and matrix were altered to maintain spatial resolution at 0.6 mm while minimizing scan duration. The velocity encoding was calibrated for the range of ±120 cm/sec for LVO sequences and ±60 cm/sec for SVC sequences. Three signal averages were used, allowing compensation of respiratory effects on cardiac output. Depending on heart rate and heart rate stability, the acquisition time for each two-dimensional PC MRI scan ranged between 2 and 4 min. No gating techniques were used to compensate for respiratory or other causes of motion.

Pilot scans were acquired to view the vessels of interest to ascertain the straightest section of the vessel adequate for the slice thickness of the PC MRI sequences and to position the imaging plane perpendicular to the centerline of the vessel to minimize partial volume effects. LVO was quantified immediately distal to the level of the aortic valve (Figure 3A). Volume of flow in the superior vena cava was quantified at the level of the pulmonary trunk as the superior vena cava begins to open into the right atrium (Figure 3B).

Sequence analysis and flow volume quantification for PC data sets were performed using a commercial workstation (ViewForum; Philips Medical Systems). Automated vessel edge detection was used for all vessels of interest, with manual correction as necessary. Once defined in the first cardiac phase, the software tracks the vessel of interest over the cardiac cycle using edge detection algorithms. Flow is then calculated at each time point of the cardiac cycle, generating a flow curve and volume of flow value for each vessel of interest.

Statistical Analysis

Measures of flow obtained by echocardiography and PC MRI were compared using simple linear regression and also as described by Bland and Altman[13]: the mean bias and limits of agreement (LOA, or "repeatability coefficient"; 1.96 × SD of differences) were calculated. Repeatability index (RI; LOA/mean of measures) was also