Dynamics of Left Ventricular Shape in Preterm Infants: Functional Geometry and Geometric Morphometrics

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Abstract

The aim of this study was to describe the left ventricular (LV) shape and its deformation during the cardiac cycle in extremely low and very low birth weight preterm at 1-3 days of age compared to term infants using functional geometry (FG) and geometric morphometrics (GM) methods. LV shape and spatio-temporal heterogeneity of LV wall motion throughout the cardiac cycle were evaluated by FG methods. We also obtained cardiac shape descriptors using GM framework, which allowed us to focus solely on inter-patient differences in shape changes associated with the cardiac cycle. Statistically significant differences between groups were observed in LV wall motion spatial heterogeneity (higher in preterm), the sphericity (lower in preterm) and shape complexity (higher in preterm) in late diastole, the first two components of the shape space obtained by GM. Thus we have demonstrated pronounced differences in shape change dynamics between term and preterm infants which can be further tackled and investigated in the GM framework.

1. Introduction

The incidence of preterm birth is increasing worldwide, affecting approximately 10% of live births [1]. Population studies have shown that preterm birth is a risk factor for early-onset heart failure and is strongly inversely associated with cardiovascular mortality in young adults[2].

Advancements in perinatal and neonatal care have increased survival rate of very low birthweight (<1500 g) infants. Every such infant is admitted to the intensive care unit. One of the main tasks in the intensive care unit is to maintain stable hemodynamics during the early neonatal period. Frequent causes of critical conditions in the early neonatal period are maladaptation of the cardiovascular system against the background of one or more conditions: respiratory distress syndrome, sepsis, shock of various etiologies and congenital pneumonia, etc. [3]. Despite advances in pediatric cardiology, the mechanisms underlying abnormal cardiac contractility are not fully understood. There is no generally accepted classification for cardiac abnormalities in preterm infants [2].

One of the most accessible and non-invasive methods to assess the state of the cardiovascular system is echocardiography (EchoCG). EchoCG in neonatology is traditionally used to diagnose congenital heart defects and is performed by functional diagnostics physicians or cardiologists. However, in the last decade, EchoCG has been actively implemented worldwide by neonatologists and anesthesiologists-resuscitators in critically ill infants. Currently, the use of EchoCG in the neonatal intensive care unit is included in the recommendations of international experts [4]. However, reference values for EchoCG parameters, including myocardial deformation characteristics, have not yet been established for extremely premature infants in the early neonatal period.

Myocardial contractility is closely related to changes in left ventricular (LV) geometry during the cardiac cycle [5]. Studies in adult patients have shown that assessment of LV shape and its change during the cardiac cycle can discriminate between pathological and healthy hearts, even in cases where standard EchoCG parameters are inconclusive [6]. LV functional geometry (FG) is defined as a set of characteristics that relate ventricular shape and function [6]. An additional set of descriptors of cardiac contractile function can be provided by geometric morphometrics (GM). GM is a mathematical framework for shape analysis commonly used in the fields of biology and ecology, and has recently been applied as a feature extraction tool for the task of classifying cardiac pathologies [7, 8].

The aim of this study is to describe the shape and deformation of the LV during the cardiac cycle in extremely low and very low birth weight premature infants at 1-3 days of age compared to term infants using FG and GM methods.

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2. Methods

Clinical data

The prospective cohort study was conducted by the Ural Research Institute for Maternal and Infant Health (Yekaterinburg) and the Regional Perinatal Center (Chelyabinsk) and was approved by the Ethics Committee. Mothers of the newborns signed an informed consent form.

The study included term newborns (n=27, gestational age 38-40 weeks, birth weight 3200-3700 g) and preterm newborns (n=19, gestational age 26-31 weeks, birth weight 500-1500 g) without clinical signs of hemodynamic disturbances. EchoCG was performed at one to three days of age using General Electric (GE) Vivid iQ and Vivid E9 XD ultrasound machines with a sector phased array transducer of 5.0-9.0 MHz. All data were anonymized and imported into the post-processing software. In addition to the standard study, video loops were recorded during the cardiac cycle of the four chamber apical position of the LV.

Segmentation and preprocessing

EchoCG images in the 4-chamber apical position were segmented frame by frame using our proprietary software package ”LKLVS - Lukas Kanade Left Ventricle Segmentation”; State Registration Certificate No. 2023619715. Starting from the manually processed end-diastolic (ED) frame we tracked the positions of 49 landmarks along the LV endocardial contour (points 0 and 48 - mitral, point 24 - apex, all the 49 points are equidistant in the ED frame) using previously developed software. Then we performed piecewise linear time warping, making each time series 59 frames long (the largest number of frames in the cardiac cycle observed in the data), with frames 0 and 58 corresponding to the ED and frame 20 to the end-systole (ES). Time warping was followed by 10-harmonic Fourier series approximation to ensure the continuity and the periodicity of the signals. For more details on segmentation and signal processing we refer to our previous work [8].

Left Ventricular Functional Geometry

The original software ”LVFG - Geometry of Left Ventricular Function”, State Registration Certificate No. 2023665251, was used to calculate the LV FG characteristics.

The LV wall motion spatial heterogeneity index (SHI) and the temporal heterogeneity index (THI) are obtained by the following procedure. The area enclosed by the LV contour in the ED is divided into regions of equal area by radial lines extending from the center of mass. Then, for each region at each time point, the areas bounded by the LV contour and the pair of radial lines defining the region are calculated. For each region, the time point where the regional area is the smallest is identified as the regional end-systole (RES). The regional ejection fraction (REF) is calculated as the ratio of the region area at the RES to the regional area at ED. Then SHI is represented by the coefficient of variation (CV) of REFs, while THI is the CV of RESs divided by the number of frames.

Moreover, LV shape indices were calculated frame by frame throughout the cardiac cycle: the standard sphericity index (SI) - the ratio of the short axis of the LV to the long axis; Gibson’s sphericity index (GSI) - the ratio of the area of the area bounded by the LV contour to the area of a circle with a perimeter equal to the LV contour; the conicity index (CI) - the ratio of the area of the triangle inscribed in the LV contour to the area bounded by the LV contour; Fourier shape power index (FSPI) - a Fourier transform based index which assesses the regularity of the LV shape.

Geometric Morphometrics

Additionally, we employed GM approach to obtain cardiac shape descriptors. Parallel transport procedure, as implemented by Linear Shift (LS), was applied to the LV configuration sequences representing cardiac cycles. Subsequently, Global Procrustes Analysis (GPA) was conducted on all LV configurations. Thus, shape coordinates were obtained for each LV configuration, eliminating inter-patient variability in cardiac anatomy. These coordinates enable us to focus solely on inter-patient differences in shape change that LV undergoes throughout the cardiac cycle [7]. Then Principal Component Analysis (PCA) was performed on 49×2 vectors of shape coordinates to eliminate feature correlations and reduce the dimensionality of the parameter set. Deterministic Parallel Analysis and Deflated Deterministic Parallel Analysis+ methods [9] were used to determine the number of principal components to retain. Consequently, a vector of shape parameters was obtained for each frame in the patient cardiac cycle video.

Statistics

The statistical analysis was conducted using the SPSS 27.0 software (IBM USA). For quantitative characteristics, normality of distribution was tested using the Shapiro-Wilk test. If the hypothesis of normal distribution was not rejected, descriptive characteristics were presented as mean ± SD. Otherwise the characteristics were described as median (25th percentile; 75th percentile). Correlations were assessed using the Pearson correlation coefficient for normal distribution and the Spearman rank correlation coefficient in the nonparametric case. Two independent group comparisons were performed using T-test for normal distribution or Mann-Whitney test in nonparametric case. The Benjamini-Yekutieli correction was used for multiple comparisons. We used Directional package for R programming language on the circular data. To test the hypothesis of equality of mean angles, we used the permutation based 2-sample mean test [10].

3. Results

Left Ventricular Functional Geometry

The comparison of FG indices between term and very preterm newborns is presented in Table 1. The SHI is larger in very preterm newborns. Furthermore, revealed significant differences between groups in mesadiastole for FSPI and SI.

Table 1. Functional geometry indices of the LV in term and very preterm newborns

	Term (n=27)	Preterm (n=19)	p
EF, %	71±5	68±4	0.121
SHI	*0.29±0.12*	*0.43±0.24*	*0.025*
THI	0.33±0.18	0.28±0.09	0.258
SI ED	0.61±0.05	0.57±0.09	0.053
SI ES	0.59±0.06*	0.56±0.09	0.179
GSI ED	0.80±0.03	0.78±0.05	0.168
GSI ES	0.76±0.04*	0.75±0.06*	0.383
CI ED	1.47±0.07	1.48±0.06	0.556
CI ES	1.49±0.09*	1.49±0.07	0.981
FSPI ED	2.50±0.74	3.22±1.38	0.051
FSPI ES	3.13±0.98*	3.52±1.58*	0.352

EF - ejection fraction, SHI - spatial heterogeneity index, THI - temporal heterogeneity index, SI - sphericity index, GSI - Gibson's sphericity index, CI - conicity index, FSPI - Fourier shape power index, ED - end-diastolic frame, ES - end-systolic frame, * - $p<0.05$ ED vs ES.

Geometric Morphometrics

First we visualized the shape changes from the ED to the ES in each group by averaging in every frame the shapes obtained by LS+GPA. The resulting Figure 1 suggests that the groups have different shape change trajectories in the systolic phase.

After PCA, only three components were retained (PC1 explains 20% of variance, PC2 - 12%, PC3 - 10%). A comparison of each PC component at each time point revealed significant differences only in the first two principal components: PC1 in the systolic phase of the cycle and in PC2 in all cardiac cycle phases. The PC scores and the group comparisons for the PC1 and PC2 in each groups are presented in Figure 2.

We have also examined more thoroughly group differences between general shape change directions from ED to ES time points. On Figure 3 vectors from ED to ES are plotted in PC1,PC2 plane for each subject. The mean angles are different between groups (p=0.001)

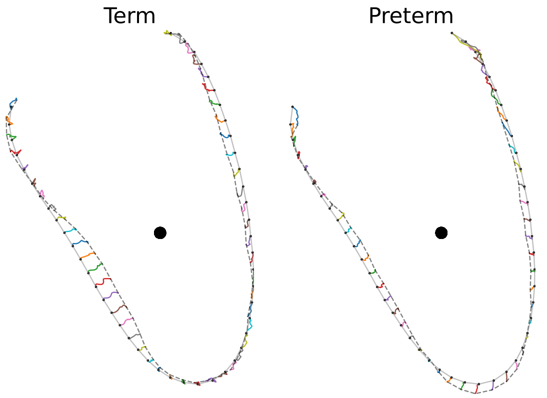

Figure 1. The mean LV contour point trajectories between ED and ES in Term and Preterm groups. The black points and the solid lines represent the shapes at the ED frame, while the dashed lines represent the shapes at the ES frame. The LV contour centers of mass are denoted by the bold points inside the contours. In the LV contour the interventricular septum is on the left and the LV free wall is on the right.

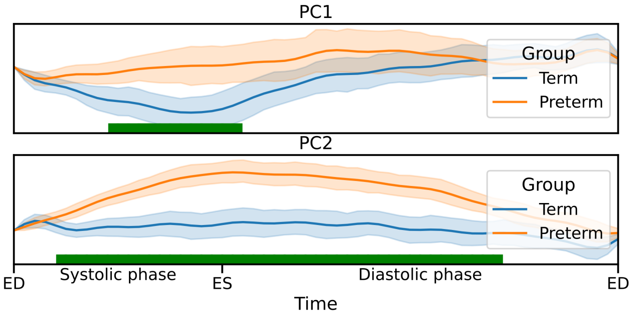

Figure 2. The mean PC scores of infants throughout the cardiac cycle are plotted along with the bootstrapped 95% confidence intervals. The thick green solid lines on the x-axis highlight the frames where there is a statistically significant difference with Benjamini-Yekutieli correction between Term and Preterm scores .

4. Conclusions

This is the frist study to employ FG and GM tools to examine the dynamics of the LV shape change during the cardiac cycle in very preterm and term infants on days 1 to 3 after birth. At this stage, the newborn is undergoing a significant transformation from fetal to postnatal blood circulation. This process is accompanied by crucial structural changes in the heart, an increase cardiac output and LV afterload. These changes lead to the establishment of a

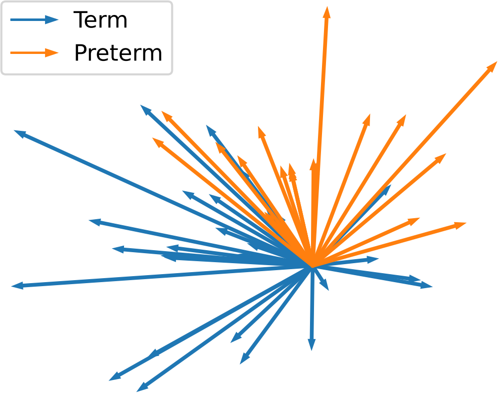

Figure 3. The vectors of LV shape change from ED to ES in PC1, PC2 plane. The arrowheads indicate the ES time points, while the arrow tails indicate the ED time points, which are identical for all vectors due to the LS+GPA transformation.

specific spatial and temporal heterogeneity of LV wall contraction, which is optimal under hemodynamic conditions [2].

Previously it was shown, that in adults the SHI is inversely proportional to the global LV ejection fraction, and in comparison to the norm, the SHI is increased in cases of LV contractile function pathologies [6]. Similarly, in this study a relationship was identified between SHI and ejection fraction (r=-0.38, p=0.010), indicating a connection between the LV wall kinetics and LV pumping function.

Despite group similarities in distribution profiles of LV regional ejection fractions, the SHI is significantly higher in preterm newborns. This highlights the distinction in wall movement patterns between term and preterm newborns. Additionally, significant group differences in sphericity and shape complexity were observed in late diastole. Preterm newborns exhibited a less spherical and more complicated LV shape in late diastole compared to the term newborns.

In term newborns all shape indices demonstrate a significant difference between ED and ES. In contrast, in preterm newborns only GSI and FSPI exhibited differences between these time points. This may be indicative of the LV shape change discoordination in preterm newborns. Concurrently, significant differences between term and preterm newborns were observed only in SI and FSPI indices in late diastole.

The GM procedure LS + GPA + PCA was used to further examine the group differences in shape changes. The directions of shape change in the first two shape components were found to be significantly different. The visualization of shape change trajectories in 2 suggests that preterm newborns exhibit less pronounced movement in the interventricular septum and more movement in the apical region during the systole. It should be noted, however, that the visualization is approximate. A more in-depth study of shape differences, which would allow us to describe what exactly happens to the shape, requires the application of appropriate statistical methods [11]. This, together with an extension of the current dataset, will be the focus of further studies.

Acknowledgments

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