Pulmonary Artery Acceleration Time Provides a Reliable Estimate of Invasive Pulmonary Hemodynamics in Children

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Background: Pulmonary artery acceleration time (PAAT) is a noninvasive method to assess pulmonary hemodynamics, but it lacks validity in children. The aim of this study was to evaluate the accuracy of Doppler echocardiography–derived PAAT in predicting right heart catheterization (RHC)–derived pulmonary artery pressure (PAP), pulmonary vascular resistance (PVR), and compliance in children.

Methods: Prospectively acquired and retrospectively measured Doppler echocardiography–derived PAAT and RHC-derived systolic PAP, mean PAP (mPAP), indexed PVR (PVRi), and compliance were compared using regression analysis in a derivation cohort of 75 children (median age, 5.3 years; interquartile range, 1.3–12.6 years) with wide ranges of pulmonary hemodynamics. To account for heart rate variability, PAAT was adjusted for right ventricular ejection time and corrected by the RR interval. Regression equations incorporating PAAT and PAAT/right ventricular ejection time from the derivation cohort were then evaluated for the accuracy of their predictive values for invasive pulmonary hemodynamics in a validation cohort of 50 age- and weight-matched children with elevated PAP and PVR.

Results: There were significant inverse correlations between PAAT and RHC-derived mPAP ($r = -0.82$) and PVRi ($r = -0.78$) and a direct correlation ($r = 0.78$) between PAAT and pulmonary compliance in the derivation cohort. For detection of pulmonary hypertension (PRVi > 3 Wood units · m^2 and mPAP > 25 mm Hg), PAAT < 90 msec and PAAT/right ventricular ejection time < 0.31 resulted in sensitivity of 97% and specificity of 95%. In the derivation cohort, the regression equations relating PAAT with mPAP and PVRi were $\text{mPAP} = 48 - 0.28 \times \text{PAAT}$ and $\text{PVRi} = 9 - 0.07 \times \text{PAAT}$. These PAAT-integrated equations predicted RHC-measured pulmonary hemodynamics in the validation cohort with good correlations ($r = 0.88$ and $r = 0.83$, respectively), small biases (<10%), and minimal coefficients of variation (<8%).

Conclusions: PAAT inversely correlates with RHC-measured pulmonary hemodynamics and directly correlates with pulmonary arterial compliance in children. The study established PAAT-based regression equations in children to accurately predict RHC-derived PAP and PVR. (J Am Soc Echocardiogr 2016;■:■-■.)

Keywords: Pulmonary artery acceleration time, Pulmonary hypertension, Pediatrics, Echocardiography

The assessment of pulmonary hemodynamics is critical in the diagnosis and management of cardiopulmonary diseases in children.[1-3] Right heart catheterization (RHC) remains the gold standard investigation for determining pulmonary vascular resistance (PVR) and pulmonary artery pressures (PAP).[1-5] However, the increased risk of an invasive procedure accompanied with radiation exposure and the frequent need for general anesthesia make RHC use as a screening or monitoring tool in children with significant cardiopulmonary disease problematic.[1,6,7] Doppler echocardiography (DE) is widely used in clinical practice as a surrogate for RHC for PAP quantification using the maximum Doppler velocity of tricuspid regurgitation. However, recent studies in children and adults comparing the Doppler velocity of tricuspid regurgitation and RHC methods have revealed clinically relevant discrepancies between Doppler-estimated and catheter-measured PAP.[1,8-10] This problem is compounded by the fact that in a significant number of children, the Doppler velocity of tricuspid regurgitation is either absent or insufficient to measure.[1-3,8-10]

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Abbreviations

AUC = Area under the receiver operating characteristic curve

DE = Doppler echocardiography

mPAP = Mean pulmonary artery pressure

PAAT = Pulmonary artery acceleration time

PAP = Pulmonary artery pressure

PVR = Pulmonary vascular resistance

PVRi = Pulmonary vascular resistance index

RHC = Right heart catheterization

ROC = Receiver operating characteristic

RV = Right ventricular

RVET = Right ventricular ejection time

sPAP = Systolic pulmonary artery pressure

WU = Wood units

There is a clinical need for a noninvasive method, other than the Doppler velocity of tricuspid regurgitation, to accurately predict PAP, PVR, and pulmonary arterial compliance in children. Pulmonary artery acceleration time (PAAT) is a quantitative method used to study the blood flow velocity characteristics in the right ventricular (RV) outflow tract in response to changes in ventricular mechanical performance and pulmonary vascular load and compliance.[4,5,11,12] A number of adult studies have shown a strong, inverse correlation between PAAT and invasively measured pulmonary hemodynamics,[3-5,12-14] but there are limited studies in children.[2,11,15-18] Currently, PAAT is not used clinically to evaluate pulmonary hemodynamics in pediatric patients, because its validity in children has not been demonstrated.

We hypothesized that PAAT would accurately predict RHC-measured pulmonary hemodynamics in pediatric patients. The aim of this study was to evaluate the correlations of DE-measured PAAT with RHC-derived PAP and PVR in children to establish and validate regression equations that use PAAT to estimate these invasive measurements.

METHODS

Study Design

In this study, we performed pulmonary hemodynamic assessment by DE and RHC in two cohorts of pediatric patients: (1) a derivation cohort to assess the correlations between DE-measured PAAT and RHC-measured PAP for the establishment of PAAT-based regression equations and (2) a validation cohort to substantiate these PAAT-based regression equation for their accuracy in predicting invasive measured pulmonary hemodynamics. In each cohort, DE and RHC were performed both simultaneously under the same loading and sedation conditions and nonsimultaneously to represent typical clinical condition in both cohorts.

Derivation Cohort

The derivation cohort consisted of 75 children (ages 1–18 years) who presented to the St. Louis Children's Hospital cardiac catheterization laboratory for clinically indicated RHC between November 2011 and December 2013. DE and RHC were performed simultaneously ($n = 50$ children) or within 6 hours ($n = 25$ children) of each other (DE followed by RHC). The data were prospectively acquired and retrospectively analyzed. The 50 children who underwent simultaneous DE and RHC were recruited from a previous study reported by our group,[1] in whom invasive pulmonary hemodynamics and PAAT were not reported. Children included in the study had a wide range of right heart pressures and diagnoses, including pulmonary arterial hypertension due to idiopathic, heritable, or connective tissue disease etiology, lesions with left-to-right shunt, and orthotopic heart transplantation, representing the spectrum of cardiopulmonary diseases seen in clinical practice (Table 1). Children with single-ventricle physiology, mechanical tricuspid valves, RV outflow tract obstruction, left heart diseases, arrhythmias, or pulmonary insufficiency or on pulmonary vasodilators were excluded.[1] Informed, written parental consent was obtained for all subjects and assent was obtained for all subjects >12 years of age. The institutional review board at Washington University School of Medicine approved all components of the study.

RHC. Fifty children underwent simultaneous DE and RHC in the cardiac catheterization laboratory under the same sedation and loading conditions, and 25 children underwent DE first without sedation, followed by sedated RHC within 6 hours. RHC-measured mean PAP (mPAP) and systolic PAP (sPAP) using a standard fluid-filled catheter. An interventional cardiologist, blinded to the patients' diagnoses and echocardiographic data, analyzed pressure tracings to evaluate pulmonary hemodynamics. Cardiac output and pulmonary blood flow were calculated using the standard Fick method and indexed to body surface area. Pulmonary artery compliance (mL/mm Hg/m^2) was calculated as the ratio of stroke volume (indexed pulmonary blood flow divided by heart rate) to pulmonary artery pulse pressure. PVR (Wood units [WU]) indexed to body surface area (PVRi; WU · m^2) was derived using pulmonary capillary wedge pressure from the following equation: (mPAP − pulmonary capillary wedge pressure)/indexed pulmonary blood flow. Oxygen consumption was assumed using the standard LaFarge methodology.[19]

Echocardiography. We acquired two-dimensional and color Doppler echocardiographic images of the parasternal and apical standard views with the patient in the supine position per the American Society of Echocardiography guidelines.[20] We developed a protocol for PAAT image acquisition and postprocessing data analysis (Appendix 1) and tested for variability using reproducibility statistical analysis.[21] A spectral Doppler image was obtained by placing a pulsed Doppler sample volume at the pulmonary valve annulus in the parasternal short-axis view (Figure 1). Maximal alignment of Doppler interrogation with blood flow direction was achieved with the placement of the sample volume at the annulus of the pulmonary valve and not more proximally in the RV outflow tract. PAAT was calculated from a spectral Doppler envelope as the time interval between the onset of systolic pulmonary arterial flow (onset of ejection) and peak flow velocity (Figure 1).

Confounding Influences. The variables confounding the PAAT measures include imaging acquisition techniques and postprocessing analysis, heart rate variability, influence of RV mechanics and function, and pulmonary compliance.[11,22] We identified and quantified the image acquisition and postprocessing analysis uncertainties with the development of a protocol (Appendix 1). To account for the potential impact of heart rate variability, PAAT was corrected for the R-R interval and also adjusted for RV ejection time (RVET) with the ratio of PAAT to RVET.[12,16,23,24] The mean PAAT/RVET ratio from three cardiac cycles was used for data analysis and further corrected by the square root of the R-R interval.[24] PAAT/RVET and the R-R interval were compared using a linear regression. We measured RV preejection time, RVET, and the ratio of RV preejection time to RVET to assess RV mechanics.[25] Preejection time was defined as the interval