

Postoperative hemodynamics of children with severe pulmonary hypertension caused by congenital heart disease

Wei-Hua Zhu, Xiong-Kai Zhu and Qiang Shu

Hangzhou, China

Background: There has been a persistent debate in pediatricians on whether or not patients with congenital heart disease with large left-to-right shunt and pulmonary hypertension (PH). The severity of pulmonary hypertension has a strong impact on the effectiveness of operative treatment and prognosis. Invasive assessment with cardiac catheterization has been used to obtain more accurate data on pre- and post-operative hemodynamic change in order to study the relationship between the age at operation and prognosis in children with severe pulmonary hypertension.

Methods: Forty children with severe PH (increased total pulmonary circulation resistance) caused by ventricular septal defect (VSD) were divided into two groups according to their age at operation. Group I were younger than 2 years old and group II older than 2 years old. The ratios of pulmonary arterial pressure to systemic arterial pressure (Pp/Ps), pulmonary resistance to systemic resistance (Rp/Rs), and the levels of pulmonary vascular resistance (PVR) to small pulmonary arterial resistance (PAR) were measured before surgery, 1 week after surgery, and 5-7 years after surgery.

Results: No differences in Pp/Ps, Rp/Rs, PVR and PAR before surgery were observed between group I and group II ($P>0.05$) in contrast to significant differences in Pp/Ps, Rp/Rs, PVR and PAR 1 week and 5-7 years after surgery ($P<0.01$). In group I a week after surgery, Pp/Ps was 0.32 ± 0.05 , Rp/Rs 0.24 ± 0.06 , PVR 235.49 ± 71.64 mmHg, and PAR 194.29 ± 46.54 mmHg; 5-7 years after surgery, Pp/Ps was $0.24\pm$

0.03 , Rp/Rs 0.19 ± 0.05 , PVR 158.26 ± 36.51 mmHg, and PAR 119.70 ± 32.48 mmHg. In group II a week after surgery, Pp/Ps was 0.50 ± 0.15 , Rp/Rs 0.42 ± 0.14 , PVR 381.23 ± 35.96 mmHg, and PAR 347.07 ± 87.52 mmHg; 5-7 years after surgery, Pp/Ps was 0.34 ± 0.08 , Rp/Rs 0.26 ± 0.08 , PVR 328.18 ± 32.65 mmHg, and PAR 274.89 ± 68.57 mmHg. During follow-up in group I, all the hemodynamic parameters were normal, whereas in group II, only Pp/Ps and Rp/Rs were close to normal and the other 6 parameters were still abnormal.

Conclusions: Early operation would be the only way to gain optimal long-term result and decrease the incidence of pulmonary vascular disease in children with PH due to VSD.

World J Pediatr 2006;1:45-48

Key words: heart defects;
hypertension pulmonary;
surgery;
follow up

Introduction

The recovery of pulmonary hypertension (PH) in patients with congenital heart disease after an operation for large left-to-right shunt has been a focus of clinical practice. If pulmonary hypertension fails to recover or even gets worse after surgery, this surgery is valueless. Although the relationships between surgical results and indications have been reported, long-term follow-up of pulmonary hemodynamics is not available in patients with this disease. In order to understand the relationship between the age of the patient at operation and the degree of PH recovery, we followed up pulmonary hemodynamics in 40 patients with a large ventricular septal defect (VSD) associated with severe pulmonary hypertension (high pulmonary resistance) before surgery, 1 week, and 5-7 years after operation.

Author Affiliations: Department of Cardiology, Children's Hospital, Zhejiang University School of Medicine, Hangzhou 310003, China (Zhu WH, Zhu XK and Shu Q)

Corresponding Author: Wei-Hua Zhu, MD, Department of Cardiology Children's Hospital, Zhejiang University School of Medicine, Hangzhou 310003, China (Tel: 86-571-87061007 ext 61211; Fax: 86-571-87033296; Email: zhuweihua54816@hotmail.com)

©2006 World J Pediatr. All rights reserved.

Methods

In the 40 patients aged from 6 months to 13 years, 18 boys and 22 girls, 18 were younger than 2 years (group I) and the other 22 older than 2 years (group II). These patients received operation for VSD associated with severe pulmonary hypertension during the period of 1990-2003. The diameters of VSDs of these patients, which were measured during the operation, ranged from 12 mm to 25 mm, greater or a 50% larger than the diameter of the aortic roots. Six patients were complicated by patent ductus arteriosus (a diameter of 2.1 mm to 8 mm) and 4 by secundum arterial septal defect with a diameter of 15 mm to 22 mm. In all patients, Pp/Ps was ≥ 0.75 (normal < 0.30), Rp/Rs > 0.32 (normal < 0.25), PVR $> 340 \text{ mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$ (normal $< 225 \text{ mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$), PAR $> 306 \text{ mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$ (normal $< 120 \text{ mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$), and arterial blood saturation $\geq 92\%$. The operation was successful in all and none of them had postoperative residual shunt. Two patients were dead in half and 5 or 7 years.

Preoperation

All patients underwent cardiac catheterization and angiocardiology under intravenous and sacral anesthesia induced by heparin $100 \mu\text{g/kg}$. Catheterization was performed percutaneously via the femoral vessel, placing an end-hole catheter in the femoral vein and an arterial cannula in the femoral artery. Pressures and blood oxygen were measured inside the heart. Pp/Ps, Rp/Rs, PVR, PAR, pulmonary-to-systemic blood flow (Qp/Qs) and arterial oxygen saturation (SaO_2) were calculated. The first week after the operation, all the hemodynamic parameters were measured repeatedly by monitoring the catheter of the pulmonary left atrium

and radical artery and 5-7 years after the operation.

Statistical analysis

All hemodynamic parameters in group I were compared with those in group II using mean $\pm$ SD. Inter-group comparison was performed with the chi-square test. Differences were considered statistically significant when a P value less than 0.05.

Results

The results after hemodynamic follow-up of group I and group II were compared before surgery and within 1 week after surgery and 5-7 years after surgery (Table).

Pp/Ps

The ratios of Pp/Ps in groups I and II were not significantly different before surgery and they exceeded 0.75. In group I, the ratio decreased to 0.32 ± 0.05 , close to the normal level, within a week. It decreased continuously to 0.24 ± 0.03 5-7 years after operation, indicating a full recovery. In group II, the ratio decreased to 0.50 ± 0.15 within a week after operation. The patients still had minor to moderate pulmonary hypertension. Follow-up for 5-7 years after surgery showed minor pulmonary hypertension in 6 patients (27%) and complete recovery in the rest.

PVR and PAR

No significant differences were seen between groups I and II in PVR and PAR before operation. In group I, PVR and PAR were close to normal within a week after

Table. Results of pre- and post-operation pulmonary hemodynamics in groups I and II (mean $\pm$ SD)

Age/cases parameter	Time	≤ 2 years $n=18$	>2 years $n=22$	F value	P value
Pp/Ps	before operation	0.89 ± 0.075	0.88 ± 0.10	2.121	>0.05
	1 week after operation	$0.32 \pm 0.05^{**}$	$0.50 \pm 0.15^*$	16.253	<0.01
	5-7 years after operation	$0.24 \pm 0.03^{**}$	$0.34 \pm 0.08^{**}$	6.514	<0.01
PVR $\text{mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$	before operation	419.55 ± 105.26	475.25 ± 71.82	1.324	>0.05
	1 week after operation	$235.49 \pm 71.64^{**}$	$381.23 \pm 35.96^*$	6.021	<0.01
	5-7 years after operation	$158.26 \pm 36.51^{**}$	$328.18 \pm 32.65^*$	5.342	<0.01
PAR $\text{mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$	before operation	354.89 ± 99.85	425.86 ± 93.84	2.361	>0.05
	1 week after operation	$194.29 \pm 46.54^{**}$	$347.07 \pm 87.52^*$	16.253	<0.01
	5-7 years after operation	$119.70 \pm 32.48^*$	$274.89 \pm 68.57^*$	12.152	<0.05
Rp/Rs	before operation	0.48 ± 0.12	0.51 ± 0.14	2.612	>0.05
	1 week after operation	$0.24 \pm 0.06^{**}$	$0.42 \pm 0.14^*$	3.896	<0.05
	5-7 years after operation	$0.19 \pm 0.05^{**}$	$0.26 \pm 0.08^*$	4.498	<0.05

Inter-group comparison, *: $P < 0.05$, **: $P < 0.01$; Pp/Ps: the ratio of pulmonary arterial pressure to systemic arterial pressure, PVR: pulmonary vascular resistance, PAR: small pulmonary arterial resistance, Rp/Rs: the ratio of pulmonary resistance to systemic resistance.

operation and PVR and PAR recovered in 5-7 years ($PVR < 225 \text{ mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$, $PAR < 120 \text{ mmHg} \cdot \text{s}^{-1} \cdot \text{L}^{-1}$ as normal). In group II, however, 6 patients showed a minor to moderate increase in PVR and PAR 5-7 years after operation. Three patients in group II showed higher levels of PVR and PAR than those before operation.

Qp/Qs and SaO₂

Qp/Qs and SaO₂ showed no significant difference between groups I and II before and after operation.

Discussion

Advances in the treatment of pulmonary hypertension during the past decade have markedly improved the survival of the patients. Pulmonary hypertension of congenital heart disease is an important determinant of morbidity and mortality in patients with pediatric diseases.^[1] Without treatment, pulmonary hypertension associated with left-to-right shunt can be possible to turn into Eisenmenger syndrome and the right heart failure.^[2-8] The patients may have a short survival (32.5 ± 14.6 years).^[9] To avoid pulmonary hypertension, early operation should be recommended. Surgical effects of congenital ventricular septal defect associated with pulmonary hypertension are dependent on the recovery of postoperative pulmonary hypertension. Reports have suggested that surgical indications and prognosis should be assessed by clinical classification of pulmonary hypertension and comprehensive judgement of organic pulmonary hypertension.^[10-15] In this study the hemodynamic parameters of 40 patients suffering from VSD associated with severe pulmonary hypertension indicated that the age at operation plays an important role in the prognosis.

In this study, all patients in groups I and II had severe pulmonary hypertension before operation, but their recovery was different after correction of cardiac malfunction. In group I, who were younger than 2 years, Pp/Ps levels were almost normal within a week after surgery but PVR and PAR levels slightly elevated, and completely recovered 5-7 years after surgery. In group II, who were older than 2 years, Pp/Ps and Rp/Rs decreased gradually, but a longer period of recovery was required. More importantly, 3 patients in group II showed higher pulmonary vascular resistance after operation. The follow-up results showed that the surgical effect of VSD with markedly elevated pulmonary vascular resistance was highly related to age at operation. In older patients, the PVR level was hard

to reduce postoperatively even if the operation was successful or sometimes pulmonary resistance could be worsened. Two patients died in 5 and half or 7 years. Since the age at operation plays such an important role in the prognosis of PVR, we recommend that surgery for VSD associated with pulmonary hypertension is suitable at 2 years old. The data of this study also indicate that in order to avoid pulmonary vascular organic lesion early operation should be performed.

In this study, the PVR levels of 6 patients in group II (27%) did not return to the normal and 3 of them showed a higher PVR level after operation than before operation. The PAR levels before operation varied from 332 to 558 mmHg and after operation from 496 to 680 mmHg. However, the Pp/Ps ratio of these patients was lower than 0.34 to 0.42. In the worst case (3 years), the PAR level was 702 mmHg before operation, and 276 mmHg in a week after operation, and completely recovered (PAR 128 mmHg) at 5 years after operation. It is suggested that the recovery from pulmonary hypertension can not be judged by pulmonary pressure,^[16] but by PVR and PAR, which are more important to assess whether the operation is successful.^[9,17-19] It is still controversial in surgical effect and indications for patients with VSD and PH.^[20,21] In this study, the long-term hemodynamic follow-up of the 2 groups showed a better recovery of pulmonary hypertension associated with VSD in the younger group, suggesting that early operation for children with PH caused by VSD should be the best way to eliminate pulmonary vascular lesion and prevent irreversible pulmonary hypertension.

Funding: This study was supported by grants from the Educational Committee of Zhejiang Province (No. 9709) and the Science and Technology Committee Funds of Zhejiang Province (No. 2003C33022), China.

Ethical approval: Not needed.

Competing interest: None declared.

Contributors: ZWH proposed the study and wrote the first draft and analyzed the data and further drafts. Z XK contributed to the design and interpretation of the study and to further drafts. All authors contributed to the intellectual content and approved the final version.

References

- 1 Ivy D. Diagnosis and treatment of severe pediatric pulmonary hypertension. *Cardiol Rev* 2001;9:227-237.
- 2 Auslender M. Pathophysiology of pediatric heart failure. *Prog Pediatr Cardiol* 2000;11:175-184.
- 3 Kay JD, Colan SD, Graham TP Jr. Congestive heart failure in pediatric patients. *Am Heart J* 2001;142:923-928.

- 4 Ueno T, Smith JA, Snell GI, Williams TJ, Kotsimbos TC, Rabinov M, et al. Bilateral sequential single lung transplantation for pulmonary hypertension and Eisenmenger's syndrome. *Ann Thorac Surg* 2000;69:381-387.
- 5 Choong CK, Sweet SC, Guthrie TJ, Mendeloff EN, Haddad FJ, Schuler P, et al. Repair of congenital heart lesions combined with lung transplantation for the treatment of severe pulmonary hypertension: a 13-year experience. *J Thorac Cardiovasc Surg* 2005;129:661-669.
- 6 Zhang H, Zhou Q, Wen S, Meng X. Perioperative lung injury in ventricular septal defect with severe pulmonary hypertension, a clinical study of 31 cases. *Zhonghua Yi Xue Za Zhi* 2002;82:1263-1266.
- 7 McDaniel NL. Ventricular and atrial septal defects. *Pediatr Rev* 2001;22:265-270.
- 8 Wessel A, Buchhorn R, Bursch J. Circulatory failure in children with left-to-right shunt in the framework of congenital heart defects: pathophysiology and therapeutic results. *Klin Pediatr* 2000;212:53-59.
- 9 Daliento L, Somerville J, Presbitero P, Menti L, Brach-Prever S, Rizzoli G, et al. Eisenmenger syndrome. Factors relating to deterioration and death. *Eur Heart J* 1998;19:1845-1855.
- 10 Roos-Hesselink JW, Meijboom FJ, Spitaels SE, Van Domburg R, Van Rijen EH, Utens EM, et al. Outcome of patients after surgical closure of ventricular septal defect at young age: longitudinal follow-up of 22-34 years. *Eur Heart J* 2004;25:1057-1062.
- 11 Zhu WH, Li JH, Zhu XK, Kang ML. Postoperative hemodynamic parameter follow-up in children with severe pulmonary resistance hypertension due to ventricular septal defect. *Zhejiang Da Xue Xue Bao Yi Xue Ban* 2003;32:149-151,166.
- 12 Zhu WH, Huang XM. Preoperative and postoperative right heart function and treatment of children with severe pulmonary resistance hypertension due to left-to-right shunt. *J Clin Pediatr* 2004;22:145-147.
- 13 Gong FQ, Lin YM, Tang HF, Gu WZ, Wang W, Kang ML. VEGFmRNA and eNOSmRNA expression in immature rabbits with bleomycin-induced pulmonary hypertension. *J Zhejiang Univ Sci* 2004;5:995-1000.
- 14 Zhu WH, Li JH, Zhu XK, Kang ML. Postoperative hemodynamic parameter follow-up in children with severe pulmonary hypertension due to ventricular septal defect. *Chin Med Sci J* 2004;19:1.
- 15 Maeda K, Yamaki S, Nishiyama M, Murakami Y, Takahashi Y, Takamoto S. Pathological lesions causing pulmonary hypertension after closure of a ventricular septal defect. *Jpn J Thorac Cardiovasc Surg* 2003;51:430-433.
- 16 Kannan BR, Sivasankaran S, Tharakan JA, Titus T, Ajith Kumar VK, Francis B, et al. Long-term outcome of patients operated for large ventricular septal defects with increased pulmonary vascular resistance. *Indian Heart J* 2003;55:161-166.
- 17 Suzuki K, Yamaki S, Mimori S, Murakami Y, Mori K, Takahashi Y, et al. Pulmonary vascular disease in Down's syndrome with complete atrioventricular septal defect. *Am J Cardiol* 2000;86:434-437.
- 18 Salzberg SP, Lachat ML, von Harbou K, Zund G, Turina MI. Normalization of high pulmonary vascular resistance with LVAD support in heart transplantation candidates. *Eur J Cardiothorac Surg* 2005;27:222-225.
- 19 Saleem K, Ahmad SA, Rashid A, Khan AA, Zameer M, Naqvi S, et al. Outcome of ventricular septal defect closure. *J Coll Physicians Surg Pak* 2004;14:351-354.
- 20 Vaidyanathan B, Roth SJ, Rao SG, Gauvreau K, Shivaprakash K, Kumar RK. Outcome of ventricular septal defect repair in a developing country. *J Pediatr* 2002;140:736-741.
- 21 Lindberg L, Olsson AK, Jogi P, Jonmarker C. How common is severe pulmonary hypertension after pediatric cardiac surgery? *J Thorac Cardiovasc Surg* 2002;123:1155-1163.

Received June 9, 2005

Accepted after revision November 12, 2005