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Assessment of Pulmonary Hypertension in the Pediatric Catheterization Laboratory:

Current Insights From the Magic Registry

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Abstract

Objectives—To assess protocols, demographics, and hemodynamics in pediatric patients undergoing catheterization for pulmonary hypertension (PH).

Background—Pediatric specific data is limited on PH.

Methods—Review of the Mid-Atlantic Group of Interventional Cardiology (MAGIC) collaboration PH registry dataset.

Results—Between November 2003 and October 2008, seven institutions submitted data from 177 initial catheterizations in pediatric patients with suspected PH. Pulmonary arterial hypertension associated with congenital heart disease (APAH-CHD) ($n = 61$, 34%) was more common than idiopathic PAH (IPAH) ($n = 36$, 20%). IPAH patients were older with higher mean pulmonary arterial pressures (mPAP) ($P < 0.01$). Oxygen lowered mPAP in patients with IPAH ($P < 0.01$) and associated PAH not related to congenital heart disease (APAH-non CHD) ($P < 0.01$). A synergistic effect was seen with inhaled Nitric Oxide (iNO) ($P < 0.01$). Overall 9/30 (29%) patients with IPAH and 8/48 (16%) patients with APAH-non CHD were reactive to vasodilator testing. Oxygen lowered pulmonary vascular resistance index (PVRI) in patients with APAH-CHD ($P < 0.01$). There was no additive effect with iNO but a subset of patients required iNO to lower PVRI below 5 WU·m². General anesthesia (GA) lowered systemic arterial pressure ($P < 0.01$) with no difference between GA and procedural sedation on mPAP or PVRI. Adverse events were rare ($n = 7$) with no procedural deaths.

Conclusions—Pediatric patients with PH demonstrate a higher incidence of APAH-CHD and neonatal specific disorders compared to adults. Pediatric PH patients may demonstrate baseline mPAP < 40 mm Hg but > 50% systemic illustrating the difficulty in applying adult criteria to children with PH. Catheterization in children with PH is relatively safe.

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Keywords

pulmonary hypertension; pediatric; cardiac catheterization; hemodynamics; vasoreactivity

INTRODUCTION

Pulmonary hypertension comprises a heterogeneous spectrum of diseases sharing the final common path way of elevated PAP and ultimately progression to right heart failure [1–3]. Several large, multi-center registries have focused on adults [4–9]. By comparison childhood PH is poorly defined with a different disease spectrum [5,10]. Importantly, several neonatal disorders are commonly associated with PH and are not represented in adult registries [11–14].

Cardiac catheterization with vasodilator testing is necessary for diagnosis, treatment stratification, and prognostication of PH in adults and children [1,15,16]. Adult catheterization PH protocols are widely reported but no pediatric specific catheterization protocols have been proposed. Generally adult criteria for diagnosis and adult definitions of reactivity are applied to children [16]. These definitions can be misleading as both pulmonary and systemic hemodynamics can be affected by age and the underlying disease process. Furthermore there is limited pediatric specific data on response to vasodilating agents.

The Mid-Atlantic Group of Interventional Cardiology (MAGIC) registry is a voluntary, prospective and multi-institutional congenital heart disease cardiac catheterization data registry begun in November 2003 to determine the long term outcome and safety of catheterization procedures. The MAGIC PH registry was developed within this framework. We used the registry to assess demographics, hemodynamics, and catheterization protocols for pediatric patients undergoing cardiac catheterization for a suspected diagnosis of PH.

METHODS

Organization of the Registry

The PH registry dataset used for this analysis began November 1, 2003 and ended October 1, 2008 when the analysis was initiated. Patients were enrolled from seven hospital centers across the United States. The submission of cardiac catheterization data was approved by the institutional review boards of the participating hospital centers. All hospital centers used PedCath (Scientific Software Solutions, Charlottesville, VA) catheterization reporting software to export cardiac catheterization and PH data electronically in an automated manner from the medical record of each patient to the central MAGIC Database for analysis [17]. Submitted data was deidentified and included patient demographics, primary diagnosis, baseline therapy, fluoroscopy time, catheterization procedural protocols, catheterization hemodynamics at baseline and following vasodilator testing, most recent echocardiographic assessment and procedure adverse events. Primary diagnosis was selected by the submitting physician from a list of potential diagnoses. Echocardiographic assessment of tricuspid regurgitation and estimates of right ventricular pressure were specified by the submitting center and represent the most recent echocardiogram performed before or following catheterization.

Recruitment and Classification

All pediatric patients (age ≤ 18 years) undergoing an initial cardiac catheterization at the participating center for suspected PH were included for data analysis. For the purposes of

data analysis, patients were compared in three cohorts: IPAH, APAH-CHD, and APAH-non CHD. Subanalysis was performed in a cohort of patients with neonatal PH, defined as PH resulting from a disorder present in the neonatal period and including: bronchopulmonary dysplasia (BPD) related, persistent PH of the newborn, congenital diaphragmatic hernia (CDH) related, newborn gastrointestinal related (including omphalocele and gastroschisis) and PH associated with pulmonary hypoplasia.

Statistical Analysis

Standard graphing and screening techniques were used to assess for outliers. Data are presented as median (25–75% inter-quartile range) in text and tables and as means $\pm$ 1 standard error of the mean in figures. Descriptive summary statistics were calculated to describe the patient and clinical characteristics for all patients taken to the catheterization laboratory for PH assessment. Binary logistic regression was utilized to assess the relationship between age and the use of sedation and to assess for risk factors associated with adverse events. A Mann Whitney U test was used to assess the relative impact of the PH cohorts on hemodynamic variables and to assess the hemodynamic effect of vasodilator agents. The effects of general anesthesia on hemodynamics were assessed using a general linear model ANOVA in which the between subject variables were age and diagnosis. Correlation between variables was assessed using Spearman's rank test. A two-tailed *P* value less than 0.05 was considered significant. Analyses were performed using SPSS for windows (version 16.0; SPSS).

RESULTS

Overall seven institutions submitted data from 414 catheterization procedures in patients with known or suspected PH. Of those procedures, 177 were performed in pediatric patients (age $\leq$ 18 years) as the initial PH catheterization at the respective centers. Patient demographics appear in Table I.

Catheterization Protocol

Details of the catheterization protocols appear in Table II. General anesthesia (GA) was used in 75% of cases and was more common in younger patients (50 vs. 82% for GA use in patients age $>$ 5 years and $<$ 5 years respectively; *P* 0.03). Fentanyl and midazolam were the most common procedural sedation agents used in 39/46 (85%). Other agents included: midazolam alone (*n* = 2), chloral hydrate + fentanyl (*n* = 1), and propofol (*n* = 2). Vasodilator testing was performed in 94% of cases. Nitric oxide and 100% oxygen were the primary vasodilators used in 85% and 81%, respectively, with 64% of cases using a combined iNO and oxygen testing phase and 11% of cases using 100% oxygen alone. When iNO vasodilator testing was performed, 100% oxygen was used concomitantly in 81%. Nitric oxide dosing varied but most cases (81/96, 84%) used inhalation concentrations of either 20 or 40 parts per million. Other vasodilator testing agents included nifedipine (*n* = 11), prostacyclin (*n* = 11), sildenafil (*n* = 1), and a calcium channel blocker (*n* = 1). Vasodilator testing protocols were similar in the various diagnostic subsets with a three phase protocol using room air, oxygen and 100% oxygen with iNO in 74% with APAH-CHD, 69% with APAH-non CHD, and 58% with IPAH.

Diagnosis and Hemodynamics

Diagnosis, median age at catheterization and hemodynamic data are listed in Table III. APAH-CHD was the most common etiology accounting for 34% with IPAH accounting for 20%. The combined group of neonatal disorders accounted for 26% of total cases. Patients with IPAH were significantly older at the time of presentation (*P* $<$ 0.01), demonstrated higher mPAP (*P* $<$ 0.01), % systemic systolic PAP (*P* $<$ 0.01), and pulmonary vascular

resistance index (PVRI) ($P < 0.01$) than those with APAH-CHD and APAH-non CHD. Overall 64% of patients had baseline mPAP < 40 mm Hg; however, 68% of those had systolic PAP $> 50\%$ systemic pressure. In patients with APAH-CHD, diagnoses were reported in 55/61 (90%) and included: isolated secundum atrial septal defect ($n = 6$), secundum atrial septal defect in association with additional defects ($n = 18$), patent ductus arteriosus ($n = 11$), ventricular septal defect ($n = 13$), coarctation of the aorta ($n = 2$), atrioventricular septal defect ($n = 9$), partial anomalous pulmonary venous return ($n = 3$), Tetralogy of Fallot ($n = 1$), and transposition of the great arteries ($n = 3$). Eight patients with APAH-CHD were reported to have trisomy 21. History of surgical intervention was not reported in the database. A pulmonary to systemic blood flow ratio (Qp:Qs) of 1:1 was reported in 19/61 (31%). In the remaining 42 patients, median Qp:Qs was 1.30 [Distribution: 12/42 (29%) Qp:Qs < 1 ; 20/42 (48%) Qp:Qs 1–2; 7/42 (17%) Qp:Qs 2–3; 3/42 (7%) Qp:Qs > 3].

There was significant but relative poor correlation between transthoracic echocardiographic estimates of right ventricular systolic pressure based on peak tricuspid regurgitation jet and pressures obtained at catheterization ($R^2 = 0.36$, $P < 0.01$). The correlation was not improved in the subset of patients with moderate or greater tricuspid insufficiency ($R^2 = 0.38$, $P = 0.13$) but was somewhat improved in those patients in which procedural sedation was used versus GA ($R^2 = 0.45$, $P = 0.02$ for procedural sedation; $R^2 = 0.35$, $P < 0.01$ for GA).

Response to Vasodilator Testing

IPAH—Mean PAP was lowered with 100% O₂ and further lowered with the addition of iNO (Fig. 1). When defining reactivity using the older definition requiring $\geq 20\%$ decrease in both mPAP and PVRI; 12/30(40%) patients undergoing vasodilator met criteria. The more recently accepted definition of reactivity requires a decrease in mPAP by ≥ 10 mm Hg to ≤ 40 mm Hg. As many of the younger patients did not have baseline mPAP > 40 , a decrease by ≥ 10 mm Hg was considered acceptable if mean PAP was ≤ 40 mm Hg. Using this definition 9/30(29%) patients with IPAH were reactive. Significantly more patients were defined as reactive using older versus revised criteria ($P < 0.01$).

APAH-non CHD—Mean PAP was significantly lowered by 100% oxygen and further lowered with the addition of iNO (Fig. 1). This effect was less pronounced than in patients with IPAH (Change in mPAP from baseline to maximal vasodilator testing 13.0 ± 9.4 mm Hg vs. 5.2 ± 9.7 mm Hg for IPAH vs. APAH-non CHD, respectively; $P < 0.01$).

Using the older definition of reactivity, 16/48 (33%) patients undergoing vasodilator testing met criteria. Using the more recent definition, 8/48 (17%) patients were reactive. Significantly more patients were defined as reactive using older versus revised criteria ($P < 0.01$).

CHD related PH—Some form of vasodilator testing was performed in 53/60 patients with a three phase vasodilator protocol used in 40 patients. Results of vasodilator testing in this subgroup appear in Fig. 2. When compared with 100% oxygen alone, the effect of iNO $\pm$ 100% oxygen on PVRI, relative pulmonary to systemic vascular resistance (Rp:Rs), relative pulmonary to systemic blood flow (Qp:Qs), and mPAP did not reach significance. However, 12/27 (44%) patients with baseline PVRI ≥ 5 Wood units $\times$ m² demonstrated an improvement to < 5 Wood units $\times$ m² with vasodilator testing and in 4/12 (33%) this improvement was not seen until the addition of iNO. Additionally 17/33 (52%) with a baseline Rp:Rs ≥ 0.33 demonstrated an improvement in their Rp:Rs to less than 0.33 and 4/17 (24%) did not reach this threshold until the addition of iNO.

Hemodynamic Effect of General Anesthesia

After controlling for age and diagnosis, use of GA significantly lowered baseline systemic pressures and tended to lower systemic vascular resistance index (SVRI) but did not significantly affect cardiac index, mPAP or PVRI (Fig. 3).

Adverse Events

Adverse events were reported in seven patients (3.9%) and included: ventricular tachycardia requiring cardioversion ($n = 1$), supraventricular tachycardia ($n = 1$), access site complications ($n = 2$), respiratory depression requiring intubation ($n = 1$), and intramyo-cardial contrast injection ($n = 1$). There were no procedural deaths reported. Mean fluoroscopy time was 21.8 ± 16.2 min. Risk of any adverse event was associated with baseline mPAP ($P = 0.02$) and percent systemic PAP ($P = 0.02$) but was not associated with age, fluoroscopy time, baseline PVRI, or cardiac index.

CONCLUSIONS

We report the first analysis of a pediatric specific PH registry for children undergoing cardiac catheterization. The major findings include a lower incidence of idiopathic PAH and a higher incidence of shunt related and neonatal specific PH than that reported in adult registries [4–9]. Most patients (64%) demonstrated baseline mPAP < 40 mm Hg but PAP were $> 50\%$ systemic in the majority of those patients. We evaluated response to vasodilating agents and demonstrate a significant pulmonary vasodilatory response to 100% oxygen. An additive effect was seen with iNO in patients with IPAH and APAH-non CHD. A lower percentage of patients were defined as reactive using revised versus older criteria for vasoreactivity. When compared with adult data, a higher percentage of pediatric patients with idiopathic PAH meet criteria for vasoreactivity. GA affected systemic hemodynamics but we found no difference between GA and procedural sedation on pulmonary hemodynamics. Finally, we describe the catheterization protocols utilized by the PH centers contributing to this registry.

PH Demographics and Hemodynamics

Data gathered from large multi-center registries has contributed significantly to our understanding of PH. However, none of the published reports have focused on pediatric patients. As we demonstrate, the spectrum of PH is different in children. In the most recent large scale adult PH registry, IPAH accounted for 39.2% of all cases with APAH-CHD accounting for 11.2% [6]. In this registry APAH-CHD was the most common diagnosis (34%). Neonatal specific disorders are obviously underrepresented in adult PH registries but account for more patients in this registry than IPAH (26% vs. 20%). As catheterization is not routinely performed for many neonatal specific causes of PH, it is likely that these data actually underestimate the prevalence of neonatal specific PH. Nonetheless this is not a benign subset of disorders. BPD related PH was the most common neonatal specific indication for cardiac catheterization and persistent echo evidence of PH has been associated with up to 40% mortality in this patient population [18].

Catheterization Lab Protocols

No standardization of catheterization laboratory protocols exists for pediatric PH. In this analysis, we report on the protocols used by seven pediatric catheterization labs with experience in the management and assessment of pediatric pulmonary hypertension. Broad generalizations include: (1) A preference for GA, particularly in younger patients. (2) A tendency to perform right as well as left heart catheterization for the initial assessment. (3) Use of a vasodilator testing protocol including 100% oxygen and iNO at a preferred dose of

20–40 parts per million. (4) Similar vasodilator testing protocols irrespective of diagnostic subgroup. Although some standardization of catheterization protocols is appropriate, the broad spectrum of childhood disease requires consideration. For example pulmonary vein stenosis is well described in congenital diaphragmatic hernia, congenital heart disease and bronchopulmonary dysplasia related PH and needs to be actively assessed in these populations [19].

Hemodynamic Assessment and Response to Vasodilator Testing

Hemodynamic interpretation must also consider the childhood spectrum of PH. Mean PAP measurements can be easily compared in adult patient populations, but in children there is age related variability. Indexed measurements such as pulmonary vascular resistance or relative values such as $R_p:R_s$ or % systemic PAP may be more useful in the pediatric population. Indeed Douwes et al. recently reported that relative values including $R_p:R_s$ and the ratio of PAP to systemic arterial pressure predict survival in children with PH [20].

Hemodynamic response to vasodilator testing has not been well studied in the pediatric PH population with the exception of patients with APAH-CHD [21]. In adult patients with IPAH, vasodilator testing is widely used as assessment of reactivity is useful for prognostic and therapeutic decision making [1,3,22]. Vasodilator testing protocols in pediatric patients have been extrapolated from adult data [23]. Previously reactivity for adults was defined as a >20% decrease in PVR and mPAP [24]. More recently vasoreactivity has been defined as a decrease in mPAP by ≥ 10 mm Hg to ≤ 40 mm Hg [25]. We assessed both definitions. In this pediatric specific cohort almost 2/3rds did not demonstrate baseline mPAP >40 mm Hg but were considered reactive if mPAP decreased by ≥ 10 mm Hg. Significantly more patients were considered reactive when using the older versus the newer definition of vasoreactivity. This was true for the overall cohort and also for the subset of patients with IPAH. This variability is consistent with the adult literature [26].

In the adult population, most reports suggest that between 10 and 15% of patients with IPAH will respond to vasodilator testing [27–29]. More patients demonstrated reactivity in this pediatric specific cohort. Further data is needed to determine if these patients may benefit from calcium channel blocker therapy or different treatment algorithms but it is enticing to speculate that earlier diagnosis and intervention may improve long term outcomes.

Different reactivity criteria are used in children with unrepaired congenital heart disease as shunting affects PAP response to vasodilator challenge [30–33]. Relative pulmonary to systemic vascular resistance and change in this ratio with vasodilator testing are considered important criterion for reactivity. In the INOP trial, Balzer et al. assessed the value of iNO in combination with 100% oxygen for preoperative assessment of vasoreactivity. They noted improved sensitivity and specificity when using an absolute value rather than % change using oxygen + iNO compared to oxygen alone [21]. Our results are consistent with this finding as a number of patients did not demonstrate an improvement in PVRI or relative $R_p:R_s$ below thresholds of the INOP study until the addition of iNO to the vasodilator regimen. Nonetheless, a specific range for operative safety remains difficult to precisely define and an element of clinical subjectivity is inevitably required.

The hemodynamic effect of anesthesia has not been well defined in pediatric patients with PH. In this database, most cases were performed under GA, particularly in the younger patients. Interestingly, in this nonrandomized assessment, GA seemed to affect systemic hemodynamics but not pulmonary hemodynamics. Standardization of anesthesia protocols would be useful, particularly if relative indicators such as percent systemic and $R_p:R_s$ are used to assess relative severity of disease.

Adverse Events

Few adverse events were reported in this registry with no procedural deaths. Carmosino et al. reviewed perioperative complications in pediatric patients with PH and noted a 5% incidence of major complications including a 1.4% mortality rate in patients undergoing cardiac catheterization [34]. Our adverse event rate is demonstrably lower, but it is possible that the design of the registry resulted in under-reporting of adverse events as the primary proceduralist was generally responsible for data input. It is unlikely that procedural deaths were underreported. These data are consistent with adult data where procedural mortality related to diagnostic catheterization for PH is very low [35]. Our data are also consistent with prior reports suggesting that baseline PH severity is the best predictor of adverse events [34]. Young age and pulmonary hypertension are both independent risk factors for serious adverse events and catheterization should be approached cautiously, particularly in patients with suspected severe disease.

Limitations of this study include the reliance of the registry on individual centers to submit data in a consistent and reliable fashion. Additionally all clinical decisions were made at the discretion of the primary proceduralist including the decision to proceed with cardiac catheterization, design of catheterization protocols including estimation of flow and shunts, as well as data interpretation. Furthermore diagnoses were defined by the submitting centers. Thus there is heterogeneity in the data but this also contributes to the real world applicability. We also do not report on long term outcomes. Overall the relative ease of data entry and the ability to capture all hemodynamic data make the MAGIC registry a useful tool for assessing demographics but limit interpretability of outcomes due to selection bias.

In summary, we present data from a large, multicenter PH catheterization registry. We demonstrate a different patient demographic than that reported in adult studies with a higher incidence of APAH-CHD and neonatal specific disorders. Overall catheterization was well tolerated with few adverse events and no mortality. Pediatric patients with IPAH demonstrate a higher incidence of reactivity than reported in adult studies. Diagnostic protocols varied by center and consensus based standardization could enhance our ability to track and better understand and treat pediatric PH. Our data suggest a preference for a three phase vasodilator testing protocol with use of 100% O₂ and iNO at a preferred dose of 20–40 ppm. Furthermore, our data suggest that indexed measurements such as pulmonary vascular resistance or relative values such as Rp:Rs or percent systemic PAP may be more useful in the pediatric population. Clearly pediatric specific prospective data are needed to improve our understanding of the pathogenesis of pediatric pulmonary hypertension.

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Fig. 1.

Effect of vasodilator testing in patients with noncongenital heart disease associated pulmonary hypertension. Data represent mean $\pm$ SEM; Idiopathic PAH represents idiopathic pulmonary arterial hypertension, Associated PAH - non CHD represents associated pulmonary arterial hypertension not related to congenital heart disease, PAP represents pulmonary arterial pressure, PVRI represents pulmonary vascular resistance index, WU represents Wood Units, NO represents Nitric Oxide.

Fig. 2.

Effect of vasodilator testing in congenital heart disease related pulmonary hypertension. Data represent mean $\pm$ SEM. PVRI represents pulmonary vascular resistance index. NO represents nitric oxide. WU represents Wood Units. Rp:Rs represents the ratio between pulmonary and systemic vascular resistance. Qp:Qs represents the ratio between pulmonary and systemic blood flow. The Qp:Qs data represents the subset with CHD related PH and residual shunts.

Fig. 3.

Effect of anesthesia on systemic versus pulmonary hemodynamics. When compared with procedural sedation, general anesthesia significantly affects systemic but not pulmonary hemodynamics. Data represent generalized marginal mean $\pm$ SEM after controlling for age. DSAo SBP represents descending aorta systolic blood pressure, SVRI represents systemic vascular resistance index, WU represents Wood units, PAP represents pulmonary arterial pressure, PVRI represents pulmonary vascular resistance index.

TABLE I**Patient Demographics**

Characteristic	N = 177
Age at diagnosis (mo)	12 (5–54)
Age at catheterization (yr)	14 (5–60)
≤ 1yr	85 (48%)
1–2yr	33 (19%)
2–12yr	38 (20%)
12–18yr	21 (12%)
Weight at catheterization (kg)	8.6 (5.2–19.2)

Data represent median with 25–75% inter-quartile range.

TABLE II

Catheterization Protocols

Characteristic	N = 177
Use of general anesthesia	131 (75%)
Age < 1yr	77 (74%)
Age 1–5yr	24 (83%)
Age > 5yr	24 (50%)
Arterial Access	166 (93%)
Left heart catheterization	125 (70%)
Vasodilator testing	164 (94%)
100% oxygen	144 (81%)
Inhaled nitric oxide	151 ^a (85%)
10 ppm	3 (3%)
20 ppm	26 (27%)
40 ppm	55 (57%)
50 ppm	2 (2%)
80 ppm	10 (10%)

^a 151 Patients underwent vasodilator testing with inhaled nitric oxide but dosing was only reported in 96 patients.

TABLE III

Baseline Hemodynamics

Diagnosis	N (%)	Age (yr)	Mean PAP (mmHg)	Systolic PAP (% systemic)	PVRI (WU/m ²)	Rp:Rs
CHD related	61 (34)	0.8 (0.3–2.5)	34.0 (26–46)	67.4 (57–92)	4.7 (3.5–7.6)	0.4 (0.3–0.5)
Idiopathic	36 (20)	4.0 (0.9–11.8)	50.0 (35–67)	87.0 (66–105)	12.0 (6.3–18.9)	0.7 (0.5–1.0)
BPD related	24 (14)	0.8 (0.5–1.3)	33.0 (28–39)	61.9 (50–74)	6.3 (5.0–8.8)	0.4 (0.3–0.6)
Persistent PH of newborn	5 (3)	0.1 (0.1–0.1)	25.0 (18–52)	82.5 (54–108)	4.2 (1.0–4.9)	0.4 (0.2–0.5)
CDH related	8 (4)	1.8 (1.0–4.8)	28.0 (27–36)	56.0 (41–68)	5.9 (5.1–6.4)	0.4 (0.3–0.5)
Assoc. with left heart Dz.	9 (5)	1.9 (0.4–9.0)	36.0 (27–50)	58.5 (55–89)	6.0 (3.3–8.5)	0.3 (0.2–0.5)
Assoc. with pulm. hypoplasia	5 (3)	1.5 (0.8–10.0)	30.0 (23–47)	76.0 (46–92)	7.6 (4.1–8.7)	0.6 (0.3–0.9)
Porto-pulmonary Htn	5 (3)	2.0 (0.5–14)	56.0 (42–66)	79.2 (59–90)	10.1 (3.9–16.4)	0.6 (0.5–0.8)
Newborn GI related	4 (2)	0.3 (0.2–0.5)	23.0 (21–33)	46.7 (37–61)	3.5 (2.3–4.2)	0.3 (0.2–0.4)
Other	20 (11)	2.7 (0.9–12.5)	28.0 (21–35)	52.9 (40–67)	4.5 (3.6–6.9)	0.3 (0.2–0.4)

Data represent median (25–75 inter-quartile range). PAP, pulmonary arterial pressure; PVRI, pulmonary vascular resistance index; WU, Wood Units; Rp:Rs, the ratio of pulmonary to systemic vascular resistance; CHD, congenital heart disease; BPD, bronchopulmonary dyspnea; PH, pulmonary hypertension; CDH, congenital diaphragmatic hernia; GI, gastrointestinal and refers to PH associated with omphalocele or gastroschisis.