Right Ventricular to Left Ventricular Diameter Ratio at End-Systole in Evaluating Outcomes in Children with Pulmonary Hypertension

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Background: Pulmonary hypertension (PH) increases right ventricular (RV) pressure, resulting in septal shift and RV dilation. Few echocardiographic measures have been used to evaluate severity and outcomes in children with PH. The aims of this study were to compare the RV to left ventricular (LV) diameter ratio at end-systole (RV/LV ratio) in normal controls and patients with PH, to correlate the RV/LV ratio with invasive hemodynamic measures, and to evaluate its association with outcomes in children with PH.

Methods: The RV/LV ratio was compared retrospectively between 80 matched normal controls and 84 PH patients without shunts. Of the patients with PH, 49 children underwent 94 echocardiographic studies and cardiac catheterizations within 48 hours (13 patients had simultaneous measurements). The RV/LV ratio was correlated against hemodynamic measures. Kaplan-Meier curves and a Cox proportional-hazards regression model were used to assess relationships between RV/LV ratio and time until an adverse clinical event (initiation of intravenous prostacyclin therapy, atrial septostomy, death, or transplantation).

Results: RV/LV ratios were lower in controls compared with patients with PH (mean, 0.51 [95% confidence interval, 0.48–0.54] vs 1.47 [95% confidence interval, 1.25–1.70], $P < .01$). The RV/LV ratio correlated significantly with mean pulmonary artery pressure, systolic pulmonary artery pressure, systolic pulmonary artery pressure as a percentage of systemic pressure, and pulmonary vascular resistance index ($r = 0.65$ [$P < .01$], $r = 0.6$ [$P < .01$], $r = 0.49$ [$P < .01$], and $r = 0.43$ [$P < .01$], respectively). Twenty-two patients with PH with RV/LV ratios > 1 had adverse events within a median of 1.1 years from their earliest echocardiographic studies. Increasing RV/LV ratio was associated with an increasing hazard for a clinical event (hazard ratio, 2.49; 95% confidence interval, 1.92–3.24).

Conclusions: The RV/LV end-systolic diameter ratio can easily be obtained noninvasively in the clinical setting and can be used in the management of patients with PH. The RV/LV ratio incorporates both pathologic septal shift and RV dilation in children with PH and correlates with invasive measures of PH. An RV/LV ratio > 1 is associated with adverse clinical events. (J Am Soc Echocardiogr 2014;27:172-8.)

Keywords: Pulmonary hypertension in children, RV/LV end-diastolic diameter ratio, Echocardiography, Outcomes

Pulmonary hypertension (PH) is defined as mean pulmonary artery pressure ≥ 25 mm Hg at rest.[1] PH is a progressive disease associated with elevations of pulmonary artery pressure and pulmonary vascular resistance, resulting in right ventricular (RV) dilation and dysfunction. The effect of RV dilation on the interventricular septum leads to a septal shift toward the left ventricle in systole. This abnormal interventricular septal shift has been previously described in patients with PH.[2-4] In those with severe PH, progressive RV dilation and dysfunction result in RV failure and death.[5-7] Hemodynamic data obtained by cardiac catheterization are used as a gold standard to assess patients with PH and to determine the severity of PH, but cardiac catheterization is an invasive procedure.[8] The inherent risks of cardiac catheterization limit its use as a surveillance tool for children with PH.

Transthoracic echocardiography is a noninvasive method used to evaluate pulmonary hemodynamics and right heart function.[9-17] It is cost effective, accessible, and safe. Several echocardiographic

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Abbreviations

LV = Left ventricular

%PAP = Systolic pulmonary artery pressure as a percentage of systemic pressure

PH = Pulmonary hypertension

RV = Right ventricular

RV/LV ratio = Right to left ventricular diameter ratio at end-systole

sPAP = Systolic pulmonary artery pressure

indices have been described to evaluate PH and its association with clinical outcomes.[3,7,17-19] Tricuspid regurgitation velocity is the most feasible noninvasive technique to estimate systolic pulmonary artery pressure (sPAP) in patients with PH; however, its precision has been debatable, and it cannot be assessed in all patients.[20] We sought to evaluate a new index, the RV to left ventricular (LV) diameter ratio at end-systole (RV/LV ratio), with the following objectives: (1) evaluate the feasibility of this index, (2) compare normal controls and patients with PH, (3) correlate with invasively obtained hemodynamic measures in PH, and (4) evaluate the association between RV/LV ratio and clinical outcomes in children with PH.

METHODS

Study Population

Normal Controls. The University of Colorado Children's Hospital Colorado pediatric normal echocardiographic database (per an institutional review board–approved protocol) was used to retrospectively identify 80 normal controls with similar age and gender distributions as the PH cohort. All 80 normal children were evaluated for heart murmurs and had normal results on echocardiography. RV/LV ratios were obtained in normal controls and compared with RV/LV ratios in patients with PH.

Patients with PH. The University of Colorado Children's Hospital Colorado pediatric PH database was used to retrospectively identify 84 patients with PH who underwent echocardiographic evaluation, cardiac catheterization, and had outcomes between March 2006 and November 2012. Inclusion criteria were adequate echocardiographic images in parasternal short-axis views at the level of the papillary muscles and patients who could have any category of PH. Exclusion criteria were inadequate-quality echocardiographic images in which the right ventricle was cut off in the parasternal short-axis view, presence of intracardiac shunts, or presence of RV outflow tract obstruction. PH patients' clinical statuses were obtained from their medical charts. This study was approved by the institutional review board at the University of Colorado.

Transthoracic Echocardiography

Echocardiography was performed on all normal controls and patients with PH using an iE33 (Philips Ultrasound, Bothell, WA) or a Vivid 7 (GE Medical Systems, Milwaukee, WI) ultrasound machine. Echocardiograms were digitally acquired using a standard protocol with appropriately sized transducers for patient size in all patients. RV/LV ratios were obtained offline from the parasternal short-axis two-dimensional view at the level of the papillary muscles with the RV free wall in view. RV and LV diameters were measured from the endocardial to endocardial surfaces at end-systole. RV/LV ratios were calculated (Figure 1).

Echocardiographic images were analyzed offline using the Agfa Heartlab system (Mortsel, Belgium). Feasibility of RV/LV ratios was assessed in normal controls and patients with PH. RV/LV ratios were compared between normal controls and patients with PH. Forty-nine of 84 patients with PH underwent echocardiography within 48 hours of cardiac catheterization. In these 49 patients, 94 echocardiographic studies and cardiac catheterizations were performed between March 2006 and November 2012. Echocardiographic images were analyzed within 48 hours of cardiac catheterization, and a small subset of patients (13 patients) had simultaneous image acquisition in the cardiac catheterization laboratory. Echocardiographic studies from all 84 patients with PH were analyzed for clinical outcomes.

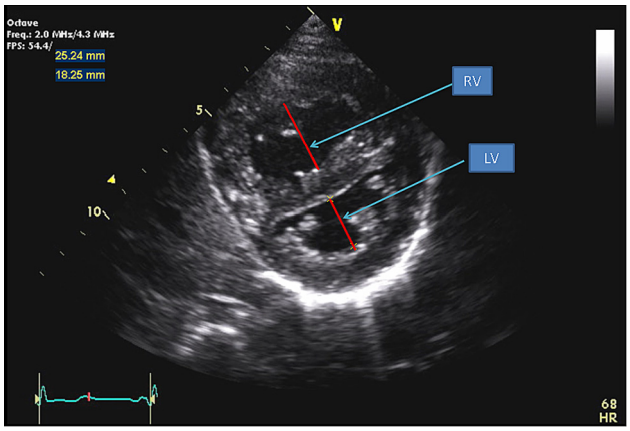

Figure 1 Parasternal short-axis view of the right and left ventricles. The RV/LV ratio was derived from RV diameter and LV diameter at end-systole.

Cardiac Catheterization

Forty-nine patients with PH underwent 94 standard right-sided heart catheterizations within 48 hours of their echocardiographic assessments. Of these 49 patients, 13 underwent simultaneous echocardiographic studies and cardiac catheterizations. General anesthesia was used in 62 of 94 studies (65%), and the rest were performed under conscious sedation. Eighty-three of 94 studies (88%) were done with the patients on room air. Three studies were performed with the patients on 100% oxygen and 8 studies with the patients on 30% oxygen. Data collected from the catheterization procedure included sPAP, sPAP as a percentage of systemic pressure (%PAP), mean pulmonary artery pressure, pulmonary vascular resistance index, pulmonary capillary wedge pressure, right atrial pressure, and cardiac index. Cardiac output was obtained using thermodilution, and cardiac index was calculated. Pulmonary vascular resistance index was calculated as (mean pulmonary artery pressure − mean pulmonary wedge pressure)/cardiac index.

Clinical Outcomes

Clinical outcomes were analyzed in all 84 patients with PH who underwent echocardiography between March 2006 and November 2012. Clinical outcomes were retrospectively obtained from medical charts in patients with PH. An adverse clinical event was defined as (1) disease progression requiring the initiation of intravenous prostacyclin, (2) clinically indicated creation of an atrial septostomy, (3) death, or (4) transplantation. The earliest echocardiographic studies available (defined as the earliest echocardiograms from 2006 onward for each patient) and the most recent echocardiographic studies (or those performed just before adverse events) were analyzed for outcome analysis. A subgroup analysis of earliest echocardiographic studies was