

Developmental Changes in Left and Right Ventricular Function Evaluated with Color Tissue Doppler Imaging and Strain Echocardiography

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Abstract

Aims: We evaluated the systolic and diastolic functions of both ventricles from the early neonatal period to adolescence using color tissue Doppler imaging and 2-dimensional tissue tracking echocardiography.

Methods: We examined 100 healthy children (aged 1–5 days, n=20; 1 month, n=20; 1 year, n=20; 6–7 years, n=20; and 12–13 years, n=20). Blood flow velocities in the mitral and tricuspid valves (E) were obtained with pulsed Doppler imaging, and longitudinal systolic (S') and early diastolic (E') peak velocities at the mid free wall segment of both ventricles were obtained with color tissue Doppler imaging. For longitudinal strain imaging, systolic peak values were obtained at the same position. In addition, peak systolic radial strain was obtained from a short-axis view of the left ventricle using the tissue tracking method. The E/E' ratio was calculated.

Results: Regarding systolic indices, S' increased during development and stabilized at 6 to 7 years, and longitudinal strain reached values of the 12- to 13-year-old group at 1 year of age in both ventricles. Like longitudinal strain, radial strain in the left ventricle reached values of the 12- to 13-year-old group at the age of 1 year. Similarly, the E/E' ratio was high at 1 month or younger and decreased by 1 year.

Conclusions: Systolic and diastolic variables change markedly from birth to 1 year of age and show only small changes thereafter.

(J Nippon Med Sch 2013; 80: 260–267)

Key words: color tissue Doppler, strain, tissue tracking, neonate, child, cardiac function

Introduction

Both myocardial contraction and relaxation

change during maturation from the neonatal period to childhood, as reported in both basic^{1,2} and clinical studies³. Some previous studies^{4–7} have assessed these age-related changes with Doppler

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echocardiography. For example, Frommelt et al.⁴ have reported a significant difference in peak systolic and early diastolic annular velocity between children younger than 1 year and children older than 1 year. Meanwhile, Swaminathan et al.⁷ have reported that only late diastolic annular velocity changes with age in healthy children. These studies indicate that developmental changes in cardiac function from the viewpoint of echocardiography remain controversial.

Measurement of strain, which is the percentage of shortening of regional area, and color tissue Doppler imaging (TDI) are more sensitive than conventional echocardiography for quantitatively assessing regional ventricular longitudinal performance⁸. Furthermore, strain measurement with 2-dimensional (2D) tissue tracking has largely overcome the angle dependency of color TDI⁹. Color TDI and 2D tissue tracking are new echocardiographic techniques that enable the measurement of systolic and diastolic performance with the tracking of acoustic markers. In the pediatric population, only limited data on myocardial velocities have been recorded with these techniques^{10,11}.

The purpose of this study was to estimate growth-related changes in the left ventricle (LV) and right ventricle (RV) with color TDI and 2D tissue tracking, from birth to adolescence.

Materials and Methods

Subjects

In this cross-sectional study, we recruited 100 age-selected healthy children (46 boys and 54 girls). We set the target ages as 0 to 5 days, 1 month, 1 year, 6 to 7 years, and 12 to 13 years. We designed this research to coincide with the timing of public health check-ups for young children (0 to 5 days, 1 month, and 1 year) and cardiac screenings for school-age children (6 to 7 years and 12 to 13 years). The study was completed when we had enrolled our target of 20 subjects in each of the 5 age groups. We chose our subjects from among children meeting our requirements who were referred to us for healthcare checks or for ruling out cardiac disease

as a cause of chest pain or heart murmur. Informed consent was obtained from children or their parents. We excluded subjects who had clinical or echocardiographic evidence of structural or functional heart disease. In addition, none of the subjects had acute or chronic illnesses, including respiratory disease. All subjects appeared to have standard proportions. Neonates aged 0 to 5 days were examined after feeding, and most of the infants aged 1 month were feeding during examination. Children 1 year old were sedated with oral triclofos sodium (80 mg/kg) before examination.

Standard Echocardiography

Echocardiographic examinations were performed with a Vivid 7 scanner (GE Yokogawa Medical Systems, Tokyo), which allowed digital storage of raw data. Images were acquired with a 2.5-, 3.5-, or 5.0-MHz transducer. To minimize interobserver variability, echocardiographic examinations were performed by 2 investigators. To reduce intraobserver variability, values were analyzed twice by a single investigator. Myocardial dimensions, such as LV end-diastolic dimension (EDD) and end-systolic dimension (ESD), were estimated with M-mode echocardiography on the short-axis view; the fractional shortening (FS) was then calculated.

Pulsed-Doppler Imaging and TDI

To measure early diastolic inflow Doppler velocity (E), pulsed Doppler imaging was performed apically with subjects in the left lateral decubitus position. By switching to tissue velocity imaging (TVI) application, we performed color TDI of 3 consecutive heart cycles at the mid-segment of the LV and RV free walls from the apical 4-chamber view. A frame rate of approximately 150 frames per second was used. The cursor was interactively tracked through all frames to keep the measurement site at approximately the same position throughout the heart cycle. The raw data were digitally stored with an EchoPAC workstation (GE Yokogawa Medical Systems) and evaluated off-line. The images were retrieved for analysis the patient's examination was completed. We measured pulsed Doppler systolic velocity (S), pulsed Doppler early diastolic velocity

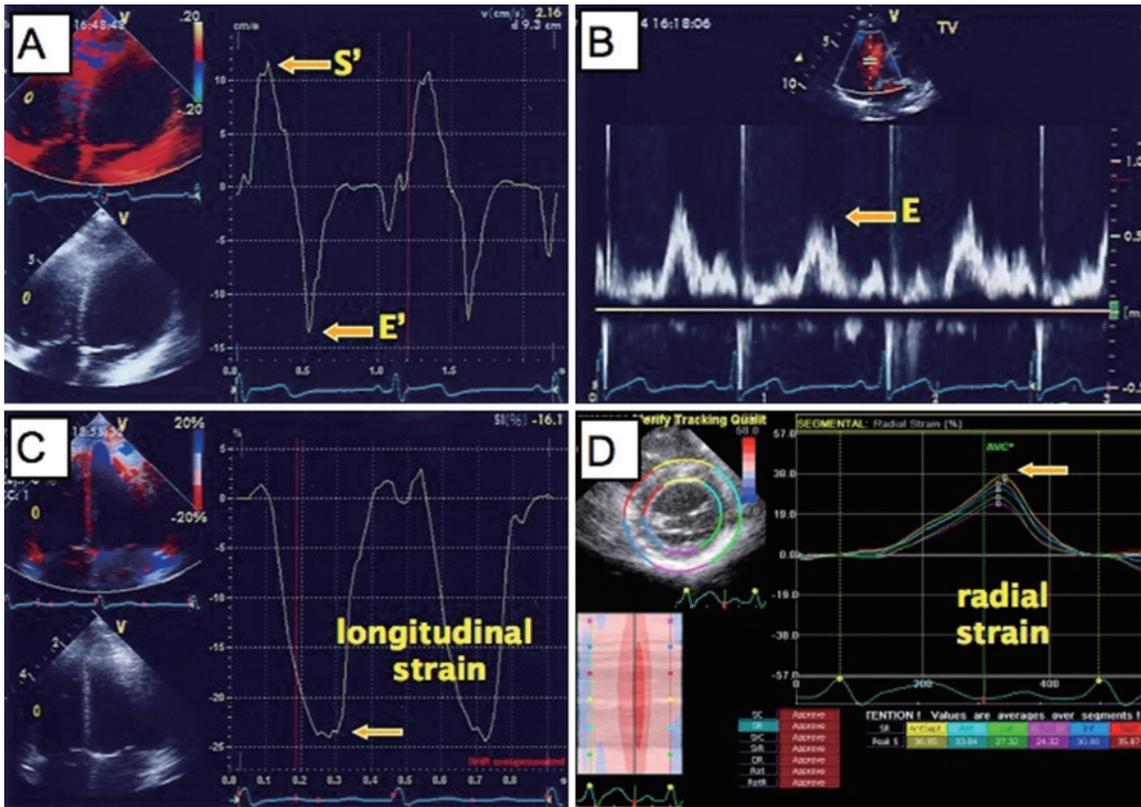


Fig. 1 Representative recordings and measuring points: A: Measuring point of S' and E' with color TDI. B: Measuring point of E at the tricuspid valve. The E/E' ratio was calculated by dividing E by E'. C: Longitudinal strain curves were obtained at the mid-segment of the RV free wall, and the peak systolic strain values were measured. D: An example of radial strain curves at the point of the midventricular portion. Data are presented as 6 time-strain plots (i.e., anteroseptal, anterior, lateral, posterior, inferior, septal segment), and the peak strain values were measured. E, blood flow velocity in mitral and tricuspid valve; E', early diastolic peak velocity; S', longitudinal systolic peak velocity

(E'), and the longitudinal peak strain (Fig. 1). The E/E' ratio was calculated.

Speckle Tracking Imaging

Speckle tracking peak radial strain values were obtained from gray-scale images of the LV short-axis view at the papillary muscle level (Fig. 1). The EchoPAC system allows analyses of peak systolic radial strain on the basis of detected natural acoustic markers. It follows the frame-by-frame movement of acoustic speckles within the myocardium over the cardiac cycle and calculates strain values for 6 predefined segments of the LV (i.e., anteroseptal, anterior, lateral, posterior, inferior, and septal segments).

Statistical Analysis

Statistical analyses were performed with IBM

SPSS Statistics version 19 (IBM Corp, Armonk, NY, USA). The various indexes in each age group are expressed as mean ± S.E. A p value < 0.05 was considered to indicate statistical significance. Differences among age groups with respect to various echocardiographic indexes were ascertained with Tukey's method.

Results

Standard Echocardiographic Variables

Standard echocardiographic variables in the 5 age groups are shown in Table 1. Heart rate (HR) decreased with age, except at 1 month, when HR was higher than in all other age groups. Echocardiographic data demonstrated expected increases in variables of cardiac growth with advancing age, including LV EDD and ESD and LV

Table 1 Echocardiographic data

	0-5 days (n=21)	1 month (n=20)	1 year (n=20)	6-7 years (n=20)	12-13 years (n=20)
HR (bpm)	128.6 ± 2.1*	141.3 ± 2.8*	111.2 ± 2.7*	90.4 ± 2.2*	68.2 ± 2.9
LVEDD (mm)	17.1 ± 0.3*	21.6 ± 0.5*	30.0 ± 0.7*	36.8 ± 0.7*	45.3 ± 0.6
LVESD (mm)	11.9 ± 0.3*	13.8 ± 0.4*	18.5 ± 0.4*	22.7 ± 0.6*	27.1 ± 0.6
LV FS (%)	33.2 ± 1.2*	35.5 ± 1.0*	38.0 ± 1.1	37.8 ± 1.0	39.7 ± 1.0
LV S' (cm/s)	2.40 ± 0.17*	2.96 ± 0.35*	5.15 ± 0.26*	6.58 ± 0.35	7.73 ± 0.56
RV S' (cm/sec)	3.71 ± 0.23*	5.47 ± 0.47*	8.06 ± 0.41*	10.29 ± 0.3	10.28 ± 0.3
Mitral E (cm/sec)	61.8 ± 3.0*	98.9 ± 3.9	102.1 ± 4.7	102.0 ± 3.5	106.5 ± 5.2
Tricuspid E (cm/sec)	53.7 ± 2.4*	77.8 ± 4.2	67.1 ± 2.3	56.4 ± 2.3*	69.6 ± 3.34
LV E' (cm/sec)	4.08 ± 0.31*	6.32 ± 1.16*	12.6 ± 0.53	14.54 ± 0.27	13.95 ± 0.62
RV E' (cm/sec)	5.28 ± 0.4*	10.64 ± 1.0	11.72 ± 0.4	11.29 ± 0.4	11.71 ± 0.6
LV strain (%)	17.1 ± 1.31*	22.6 ± 1.2	27.6 ± 1.2	27.4 ± 1.0	25.7 ± 1.2
RV strain (%)	17.9 ± 0.9*	25.3 ± 1.5*	28.8 ± 0.9	29.8 ± 1.0	30.6 ± 0.9
LV mass (g/m ²)	23.9 ± 1.8*	26.8 ± 1.5*	39.2 ± 3.1*	58.2 ± 2.8*	81.9 ± 4.3

Values are expressed as mean ± SE. Data with * show a statistically significant difference ($p < 0.05$) with the 12- to 13-year-old group.

E, early diastolic inflow Doppler velocity; EDD, end-diastolic dimension; ESD, end-systolic dimension; E', pulsed Doppler early diastolic velocity; FS, fractional shortening; HR, heart rate; LV, left ventricle; RV, right ventricle; S', pulsed Doppler systolic velocity

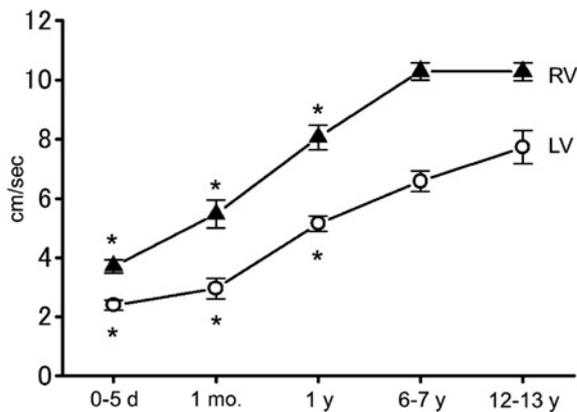


Fig. 2 S' in RV and LV in the 5 age groups: S' was obtained from color TDI. Values are expressed as mean ± SE. * indicates a statistically significant difference ($p < 0.05$) compared with the 12- to 13-year-old group in the RV and LV. Note that S' in both the RV and LV increased during development and stabilized at 6 to 7 years. The S' in the RV was higher than that in the LV in all age groups. LV, left ventricle; RV, right ventricle; S', longitudinal systolic peak velocity.

mass. The LV FS, a measure of ventricular function, was significantly lower at 0 to 5 days and 1 month than at 12 to 13 years. The E of both the mitral and tricuspid valves were lower at 0 to 5 days than at 12 to 13 years.

Changes in LV and RV Contractile Function with Age

From the longitudinal direction, 2 variables were measured to evaluate contractile function: the S' and strain. The S' measured at the middle of the LV and RV free walls increased during development and stabilized at 6 to 7 years (Fig. 2). At all ages, RV S' exceeded LV S'.

Similarly, peak longitudinal strain measured at the middle of the free walls of the LV and RV increased during development (Fig. 3). Unlike S', peak strain reached values of 12 to 13 years at the age of 1 year in both the LV and RV. Like S', peak longitudinal strain was greater in the RV than in the LV in all age groups. In addition, LV radial strain showed the same tendency as longitudinal strain, also reaching the value of 12 to 13 years at the age of 1 year (Fig. 4).

Changes in LV and RV Relaxation Function with Age

To evaluate diastolic function with echocardiography, we used the index of the E/E' ratio, which was calculated as shown in Figure 1. The E/E' ratio in the LV and RV decreased significantly with development and stabilized at 1 year (Fig. 5).

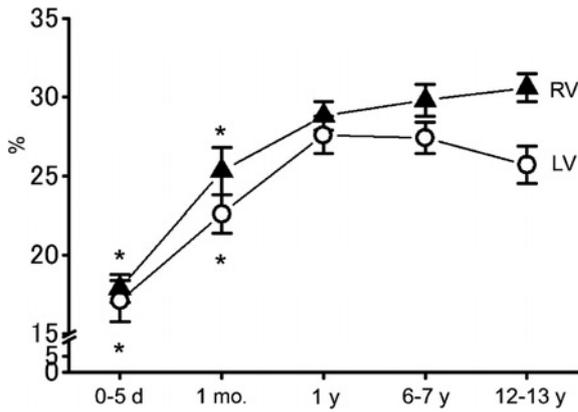


Fig. 3 Longitudinal peak systolic strain in RV and LV in the 5 age groups: Longitudinal peak systolic strain was obtained from color TDI. Values are expressed as mean \pm SE. * indicates a statistically significant difference ($p < 0.05$) compared with the 12- to 13-year-old group in the RV and LV. Note that peak systolic strain in both the RV and LV reached values of the 12- to 13-year-old group at the age of 1 year. Similarly to S', peak systolic strain in the RV was higher than that in the LV in all age groups. LV, left ventricle; RV, right ventricle

Discussion

Our results demonstrate developmental changes in cardiac function in terms of systolic and diastolic function in the LV and RV. This report is, to our knowledge, the first of normal values of systolic and diastolic function of the LV and RV obtained with color TDI and speckle tracking in childhood.

Contractile function in the LV is traditionally assessed with noninvasive echocardiography. Specifically, ejection fraction, stroke volume, cardiac output, FS, and the mean velocity of circumferential FS are measured. Diastolic function in the LV has been derived by dividing the E by atrial filling velocity (A) to obtain the E/A ratio. However, the usefulness of these standard echocardiographic indices may be limited by the confounding effects of ventricular pressure or preload or by the pseudonormalization of transmitral flow patterns. Moreover, RV function is difficult to assess with conventional echocardiography, and few reports of

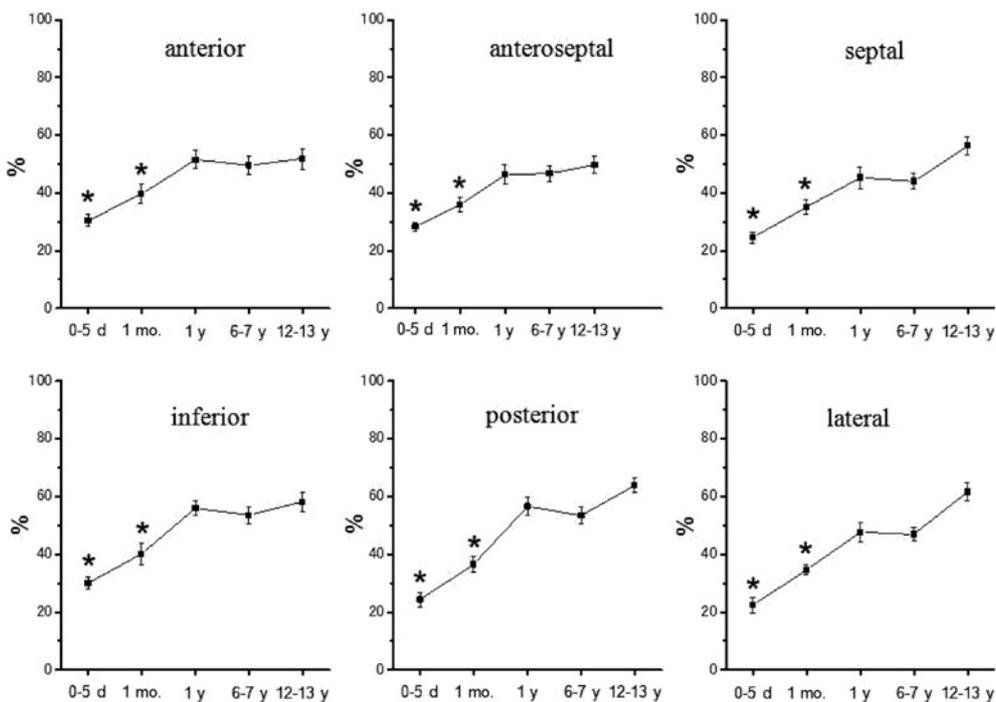


Fig. 4 Segmental radial strain in the 5 age groups: Radial strain was obtained from the two dimensional tissue tracking method. Values are expressed as mean \pm SE. * indicates a statistically significant difference ($p < 0.05$) compared with the 12- to 13-year-old group. Note that radial strain reached values of the 12- to 13-year-old group at the age of 1 year, showing the same tendency as longitudinal peak systolic strain. LV, left ventricle; RV, right ventricle

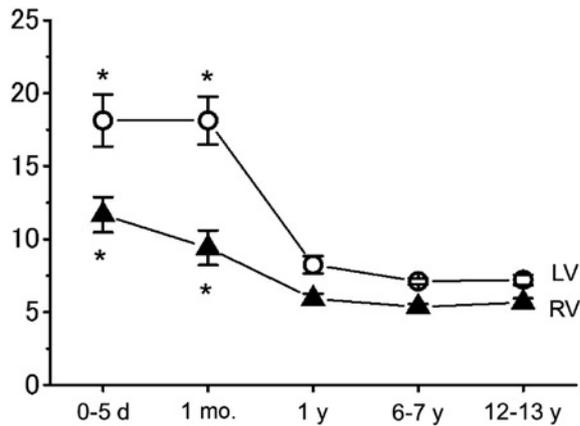


Fig. 5 E/E' in RV and LV in the 5 age groups: The E was obtained at the mitral and tricuspid valves with the pulsed Doppler method. The E' was obtained from color TDI. Values are expressed as mean \pm SE. * indicates a statistically significant difference ($p < 0.05$) compared with the 12- to 13-year-old group in the RV and LV. Note that the E/E' ratio in both the RV and LV reached values of the 12- to 13-year-old group at the age of 1 year. The E/E' ratio in the LV is higher than that in the RV in all age groups. E, blood flow velocity in the mitral and tricuspid valve; E', early diastolic peak velocity; LV, left ventricle; RV, right ventricle

RV function in the pediatric population have been published¹²⁻¹⁴.

The recently developed technique of color TDI is useful for quantifying regional myocardial function by measuring velocities directly from myocardium. Therefore, color TDI allows separate measurement of myocardial strain in the LV and RV. Color TDI can be used to evaluate not only regional myocardial contractile function but also global contractile cardiac function¹⁵⁻¹⁸.

The S' and longitudinal strain (**Fig. 2, 3**) were higher in the RV than in the LV, and the E/E' ratio (**Fig. 5**) was lower in the RV than in the LV. This difference may be related to differences between the LV and RV in afterload, ventricular thickness, and cardiac myocyte function. Furthermore, an improvement in physiologic pulmonary hypertension may be a reason for the marked reduction in the RV E/E' ratio during early infancy.

Even with color TDI, technical issues, such as angle dependence, signal noise, and measurement variability, remain. Color TDI is better suited for the

assessment of long-axis ventricular shortening and lengthening. Calculation of 2D strain from speckle tracking has largely overcome this angle dependence and enables myocardial strain to be calculated in any direction.

Concerning the developmental changes in LV and RV function evaluated with TDI, previous studies of children are controversial. For example, Swaminathan et al.⁷ reported the lack of a linear correlation of age with the majority of TDI velocities in 151 healthy children aged 1 to 18 years. In that study, only late diastolic TDI velocities at the lateral mitral and tricuspid annuli had a negative linear correlation with age. Kapusta et al.¹⁹ reported similar findings in a group of healthy children aged 4 to 17 years. In contrast, both Mori et al.⁵ and Harada et al.²⁰ have reported significant correlations of age with systolic and diastolic TDI velocities at the lateral mitral and tricuspid annuli in pediatric patients. Meanwhile, Lorch et al.¹⁰ evaluated longitudinal strain and strain rate with speckle tracking echocardiography in 284 healthy infants and children from birth to 18 years of age. They concluded that longitudinal strain and strain rate are independent of maturational changes. Similarly, the E/E' ratio is also controversial. Swaminathan et al.⁷ have documented E/E' ratios in healthy children at both the lateral tricuspid and mitral annuli and found a weak association with age for only the mitral E/E' ratio. Eidem et al.⁶ reported that E/E' ratios at the mitral and tricuspid annuli and ventricular septum were highest in neonates and steadily decreased during childhood. These differences with the present data might be explained by different stratification of age groups. That is, we divided infants younger than 1 year into 3 age groups: 0 to 5 days, 1 month, and 1 year.

We conclude that the contractile and relaxation functions are weak in the immature heart and that the marked age-related changes in cardiac variables in the present study reflect both physiological change of loading conditions and myocardial mechanical maturation²¹.

Limitation

Most subjects aged 0 to 5 days and 1 month were

examined soon after feeding, and the echocardiographic data might have been affected by volume loading in the immature heart. Similarly, most subjects 1-year-old subjects were examined while sedated. These conditions might have influenced our results.

The echocardiographic data obtained in the present study are restricted to a certain age range. Similar data should still be derived from a large population of unrestricted age to more accurately evaluate age-related changes.

Clinical Implication

A degree of immaturity of cardiac function is present in the immature heart; therefore, the capacity of the immature heart should be considered when infusion therapies are chosen.

Conclusions

Echocardiographic indices of systolic and diastolic function in both the LV and RV changes significantly from the early neonatal period to 1 year of age. By 6 to 7 years, these indices stabilize at levels close to those observed at 12 to 13 years. On the other hand, variables of cardiac growth, such as ESD, EDD, and LV mass, continue to change as children mature. Our findings suggest that the maturation of cardiac function, including systolic and diastolic function of both ventricles, occurs much faster than cardiac growth.

Conflict of Interest: The authors declare no conflict of interest associated with this manuscript.

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(Received, July 12, 2012)

(Accepted, February 8, 2013)