Clinical Utility of Stroke Volume Index in Children with Idiopathic and Heritable Pulmonary Arterial Hypertension

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Take Home Points:

- In children with idiopathic and heritable pulmonary arterial hypertension, stroke volume index (SVi) may provide additional prognostic information beyond cardiac index.
- An SVi less than 33 mL/m^2 was associated with a higher risk of death or lung transplantation, and may be a useful threshold for risk stratification in pediatric PAH.

Summary

Pediatric pulmonary arterial hypertension (PAH) remains a progressive disease characterized by pathologic remodeling of the pulmonary arterioles, increasing pulmonary vascular resistance, right ventricular dysfunction, and ultimately right heart failure and premature death. Mortality in pediatric PAH is largely driven by progressive RV failure and the inability to maintain cardiac output. Although targeted therapies have improved survival, outcomes remain unsatisfactory, making accurate risk stratification essential for guiding therapy and predicting prognosis. Current pediatric PAH risk assessment incorporates clinical, functional, biomarker, imaging and hemodynamic variables, with prior studies demonstrating the prognostic value of right atrial pressure, PVRi and cardiac index[1], however, stroke volume index (SVi) has not been incorporated into pediatric risk assessment, despite its established prognostic role in adult PAH.

Unlike cardiac index, which may remain preserved through compensatory tachycardia despite worsening RV performance, SVi may provide a more direct assessment of RV adaptation to increased afterload. This distinction may be particularly relevant in children with PAH, in whom cardiac output may be maintained despite progressive reductions in stroke volume. The clinical relevance of SVi is underscored by its incorporation into the 2022 European Society of Cardiology/European Respiratory Society risk-stratification framework for adult PAH, in which an SVi <31 mL/m^2 is considered a high-risk hemodynamic feature. Notably, this threshold may identify severe hemodynamic impairment in patients who would otherwise be classified as intermediate risk and for whom initial triple-combination therapy, including a prostacyclin analogue, should be considered.[2]

The prognostic significance of SVi in pediatric PAH remains poorly defined. In the April 2026 issue of *Pediatric Cardiology*, Takatsuki *et al* sought to determine whether SVi offers prognostic

value in children with idiopathic and heritable PAH. This retrospective multicenter study titled "Clinical Utility of Stroke Volume Index in Children with Idiopathic and Heritable Pulmonary Arterial Hypertension" included 103 children with newly diagnosed idiopathic or heritable PAH who underwent diagnostic right heart catheterization at the Toho University Omori Medical Center and the University of Colorado School of Medicine, Children's Hospital Colorado between 2004 and 2022. The primary composite outcome included cardiac death or lung transplantation. Cardiac output was measured using the Fick method, and the stroke volume index was calculated by dividing cardiac output by heart rate and indexing the resulting stroke volume to body surface area. The patients were followed for a median of 89 months (range 6 to 315 months).

Twenty-three patients (22%) experienced an adverse outcome (cardiac death or lung transplantation) during follow-up. Compared with patients who remained event-free, those who experienced an adverse outcome had significantly higher right atrial pressure, pulmonary artery pressure and PVRi, along with lower SVi at baseline (median 29.1 vs. 35.6 mL/m^2, p<0.05), while heart rate and cardiac index remained similar between the groups. Lower SVi was associated with an increased risk of cardiac death or lung transplantation (HR 0.92; 95% CI 0.89-0.97; p=0.001) and was significantly correlated with established markers of disease severity, including 6-minute walk distance, BNP and WHO functional class. On univariate Cox regression analysis, mean PAP, systolic and diastolic PAP, PVRi, PVR/SVR ratio, CI and SVi were associated with adverse outcomes. Receiver-operating characteristic analysis identified an SVi threshold of 33 mL/m^2 for predicting adverse outcomes in children with idiopathic and heritable PAH. However, no hemodynamic variable remained independently associated with adverse outcomes on multivariable analysis, with the association between SVi and outcomes narrowly missing conventional statistical significance (HR 0.83, 95% CI 0.67-1.03, p=0.05). The authors' findings should be interpreted as demonstrating an association between lower SVi and adverse outcomes, rather than establishing SVi as an independent predictor of outcome. The absence of statistically significant independent predictors on multivariable analysis may reflect the relatively small sample size and the interrelationships among hemodynamic measures of PAH severity, which may limit the ability of multivariable models to distinguish the prognostic contribution of individual variables.

However, the authors present several findings that support the potential clinical relevance of SVi in pediatric PAH. Patients who experienced an adverse outcome had significantly lower SVi at baseline than those who remained event-free, despite similar heart rate and cardiac index, supporting the premise that cardiac index may be preserved through compensatory tachycardia despite declining stroke volume. Consequently, SVi may capture an aspect of declining RV function that is not apparent from cardiac index alone.

Takatsuki *et al*'s findings are consistent with observations in adults with PAH, in whom SVi has emerged as a potential marker of disease severity and prognosis. van Wolferen *et al* evaluated 64 adults with idiopathic PAH using cardiac magnetic resonance imaging and found that a lower

baseline SVi was independently associated with mortality. In their cohort, patients with a baseline SVi > 25 mL/m^2 had significantly better survival than those with lower SVi. These authors also found a stronger association between SVi and prognosis than between cardiac index and prognosis, suggesting that stroke volume may provide more direct information regarding RV function. They also proposed that the discrepancy may reflect compensation for declining stroke volume by an increase in heart rate, which can preserve cardiac output despite worsening RV function.[4]

More recently, Weatherald *et al* assessed 763 newly diagnosed adult patients with idiopathic, heritable or drug-induced PAH who underwent follow-up right heart catheterization after treatment initiation in the French Pulmonary Arterial Hypertension Network. At first follow-up, SVi and right atrial pressure were the only hemodynamic variables independently associated with death or lung transplantation. Importantly, lower SVi identified patients at higher risk for death or lung transplantation, even among those with otherwise low-risk features such as NYHA functional class I or II and a cardiac index ≥2.5 L/min/m^2. The optimal SVi threshold for predicting adverse outcomes in their study was 38 mL/m^2. These authors proposed that SVi may provide a more direct reflection of RV function and adaptation than cardiac index, as cardiac index may be maintained through an increase in heart rate despite persistent or worsening RV dysfunction.[5]

Takatsuki *et al*'s findings extend these observations to a pediatric cohort and suggest that SVi may identify pediatric patients at increased risk of adverse outcomes despite preserved cardiac output. Thus, SVi may provide complementary prognostic information beyond cardiac index alone in pediatric idiopathic and heritable PAH. Although the findings do not establish SVi as an independent predictor, the consistency of its association with adverse outcomes, correlation with established markers of PAH severity, and similarity of the identified pediatric threshold of 33 mL/m^2 to the adult guideline threshold (31 mL/m^2) support further investigation of SVi as a potential component of pediatric PAH risk assessment.

An important consideration in interpreting these findings is the effect of anesthesia on hemodynamic measurements obtained during pediatric right heart catheterization. Most children require sedation or general anesthesia for right heart catheterization, and anesthetic agents can alter heart rate, myocardial function and pulmonary and systemic vascular tone. This may be particularly relevant to SVi, which is calculated from cardiac output and heart rate. Dexmedetomidine, an alpha-2 adrenergic agonist, is commonly used as a sedative or adjunct to general anesthesia during pediatric cardiac catheterization. In a cohort of 25 children with congenital heart disease and pulmonary hypertension, Kanchi *et al* demonstrated a significant reduction in heart rate from 111 to 102 bpm (p<0.01) following administration of 1 mcg/kg of dexmedetomidine over 10 minutes, without a clinically significant hemodynamic effect[6]. Although these findings have not been specifically demonstrated in children with idiopathic or heritable PAH, they highlight the potential for anesthetic-related changes in heart rate to influence SVi measurements obtained during right heart catheterization.

The Takatsuki *et al* study is limited by its retrospective nature, spanning nearly two decades, over which treatment strategies have evolved considerably. The retrospective design also limited standardization of anesthetic and sedation practices during RHC, which may have influenced heart rate, and consequently SVi measurements. Additionally, 25% of the patients were being treated with pulmonary vasodilator therapies at the time of initial right heart catheterization, introducing a potential bias that might influence the results of the hemodynamic parameters. However, the association between SVi and adverse outcomes remained significant in the treatment-naïve group.

Although these findings require prospective validation before incorporation into pediatric PAH guidelines, the association between lower SVi and adverse outcomes and the identification of a threshold of 33 mL/m^2 support further investigation of SVi as a potential component of pediatric PAH risk assessment.

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