# Systolic and Diastolic Myocardial Response to Exercise in a Healthy Pediatric Cohort

Barbara Cifra, MD, Luc Mertens, MD, PhD, Moniba Mirkhani, MsC, Cameron Slorach, RDCS, Wei Hui, MD, Cedric Manlhiot, PhD, Mark K. Friedberg, MD, and Andreea Dragulescu, MD, PhD, *Toronto, Ontario, Canada*

*Background:* The aims of the present study were to evaluate the feasibility and reproducibility of color Doppler tissue imaging (DTI) and two-dimensional speckle-tracking echocardiography during semisupine cycle ergometric stress echocardiography and to establish normal myocardial systolic and diastolic left ventricular (LV) and right ventricular (RV) response to exercise in children.

*Methods:* This was a single-center prospective study of 62 healthy children (35 girls). The median age was 14 years (range, 8–19 years). A stepwise semisupine cycle ergometric protocol was used. Color DTI peak systolic (s′) and peak diastolic (e′) velocities and myocardial acceleration during isovolumic contraction were measured in the LV lateral wall, RV free wall, and septum. Early mitral inflow Doppler (E) was measured from the apical four-chamber view, and the ratio of diastolic filling to tissue early diastolic velocity (E/e′) was calculated. LV and RV longitudinal strain were measured from four-chamber apical views. LV circumferential strain was derived from the parasternal short-axis view at the midventricular level. The relationship of each parameter with increasing heart rate was evaluated at each stage of exercise.

*Results:* During exercise color DTI, velocities were obtained in 96% of subjects, with isovolumic contraction having the lowest feasibility among DTI measurements (89%). Strain analysis was measurable in 87% of subjects, with LV longitudinal strain measured in 98% of the subjects compared with 93% for circumferential strain. RV longitudinal strain had the lowest feasibility (70%). A linear relationship was observed between heart rate and color DTI velocities, E, E/e′, and myocardial longitudinal and circumferential strain. The relationship between isovolumic contraction and heart rate was exponential.

*Conclusions:* This study provides reference values for systolic and diastolic reserve during exercise in healthy children as measured by color DTI and two-dimensional speckle-tracking echocardiography. These data allow the evaluation of myocardial response in pediatric cardiac disease. (J Am Soc Echocardiogr 2016;■:■-■.)

*Keywords:* Reference values, Speckle-tracking, Doppler tissue imaging, Children, Exercise, Stress imaging

Stress echocardiography is a noninvasive method for the assessment of global and regional cardiac function and can be used to diagnose subclinical cardiac dysfunction that is not apparent at rest. Stress echocardiography has also been used to evaluate dynamic valve function by measuring changes in hemodynamic gradients or the severity of regurgitation during exercise.[1,2] Although stress echocardiography has been widely used in adult heart disease, its application in children with acquired or congenital heart disease (CHD) is less defined.[3] An increasing body of evidence suggests that exercise stress echocardiography can provide important physiologic information on ventricular function and functional reserve in patients with CHD and can detect subclinical cardiac dysfunction not apparent at rest.[3-6]

Compared with treadmill exercise stress, during which images are acquired at rest and at peak exercise or within the first minute of recovery, semisupine cycle ergometric (SSCE) stress echocardiography allows image acquisition at different exercise intensities. Thus, the dynamic myocardial response to increasing levels of exercise can be evaluated.[7,8] Doppler tissue imaging (DTI) and two-dimensional (2D) speckle-tracking echocardiography (STE) allow the quantification of global and regional myocardial function with good temporal resolution and are robust under difficult imaging conditions.[9,10] These techniques do not depend on geometric assumptions, an advantage in patients with CHD.[9,11] Therefore, these techniques are well suited to evaluate myocardial response to exercise in children.

Although normal resting pediatric DTI and speckle-tracking echocardiographic values have been published,[12,13] there are only limited data on the normal myocardial response to exercise. The aims of the present study was to evaluate the feasibility and reproducibility of color DTI and 2D STE during SSCE stress echocardiography and to establish normal systolic and diastolic response to exercise in a healthy pediatric cohort.

---

From the Division of Cardiology, The Labatt Family Heart Centre, Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada (B.C., L.M., M.M., C.S., W.H., C.M., M.K.F., A.D.).

Reprint requests: Luc Mertens, MD, PhD, The Labatt Family Heart Center, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada (E-mail: *luc.mertens@sickkids.ca*).

0894-7317/$36.00

http://dx.doi.org/10.1016/j.echo.2016.02.015

**Abbreviations**

**CHD** = Congenital heart disease

**DTI** = Doppler tissue imaging

**HR** = Heart rate

**IVA** = Isovolumic contraction

**LV** = Left ventricular

**RV** = Right ventricular

**SSCE** = semisupine cycle ergometric

**STE** = Speckle-tracking echocardiography

**2D** = Two-dimensional

## METHODS

### Patients

Sixty-two healthy volunteers were prospectively recruited from January 2010 to March 2014. Inclusion criteria were a structurally normal heart as demonstrated on resting echocardiography and normal sinus rhythm. Exclusion criteria were a personal or family history of CHD or cardiomyopathy and intense athletic training, defined as >10 hours of sports per week. In addition, children needed to be 140 cm tall in order to be able to reach the bicycle pedals. Parental consent was obtained. The study was approved by the institutional research ethics board.

### SSCE Stress Echocardiographic Protocol

A semisupine bicycle (Lode BV, Groningen, The Netherlands) was used for all echocardiographic stress studies. A standardized Bruce exercise protocol was used with 20-W increments every 3 min for children <14 years of age and 25-W increments for those >14 years of age. All subjects were asked to pedal at a speed of 60 revolutions/min. The target heart rate (HR), for considering the test maximal, was defined as 85% of the maximal HR, calculated as 220 minus age. Patients were monitored with continuous 12-lead electrocardiography. Blood pressure was measured at baseline and during the last 30 sec of each exercise stage (Dinamap; GE Medical Systems, Milwaukee, WI). The test was terminated if predefined adverse events occurred, including arrhythmia, ischemic electrocardiographic changes, chest pain, >10% decrease in systolic blood pressure, or severe hypertension. Predefined criteria for terminating the test were fatigue, shortness of breath, achieving the target HR, and inadequate image quality.

### Image Acquisition and Analysis

Images were acquired using a Vivid 9 ultrasound system (GE Medical Systems) during the last 2 min of each exercise stage and during recovery. We also used the Smart Stress application, which allows the baseline images to be visible during the image acquisition at each stage of exercise. At each stage, parasternal long-axis, parasternal short-axis at the level of the left ventricular (LV) papillary muscles and apical four-, three-, and two-chamber views were recorded. The images were acquired at frame rates of >60 frames/sec and optimized for offline 2D speckle-tracking echocardiographic analysis. We also acquired spectral pulsed-wave Doppler of mitral inflow and high–frame rate, narrow-sector, color DTI of the LV and right ventricular (RV) lateral walls and of the interventricular septum from the apical four-chamber view. Two dedicated sonographers performed all tests. Images were digitally stored in raw Digital Imaging and Communications in Medicine format. The data were analyzed offline using an EchoPAC system (version 110.1.3; GE Medical Systems). Color DTI velocities (s′ and e′) were measured from three consecutive cardiac cycles. In all subjects, fusion of the e′ and a′ waves was seen during exercise. The peak fused wave was measured as peak diastolic e′. Isovolumic contraction (IVA) was measured as the mean acceleration of the velocity spike during the isovolumetric contraction period.[14] LV longitudinal and circumferential strain values were calculated from the apical four-chamber and short-axis views, respectively, using 2D STE. The endocardial border was manually traced and strain analysis automatically generated. Speckle-tracking strain analysis was accepted when the software and visual inspection indicated adequate tracking. If tracking was inadequate, further manual adjustments were made. Only images with at least four adequate segments were accepted for analysis. Circumferential strain was analyzed for six LV segments (anterior septum, anterior, lateral, posterior, inferior, and septum). Longitudinal strain was analyzed from the apical four-chamber view for six segments (basal septum, mid septum, apical septum, apical lateral, mid lateral, and basal lateral). From the apical four-chamber view, RV longitudinal strain was calculated for the RV free wall (basal, mid, and apical segments). Global RV free wall strain measurements were calculated by averaging the segmental values.

### Reproducibility

Fifteen randomly selected studies were used for the assessment of intra- and interobserver variability of color DTI, IVA, and strain measurements. For intraobserver variability, the same observer reanalyzed the studies, blinded to the initial results, ≥2 weeks after the initial analysis. For interobserver variability, a second observer analyzed the same studies, blinded to the results of the first analysis.

### Statistical Analysis

Data are presented as mean ± SD, medians with ranges, and frequencies as appropriate. Linear regression models adjusted for repeated measures through an autoregressive covariance structure were used to determine change in outcome associated with increasing HR and the slope of change over time. Both linear and nonlinear transformations of HR were tested for each parameter, and the model with the best fit according to the Akaike information criterion was evaluated. All figures report the line of best fit and 95% prediction bands. Intraclass correlation coefficients were calculated for inter- and intraobserver variability. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

## RESULTS

Sixty-two healthy volunteers (35 girls) were included in the study. Demographic data are summarized in Table 1. All subjects had normal baseline LV systolic function, with a mean ejection fraction of 64 ± 4% and mean fractional shortening of 35 ± 3%. At rest, the mean HR was 72 ± 11 beats/min and mean systolic blood pressure was 104 ± 13 mm Hg. At peak exercise, the mean highest HR achieved was 154 ± 12 beats/min, and mean systolic blood pressure was 148 ± 21 mm Hg (Table 2). No test was terminated for adverse medical events. With the increase of HR, we noticed a progressive decline of image quality for myocardial assessment, so all tests were terminated before the target HR (220 − age) was achieved, and they were classified as submaximal.

### Feasibility

Systolic and diastolic echocardiographic parameters could be measured in all subjects at rest and at the highest HR achieved during SSCE stress echocardiography. Absolute values are presented in Tables 2 and 3. The relationship between HR and e′ and s′ velocities