

# Residual pulmonary hypertension after left to right shunt closure in common pediatric congenital heart diseases: rate and risk factors

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## ABSTRACT:

**Introduction:** Left to right shunt in congenital heart disease is the common causes of pulmonary hypertension (PH) in children, and the pulmonary pressure sometime isn't recovered to normal value after the shunts closed. Residual PH after correcting these shunts may cause deaths. The purpose of this study was to describe the rate of residual PH after surgical closure the left to right shunts in pediatric congenital heart disease and determine its risk factors.

**Patients and methods:** A retrospective study was performed on the medical recorded documents of 59 children who were diagnosed pulmonary artery hypertension associated with common left to right shunt congenital heart diseases and performed shunt closure surgically at Cho Ray hospital between January 2020 and May 2022. Systolic pulmonary artery pressure (PAPs) was measured via tricuspid regurgitation jet on transthoracic echocardiography (mode: continuous wave doppler, plane: apical 4-chamber). PH was defined as PAPs  $\geq$  40mmHg. Postoperative PAPs was measured 1 day before discharge.

**Results:** The median age and weight at surgery were 7 months (2 – 215) and 5.9 kg (3.6 – 35), 59.3% was female. Preoperatively, 66.1% were mild PH, 33.9% moderate. Postoperatively, 10 patients (17%) diagnosed residual PH and all was mild. Among 10 patients with residual PH: 7

were combined defects (5 VSD-PDA, 2 VSD-ASD), 3 simple defects (2 VSD, 1 ASD). Preoperative high pulmonary pressure was associated with residual PH (correlation coefficient 0.116,  $p = 0.001$ ). **Conclusions:** The proportion of patients with postoperatively residual PH is significant and most of these cases are combined shunt. Preoperative high pulmonary pressure is related to residual PH.

**Keywords:** Residual pulmonary hypertension, Left to right shunt closure, Congenital heart disease.

## 1. INTRODUCTION

Common left to right (L-R) shunt congenital heart disease (CHD) includes atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), and atrioventricular septal defect (AVSD) [1]. L-R shunts increase in both volume and pressure of pulmonary blood flow, result in pulmonary vascular wall remodeling and lead to the pulmonary artery hypertension (PH). PH is defined as mean pulmonary artery pressure  $>$  20 mmHg measured by right heart catheterization at rest [2]. In the developing countries, the

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transthoracic echocardiography is useful in this situation and PH is diagnosed as systolic pulmonary artery pressure (PAPs)  $\geq 40$ mmHg [3].

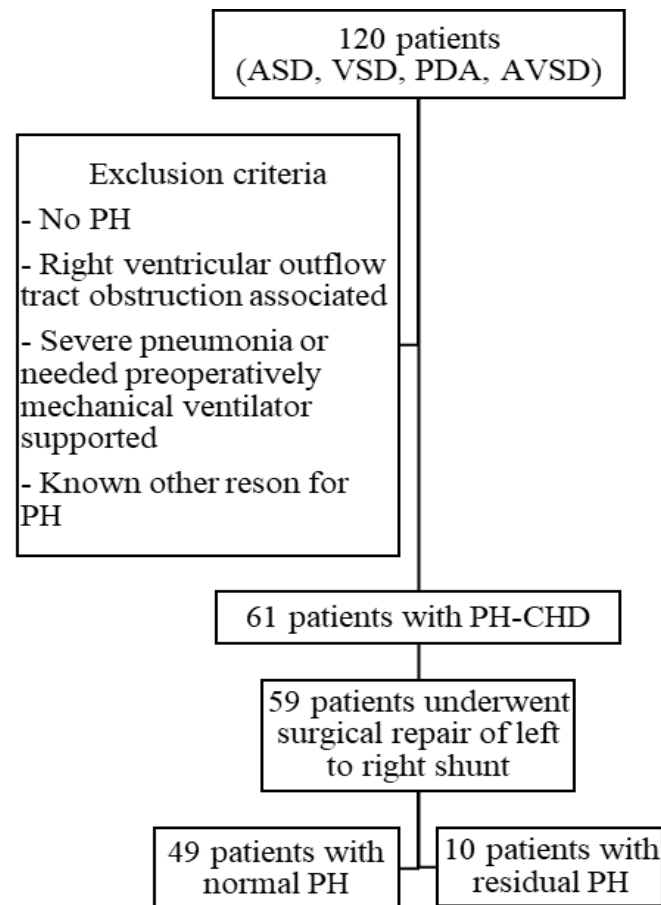
Despite anatomically successful repair early, residual pulmonary hypertension is found in many children [4]. Residual PH reduces the patient's quality of life and may cause death with the 5-year mortality rate is about 17% - 49% [4]. The purpose of this study was to describe the rate of residual PH after surgical closure of common L-R shunts in CHD children and determine the its risk factors.

## 2. PATIENTS AND METHODS

A retrospective study was performed on the medical recorded documents of 59 patients who were diagnosed PH associated with common left

to right CHD and performed shunt closure surgically at the Department of Pediatric Cardiac Surgery, Cho Ray hospital from January 2020 to May 2022 (Figure 1).

CHD was initially diagnosed via preoperatively transthoracic echocardiography and then intraoperatively confirmed. The simple defect was determined when there was one of four defects: ASD, VSD, partial AVSD, PDA; the combined defect was determined when they had more than 1 simple defect and the complex defect was completed AVSD case. PAPs was measured via tricuspid regurgitation jet on transthoracic echocardiography (continuous wave doppler, apical 4-chamber).



**Figure 1. Flowchart of patient selection process**

Diagnosis of PH was diagnosed when the transthoracic PAPs  $\geq 40$ mmHg. Three degrees of PH included mild (PAPs: 40 to 60 mmHg), moderate (PAPS: 61 to 90 mmHg) and severe (PAPs  $> 90$ mmHg). Postoperative PAPs was measured 1 day before hospital discharge. STATA 14 was used to analyze data. The statistically significant was  $P < 0.05$ .

### 3. RESULTS

#### 3.1. Preoperative characteristics

59 patients with PH-CHD, the median age and weight at surgery were 7 months (2 – 215 months) and 5.9 kg (3.6 – 35kg ) respectively. 35 patients (59.3%) were female. 09 patients were associated with Down syndrome.

The defects and severity of PH were classified as groups (Table 1). Preoperatively, PAPs was  $54,2 \pm 13,2$  mmHg (40 – 90 mmHg).

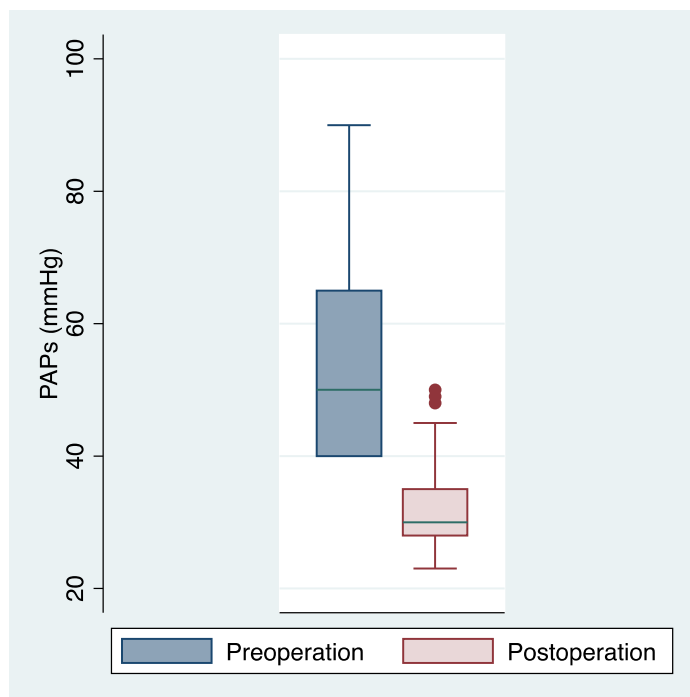
*Table 1. Characteristics of defect and PH preoperatively*

Variable	n, %
<b>Simple defect</b>	21 (35.6)
ASD	9
VSD	13
<b>Combined and complex defect</b>	38 (64.4)
ASD-VSD	3
ASD-PDA	3
VSD-PDA	27
cAVSD	5
<b>Severity of preoperative PH</b>	
Mild	39 (66.1)
Moderate	20 (33.9)
Severe	0 (0)

#### 3.2. Postoperative characteristics

After operations, the median of mechanical ventilation duration was 25 hours (range: 6 – 169 hours), the median of ICU length of stay was 88 hours (6 – 784 hours), the medium of hospital stay was 10 days (5 – 42 days). No patient reported death or reoperated during hospital stay

Before discharge, the postoperative PAPs was  $32,5 \pm 6,6$  mmHg, and it was statistically significant comparing to the preoperative one ( $p < 0.001$ ) (Figure 2).



**Figure 2. Systolic pulmonary artery pressure at pre- and post-operation**

10 patients (17%) were diagnosed residual PH, many of them were female, combined and complex defects (Table 2).

**Table 2. Characteristics of residual PH patients**

No	Age (month)	Gender	Down syndrome	Defect	Preop. sPAP (mmHg)	Postop. sPAP (mmHg)
1	2	Female	No	VSD-ASD	70	40
2	3	Female	No	VSD	85	45
3	3	Female	No	VSD-PDA	70	42
4	5	Female	No	VSD-PDA	45	43
5	5	Male	No	VSD-PDA	70	49
6	6	Female	No	VSD-PDA	75	40
7	8	Female	No	VSD-PDA	75	40
8	9	Female	No	VSD-ASD	75	48
9	12	Male	Yes	VSD	80	50
10	215	Female	No	ASD	65	45

10 patients with residual PH (1 older than 12 months, 8 female, 1 associated with Down syndrome, 3 simple defects, 1 mild PH preoperatively), the mean preoperative PAPs was  $71 \pm 10.75$  mmHg and the mean postoperative PAPs was  $44.2 \pm 3.824$  mmHg.

Female, Down syndrome, combined defects and complex defects, age at surgery, preoperative PH and the severity of preoperative PH were analyzed and suggested as risk factors of residual PH (table 3, 4 ,5).

**Table 3. Binary logistic regression analysis of the age at surgery and preoperative sPAP related to residual PH**

Variable	Coefficient	P value	Range
Age at surgery	0.005	0.531	0.01 – 0.021
Preoperative PAPs	0.116	0.001	0.046 – 0.185

**Table 4: Binary logistic regression analysis of the clinical characteristics**

Variable	N, %	Odd ratio	P value	95% CI
Female	8, 22.6	3.57	0.135	0.673 – 18.988
Down syndrome	1, 11.1	0.41	0.443	0.043 – 3.966
Combined and complex defects	7, 18.4	1.46	0.628	0.318 – 6.667

**Table 5: Fisher's exact analyzing severity of preoperative PH and residual PH**

Severity of preoperative PH	Residual PH	Total	P- value
Mild (n,%)	2, 5.1%	39	0.002
Moderate (n,%)	8, 40%	20	

The correlating between preoperative PAPs and residual PH was found ( $p = 0.001$ )

#### 4. DISCUSSION

PH was the common consequence of L-R shunt CHD, and we found 10 patients had residual PH after closing L-R shunts and the high preoperative PAPs was correlated to the residual PH.

##### 4.1. Rate of residual pulmonary hypertension

Our study revealed that 17% of patients had residual PH after closed L-R shunts and there was different between current studies about this proportion (table 6).

**Table 6. Current studies of PH-CHD**

Study	N	Residual PH (%)	Type of defect
Jančauskaitė, et al (2020) [4]	88	30.7%	ASD, VSD, PDA, AVSD (complete and partial), TA, TGA, TOF.
Arafuri, et al (2021) [5]	103	24.3%	ASD, VSD, PDA, cAVSD, TA, TGA, Single ventricle physiology with unobstructed pulmonary blood flow
Thảo ĐP et al (2021) [6]	60	15.3%	VSD with preoperative severe PH
<b>Our results</b>	59	17%	ASD, VSD, PDA, cAVSD

Different types of L-R shunt allow different blood volume and pressure to pulmonary artery.. Conotruncal defects (such as aortopulmonary window, truncus arteriosus, transposition of the great arteries with VSD), cAVSD were known as high flow defects that may damage pulmonary vasculature irreversibly soon, even under 6 months of age.

#### **4.2. Risk factors of residual pulmonary hypertension:**

Down syndrome was known as a risk factor of pulmonary artery damage that may lead to PH, especial in the context of L-R shunt CHD, and may also remodel pulmonary vasculature irreversibly soon, even under 6 months-old [7]. This study also showed that Down syndrome was not related to residual PH. However, the number of Down syndrome patients in our study (n = 9) was not enough to firmly conclude.

Age at surgery was also considered related to reversibility of pulmonary vasculature after closing shunts. Some studies showed that

children who close L-R shunt beyond the 2 years of age can have normal pulmonary artery pressure postoperatively, while others showed that although closing L-R shunts during infancy, many children may have residual PH [8,9]. In this study, preoperative PAPs of patients aged upper 2 years was not higher other. Postoperatively, only 1 out of 10 patients aged upper 2 years had residual PH and age at surgery was not correlated to residual PH (table 3, 4, 5). In developing countries like Vietnam, not many children have been undergone CHD screening before or right after birth. They were instead diagnosed CHD while managed the consequences of L-R shunt such as pneumonia, heart failure, PH and malnutrition. Children with large L-R shunt may be diagnosed and closed during their infancy while others with simple and small defects were intervened at latter stage. Age at surgery should be put in the context of the same type and size of defects to analyze the relation to pulmonary vascular reversibility.

8 out of 10 residual PH patients were female, however there was no relationship between gender and residual PH. Other studies were also found that gender was not a risk factor of residual PH. Combined and complex L-R shunts increased more blood volume with high pressure to pulmonary artery so these patients may present to hospital and also perform L-R shunt closing soon. In our study, preoperative PAPs of patients with combined and complex defects was not higher than patients with simple one, and there was also no relationship between types of defects and residual PH. It seems that with the same in preoperative PAPs, pulmonary artery was remodeled at the similar grade so there was no relationship between type of defects and residual PH.

Under higher pressure, pulmonary vessels were looked like extremely damaged and decrease the reversibility after corrected defects. Jančauskaitė, et al and Michele D'Alto, et al found that higher preoperative PVR was associated with residual PH [4,10]. Look back to the formula:  $mPAP = PCWP + (PVR * Q)$  (mPAP: mean pulmonary arterial pressure, Q: pulmonary flow, PCWP: capillary wedge pressure, and PVR: pulmonary vascular resistance), pulmonary pressure and resistance have a positive correlation, and both also has the same meaning in residual PH prediction. To decrease risk of residual PH, medication management to relieve pulmonary pressure before closing shunt should be considered.

## 5. CONCLUSION

Residual PH was observed in nearly 20%

children with common left to right CHD. High preoperative PAPs was associated to residual PH.

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