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Left ventricular rotational mechanics in early infancy: Normal reference ranges and reproducibility of peak values and time to peak values

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ABSTRACT

Introduction: Left ventricular cardiac twist and torsion values have been described in premature and term neonates, but not in early infancy. Early and late peak untwist rates and time to peak (TTP) values have not been described in infants.
Methods: 53 term infants were enrolled prospectively. The following parameters were obtained by two blinded observers at 1–2 months postnatal age: peak twist and torsion (twist indexed to LV length), peak twist rate and torsion rate, TTP twist, early peak untwist rate, TTP early untwist rate, late peak untwist rate, TTP late untwist rate. Reproducibility was assessed using intraclass correlation and Bland Altman analysis.
Results: Intraclass correlation was ≥0.87 for all peak rotational mechanics values. Measures of TTP values had intraclass correlation (ICC) values ≤0.77, with TTP twist rate demonstrating the lowest ICC (0.69). The only measure which demonstrated significant bias was TTP twist rate. Peak twist demonstrated modest correlation ($R = 0.52$, $p < 0.001$) with global circumferential strain, and no correlation with ejection fraction, global longitudinal strain, or left ventricular myocardial performance index.
Conclusions: Measurements of rotational mechanics and timing to peak values have acceptable reproducibility. Peak twist, twist rate, and early untwist rate values in early infancy are similar to those reported in premature neonates, and higher than those reported in older children. Twist indexed to LV length (torsion) is lower in early infancy than in premature neonates, but higher than in term neonates.

1. Introduction

Early in life, dramatic maturational changes take place in the circulatory system. In contrast to the adult heart, neonatal myocardium is less compliant due to a higher proportion of fibrous tissue and intracellular water. In addition, resolution of the patent ductus arteriosus, decreases in pulmonary vascular resistance and increases in systemic vascular resistance result in preload and afterload changes on the left ventricle. These differences are reflected in differences in echocardiographic measures, including spectral Doppler inflow ratios, tissue Doppler values and strain and strain rate values [1,2].

Throughout the cardiac cycle, the rotational movement of the left ventricle (LV) contributes substantially to both the ejection of blood in systole and LV filling in diastole. Across age ranges, the LV base exhibits clockwise rotation, and the apex exhibits counterclockwise rotation [3]. The difference in degree of rotation of the apex and base is referred to as net LV twist. As subendocardial shortening tends to occur earlier than subepicardial shortening, transient dysfunction of a region of myocardium may result in apical clockwise rotation in the pre-ejection phase, resulting in net increase or decrease in LV twist [4]. In adults, over 50% of LV recoil, or untwisting, appears to take place during isovolumetric relaxation early in diastole, while the remainder takes place during LV filling [3]. LV twist appears to increase with higher preload, decrease with higher afterload, and increase with higher myocardial contractility. However, the impact of these factors on LV untwisting is not well understood [5,6]. While changes in rotational mechanics have been studied in both neonates and school age children, the early infancy period has not been studied [7,8]. Furthermore, rotational mechanics of diastolic events have not

Abbreviations: LV, (left ventricle); ICC, (Intraclass correlation coefficient); TTP, (time to peak).

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been studied extensively in children. The objectives of the current study are to: describe normal reference ranges and interobserver variability for measures of left ventricular rotational mechanics and timing to the peak values of these measures in early infancy.

2. Methods

We performed a post-hoc analysis of echocardiograms obtained during a previously published prospective study on myocardial deformation values through fetal life, and at a single, postnatal time point at 4–8 weeks of age [9]. Rotational mechanics were not examined during the initial study. Participants were identical between the two studies. Mothers who were undergoing routine obstetric ultrasonography at Texas Children's Hospital Pavilion for Women were invited to enroll in this institutional review board–approved study at the time of the routine second-trimester ultrasound scan. Informed consent was obtained, and participants were compensated for parking and time spent participating in the study. Criteria for inclusion in the study included: absence of cardiac abnormalities during the screening obstetric ultrasound and maternal body mass index <30 kg/m^2. Exclusion criteria included: preexisting or history of maternal diabetes, maternal hypertension, growth restriction, thyroid disease, and other significant chronic disease or obstetric complication. No additional postnatal factors were used to exclude patients. The sample size for the current study was predetermined from the prior investigation of systolic myocardial deformation where a total sample size of 53 patients was chosen to obtain a 99% confidence interval ($a = 0.01$) [9]. The type I error rate was assumed to be 0.01 for sample-size considerations to allow multiple hypothesis testing and control the overall probably of a type I error. Additional patients were enrolled because of a presumed attrition rate of about 10%. To confirm that the sample size would be large enough to adequately power the present study, a repeat (post-hoc) power analysis was performed. We specifically tested the ability to test interobserver variability of LV twist. We found that in order to achieve a power of 0.8, a sample size of 51 would be needed to find a difference of 3 degrees (°) based upon the measured SD of 5.4°.

3. Image acquisition and analysis

Short axis images at the mitral valve level and at the apex were obtained using a GE Vivid E9 ultrasound system using a 5- or 6-MHz phased-array probe and stored as raw, uncompressed data. In order to measure LV length, a 4 chamber view was also employed. Spatial and temporal resolution were optimized with an minimum frame rate of 70 frames per second. Data were sent to an independent workstation for analysis, which uses speckle tracking for calculation of basal and apical rotation (EchoPAC version 110.0.2; GE Healthcare, Milwaukee, WI). For each measure, in all study subjects, offline image analysis was performed by two examiners, each blinded to the results of the other: a pediatric cardiologist with expertise in fetal imaging (S.A.M.) and a sonographer with substantial experience in functional analysis who works exclusively as a research sonographer (D.K.F.). Observers placed points of interest along the LV endocardium to initiate automated tracking throughout the cardiac cycle. Observers adjusted points as necessary to ensure adequate tracking. Observers analyzed data obtained on the same acquisition and were free to choose which cardiac cycle in the particular acquisition to analyze. The onset of the q wave was marked on the electrocardiogram tracing. Aortic valve closure was determined using a pulse wave Doppler waveform. To ensure adequate blinding, data from each observer were saved in separate folders on a research server.

Apical and basal rotation were presented graphically for each case (Fig. 1). Twist was calculated in degrees (°) as the difference between apical and basal rotation. In order to account for ventricular size, we then indexed twist to LV length (torsion). The rate of change in twist and torsion (twist rate and torsion rate) were then automatically calculated. Peak twist, peak torsion, peak twist and torsion rate, and peak early and late untwist rate were then measured and recorded. The first (early) and second (late) peak untwist values were then identified. Time to peak (TTP) values were then measured, with the q wave on the electrocardiogram used as the onset of systole.

In addition to measures of rotational mechanics, the following functional measures were also obtained: ejection fraction, global left ventricular longitudinal strain, global left ventricular circumferential strain, and left ventricular myocardial performance index. For this purpose, we used the ejection fraction and global left ventricular longitudinal strain derived after speckle tracking was performed on acquisitions in the 4 chamber, 2 chamber and 3 chamber views. Circumferential speckle tracking was obtained after speckle tracking was performed on short axis acquisitions at the basal, mid papillary and apical levels.

4. Statistical analysis

Interobserver variability was measured by two means: calculating intraclass correlation coefficients (ICCs) and Bland-Altman analysis. Correlation of LV twist with ejection fraction, global longitudinal and circumferential strain and left ventricular myocardial performance index was performed using Spearman's rho. Measures of rotational mechanics were also correlated with heart rate using Spearman's rho.

5. Results

A total of 60 gravid mothers were enrolled in our previously published prospective study of fetal myocardial deformation characteristics. Of these, 53 completed the study through birth and had early infancy echocardiograms performed. Of the 7 who did not have postnatal echocardiograms, one developed preeclampsia during pregnancy, one developed supraventricular tachycardia during pregnancy, and the remaining 5 disenrolled voluntarily at various points throughout the study. All infants were born at term, clinically well at the time of the echocardiogram, and no infant had a patent ductus arteriosus or other identifiable structural heart lesion, other than a patent foramen ovale. The median gestational age at birth was 39.5 weeks (range 37.2–41.4 weeks). In all infants, the heart was adequately imaged and the myocardium appeared to track appropriately during rotational mechanics analysis. The mean ± SD frame rate of acquisitions obtained for rotational mechanics analysis was 92.7 ± 20.0 frames per second (range 70–131), with mean ± SD frame rate to heart rate ratio of 0.63 ± 0.15 frames per second. Normative data for all parameters are depicted in Table 1.

Table 2 depicts the intraclass correlation values and mean bias between observers for all measures. Intraclass correlation was ≥0.87 for all peak rotational mechanics values. Measures of TTP values had ICC values ≤0.77, with TTP twist rate demonstrating the lowest ICC (0.69). Fig. 2 depicts Bland-Altman diagrams for the 6 measures of rotational mechanics and 4 measures of TTP values. The only measure which demonstrated significant bias was TTP twist rate (Fig. 2F). Peak twist demonstrated modest correlation ($R = 0.52$, $p < 0.001$) with global circumferential strain. Peak twist did not correlate with ejection fraction, global longitudinal strain, or left ventricular myocardial performance index. Higher heart rate correlated with higher peak twist and peak torsion rate, and there was a trend towards an association with peak late untwist rate (Table 3).

6. Discussion

We performed a post-hoc analysis of patients who had been enrolled prospectively for the purposes of identifying normal fetal and infant values of myocardial deformation and describing interobserver agreement for these measures. We found that measures of rotational mechanics values were reproducible in infants in our cohort between ages 3.8 and 8 weeks, while timing to peak values were less reliable.