Shape of Pulmonary Artery Doppler Flow Profile and Right Ventricular Hemodynamics in Neonates

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Objectives To characterize pulmonary artery Doppler flow profile (PAFP) patterns among infants receiving care in neonatal intensive care units and to examine the association of PAFP patterns with pulmonary and right ventricular (RV) hemodynamics.

Study design This is a retrospective study at 2 tertiary intensive care units over 4 years that included neonates who demonstrated a complete tricuspid regurgitation envelope on targeted neonatal echocardiography. Separate personnel reviewed TNEs to characterize PAFP patterns, divide cohort into PAFP groups, and measure quantitative indices of RV hemodynamics (RV systolic pressure, pulmonary artery acceleration time and its ratio with RV ejection time, tricuspid annular plane systolic excursion, and RV output), for intergroup comparisons.

Results We evaluated TNEs from 186 neonates with median gestational age of 28.5 weeks (IQR, 25.9-35.9 weeks). Four distinct PAFP patterns were identified (A) near-isosceles triangle (22%), (B) right-angled triangle (29%), (C) notching (40%), and (D) low peak velocity (<0.4 m/s; 9%). Groups A-C demonstrated a stepwise worsening in all indices of PH, whereas pattern D was associated with lower tricuspid annular plane systolic excursion and RV output. Using common definitions of pulmonary hypertension (PH), pattern A performed best to rule out PH (sensitivity range, 81%-90%) and pattern C for diagnosing PH (specificity range, 63%-78%).

Conclusions Inspection of PAFP is a simple bedside echocardiography measure that provides clinically meaningful information on underlying RV hemodynamics and may aid in screening and monitoring of patients for PH in intensive care units. *(J Pediatr 2024;266:113864)*.

Pulmonary hypertension (PH) is a major complication of prematurity and frequently encountered in tertiary neonatal intensive care units (NICUs).[1-3] Although the gold standard investigation for diagnosing and characterizing the severity of PH is right heart catheterization, it cannot be used routinely in neonatal practice because of its invasive nature and high risk of complications.[3,4] Moreover, some studies have shown that foregoing catheterization before the initiation of therapy could be a reasonable strategy.[4,5] In NICUs, echocardiography is considered the modality of choice to diagnose and monitor PH and related right ventricular (RV) hemodynamics.[1-4,6-8] On echocardiography, calculation of RV peak systolic pressure (RVSP) by measuring peak tricuspid regurgitation jet velocity (TRJV) is usually considered as the first-line method in evaluation for PH.[1-4,6-8] However, a complete TRJV envelope is often not available for interrogation, prompting use of alternate echocardiography indices.[6,7] Although several known echocardiography markers for PH have been described for clinical use in neonates, most remain untested in validation studies.[1]

One such relevant marker is the shape of the pulmonary artery Doppler flow profile (PAFP), which is known to vary with the presence and severity of PH in older patients.[9-12] Under physiological conditions, PAFP demonstrates an acceleration and deceleration phase, which resembles a near-isosceles triangular shape.[9-12] With increasing afterload, the RV ejection's acceleration phase shortens, and the deceleration phase lengthens, which resembles a right-angled triangular shape. Further, greater resistance across the pulmonary vascular bed may cause a reflective wave of blood partway through the RV ejection, producing a notched PAFP shape. In adult patients, the occurrence of a notched PAFP is indicative of increased pulmonary vascular resistance (PVR) measured invasively, with a midsystolic notch showing a specificity and sensitivity of 96% and 71%, respectively, for diag-

NICU	Neonatal intensive care unit	RVET	Right ventricular ejection time
PAAT	Pulmonary artery acceleration time	RVSP	Right ventricular systolic pressure
PAFP	Pulmonary artery Doppler flow profile	SBP	systolic blood pressure
PDA	Patent ductus arteriosus	TAPSE	tricuspid annular plane systolic excursion
PH	Pulmonary hypertension	TNE	Targeted neonatal echocardiography
PVR	Pulmonary vascular resistance	TRJV	Tricuspid regurgitation jet velocity
RV	Right ventricular		
RVO	Right ventricular output		

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nosing PH (defined as PVR ≥5 Wood units).[9-12] Although PAFP is a simple tool that can be easily obtained in most patients and is suitable for bedside application in NICUs, the type of PAFP profiles seen in neonates and their relationship with pulmonary pressures and RV hemodynamics are not understood fully.

The overall goal in this project was to examine the usefulness of PAFP shape patterns in the assessment of pulmonary and RV hemodynamics in neonates. Our specific objectives were to (1) identify different PAFP patterns in neonates that underwent echocardiograms in our NICU and had a complete TRJV envelope, (2) examine the association between different PAFP patterns and RVSP and RV performance, (3) calculate sensitivity and specificity for PAFP patterns in diagnosing PH and severe PH, predefined by RVSP thresholds, and (4) examine inter-rater reliability for categorizing PAFP shape patterns. We hypothesized that PAFP shape patterns would differ based on the presence or absence of PH and its severity in neonates.

Methods

Design and Patient Selection

A retrospective cohort study was conducted at the tertiary NICUs of the Mount Sinai Hospital and the Hospital for Sick Children, University of Toronto, over a 4-year period (January 2014 to December 2017), when both units had an established in-house targeted neonatal echocardiography (TNE) program.[13] The study was approved by the institutional research ethics boards.

We included all infants who had a TNE during the study period, with the presence of a complete envelope of tricuspid regurgitation to allow estimation of RVSP and availability of a pulse wave Doppler obtained at the level of pulmonary valve to allow characterization of PAFP in the same TNE. Neonates with congenital structural or genetic anomalies, except for patent ductus arteriosus (PDA) and patent foramen ovale, were excluded. Eligible patients were identified by reviewing all electronically archived TNE reports, and the review of TNEs and health charts for those with reported RVSP on reports. Only the first eligible scan for each patient was included for analysis to avoid bias from interdependency of repeat measures.

Echocardiography Methods

All TNEs were performed with a GE Vivid E9 ultrasound machine (GE Healthcare) and a 6- or 12-MHz sector probe, using a modified standard imaging protocol informed by the American Society of Echocardiography guidelines,[13,14] and saved in RAW data format. For this study, included TNEs were reanalyzed on a dedicated workstation (EchoPAC version BT10; GE Healthcare), to measure the predefined variables related to pulmonary and RV hemodynamics. The TNE analyses was carried out in 2 phases, performed by separate personnel while remaining blinded to each other's results: (i) measurement of quantitative indices and (ii) assessment and categorization of PAFP. The quantitative indices included calculation of RVSP from TRJV (direct measure of pulmonary pressures), ratio of RVSP to systolic blood pressure (a measure of pulmonary pressures in relation to systemic), pulmonary artery acceleration time (PAAT; an indirect measure with lower value indicating relatively higher PVR), ratio of RV ejection time (RVET) and PAAT (an indirect measure with higher value indicating relatively higher PVR), tricuspid annular plane systolic excursion (TAPSE; a measure of RV longitudinal systolic function with higher value indicating better function) and RV output (RVO; a measure of global pump function). All analyses were performed using standard published methods (detailed methods provided in the **Appendix**; available at www.jpeds.com).[14-20] In addition, we also recorded presence or absence of significant PDA, defined as a PDA of ≥1.5 mm in diameter shunting from left to right. This process facilitated subgroup comparison because a left-to-right shunting PDA may affect the relationship between PAFP and markers of PH and RV hemodynamics.

To facilitate an unbiased assessment of PAFP, the cleanest pulsed wave Doppler trace from each TNE was saved as an image file, labelled with study ID, for later assessment. The shapes of PAFP that may be encountered in neonatal practice are not known fully. Therefore, as a first step, study personnel independently inspected and characterized all study traces to define distinct patterns, informed in part by previous studies in adult and pediatric patients.[9-12,21] Subsequently, different study personnel used the identified categories and classified TNEs into relevant PAFP groups. PAFP was observed in long and short parasternal and apical RV 3-chamber views, and when multiple PAFP shapes were observed on the same TNE, the pattern considered most severe was used for classification. The personnel involved in the initial overall PAFP characterization and subsequent classification of patients into different PAFP groups worked independent of each other and remained blinded to the results of the quantitative analysis.

Robust validated definition of PH and severe PH are not established for neonates. Hence, for this study we used the following commonly used definitions: (i) RVSP of ≥40 mm Hg, (ii) RVSP:SBP of ≥0.5 (pulmonary pressure at or higher than half-systemic), and for severe PH, and (iii) RVSP:SBP of ≥1.0 (systemic or suprasystemic PH).[1,3,22]

Statistical Analyses

All study data were entered into a Microsoft Excel spreadsheet and statistical analysis were done using STATA13. Patient demographics and quantitative echocardiography data were assessed for normality using skewness/Kurtosis test and presented as mean ± SD or median (IQR), as appropriate. The study cohort was divided into 4 groups based on the qualitative categorization of PAFP patterns observed. Intergroup comparisons were performed to examine the associations between PAFP pattern (group) and measured quantitative indices (RVSP, RVSP:SBP, PAAT, RVET:PAAT, TAPSE, and RVO), using the *t* test

or Wilcoxon rank-sum test for continuous variables and the χ^2 test or Fischer's exact test for categorical variables, as appropriate. Similar analyses were performed for the subgroup of patients without significant PDA. As relevant, the sensitivity and specificity of PAFP patterns were determined for diagnosing or ruling out PH/severe PH using probability statistic. A P value of <.05 was considered statistically significant.

The intra- and interobserver agreement for categorizing PAFP patterns were assessed using the Cohen's Kappa method.[23,24] For intraobserver agreement, 1 observer categorized 50 randomly selected Doppler trace images on 2 separate occasions 8 weeks apart to avoid recall bias. Two observers categorized the same 50 images independently for assessing the interobserver agreement. The latter was assessed between 2 observers fully trained in TNE, and between a TNE-trained and an untrained novice observer. Kappa values were categorized as almost perfect agreement (0.81-1.00), substantial (0.61-0.80), moderate (0.41-0.60), fair (0.21-0.40), and none to slight (0.01-0.20).[24]

Results

Between January 2014 and December 2017, we identified 194 infants who had a TNE with a complete envelope of TRJV to calculate RVSP. Of these, 8 patients were excluded on account of TNE not having an image sufficient to categorize PAFP. The median gestational age and weight at birth for the final cohort were 28.5 weeks (IQR, 25.9-35.9 weeks) and 1100 g (IQR, 760-2380 g), respectively, and at TNE evaluation were 32.9 weeks (IQR, 28.6-38.0 weeks) and 1650 g (IQR, 890-2916 g), respectively. The cohort demonstrated a median RVSP of 42 mm Hg (IQR, 35-53 mm Hg) . There were 4 distinct PAFP patterns identified, as follows: group A, with near-isosceles triangular shape PAFP (slow and near equal time of flow acceleration and deceleration); group B, with near right-angled triangular shape PAFP (shorter acceleration and longer deceleration phase); group C, presence of mid or late systolic notch; and group D, low velocity flow (peak velocity of PAFP trace of <0.4 m/s) (**Figure**). Patients in group D demonstrated low peak velocity across all beats in the Doppler trace and were classified as such, irrespective of the PAFP shapes. In contrast, in traces classified as groups A-C, all beats had a peak velocity of >0.4 m/s.

Intergroup comparison

Comparison of baseline characteristics revealed group A infants to be relatively less mature at birth and less frequently had a significant PDA at the time of TNE in comparison to other groups (**Table I**). Infants with a group D pattern (low velocity PAFP) had TNE evaluation performed at a young postnatal age; 94% of traces occurring within the first 3 days of birth and in the context of TNEs performed for acute PH. The notched PAFP patterns were observed in TNEs performed at a relatively advanced postnatal age. On comparison of quantitative TNE indices measured for this study, a stepwise increase in RVSP was observed from groups A-C, before it lowered for group D (**Table II**). The PAAT, RVSP:SBP and RVET:PAAT ratios also demonstrated incremental worsening from group A to group C. Group D had PAAT similar to group C; however, it was also associated with lower TAPSE and RVO. Analysis stratified by the presence or absence of significant PDA (diameter of ≥1.5 mm with left to right shunt) showed similar associations as for the whole cohort (**Table III**).

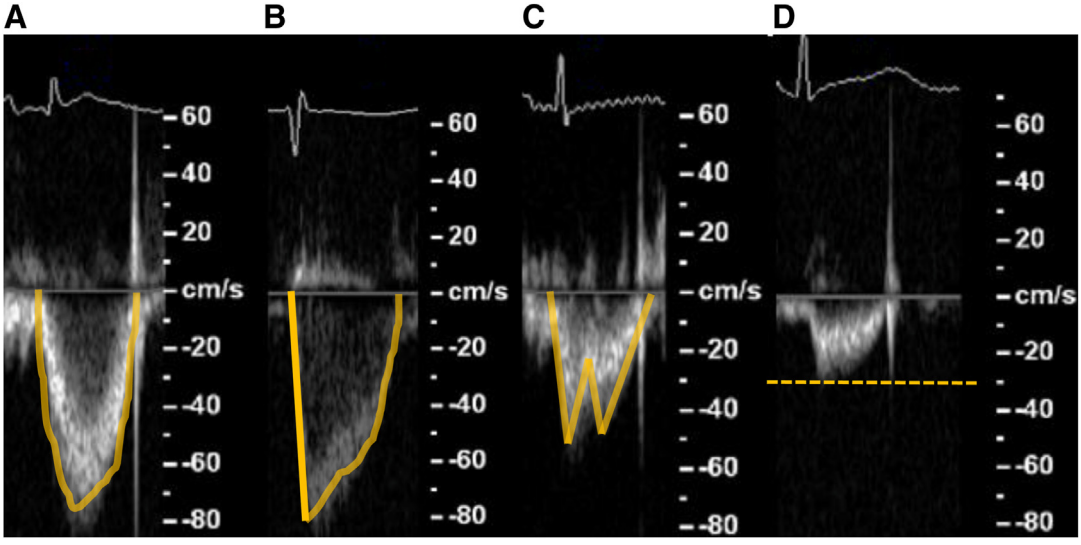

Figure. Illustration of the four distinct patterns categorized, as acquired using a pulsed wave doppler tracing from the RV outflow tract at the level of the pulmonary valve. **(A)** Group A. Near-isosceles triangular shape. **(B)** Group B. Near right-angled triangular shape (slope of flow acceleration qualitatively of shorter duration than deceleration). **(C)** Group C. Presence of mid or late systolic notch. **(D)** Group D. Low flow (peak flow velocity of <0.4 m/s).

Table I. Baseline demographics of the different groups

Characteristics	Overall population (n = 186 [100%])			
	Group A (n = 41 [22%])	Group B (n = 54 [29%])	Group C (n = 74 [40%])	Group D (n = 17 [9%])
Gestational age at birth, weeks	26.6 (24.7-29.3)	28.6* (26.3-35.9)	30.8* (26.6-37.7)	28.4 (25.4-31)
Weight at birth, g	860 (660-1210)	1010* (780-2360)	1345* (800-3050)	1080 (810-1580)
Gesta tional age at TNE, weeks	29.9 (28.9-36.1)	30.4 (27.4-37.9)	35.6*† (30.6-39.4)	28.4‡ (27-31.1)
Weight at TNE, g	1310 (870-2500)	1310 (800-2450)	2200*† (1330-3180)	1080‡ (800-1580)
Day of life at TNE, days	13 (4-52)	4 (2-13)	6 (3-36)	1 (1-3)
SBP at TNE, mm Hg	61 (51-77)	53* (40-66)	63† (55-74)	50*‡ (45-55)
Sex: Male	26 (63)	31 (57)	42 (57)	8 (47)
Invasive ventilation at TNE	23 (56)	17* (32)	21* (28)	3* (18)
PDA with diameter ≥ 1.5 mm	14 (34)	30* (56)	40* (54)	9 (53)

Group A, near-isosceles triangular shape; *Group B*, near right-angled triangular shape; *Group C*, presence of mid or late systolic notch; *Group D*, peak flow velocity < 0.4 m/s.
Values are median (IQR) or number (%).
*$P < .05$ vs A.
†$P < .05$ vs B.
‡$P < .05$ vs C.

Diagnostic characteristics for PH

Given the observed association between group D pattern and low RV function, probabilistic analyses were restricted to the other 3 groups. Using study definitions of RVSP of ≥40 mm Hg, RVSP:SBP of ≥.5 and RVSP:SBP of ≥1.0, the group A PAFP pattern demonstrated the greatest discriminatory ability to rule out a diagnosis of PH, with sensitivity of 90% (95% CI, 86%-95%), 81% (95% CI, 75%-87%), and 88% (95% CI, 83%-93%), respectively, for the 3 definitions examined. In contrast, the group C pattern performed best to diagnose PH, with a specificity of 78% (95% CI, 72%-85%), 73% (95% CI, 67%-80%), and 63% (95% CI, 55%-70%), for respective definitions. The corresponding sensitivities, however, were low at 59% (95% CI, 52%-66%), 48% (95% CI, 40%-55%), and 59% (95% CI, 52%-67%), respectively. The group B pattern demonstrated only moderate performance for ruling out suprasystemic PH (sensitivity, 71%; 95% CI, 65%-78%).

Inter-rater agreement

The agreement between TNE-trained observers was excellent for both interobservers (Kappa, 0.91; 95% CI, 0.86-0.96; 94% agreement) and intraobservers (Kappa, 0.91; 95% CI, 0.86-0.96; 94% agreement). However, the interobserver agreement between trained and untrained observers was only moderate (Kappa, 0.61; 95% CI, 0.52-0.69; 72% agreement).

Discussion

In our cohort of neonates receiving neonatal intensive care, a simple visual inspection of the pulmonary artery Doppler flow pattern on echocardiography was reliable between experienced TNE operators and may aid in identifying underlying pulmonary and RV hemodynamics. Specifically, we identified four distinct PAFP patterns across a range of RVSP. The first 3 patterns correlated linearly with increasing pulmonary pressures, whereas the fourth (low velocity PAFP) was associated with reduced TAPSE (RV longitudinal systolic function) and lower RVO. Further, these associations were found both in the presence or absence of a significant left to right shunting PDA, a common potential confounder in preterm neonates.

Acute and chronic pulmonary hypertensive disorders are frequently encountered in tertiary neonatal practice and are associated with adverse clinical outcomes. Given the constraints of clinical examination and the nonspecific nature of symptoms in this patient population, bedside echocardiography has remained the clinical investigation of choice for the diagnosis and longitudinal monitoring of disease progression.[25] There has been an increasing emphasis on developing, adapting, and understand the applications of echocardiographic indices related to pulmonary and RV hemodynamics in older patients.[26,27] Although several

Table II. Echocardiography measurements of the groups in the overall population

Variables	Overall population (n = 186 [100%])			
	Group A (n = 41 [22%])	Group B (n = 54 [29%])	Group C (n = 74 [40%])	Group D (n = 17 [9%])
RVSP, mm Hg	34.8 (31.2-39.2)	41.5* (36-48.4)	53.3*† (42.3-66.6)	37.9‡ (30.2-45.4)
RVSP/SBP, %	0.53 (0.43-0.72)	0.80* (0.62-0.96)	0.88* (0.63-1.1)	0.75* (0.57-0.96)
RVET/PAAT, %	3.3 (2.6-4.3)	3.9 (3.2-4.4)	4.9*† (3.9-5.7)	4.3* (3.8-4.5)
PAAT, ms	52 (41-77)	44* (38-53)	37*† (32-45)	34*† (31-36)
TAPSE, mm	6.7 (5.9-9.2)	6.9 (5.4-7.8)	7.0 (6.0-8.4)	4.5*†‡ (3.7-5.1)
RVO, mL/kg/min	230 (190-276)	209 (147-300)	225 (157-273)	106*†‡ (92-135)

Group A, near-isosceles triangular shape; *Group B*, near right-angled triangular shape; *Group C*, presence of mid or late systolic notch; *Group D*, peak flow velocity < 0.4 m/s.
Values are median (IQR).
*$P < .05$ vs A.
†$P < .05$ vs B.
‡$P < .05$ vs C.

Table III. Echocardiography measurements of the groups in the 2 subgroups, one with a closed PDA and the other with an open PDA

	Patient with PDA ≥1.5 mm (n = 93 [50%])				Patient without PDA ≥ 1.5 mm (n = 93 [50%])			
Variables	Group A (n = 14 [15%])	Group B (n = 30 [32%])	Group C (n = 40 [43%])	Group D (n = 9 [10%])	Group A (n = 27 [29%])	Group B (n = 24 [26%])	Group C (n = 34 [37%])	Group D (n = 8 [9%])
RVSP mm Hg	37.7 (31.2-45.6)	45.3 (38.6-49.8)	53.3*† (45.9-61.9)	42.1‡ (31.3-43.3)	34.8 (29.1-37.1)	39.2* (32.5-44.1)	52.8*† (39.7-72.3)	36.3‡ (30.0-50.2)
RVSP/SBP, %	0.81 (0.64-0.78)	0.88 (0.77-0.97)	0.93* (0.72-1.0)	0.82 (0.71-0.94)	0.48 (0.42-0.61)	0.64* (0.48-0.87)	0.74* (0.58-1.2)	0.63* (0.57-0.98)
RVET/PAAT, %	3.7 (3.2-4.3)	4 (3.2-5.1)	4.2* (3.7-5.6)	4.3* (4.2-4.4)	3.1 (2.5-4.2)	3.7 (3.0-4.2)	5.2*† (4.2-5.8)	3.9 (3.1-4.9)
PAAT, ms	47 (41-58)	41* (34-48)	38*† (32-44)	33* (27-35)	62 (41-90)	49 (40-61)	35*† (32-45)	36*† (31-37)
TAPSE, mm	6.5 (5.6-6.7)	7.2 (5.9-7.9)	6.9 (6.0-8.1)	4.5*†‡ (3.7-5.1)	8.5 (6.1-9.5)	6.3* (3.8-7.4)	7.5 (6.5-8.6)	4.6*†‡ (3.6-4.9)
RVO, mL/kg/min	202 (177-230)	248 (170-335)	214 (148-272)	94*†‡ (82-118)	249 (199-312)	191* (145-235)	230 (167-274)	121*‡ (100-187)

Group A, near-isosceles triangular shape; *Group B*, near right-angled triangular shape; *Group C*, presence of mid or late systolic notch; *Group D*, peak flow velocity < 0.4 m/s.
Values are median (IQR).
*$P < .05$ vs A.
†$P < .05$ vs B.
‡$P < .05$ vs C.

quantitative indirect echocardiographic measures are used in neonates, efforts to validate and establish specific thresholds related to adverse outcomes are still underway.[28,29] In typical neonatal practice, the assessment of RVSP and ductal shunt characteristics are used as the first-line measures for PH assessment. However, these modalities are often not available, particularly late in the postnatal course, which underlines the need to develop additional noninvasive measures.[30,31] If validated, visual inspection of PAFP could be a simple and quickly acquired qualitative measure for bedside application in neonates receiving intensive care.

Alterations in PAFP shape have been recognized to reflect underlying PVR and are well-studied and incorporated in clinical guidelines for assessing older patients with PH.[32] Under pathological conditions, as the RV gets pressure loaded with reduced pulmonary arterial compliance and increased impedance, blood flow accelerates leading to a shorter time to reach peak velocity. Further, a stiff pulmonary vascular tree (reduced compliance) causes elevated pulse pressure and pulsatile afterload, and premature reflection of blood flow from the distal arteries to main pulmonary artery during systole. This process produces a Doppler pattern of deceleration of forward systolic flow in the main pulmonary artery. However, as the RV contraction continues, a second briefer period of acceleration occurs, producing a notched PAFP profile.[32,33] Among children, a relatively short PAAT is indicative of higher PVR.[16] Similarly, in adults, the presence of notching indicates high PVR and may distinguish PH occurring from pulmonary vascular disease vs secondary to left heart disease.[10,11] The types and validity of PAFP Doppler patterns in NICU patients required separate investigation owing to the inherent differences from older patients, including physiologically smaller hearts, higher heart rates, different etiologies for PH and concurrent presence of ductal shunt, all of which may affect its clinical application.[1,16,34,35] Further, in neonates, PVR is physiologically higher in the period immediately after birth and decreases over days to weeks. In otherwise well preterm neonates, the PAAT increases over the first few weeks of age.[34] In term-born healthy neonates, the PAFP pattern changes over the first 24 hours of transition after birth, with notching seen in the first hour of age, which evolves into a right-angled triangular pattern by 8-12 hours and more of an isosceles triangular pattern by 24 hours of age.[36] We add to these observations through our systematic examination of PAFP patterns among neonates receiving care in the NICU and assessment of their validity relative to described patterns in adult and pediatric patients.[9-12,21]

Our observations in neonates demonstrate several similarities with investigations by Lopez-Candales and Edelman who also recognized 4 distinct patterns from 120 adult patients with PH.[12] Patterns I and II were visually comparable with the isosceles and right-angled triangular shapes, respectively. They described pattern III as mid-systolic notching; however, we found distinguishing mid vs late-systolic notching challenging in neonates, possibly owing to their higher heart rates, and instead recorded presence of any systolic notching. Last, they described pattern IV as reduction in signal volume resulting in a spiked appearance, whereas we found the presence of a low peak velocity (<0.4 m/s) to be the unifying feature where the Doppler shape may be variable. Although we were able to describe the PAFP patterns observed in NICU patients and establish their relevance to RV and pulmonary hemodynamics, the relative specificity of notched pattern to diagnose PH was lower than what has been described in studies in adults and children.[10,11] This result may be due to the use of echocardiography-derived RVSP as our comparator instead of cardiac catheterization used in adult and pediatric studies. This is a practical limitation of studies involving newborn infants. In

comparison with invasive assessment, RVSP measured on echocardiography has been shown to be overestimate pulmonary artery systolic pressure.[3] Further, RVSP is expected to underestimate pulmonary pressures in the presence of RV systolic dysfunction, as we also found in group D.

Unlike previous studies in adult patients where a stepwise increase in pulmonary artery systolic pressure across 4 patterns was also associated with progressive decreases in TAPSE, we found decreased TAPSE and RVO only in association with low velocity traces, even though there was a stepwise increase in pulmonary pressures across all patterns. This observation may reflect the differences between patient populations and underlying etiology of PH. For instance, we found that group D traces typically occurred in acutely sick neonates, early in their postnatal course, and in the context of persistent PH of the newborn. In contrast, groups B and C patterns were seen more often later in the postnatal course in the context of chronic pulmonary vascular changes. It is also our anecdotal experience that, unlike acute PH, overt RV systolic dysfunction and low RVO are uncommon in the context of chronic PH in neonates, other than in decompensated end-stage disease. However, it is important to note that we only used select echocardiographic markers that may identify gross RV systolic dysfunction (TAPSE, RVO). Other parameters, such as longitudinal strain and strain rates, and tissue Doppler imaging were not evaluated and may be more sensitive to subtle alterations in RV function in relation to PAFP patterns. Although our data indicate that low velocity traces could alert clinicians to the underlying RV systolic dysfunction, PAFP patterns do not reflect cardiac function and should not be considered in lieu of comprehensive functional assessments.

Our study results should be interpreted in the context of other limitations. Because our goal was to understand PAFP patterns in neonates and their physiological relationship with pulmonary pressures and overt RV systolic function, only 1 TNE was included per patient. Future studies should examine the usefulness of PAFP patterns for longitudinal monitoring. Further, the relationship between presence of different PAFP patterns, their change over time, and relevant clinical outcomes need investigation. Additionally, our probabilistic analyses may be limited by the inclusion of only neonates who demonstrated a complete TR envelope to allow calculation of RVSP. We could not examine patients with lower pulmonary pressures; our study only had 6 infants with an RVSP of <25 mm Hg. However, this factor reflects pragmatic neonatal practice, where most patients do not demonstrate a full TR envelope and where PAFP may be a useful adjunctive qualitative measure. Similarly, in neonates, >1 PAFP pattern may be present on the same trace, which may have affected our analyses. We are also unable to comment whether PAFP patterns can help to distinguish PH owing to pulmonary vascular disease from other causes such as flow-driven PH or from left heart dysfunction. Unlike in older patients, most PH seen in neonates occurs in the context of an acute or chronic increase in PVR. Hence, alternate pathophysiologies are likely to be underrepresented in our cohort. Last, the interaction between level of operator experience and impact of education on reliability of identifying PAFP needs examination to optimize its use in the clinical setting.

In conclusion, this study suggests that, similar to previous work in adult patients with PH, visual inspection of pulmonary artery Doppler waveform on echocardiography may provide clinically meaningful information on the underlying pulmonary and RV hemodynamics in neonates receiving care in NICUs. We recognized four distinct PAFP patterns in neonates, indicating a stepwise increase in pulmonary pressures and the fourth pattern also indicating reduced RV systolic function. The PAFP profile is a simple bedside tool that may aid in routine screening and monitoring of neonates for PH when measurement of RVSP is not feasible. ■

Declaration of Competing Interest

The authors declare no conflicts of interest.

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