Congenital Heart Disease

Long-Term Outcome of Outlet-Type Ventricular Septal Defect: Focus on Congestive Heart Failure and Aortic Valve Disorder

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Purpose: To investigate the outcome of outlet-type ventricular septal defect (VSD) after surgery in pediatric patients.

Methods: A total of 152 children who underwent surgical repairs for outlet-type VSD were enrolled. Clinical features associated with development of congestive heart failure (CHF), aortic valve prolapse (AVP), and aortic regurgitation (AR) were analyzed.

Results: CHF was noted in 34 (22.4%) of 152 patients. Patients with CHF had a larger VSD size ($p < 0.0001$), a higher Qp/Qs ratio ($p < 0.0001$), and a higher mean pulmonary pressure ($p < 0.0001$) compared with patients without CHF. AVP was noted in 106 (69.7%) of 152 patients. Patients with AVP had an older operation age ($p < 0.0001$), a smaller Qp/Qs ratio ($p < 0.0001$), a higher systolic pressure gradient between the left and right ventricles ($p < 0.0001$), and a higher diastolic pressure gradient between the aorta and the right ventricle ($p = 0.022$) compared with the patients without AVP. Among 43 (28.3%) patients with AVP and AR, 17 had mild and 4 had moderate-severe AR after surgery. Severe AVP ($p = 0.0231$) and pre-operative AR ($p < 0.001$) are two risk factors for the presence of postoperative residual AR.

Conclusion: Long-term outcome of surgical repairs for outlet-type VSD is excellent in most pediatric patients without severe CHF or moderate-severe AR. AVP and AR are more frequent and severe in patients with delayed surgery, highlighting the importance of early surgical treatment of outlet-type VSD.

Key Words: Aortic regurgitation • Aortic valve prolapse • Congestive heart failure • Outlet-type ventricular septal defect

INTRODUCTION

Outlet-type ventricular septal defects (VSDs) are relatively common among Orientals.[1-3] Such patients may have severe congestive heart failure (CHF) at a young age, and some are accompanied by a high incidence of aortic valve prolapse (AVP) or aortic regurgitation (AR) ranging from 36% to 79% and 52% to 78%, respectively.[4-6] Early surgical repair of the defect has been advocated,[7,8] but the timing of surgical closure of VSD with or without concomitant aortic valve abnormalities remains controversial.[5,7-9] Furthermore, most previous studies have enrolled adult patients.[1,2,11-14] The

Received: September 10, 2010 Accepted: December 30, 2010
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purpose of this study was to investigate the clinical features associated with the development of CHF, AVP, and AR as well as the long-term outcome of outlet-type VSD in 152 surgically proven children.

MATERIALS AND METHODS

From July 1991 to December 2009, a total of 152 pediatric patients (age ≤ 18 years) who had undergone surgical repairs for outlet-type VSD in Chang Gung Memorial Hospital at Kaohsiung were included in this study. The indications for surgery included CHF, AVP with or without AR, and prevention of VSD-related aortic valve disorders. Patients with major cardiovascular anomalies (e.g. tetralogy of Fallot, transposition of the great arteries, double-outlet right ventricle, or tricuspid atresia) were excluded. The medical records of these patients were retrospectively analyzed. The study was approved by the Human Investigation Committee of our Institutional Review Board.

The VSDs were classified according to the method of nomenclature published by the Society of Thoracic Surgeons in 2000.[15] Outlet-type VSD indicates that the defect lies beneath the semilunar valve(s) in the conal or outlet septum. The size of the VSD was estimated by the surgeon with calipers to measure the short and long axes of the VSD. We took the longer diameter to represent the VSD size. In the study, the true size of the VSD was determined by surgical findings in order to prevent underestimation of echocardiogram due to occult prolapsed cusp. Muscle bar was defined as the presence of muscle found between the VSD and the semilunar valves. CHF was diagnosed if infants had at least 2 of the following conditions: prolonged feeding time > 30 minutes for a single meal, respiratory rate > 60/min or respiratory distress, heart rate > 160/min, hepatomegaly, capillary refilling time > 2 seconds, failure to thrive (weight percentile less than the 3rd percentile),[16] or for patients with heart function in New York Heart Association class II to IV.[17] AVP was defined as the presence of aortic valve leaflet protruding into the VSD. Severe AVP was defined as the formation of sinus of Valsalva aneurysm or windsock deformity of the aortic cusp.[18,19] The grading of AR assessed by echocardiograms was based on the Omoto scale system.[20] The timing of aortic valvuloplasty (Spencer's commissural suspension) was judged and performed by the surgeon if the preoperative evaluation showed a moderate-severe degree of AR. Failure of aortic valve repair was defined by the persistence of moderate-severe AR, or the requirement of aortic valve replacement (AVR) during follow-up. Patients were followed up at the outpatient clinic every 3-6 months in the first year after surgery, and then once annually.

The clinical data included patients' age at surgery, gender, body weight percentile, pulmonary flow/systemic flow ratio (Qp/Qs), mean pulmonary artery pressure, and VSD size found during surgery; associated anomalies including atrial septal defect (ASD), patent ductus arteriosus (PDA) or coarctation of the aorta (CoA), age at which AVP was first diagnosed, the onset age of AR, and outcome were recorded.

Statistical analysis

Results are expressed as mean ± SD. Comparison of the parameters between the groups was performed using the Student *t* test, chi-squared test, Fisher exact test, and Mann-Whitney *U* test as appropriate. Logistic regression was used for multivariate analysis. Statistical analysis was performed using the Statistics Package for Social Sciences 12.0 for Windows XP (SPSS, Chicago, IL). A p value < 0.05 was considered statistically significant.

RESULTS

The study recruited 152 patients with outlet-type VSD. There were 92 boys and 60 girls. The mean age at the time of surgery was 50.4 ± 4.0 months and the mean weight was 16.4 ± 0.9 kg. Forty-six patients had other associated cardiac anomalies, including ASD (n = 37), ASD + PDA + CoA (n = 3), CoA (n = 2), PDA (n = 2), ASD + CoA (n = 1), and PDA + CoA (n = 1). The mean diameter of VSD was 10.0 ± 0.4 mm. The mean Qp/Qs ratio was 1.8 ± 0.1, and pulmonary artery pressure was 32.5 ± 1.5 mmHg. Thirty-four patients (22.4%) had CHF. CHF in 33 patients was due to a left-to-right shunt and in 1 patient due to severe AR. Patients with CHF had a larger VSD size (13.1 ± 0.9 mm vs. 9.1 ± 0.4 mm, $p < 0.0001$), a higher Qp/Qs ratio (3.1 ± 0.2 vs. 1.5 ± 0.1, $p < 0.0001$), a higher mean pulmonary pressure (37.8 ± 3.2 mmHg vs. 16.8 ± 0.5 mmHg, $p < 0.0001$),

and a lower body weight percentile (5 ± 2 vs. 42 ± 3, p < 0.0001) compared with patients without CHF (Table 1). Logistic regression analysis revealed a pulmonary arterial pressure larger than 34 mmHg (p < 0.0001), and a Qp/Qs ratio larger than 2.0 (p = 0.026), as the significant risk factors for the development of CHF.

Among the 34 patients with CHF, three with severe CHF before surgery had early postoperative mortality due to persistent pulmonary hypertension and intractable CHF. There were no atrioventricular blocks or other major operative complications noted. Twelve patients also had AVP. There were two patients with mild AR, and only one patient had severe AR associated with severe AVP. It is noteworthy that this patient first came to our hospital at 10 years of age and, with the exception of this patient, no patient had significant AR after surgery. Failure to thrive was noted in 23 of 34 patients (67.6%) before VSD repair, and good body weight gain was achieved, with an increase of 37 ± 6 percentile after surgery at a mean interval of 98.0 ± 5.5 months.

Out of the152 patients, 106 patients (69.7%) developed AVP. The mean age of diagnosis by echocardiography was 52.3 ± 4.8 months. The mean age at surgery was 58.4 ± 5.1 months. A comparison of clinical characteristics in the patients with and without AVP is summarized in Table 2. Logistic regression analysis revealed the absence of a muscle bar (p = 0.002) and systolic pressure gradient between the left and right ventricles (p < 0.0001) as the risk factors for development of AVP. Among 106 patients with AVP, 69 patients had mild AVP and 37 patients had severe AVP. Patients with mild AVP were significantly younger (42.1 ± 4.6 months vs. 88.9 ± 10.0 months, p < 0.0001), had smaller VSD size (7.6 ± 0.5 mm vs. 13.5 ± 0.6 mm, p < 0.0001), and showed a higher incidence of muscle bar (49.3% vs. 10.8%, p < 0.0001) than those with severe AVP. Logistic regression analysis revealed the absence of a muscle bar (p = 0.002) and delayed operation (p = 0.048) and larger VSD size (p = 0.025) as the risk factors for development of severe AVP. Among the patients with AVP, there were 43 patients associated with AR, including 37 cases of mild AR and 6 cases of moderate-severe AR. The mean

Table 1. Comparison of clinical characteristics in patients with and without congestive heart failure

Parameter	Non-CHF (n = 118)	CHF (n = 34)	p value
Sex (male/female)	72/46	20/14	0.818
Mean operation age (months)	59.1 ± 4.5	20.1 ± 6.1	< 0.0001
BW percentile	42 ± 3	5 ± 2	< 0.0001
VSD size	9.1 ± 0.4	13.1 ± 0.9	< 0.0001
Qp/Qs	1.5 ± 0.1	3.1 ± 0.2	< 0.0001
Mean pulmonary arterial pressure (mmHg)	16.8 ± 0.5	37.8 ± 3.2	< 0.0001
Presence of AVP	92 (78.0%)	12 (35.3%)	< 0.0001

CHF, congestive heart failure; BW, body weight; VSD, ventricular septal defect; AVP, aortic valve prolapse.

Table 2. Comparison of clinical characteristics in patients with and without aortic valve prolapse

	Non-AVP (n = 46)	AVP (n = 106)	p value
Sex (male/female)	27/19	65/41	0.761
Mean operation age (months)	31.8 ± 5.3	58.45 ± 5.1	< 0.0001
VSD size (mm)	10.7 ± 0.9	9.7 ± 0.5	0.278
Qp/Qs	2.6 ± 0.2	1.5 ± 0.1	< 0.0001
Systolic pressure gradient between LV and RV (mmHg)	41.6 ± 5.1	68.5 ± 2.0	< 0.0001
Diastolic pressure gradient between aorta and RV (mmHg)	50.0 ± 2.0	56.5 ± 1.5	0.022
Diastolic pressure gradient between aorta and LV (mmHg)	47.5 ± 1.9	52.9 ± 1.5	0.070
Presence of muscle bar	31 (67.4%)	38 (35.8%)	< 0.0001
Pre-op AR	0	43 (40.6%)	< 0.0001

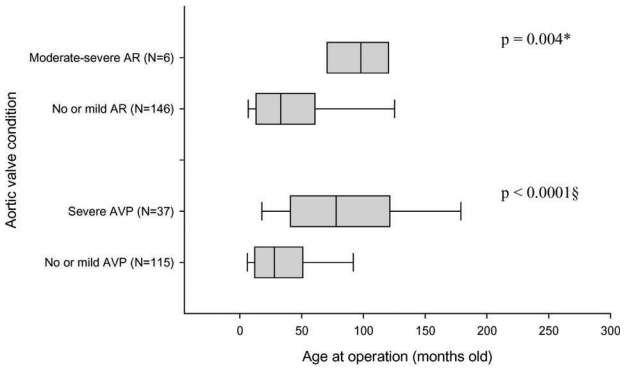
AVP, aortic valve prolapse; VSD, ventricular septal defect; LV, left ventricle; RV, right ventricle; Pre-op AR, pre-operative aortic regurgitation.

age of the patients with AR as noted by echocardiography was 55.1 ± 7.2 months. Mild AR was noted in 37 patients; 13 patients of the group had severe AVP. The mean age at surgery was 53.8 ± 7.3 months. Six patients had moderate-severe AR, all had severe AVP. The mean age at surgery was 97.5 ± 11.2 months. Logistic regression analysis revealed that severe AVP (p = 0.006) was the risk factor for the development of pre-operative moderate-severe AR. The mean age at surgery of patients with severe AVP and moderate-severe AR was also significantly higher than that of patients with less severe AVP and AR (88.9 ± 10.0 months vs. 38.0 ± 3.5 months, p < 0.0001; 97.5 ± 11.2 months vs. 48.4 ± 4.1 months, p = 0.004, respectively) (Figure 1).

Of the 149 survivors who were regularly followed up with median duration of 96.8 months and range of 12 to 353 months, 21 had residual AR, and among these, 17 had mild and 4 had moderate-severe AR. None of the patients without AR before surgery developed AR after VSD repair. A comparison of patients with or without significant postoperative AR is summarized in Table 3. Six patients with preoperative moderate-severe AR who underwent VSD repair required concomitant aortic valvuloplasty. Among these, failure of aortic valve repair was seen in 4 patients, and 3 patients underwent AVR 6, 25, and 85 months after VSD repair, respectively. The remaining one patient refused reoperation and chose medical treatment. Logistic regression analysis revealed that preoperative moderate-severe AR (p < 0.0001) was the risk factor for the failure of aortic valve repair. For patients with outlet-type VSD without AR or with mild AR before surgery, no AR deterioration was found during follow-up echocardiography.

DISCUSSION

In the present study, 22% of patients with outlet-type VSD presented with severe CHF and pulmonary hypertension. Clinically, these patients harbored large VSD with a high Qp/Qs ratio, leading to pulmonary hypertension. Consistent with prior studies,[21,22] our results indicate that early operation is mandatory in such patients and results in remarkable clinical improvement with relief of CHF, a substantial increase in body growth



AVP represents aortic valve prolapse.
AR represents aortic regurgitation.
*Mann-Whitney test.
§Independent Student's *t*-test.

Figure 1. *Age at operation versus complications of aortic valve.*

Table 3. Comparison of patients with or without significant postoperative aortic regurgitation

Parameter	None-to-Mild AR (n = 145)	Moderate-to-Severe AR (n = 4)	p value
Sex (male/female)	88/57	2/2	0.649
Mean operation age (months)	49.6 ± 4.1	111.8 ± 10.5	0.012
Presence of severe AVP	33 (22.8%)	4 (100.0%)	0.003
Presence of muscle bar	69 (47.6%)	0	0.124
Pre-operative moderate-severe AR	2 (1.4%)	4 (100.0%)	< 0.0001
VSD Size (mm)	9.8 ± 0.4	13.8 ± 1.3	0.130
Qp/Qs	1.8 ± 0.1	2.1 ± 0.2	0.636
Presence of pulmonary hypertension*	26 (17.9%)	1 (25.0%)	0.560
Systolic pressure gradient between LV and RV (mmHg)	60.9 ± 2.3	72.8 ± 12.3	0.394
Diastolic pressure gradient between aorta and RV (mmHg)	55.2 ± 1.3	44.0 ± 8.4	0.109
Diastolic pressure gradient between aorta and LV (mmHg)	51.8 ± 1.3	44.5 ± 10.0	0.301

*Pulmonary hypertension is defined as mean pulmonary artery pressure ≥ 25 mmHg.
AR, aortic regurgitation; AVP, aortic valve prolapse; VSD, ventricular septal defect; LV, left ventricle; RV, right ventricle.

and abolition of the development of aortic valve complications. On the other hand, in patients with large VSD, the presence of severe CHF might indicate advanced impairment of heart function. Although VSD repair was successfully accomplished, 3 of our patients had early mortality, highlighting that early surgical treatment is of the utmost importance once mild CHF is recognized in patients with outlet-type VSD.

In patients without CHF, outlet-type VSD may be complicated with the development of AVP. Several mechanisms have been hypothesized, including the Venturi effect of the VSD jet, lack of adequate support due to the absence of an infundibular muscle bar, and intrinsic discontinuity of aortic valve annulus and aortic media.[23,24] The Venturi effect is defined as a high-velocity jet flow of blood created by the VSD below the aortic valve. This effect has been considered as the most probable cause of AVP[25,26] because such a high-velocity jet flow is potentially capable of progressive elongation of the adjacent aortic valve cusp, gradually leading to the formation of windsock deformity over time, and eventually causing the development of AVP. With further deterioration, the aortic valve may be distorted, and then AR may occur. In the present study, patients with AVP had a higher pressure gradient between the left and right ventricles (RV) during systole compared with those without AVP. This finding supports the Venturi effect hypothesis that the higher the pressure gradient, the higher the velocity of the Venturi jet, and thus the higher the chance of AVP development.[5,25,27] In addition, our results also showed that the pressure gradient between the aorta and RV during diastole was higher in patients with AVP, which may be suggestive of a higher chance of downward dragging of the aortic cusp into the RV. The presence of an infundibular muscle bar has also been described as an important support for the aortic valve.[21,24,28,29] Consistent with prior studies,[5,27,30] our results also showed that patients without an infundibular muscle bar ($p < 0.0001$) had a significantly higher frequency of AVP development.

Large VSD frequently associated with AVP development has also been reported,[24,31] with VSD size assessment based on surgical results. On the other hand, this association has not been addressed in studies in which VSD size assessment was based on echocardiographic results.[21,32] This finding indicated the possibility of underestimation of outlet-type VSD in preoperative imaging studies in patients with AVP. In retrospect, an underestimation of VSD diameter was usually associated with the presence of AVP, such that the size of the defect seen on echocardiogram seemingly appeared smaller than the actual size. From a clinical perspective, spontaneous decrement or closure of outlet-type VSD is rare, particularly when the patient presents with no parallel clinical improvement. Therefore, assessment of outlet-type VSD presented with AVP by echocardiography is a challenge in clinical practice. In our experience, a decrement of the outlet-type VSD size noted on an echocardiogram may be considered as an indirect sign of AVP development.

Aortic valvuloplasty in VSD patients with severe AVP has been advocated to prevent AR.[24] In our study, 31 out of the 37 patients who presented with severe AVP without AR or with mild AR were successfully managed with simple closure of the defect without aortic valvuloplasty, and none of these 31 patients developed AR progressions after operation. Trivial or mild AR may sometimes be observed by echocardiography after surgical repair of VSD.[33,34] Simple closure of the defect with reduction of the Venturi effect has also been proved to be effective in the prevention of AR deterioration.[7,21] From our experience, routine aortic valvuloplasty in patients with severe AVP without significant AR might not be needed. For children and adolescents with moderate or severe AR, aortic valvuloplasty is reported as a valid option with good intermediate results.[35] However, in 4 of 6 patients with moderate-severe AR who were managed with defect closure and concurrent valvuloplasty, residual severe AR was still found after surgery. Severe AVP ($p = 0.0231$) and pre-operative AR ($p < 0.001$) are two risk factors of postoperative residual AR. In our study, valvuloplasty was effective in two patients to restore the aortic valve function and prevent further deterioration.

CONCLUSION

Long-term outcome of surgical repairs for outlet-type VSD is excellent in most pediatric patients without severe CHF or moderate-severe AR. AVP and AR are more frequent and severe in patients with delayed sur-

gery, highlighting the importance of early surgical treatment of outlet-type VSD.

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