Original Article

Clinical outcomes of the neonates with critical pulmonary stenosis: intrauterine versus postnatal transport

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Background: Pulmonary stenosis (PS) is one rare congenital heart disease (CHD) featuring obstruction of right ventricular outflow tract. Critical pulmonary stenosis (CPS) is neonatal PS having cyanosis and evidence of patent ductus arteriosus (PDA) dependency. There is limited data on the clinical outcomes of CPS with different modes of transportation. This study aimed to investigate clinical features and outcomes of CPS through the intrauterine transport (IT) and postnatal transport (PT).

Methods: Single-center retrospective research was performed. Neonates with CPS were grouped into the IT group and PT group. Clinical characteristics and outcomes of the neonates were compared between the two groups.

Results: Totally 110 neonates with PS were included in this study, 77 with CPS and 33 with non-CPS. In the infants with CPS, there were 53 and 24 in the IT and PT group respectively. Echocardiography showed that transvalvular pulmonary gradient (TVG) stayed lower in the IT group than that in the PT group {77.0 [interquartile range (IQR), 60.5–91.5] *vs.* 92.0 (IQR, 73.3–125.0) mmHg, P=0.006}. Levels of serum N-terminal pro-brain natriuretic peptide (NT-proBNP) and troponin I also remained lower in the IT group than those in the PT group [2,256 (IQR, 1,054–4,527) *vs.* 3,708 (IQR, 2,138–6,789) pg/mL, P=0.02; 0.020 (IQR, 0.011–0.034) *vs.* 0.042 (IQR, 0.027–0.072) ng/mL, P<0.001, respectively]. All infants with CPS received percutaneous balloon pulmonary valvuloplasty (PBPV) therapy in neonatal period and were discharged from the hospital. Length of hospital stay remained shorter in the IT group than that in the PT group [13.0 (IQR, 11.0–15.0) *vs.* 15.5 (IQR, 10.8–22.8) days, P=0.03].

Conclusions: IT and early management after birth could effectively reduce the severity of CPS before PBPV treatment and shorten the length of hospital stay among neonates suffering from CPS.

Keywords: Critical pulmonary stenosis (CPS); intrauterine transport (IT); newborn; percutaneous balloon pulmonary valvuloplasty (PBPV)

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Introduction

Pulmonary stenosis (PS) is one rare congenital heart disease (CHD) featuring obstruction of right ventricular (RV) outflow tract. It happens in around 1 per 2,000 live births globally and is around 8% of entire CHD (1). PS featured a thickened dooming pulmonary valve and flow acceleration on color and pulse Doppler mapping. Critical pulmonary stenosis (CPS) is a condition characterized by an extremely small or pin-hole orifice in the pulmonary valve (PV). CPS can cause cyanosis and death in the newborn because of inadequate antegrade pulmonary flow through RV outflow tract, which might lead to RV hypoplasia and dysfunction (2). Left-to-right shunting through patent ductus arteriosus (PDA) offers an additional source of pulmonary blood flow among patients with reduced prograde flow through critically stenotic pulmonary valve (3). If the CPS is unrecognized by echocardiography at birth, closure of ductus arteriosus within certain days after birth will lead to rapid deterioration with cardiogenic shock, cardiac arrest, severe metabolic acidosis, and other organ dysfunction, even death (4). Therefore, early detection and diagnosis of neonatal CPS have important clinical significance for guiding treatment. Administration of prostaglandin E1 (PGE1) shortly after birth to dilate the ductus arteriosus can augment pulmonary artery blood flow and enhance hypoxemia, which can improve the prognosis of newborns with CPS (5). Percutaneous balloon pulmonary valvuloplasty (PBPV) needs to be done in hospitals with CPS treatment capabilities following stabilization of patient's general conditions (6). Failure to diagnose and refer to a tertiary care center owning pediatric cardiac experts augments risks of complications and death among infants suffering from CPS (7).

Ronai *et al.* reported that the prenatal diagnosis rate of CPS was 37% at routine second trimester screening by 2D imaging between 2000 and 2014 (8). Optimal timing for performance of comprehensive transabdominal fetal echocardiography is 18 to 22 weeks' gestation (9). Fetal PS is defined by the presence of pulmonary valve dysplasia (valve hyperechogenicity, thickening or hypomobility) combined with systolic flow acceleration (peak velocity>1.4 m/s) (10). PS is subclassified as: critical (presence of reversed flow in the ductus arteriosus), moderate (right ventricle hypoplastic with significant tricuspid regurgitation), or mild (the remainder) (11). When fetal CPS is screened and diagnosed by echocardiography, CHD counselling, fertility guidance and multidisciplinary collaboration are required (12). The pregnant woman may be transferred to a delivery facility with neonatal CPS treatment capabilities before delivery, which is called as intrauterine transport (IT) (13). If the fetus is not diagnosed, the neonate will be transported to tertiary hospitals after postnatal diagnosis because of cyanosis or heart murmurs (14,15). It was reported that planned IT was of great significance for the successful treatment of neonates with congenital diaphragmatic hernia, and tracheoesophageal fistula, etc. (16). However, there are few studies concerning the effect of IT for neonatal CPS. Therefore, our research targeted at investigating and comparing clinical features and outcomes of neonates with CPS having IT and postnatal transport (PT). We present this article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-42/rc).

Highlight box

Key findings

- Intrauterine transport (IT) and early management after birth could effectively reduce the severity of critical pulmonary stenosis (CPS) before percutaneous balloon pulmonary valvuloplasty (PBPV) treatment and shorten the length of hospital stay in neonates with CPS.

What is known and what is new?

- Studies have shown that prenatal diagnosis is crucial for the prognosis of CPS patients, which is generally diagnosed by echocardiography during the fetal period.
- There are few studies on the clinical outcomes of these patients with different transports. This study found that prompt transfer to a tertiary care center with pediatric cardiac expertise is important for the prognosis of the neonates with CPS.

What is the implication, and what should change now?

- For neonatal CPS, establishing regional three-level prenatal diagnosis network and increasing the proportion of planned IT might be meaningful.

Methods

Participant selection

This cross-sectional study included all the neonates diagnosed with PS with intact ventricular septum in neonatal intensive care unit (NICU) of Xinhua Hospital Shanghai Jiao Tong University School of Medicine from January 2014 to June 2023. Exclusion criteria were as below: PS and ventricular septal defect (VSD), pulmonary

atresia (PA), other diagnosed complicated CHD, and serious diseases of other systems. According to the type of transport, neonates with CPS were grouped into the IT group and the PT group. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (No. XHEC-D-2023-172). Written informed consent was obtained from the parents or their legal guardians for all study participants prior to participation.

Data collection

Clinical data came from electronic medical record system, information on clinical features and managements included. Percutaneous pulse oxygen saturation (SpO_2), heart rate (HR), blood pressure and serum cardiac biomarkers were measured immediately after admission. Serum N-terminal pro-brain natriuretic peptide (NT-proBNP), troponin I, creatine kinase-MB isoenzyme (CK-MB) and myohemoglobin levels were measured through chemiluminescent immunoassay via Access 2 Immunoassay System (Beckman Coulter, Inc., CA, USA) right after blood collections and centrifugations. Fetal echocardiogram was performed through ultrasound system Vivid 5 via 3.5- or 5-MHz sector probes (GE Medical Systems, Bucks, UK) by experienced pediatric cardiologists at gestational age of 18–22 weeks in second trimester. Neonatal bedside echocardiography was done with an ultrasonographic unit having one 5–10 MHz probe within 2 days after admission. Pulmonary artery velocity maximum (PAVmax, m/s) and tricuspid regurgitation velocity (TRV, m/s) were measured and transvalvular pulmonary gradient (TVG, mmHg) and transvalvular tricuspid gradient (TTG, mmHg) were calculated via modified Bernoulli equation (TVG = 4× $PAVmax^2$). Right ventricular systolic pressure (RVSP, mmHg), pulmonary artery systolic pressure (PASP, mmHg) and peak-to-peak gradients (PPG, mmHg) were examined after the treatment of PBPV.

Statistical analysis

Data analysis was done via SPSS 26.0 software program. Continuous variables were displayed as means ± standard deviations (SD), while for non-normally distributed datasets, the median and interquartile range (IQR) were adopted. Proportions were displayed as percentages. T-test was adopted for analyzing normally distributed variables. Non-normally distributed data were compared via rank-sum test. Enumeration data were displayed as n (%) and comparison between groups was done via Chi-square test or Fisher's exact probability approach. Significance statistically was defined if P value stayed below 0.05 (P<0.05).

Results

There were 127 newborns diagnosed with PS through echocardiography between January 2014 and June 2023 in Xinhua Hospital. Among them, 6 neonates were diagnosed with PA ultimately, 11 neonates suffered from other complicated CHDs (1 suffering from RV diverticulum, 4 double outlet right ventricle, 3 complete transposition of great artery, 1 single ventricle, and 2 aortic stenosis). Overall, 110 neonates were included in our research, having 77 in CPS group and 33 in non-CPS groups. In the CPS group, 53 cases were transported prenatally and 24 postnatally. In non-CPS group, 21 cases were transported to our hospital prenatally and 12 were transported postnatally. The patient enrollment flowchart is shown in *Figure 1*.

Basic clinical features of all neonates are detailed as *Table 1*. There were no statistical differences in gestational age (GA), birth weight (BW), gender, delivery mode between the IT and PT group (P>0.05). Among 77 neonates with CPS, SpO_2 was significantly high in the IT group relative to the PT group (P<0.001). Among infants with CPS, age of admission stayed much larger in the PT group relative to the IT group [6.00 (IQR, 0.28–14.75) *vs.* 0.04 (IQR, 0.03–0.08) days, P<0.001]. However, among the infants with non-CPS, the age of admission was slightly larger in the PT group relative to the IT group [0.54 (IQR, 0.20–10.00) *vs.* 0.04 (IQR, 0.02–0.05) days, P<0.001] because 75% infants in the PT group were born locally.

A comparison of echocardiography index and cardiac biomarkers between the IT group and the PT group are shown in *Figure 2*. Among the neonates with the non-CPS, there were no significant differences in PAVmax and TVG between the IT and PT group (P>0.05). In the neonates with CPS, TVG and PAVmax remained greatly lower in the IT group relative to the PT group [77.0 (IQR, 60.5–91.5) *vs.* 92.0 (IQR, 73.3–125.0) mmHg, P=0.006; 4.25±0.71 *vs.* 4.88±0.83 m/s, P<0.001, respectively].

Among the neonates with non-CPS, the levels of serum NT-proBNP and troponin I were greatly low in the IT group relative to the PT group [1,488 (IQR, 706–2,181) *vs.* 2,504 (IQR, 1,841–2,924) pg/mL, P=0.006; 0.018 (IQR,

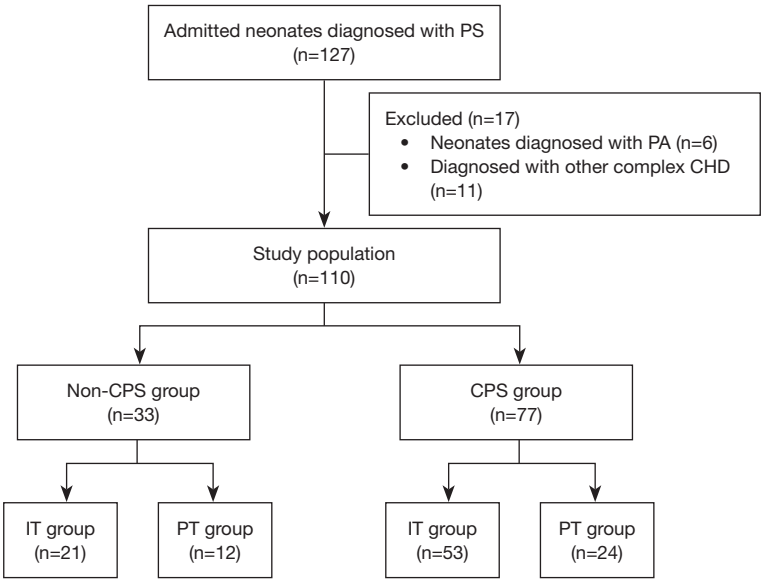

Figure 1 Patient enrollment flowchart. PS, pulmonary stenosis; PA, pulmonary atresia; CHD, congenital heart diseases; CPS, critical pulmonary stenosis; IT, intrauterine transport; PT, postnatal transport.

Table 1 Clinical characteristics of all the neonates in the study

Characteristics	Non-CPS (n=33)			CPS (n=77)		
	IT group (n=21)	PT group (n=12)	P value	IT group (n=53)	PT group (n=24)	P value
General information						
GA, weeks	38.57±2.57	38.23±2.01	0.69	38.61±1.38	38.30±1.76	0.98
BW, g	3,336±694	2,835±681	0.054	3,211±501	3,067±690	0.93
Male	8 (38.1)	5 (41.7)	0.56	32 (60.4)	14 (58.3)	0.87
Cesarean delivery	10 (47.6)	6 (50.0)	0.71	28 (52.8)	12 (50.0)	0.82
1-min Apgar score	10.0 (9.0–10.0)	9.0 (9.0–10.0)	0.53	9.0 (9.0–9.0)	9.5 (9.0–10.0)	0.38
5-min Apgar score	10.0 (9.5–10.0)	9.5 (9.0–10.0)	0.28	9.0 (9.0–10.0)	10.0 (9.0–10.0)	0.20
Age of admission, days	0.04 (0.02–0.05)	0.54 (0.20–10.00)	<0.001	0.04 (0.03–0.08)	6.00 (0.28–14.75)	<0.001
Vital sings at admission						
SpO_2, %	91.7±6.8	92.5±10.9	0.80	91.6±6.1	89.7±7.65	<0.001
HR, bpm	139.2±10.5	144.7±12.1	0.19	139.4±11.5	141.4±11.6	0.14
MAP, mmHg	48.9±6.3	49.7±7.6	0.72	49.3±5.9	52.0±7.7	0.06

Data are presented as mean ± SD, mean (IQR), or n (%). CPS, critical pulmonary stenosis; IT, intrauterine transport; PT, postnatal transport; GA, gestational age; SD, standard deviation; BW, birth weight; IQR, interquartile range; SpO_2, percutaneous pulse oxygen saturation; HR, heart rate; MAP, mean arterial pressure.

0.010–0.023) *vs.* 0.026 (IQR, 0.019–0.073) ng/mL, P=0.04, respectively]. Within neonates with CPS, level of serum NT-proBNP and troponin I was also significantly low in the IT group relative to the PT group [2,256 (IQR, 1,054–4,527) *vs.* 3,708 (IQR, 2,138–6,789) pg/mL, P=0.02; 0.020 (IQR, 0.011–0.034) *vs.* 0.042 (IQR, 0.027–0.072) ng/mL, P<0.001, respectively]. There were no significant differences in serum CK-MB and myoglobin levels between the IT and

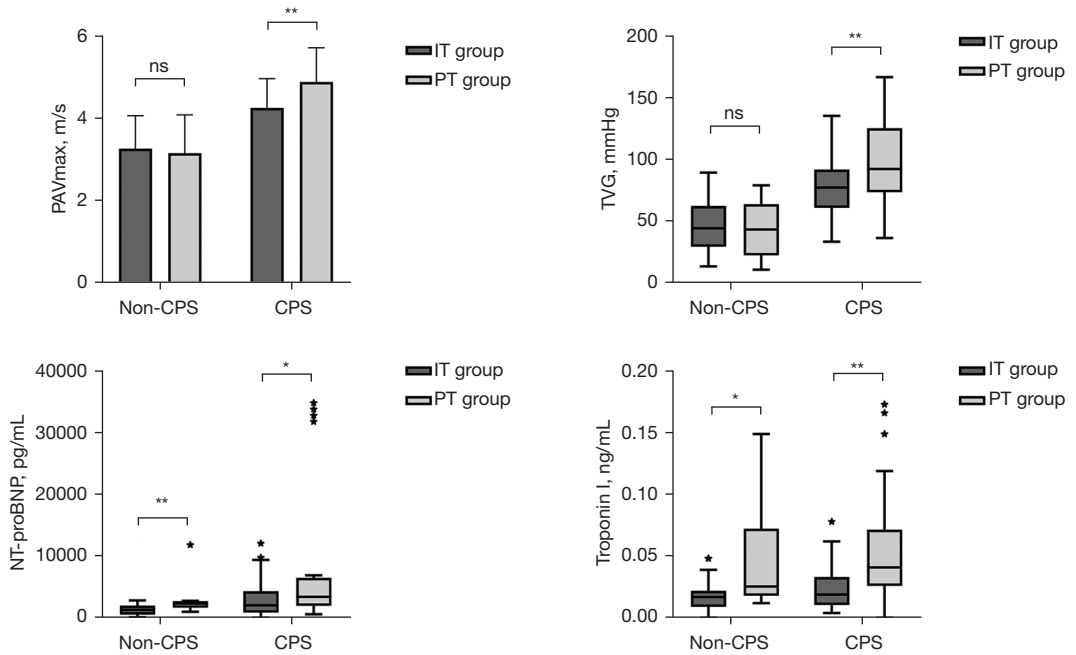

Figure 2 PAVmax, TVG, NT-proBNP, troponin I in neonates with PS between the IT group and PT group. *, P<0.05; **, P<0.01; ns, not significant. PAVmax, pulmonary artery velocity maximum; TVG, transvalvular pulmonary gradient; NT-proBNP, N-terminal pro-brain natriuretic peptide; PS, pulmonary stenosis; CPS, critical pulmonary stenosis; IT, intrauterine transport; PT, postnatal transport; ns, no significance.

Table 2 Treatment and post-PBPV complications in the neonates with CPS

Treatment and post-PBPV complications	IT group (n=53)	PT group (n=24)	P value
Age of the patients receiving PBPV, days	5.0 (4.0–7.0)	11.0 (5.0–18.8)	0.001
Mechanical ventilation >7 days after PBPV	0	2 (8.3)	0.09
Heart failure after PBPV	0	1 (4.2)	0.31
Arrhythmia after PBPV	0	1 (4.2)	0.31
Hydropericardium after PBPV	1 (1.9)	1 (4.2)	0.53
Length of hospital stay, days	13.0 (11.0–15.0)	15.5 (10.8–22.8)	0.03

Data are presented as mean (IQR) or n (%). CPS, critical pulmonary stenosis; PBPV, percutaneous balloon pulmonary valvuloplasty; IT, intrauterine transport; PT, postnatal transport; IQR, interquartile range.

PT group (P>0.05).

Neonates with non-CPS had no or mild symptoms, did not need surgical intervention and only regular follow-up. All infants in the CPS group received PBPV therapy in neonatal period. All newborns with CPS used PGE1 shortly after admission. Treatment and post-operation complications in the neonates with CPS between the IT and PT group are summarized in *Table 2*. Among the infants with CPS, age of the patients receiving PBPV was younger in the IT group relative to the PT group [5.0 (IQR, 4.0–7.0) *vs.* 11.0 (IQR, 5.0–18.8) days, P=0.001], and length of hospital stay remined shorter in the IT group relative to the PT group [13.0 (IQR, 11.0–15.0) *vs.* 15.5 (IQR, 10.8–22.8) days, P=0.03]. All cases had tricuspid regurgitation, but none of them had right ventricular dependent coronary circulation (RVDCC). In the CPS group, 2 cases received mechanical ventilation for over 7 days, 1 case had arrhythmia, 1 case had heart failure and 2 cases had hydropericardium. All cases were discharged from hospital and attended follow-up clinic. In the follow-up period, 2 cases in the IT group received the second PBPV

Table 3 Pre-operative and post-operative echocardiography and cardiac catheterization index in the CPS group

Parameter	Pre-operation (n=77)	Post-operation (n=77)	P value
Echocardiography index			
PAVmax, m/s	4.45±0.80	2.57±0.49	<0.001
TVG, mmHg	81.0 (64.5–100.0)	28.6 (21.4–35.3)	<0.001
TRVmax, m/s	5.24±0.68	3.36±0.45	<0.001
TTG, mmHg	116.9 (114.5–128.0)	52.5 (39.0–56.8)	<0.001
Cardiac catheterization index			
RVSP, mmHg	92.01±17.21	48.83±11.61	<0.001
PASP, mmHg	23.65±4.73	33.23±8.11	<0.001
PPG, mmHg	69.84±11.11	15.68±9.37	<0.001

Data are presented as mean ± SD or mean (IQR). CPS, critical pulmonary stenosis; PAVmax, pulmonary artery velocity maximum; SD, standard deviation; TVG, transvalvular pulmonary gradient; IQR, interquartile range; TRV, tricuspid regurgitation velocity; TTG, transvalvular tricuspid gradient; RVSP, right ventricular systolic pressure; PASP, pulmonary artery systolic pressure; PPG, peak-to-peak gradients.

treatment in our hospital at 3 and 13 months, respectively.

After PBPV therapy, all the infants underwent post-operative echocardiography. A comparison of echocardiography and cardiac catheterization index between pre-operation and post-operation is shown in *Table 3*. Alleviation of obstruction in RV outflow tract caused a great reduction on PAVmax, TVG, TRV, TTG (P<0.01). Cardiac catheterization showed that RVSP decreased and PASP increased significantly after PBPV treatment (P<0.01).

Discussion

CPS requires urgent neonatal intervention after birth. In this study, around two-thirds of the neonates with CPS were transferred to our hospital through IT, and they were admitted to NICU shortly after birth. It was found that IT and early management after birth could effectively reduce the severity of CPS, schedule early PBPV and shorten length of hospital stay among neonates with CPS.

There are several studies about the biomarkers of CPS in neonates. Our team found serum NT-proBNP was positively correlated with PS severity and could be used as a biomarker to identify CPS in neonates (17). El Tahlawi *et al.* (18) reported that serum troponin I was correlated positively with PS severity. RV pressure volume overload causes alterations in myocardial cell function and damage, leading to a significant increase in NT-proBNP and troponin I level in neonatal CPS (19), which is similar to the results of this study.

Infants with CPS usually experience serious cyanosis and right heart dysfunction shortly after birth, which can lead death without timely treatment (5). Timely maintenance of arterial catheterization and early intervention to pulmonary artery blood flow establishment can significantly improve clinical symptoms (20). PBPV is a common treatment for CPS to enlarge diameter of pulmonary valve and reduce stenosis degree (21). The successful rate of PBPV surgery in newborns is about 93% to 98%, and complications during and after surgery mainly include arrhythmia, pericardial effusion, the long duration of mechanical ventilation, etc. (22). In this study, all CPS neonates underwent PBPV surgery and none of the infants died of PBPV.

Prenatal cardiac screening has been applied in most advanced and developing countries (23). In China, routine prenatal ultrasound screening is performed in second trimester, including screening for cardiac abnormalities. When suspected PS is detected through regular screening, the pregnant woman will visit a fetal cardiac expertise for detailed fetal heart assessment, and fetal echocardiography will be performed every 4–6 weeks to further clarify the diagnosis, detect changes in the severity of PS and cardiac function during fetal growth (24). If the fetal CPS is diagnosed, the pregnant woman will be referred to a delivery facility with neonatal CPS treatment capabilities. A consultation of multidisciplinary consultation will be provided, by an integrative team including pediatric cardiologists, obstetrician, ultrasound physician, neonatologist, and geneticist. The pregnant woman will be admitted to the hospital before delivery and the neonate will be transferred to NICU shortly after birth.

Fetal cardiac intervention (FCI) is a novel invasive intrauterine technique that reduces mortality and morbidity associated with CHD and increases the possibility of biventricular circulation (25). FCI is performed for three main CHDs: CPS/PA with intact ventricular septum (CPS/PAIVS) with worsening RV hypoplasia, critical aortic stenosis (CAS) with evolving hypoplastic left ventricle (LV), and hypoplastic left heart syndrome (HLHS) with intact or restrictive atrial septum (26). Hogan *et al.* (27) analyzed data from 84 patients with CPS/PAIVS of 14 international institutions and found right heart structures grew significantly more from midgestation to late gestation in fetuses who underwent intrauterine intervention, compared with fetuses who received postnatal intervention. Intrauterine valvuloplasty promotes ventricular growth and function in PS, but unified standards for FCI are not well-established, and outcomes are related to various factors, such as the experience of the surgical team, available resources, etc. (28). In our fetal medical center, five fetal aortic or pulmonary valvuloplasty procedures were successfully performed between August 2018 and May 2022 (29).

In this study, the neonates with IT were transferred to the NICU shortly after birth and had better oxygen saturation after admission. We also found the neonates with IT had lower levels of TVG, PAVmax, serum NT-proBNP and troponin I level, indicating that IT and early management after birth can improve the clinical symptoms in the neonates. Meanwhile, the neonates with IT had earlier PBPV treatment and shorter hospital stays than those with PT. Chakraborty *et al.* (30) reported that prenatal diagnosis of CHD could reduce preoperative prevalence of acidosis, intubation, rescue, and could provide better preoperative conditions for subsequent cardiac surgery, especially in ductal-dependent cardiac anomalies. Li *et al.* reported perinatal integrative management and IT could enhance the advantage of prenatal diagnosis and benefit functional restoration of RV in neonatal CPS (31). Therefore, prenatal diagnosis, IT and earlier PBPV could improve the outcomes of CPS. Establishing regional three-level prenatal diagnosis network for neonatal CPS and increasing the proportion of planned IT might be meaningful.

Conclusions

IT and early management after birth could effectively reduce the severity of CPS before PBPV treatment and shorten length of hospital stay among neonates suffering from CPS.

Limitations

This study was a single-center retrospective study with a relatively small sample size, so there could be some missing data and possible ascertainment bias.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-24-42/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-24-42/dss

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-24-42/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-42/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (No. XHEC-D-2023-172). Written informed consent was obtained from the parents or their legal guardians for all study participants prior to participation.

References

1. Liu Y, Chen S, Zühlke L, et al. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol 2019;48:455-63.
2. Cuypers JA, Witsenburg M, van der Linde D, et al. Pulmonary stenosis: update on diagnosis and therapeutic options. Heart 2013;99:339-47.
3. Rigby ML. Severe aortic or pulmonary valve stenosis in premature infants. Early Hum Dev 2012;88:291-4.
4. Khalil M, Jux C, Rueblinger L, et al. Acute therapy of newborns with critical congenital heart disease. Transl Pediatr 2019;8:114-26.
5. Marchini F, Meossi S, Passarini G, et al. Pulmonary Valve Stenosis: From Diagnosis to Current Management Techniques and Future Prospects. Vasc Health Risk Manag 2023;19:379-90.
6. Hoetama E, Prakoso R, Roebiono PS, et al. Balloon pulmonary valvuloplasty in neonates with critical pulmonary stenosis: Jugular or femoral. Ann Pediatr Cardiol 2020;13:11-5.
7. Mortezaeian H, Khorgami M, Omidi N, et al. Percutaneous Balloon Pulmonary Valvuloplasty of Critical Pulmonary Stenosis and severe pulmonary stenosis in Neonates and Early Infancy: A Challenge in the Cyanotic. J Cardiovasc Thorac Res 2021;13:156-61.
8. Ronai C, Freud LR, Brown DW, et al. Low prenatal detection rate of valvar pulmonary stenosis: What are we missing? Prenat Diagn 2020;40:966-71.
9. Carvalho JS, Axt-Fliedner R, Chaoui R, et al. ISUOG Practice Guidelines (updated): fetal cardiac screening. Ultrasound Obstet Gynecol 2023;61:788-803.
10. Moon-Grady AJ, Donofrio MT, Gelehrter S, et al. Guidelines and Recommendations for Performance of the Fetal Echocardiogram: An Update from the American Society of Echocardiography. J Am Soc Echocardiogr 2023;36:679-723.
11. Guirado L, Crispi F, Masoller N, et al. Biventricular impact of mild to moderate fetal pulmonary valve stenosis. Ultrasound Obstet Gynecol 2018;51:349-56.
12. Zhang Y, Wang J, Zhao J, et al. Current status and challenges in prenatal and neonatal screening, diagnosis, and management of congenital heart disease in China. Lancet Child Adolesc Health 2023;7:479-89.
13. Thakur V, Dutil N, Schwartz SM, et al. Impact of prenatal diagnosis on the management and early outcome of critical duct-dependent cardiac lesions. Cardiol Young 2018;28:548-53.
14. McElhinney DB, Asija R, Zhang Y, et al. 20-Year Experience With Repair of Pulmonary Atresia or Stenosis and Major Aortopulmonary Collateral Arteries. J Am Coll Cardiol 2023;82:1206-22.
15. Poupart S, Navarro-Castellanos I, Raboisson MJ, et al. Supravalvular and Valvular Pulmonary Stenosis: Predictive Features and Responsiveness to Percutaneous Dilation. Pediatr Cardiol 2021;42:814-20.
16. Chakraborty P, Roy S, Mandal KC, et al. Esophageal Atresia and Tracheoesophageal Fistula: A Retrospective Review from a Tertiary Care Institute. J West Afr Coll Surg 2022;12:30-6.
17. Lin Z, Chen Y, Zhou L, et al. Serum N-Terminal Pro-B-Type Natriuretic Peptide as a Biomarker of Critical Pulmonary Stenosis in Neonates. Front Pediatr 2021;9:788715.
18. El Tahlawi M, Morsy M, Elawady M, et al. Is there any relationship between biomarkers and echocardiographic markers in patients with pulmonary stenosis underwent balloon valvuloplasty? Echocardiography 2021;38:924-31.
19. Uner A, Doğan M, Ay M, et al. The evaluation of serum N-terminal prohormone brain-type natriuretic peptide, troponin-I, and high-sensitivity C-reactive protein levels in children with congenital heart disease. Hum Exp Toxicol 2014;33:1158-66.
20. Arunamata A, Goldstein BH. Right ventricular outflow tract anomalies: Neonatal interventions and outcomes. Semin Perinatol 2022;46:151583.
21. Barry OM, Bouhout I, Turner ME, et al. Transcatheter Cardiac Interventions in the Newborn: JACC Focus Seminar. J Am Coll Cardiol 2022;79:2270-83.
22. Bouhlel I, Ajmi H, Slim M, et al. Immediate results of balloon valvuloplasty in congenital pulmonary valve stenosis. Tunis Med 2021;99:291-7.
23. Lesieur E, Zaffran S, Chaoui R, et al. Prenatal screening and diagnosis of pulmonary artery anomalies. Ultrasound Obstet Gynecol 2023;61:445-57.
24. Pang C, Wang Y, Shen J, et al. Echocardiographic characteristics and clinical outcomes in fetuses with pulmonary stenosis or pulmonary atresia with intact ventricular septum. Pediatr Neonatol 2023;S1875-

9572(23)00176-6.
25. Friedman KG, Tworetzky W. Fetal cardiac interventions: Where do we stand? Arch Cardiovasc Dis 2020;113:121-8.
26. Tulzer A, Arzt W, Tulzer G. Fetal aortic valvuloplasty may rescue fetuses with critical aortic stenosis and hydrops. Ultrasound Obstet Gynecol 2021;57:119-25.
27. Hogan WJ, Grinenco S, Armstrong A, et al. Fetal Cardiac Intervention for Pulmonary Atresia with Intact Ventricular Septum: International Fetal Cardiac Intervention Registry. Fetal Diagn Ther 2020. [Epub ahead of print]. doi: 10.1159/000508045.
28. Diniz AMB, Manso PH, Santos MV, et al. A Systematic Review of Benefits and Risks of Fetal Surgery for Congenital Cardiac Defects Such as Pulmonary Valve Stenosis and Critical Aortic Stenosis. Braz J Cardiovasc Surg 2023;38:398-404.
29. Zhao L, Wang L, Xia H, et al. Prognosis and outcome of intrauterine treatment of fetuses with critical congenital heart disease. Chin Med J (Engl) 2024;137:1431-6.
30. Chakraborty A, Gorla SR, Swaminathan S. Impact of prenatal diagnosis of complex congenital heart disease on neonatal and infant morbidity and mortality. Prenat Diagn 2018;38:958-63.
31. Li J, Li G, Shi X, et al. Integrative Perinatal Management Enhanced the Advantage of Prenatal Diagnosis on Critical Pulmonary Valve Stenosis: An Observational Preliminary Study. Front Pediatr 2020;8:572238.

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