Left Ventricular Function in Healthy Term Neonates During the Transitional Period

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Objectives To evaluate whether incorporating conventional, tissue Doppler imaging and speckle tracking echocardiography are reliable and can characterize changes in left ventricular (LV) function properly in healthy neonates in the early transitional newborn period.

Study design A prospective observational study was conducted in 50 healthy term neonates with a mean ± SD gestational age and birth weight of 39.3 ± 1.2 weeks and 3.5 ± 0.44 kg, respectively. All infants underwent serial echocardiograms at 15 ± 2 (day 1) and 35 ± 2 hours (day 2) of age. The LV dimensions and various functional indices including tissue Doppler imaging velocities and speckle tracking echocardiography-derived peak longitudinal strain, and systolic and diastolic strain rate were acquired and compared between time points.

Results All measurements were feasible from each scan except speckle tracking echocardiography in 10% and 20% of images on days 1 and 2 of age, respectively. LV dimensions, but not functional measures, demonstrated a small to moderate positive correlation with birth weight. On day 2, a small reduction was observed in LV basal diameter, mitral valve inflow velocity time integral, and systolic velocity of the lateral wall and septum. Other indices remained unchanged. Tissue Doppler imaging-derived functional and flow-derived hemodynamic measures demonstrated the least measurement bias, and strain measurements demonstrated better reliability than strain rate, fractional shortening, and ejection fraction.

Conclusion The relative reliability of various echocardiographic indices to quantify LV function in neonates establish a normative dataset and provide evidence for their validity during the first 2 days of life. *(J Pediatr 2017;182:197-203).*

Impaired left ventricular (LV) function is associated with many disorders of the early neonatal period, including infants of mothers with diabetes, birth asphyxia, persistent pulmonary hypertension of the newborn, sepsis, and intrauterine growth restriction.[1-5] Two-dimensional echocardiography is considered the clinical reference investigation to evaluate LV size and function in neonates. Traditionally, the most common echocardiographic methods used to assess LV systolic function objectively are M-mode derived shortening fraction and B-mode derived ejection fraction (EF). Although these methods provide a simple index of LV function and size, their usefulness in the first few days of life is hampered by physiological changes in interventricular septal motion and LV geometry.[6] This is owing to a progressive increase in systemic vascular resistance, a decrease in pulmonary vascular resistance, and a decrease in LV preload with closure of the patent ductus arteriosus (PDA) during this period. Further, fractional shortening measures change in LV cavity dimension at a single point in 1 plane, which makes it highly operator dependent and not always reflective of global LV function.

Tissue Doppler imaging (TDI) and speckle tracking echocardiography (STE) assess regional and global LV function by directly measuring muscle wall characteristics rather than cavity dimensions. TDI measures the velocity of muscle movement of the LV free wall and septum in systole and diastole, as well as the timing of cardiac events in a cardiac cycle.[7] STE is used to measure LV longitudinal deformation, which is expressed as percentage change in muscle length in systole compared with end diastole (strain), as well as provide a measure of the speed

EF	Ejection fraction
IVRT	Isovolumic relaxation time
LV	Left ventricle(ular)
MV	Mitral valve
PDA	Patent ductus arteriosus
STE	Speckle tracking echocardiography
TDI	Tissue Doppler imaging
VTI	Velocity time index

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with which this deformation occurs (strain rate).[8] Quantitative measure of LV function have been shown to be feasible in recent neonatal studies.[2,4,9-11]

We aimed to characterize LV function with a comprehensive echocardiographic protocol that incorporates conventional imaging, TDI, and STE to compare measurement reliability, establish reference values, and determine their maturational patterns during the early neonatal transitional period.

Methods

This prospective, observational study was carried out in the Mother and Baby Unit of Mount Sinai Hospital, Toronto, Ontario, Canada, over a 10-month period in 2013. The study was approved by institutional research ethics board and the parents of eligible infants provided consent within 12 hours of birth. Eligible infants included healthy, term, singleton neonates born after uncomplicated, low-risk pregnancies with a gestational age ranging between 37 and 42 weeks and birth weights between the 10th and 90th percentiles for the given gestation. We excluded infants with the following characteristics: infants born to mothers with medical conditions that could influence the infant's cardiac function or physiological postnatal transition (diabetes mellitus/gestational diabetes, preeclampsia, clinical chorioamnionitis, absent/reversed end-diastolic flow in the umbilical arteries on the most recent fetal ultrasound examination, use of antidepressant medication), evidence of perinatal ischemic insult (as defined by any one of the following: cord pH < 7.0, 5-minute Apgar score of ≤ 5 or need for active resuscitation), admission to the neonatal intensive care unit for any length of time, evidence of congenital or chromosomal abnormalities, and congenital heart disease other than a patent foramen ovale or a PDA. None of the patients recruited to this study were exposed to an antenatal course of corticosteroids. We have described previously a comprehensive echocardiographic protocol for assessing neonatal right ventricular dimensions and function in the transitional period,[12] but have never reported measures of LV function and structure in this population.

Each infant underwent 2 echocardiographic evaluations at a mean (SD) age of 15 ± 2 hours of age (range 12-19 [day 1]) and 35 ± 2 hours of age (range, 30-40; day 2) using a Vivid 7 ultrasound system and a 10 MHz transducer (GE Medical Systems, Milwaukee, Wisconsin). These times were based on the fact that at our institute the majority of healthy newborns are discharged home on day 2 of age. Discharge from hospital was not delayed specifically for this study. All patients were assessed using a comprehensive neonatal protocol of LV functional assessment, which included the recommendations of the American Society of Echocardiography.[13] Infants were in a quiet resting state during the examination. Simultaneous electrocardiogram recordings were also taken and the blood pressure was recorded just before performing the echocardiogram using an oscillometeric method (DINAMAP Pro 100; GE Healthcare, Tampa, Florida). All studies were stored to an archiving system for later analysis using a dedicated work station (EchoPAC version BT10; GE Medical Systems).

LV Dimensions

LV dimensions were obtained in end diastole from the apical 4-chamber view, the long axis parasternal view, and the short axis parasternal view. From the apical 4-chamber view, the mitral valve (MV) annulus diameter was measured by joining a straight line between the 2 leaflet hinge points; the basal diameter was measured by drawing a straight line at the basal segment of the LV cavity, parallel to the MV annulus to get the maximal distance between LV free wall and septum; and the LV length was determined by a straight line joining the midpoint of the MV annulus and LV apex. The LV end-diastolic diameter was determined using M-mode of the long and short axis parasternal views at the level of the MV leaflet tips. Finally, the LV end diastolic circumference was determined in 2 dimensions from the short axis parasternal views at the level of the papillary muscles just below the MV chordae.

Conventional Echocardiography Functional Assessment

The following conventional LV function measurements were made: shortening fraction from the long axis parasternal view; EF using Simpson Biplane Method from the apical 4- and 2-chamber views; MV E-wave velocity, A-wave velocity, E:A ratio, MV velocity time index (VTI), and isovolumic relaxation time (IVRT) obtained from the apical 4-chamber view using pulse wave Doppler with the sample gate of 2 mm placed approximately at the level of the tips of the MV leaflets. The diastolic time was obtained from the duration of the MV inflow wave. In addition, we measured the velocity of circumferential fiber shortening using M-mode of the short axis parasternal view at the level of the papillary muscles. The LV ejection time was measured from the apical 5-chamber view at the level of the aortic valve using pulsed wave Doppler.[14-16]

Tissue Doppler Imaging

Tissue Doppler velocities were obtained from the apical 4-chamber view by placing a pulsed wave Doppler sample gate of 1-2 mm, positioned just below the lateral mitral annulus, and the basal septal area. Offline analysis used average readings of peak systolic (s′), early diastolic (e′), and late diastolic (a′) myocardial velocities in 3 consecutive cardiac cycles.[7] On the tissue Doppler traces (lateral mitral annulus) we measured the isovolumic contraction time (IVCT′, between the end of the a′ wave to the beginning of the s′ wave) and the IVRT (IVRT′, between the end of the s′ wave to the beginning of the e′ wave). In addition, we measured systolic time (duration of the s′ wave) and diastolic time (duration of the e′ and a′ waves combined). The myocardial performance index was calculated using the formula: IVRT′ + IVCT′/systolic time (**Figure 1**, A; available at www.jpeds.com).[17]

Speckle Tracking Echocardiography

Longitudinal strain analysis was carried out by obtaining grey scale images of the LV in 3 views (the 4-, 2-, and 3-chamber apical views) at a frame rate of 80-100 frames per second, resulting in a frame rate to heart rate ratio between 0.60 and 0.95.