Validation of Noninvasive Measures of Left Ventricular Mechanics in Children: A Simultaneous Echocardiographic and Conductance Catheterization Study

Shahryar M. Chowdhury, MD, MSCR, Ryan J. Butts, MD, Carolyn L. Taylor, MD, Varsha M. Bandisode, MD, Karen S. Chessa, RDCS, Anthony M. Hlavacek, MD, MSCR, Girish S. Shirali, MBBS, and G. Hamilton Baker, MD, *Charleston, South Carolina; and Kansas City, Missouri*

Background: The accuracy of echocardiography in evaluating left ventricular contractility has not been validated in children. The objective of this study was to compare echocardiographic measures of contractility with those derived from pressure-volume loop (PVL) analysis in children.

Methods: Patients with relatively normal loading conditions undergoing routine left heart catheterization were prospectively enrolled. PVLs were obtained via conductance catheters. The gold-standard measure of contractility, end-systolic elastance (Ees), was obtained via balloon occlusion of one or both vena cavae. Echocardiograms were performed immediately after PVL analysis under the same anesthetic conditions. Single-beat estimations of echocardiographic Ees were calculated using four different methods. These estimates were calculated using a combination of noninvasive blood pressure readings, ventricular volumes derived from three-dimensional echocardiography, and Doppler time intervals.

Results: Of 24 patients, 18 patients were heart transplant recipients, and six patients had small patent ductus arteriosus or small coronary fistulae. The mean age was 9.1 ± 5.6 years. The average invasive Ees was 3.04 ± 1.65 mm Hg/mL. Invasive Ees correlated best with echocardiographic Ees by the method of Tanoue ($r = 0.85$, $P < .01$), with a mean difference of −0.07 mm Hg/mL (95% limits of agreement, −2.0 to 1.4 mm Hg/mL).

Conclusions: Echocardiographic estimates of Ees correlate well with gold-standard measures obtained via conductance catheters in children with relatively normal loading conditions. The use of these noninvasive measures in accurately assessing left ventricular contractility appears promising and merits further study in children. (J Am Soc Echocardiogr 2016;■:■-■.)

Keywords: Pressure-volume relationship, pediatric, contractility, echocardiography

The advanced assessment of left ventricular (LV) mechanics in the pediatric population has the potential to provide valuable insights into the natural history and results of medical and surgical interventions in patients with congenital heart disease. However, such an assessment is rarely performed in children, because of the invasive nature of the studies that are required to carry out pressure-volume loop (PVL) analysis.[1] As such, the development of accurate noninvasive indices of myocardial mechanics has long been a goal in pediatric echocardiography.[2]

LV end-systolic elastance (Ees) is a load-independent measure of myocardial contractility, defined as the slope of the end-systolic pressure-volume relationship.[3] The ratio of arterial elastance (Ea) to Ees (Ea/Ees) is the reference-standard measure of ventriculoarterial coupling, as it describes the interaction between myocardial performance and vascular function.[4] A number of studies have been performed in animals and humans attempting to develop noninvasive estimates of these measures.[5-8] Few studies have been performed attempting to independently validate these methods in adults.[9] However, it is clear that adult data supporting the accuracy of noninvasive assessments of myocardial mechanics may not be applicable in children.[10] As such, before these noninvasive measures can be used in children, they should be validated against the reference standard.

The goal of this study was to assess the validity of echocardiographic indices of contractility and ventriculoarterial coupling by direct comparison with reference-standard indices derived from PVL analysis in children. We hypothesized that noninvasive estimates

From the Department of Pediatrics, Division of Cardiology, Medical University of South Carolina, Charleston, South Carolina (S.M.C., R.J.B., C.L.T., V.M.B., K.S.C., A.M.H., G.H.B.); and The Ward Family Heart Center, Children's Mercy Hospital, Kansas City, Missouri (G.S.S.).

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Reprint requests: Shahryar M. Chowdhury, MD, MSCR, Medical University of South Carolina, Department of Pediatrics, Division of Cardiology, 165 Ashley Ave, MSC 915, Charleston, SC 29425 (E-mail: chowdhur@musc.edu).

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Abbreviations

Ea = Arterial elastance

Ees = End-systolic elastance

Ees_{sb} = Single-beat estimation of end-systolic elastance

LV = Left ventricular

PVL = Pressure-volume loop

3D = Three-dimensional

2D = Two-dimensional

of Ees and Ea/Ees would correlate well with invasive Ees and Ea/Ees, respectively.

METHODS

Children (<21 years of age) with biventricular circulation undergoing clinically indicated diagnostic left heart catheterization were recruited prospectively. Exclusion criteria were (1) medical status for which participation in the study presented more than minimal risk as determined by the attending physician, (2) nonsinus rhythm, (3) right-sided cardiac pathology (tetralogy of Fallot, atrial septal defect, etc), and (4) significantly abnormal loading conditions (ratio of pulmonary to systemic blood flow > 1.5 or LV outflow tract gradient > 15 mm Hg); a significant left-to-right shunt would adversely affect conductance catheter volume calibration and LV outflow tract obstruction would significantly affect the noninvasive estimation of LV pressure. Therefore, patients with significantly abnormal loading conditions were excluded, keeping the study population relatively homogenous. The protocol was approved by our institutional review board. Informed consent was obtained from the parents or legal guardians of minors and from participants ≥18 years of age.

Study Catheterization and PVL Analysis Protocol

All patients underwent general anesthesia per institutional protocol. All study data were collected after the patient's primary diagnostic and interventional procedures. A 4-Fr high-fidelity microconductance catheter (CD Leycom, Zoetermeer, The Netherlands) was placed in the apex of the left ventricle via the femoral approach. The conductance catheter's micromanometer was calibrated in normal saline for 15 sec before placement. PVLs were volume calibrated using hypertonic saline to account for parallel conductance. Conductance catheter volumes have been shown to correlate well with cardiac magnetic resonance imaging volumes, though they do underestimate absolute volumes.[11,12] Cardiac output was determined by thermodilution. Conductance electrodes outside of the ventricle were excluded from analysis. Preload reduction was achieved via balloon occlusion of one or both vena cavae. Ees was then calculated using the iterative regression method.[13] Invasive Ea was calculated as end-systolic pressure divided by invasive stroke volume.[14] All PVL data were recorded in triplicate over 10 sec during an expiratory breath hold. Microconductance data were recorded at a sampling rate of 250 Hz. Invasive data were obtained using standard equipment approved for use in human subjects (INCA intracardiac analyzer; CD Leycom). PVL analysis was performed offline using specialized software (ConductNT version 3.18; CD Leycom).

Echocardiographic Acquisition and Analysis Protocol

Echocardiograms were obtained immediately after PVL analysis under the same anesthetic conditions using a Philips iE33 system (Philips Medical Systems, Andover, MA). Echocardiograms were sent uncompressed and at native frame rates to the encrypted server for analysis. All measurements were made offline by a single blinded reviewer (S.M.C.) and averaged over three beats. Ventricular volumes and ejection fraction used in the calculation of Ees were derived from three-dimensional (3D) echocardiography (QLAB version 9.0; Philips Medical Systems). Electrocardiographically gated 3D echocardiographic volumes were acquired during expiratory breath hold over four beats, and the subvolumes were stitched together. The average frame rate of the 3D echocardiographic volumes was 29.7 ± 5.1 frames/sec, with an average heart rate during acquisition of 86.8 ± 17.2 beats/min.

Single-beat estimations of echocardiographic Ees (Ees_{sb}) were calculated using four different methods, which have been previously validated in adult patients. Method 1 (Ees_{sb1}),[5] method 2 (Ees_{sb2}),[6] and method 3 (Ees_{sb3})[7] use echocardiographic ventricular volumes, Doppler time intervals, and blood pressure cuff measurements to estimate Ees. In addition, Ees_{sb2} and Ees_{sb3} require an estimation of ventricular end-diastolic pressure. Method 4 (Ees_{sb4})[8] is a simpler method that requires only echocardiographic ventricular volumes and blood pressure cuff measurements to estimate Ees. Please see the Appendix for details on the methods to calculate these Ees_{sb} estimates.

Echocardiographic Ea was calculated as (0.9 × systolic blood pressure)/(3D echocardiographic stroke volume). A second set of calculations of Ees and Ea was made using two-dimensional (2D) echocardiography by calculating volumes using the 5/6 area-length method. Noninvasive blood pressures (systolic, diastolic, and mean) were obtained supine at the time of echocardiography by automated sphygmomanometer and averaged over three measurements. Intra- and interobserver variability of Ees_{sb} was assessed in 50% of studies by observers blinded to the original measurements.

Table 1 Patient demographics and invasive data

Variable	Value
Age (y)	9.6 ± 5.8
Female, *n* (%)	12 (50%)
Height (cm)	126 (58.1)
Weight (kg)	32.9 (36.4)
BSA (m^2)	0.96 (0.85)
Systolic blood pressure (mm Hg)	88 ± 9
Diastolic blood pressure (mm Hg)	47 ± 7
Baseline heart rate (beats/min)	86 ± 18
Oxygen saturation	99 (2.8)
EDP (mm Hg)	10.6 ± 3.3
Cardiac index (L/min/m^2)	3.5 ± 1.2
MvO_2 (%)	75 ± 5
Rp (Wood units)	1.8 ± 0.7
Rs (Wood units)	19.2 ± 6.0
Qp/Qs	1.03 ± 0.21
Ees (mm Hg/mL)	2.9 ± 1.6
Ea (mm Hg/mL)	2.2 ± 0.9
Ea/Ees	0.88 ± 0.35

BSA, Body surface area; *EDP*, end-diastolic pressure; *MvO_2*, mixed venous oxygen saturation; *Rp*, pulmonary vascular resistance; *Rs*, systemic vascular resistance, *Qp/Qs*, ratio of pulmonary to systemic blood flow.
Data are expressed as mean ± SD for parametric data and median (interquartile range) for nonparametric data.