Aortic Valve Prolapse Associated With Outlet-Type Ventricular Septal Defect

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Background. **Aortic valve prolapse is frequently associated with juxta-arterial ventricular septal defect. The significance of its association with other outlet types of ventricular septal defect, however, remains unclear.**

Methods. **From 1987 to 2002, 677 patients (male:female ratio, 424:253) who received surgical repair for ventricular septal defect extending to the outlet septum were reviewed. Based on surgical findings, ventricular septal defects were classified as juxta-arterial, perimembranous outlet, or muscular outlet type.**

Results. **Aortic valve prolapse occurred in 373 of 677 patients (57.2%) with 209 juxta-arterial, 103 perimembranous outlet, and 61 muscular outlet type. Significant aortic regurgitation developed in 51 of 373 (14%). Among 252 patients with regular follow-up, the mean onset ages of aortic valve prolapse in juxta-arterial, perimembranous outlet, and muscular outlet type were 4.9, 5.0, and 5.1 years, respectively (no statistical difference). The presence of larger shunt and probably anterior malalignment predicted an earlier onset of aortic valve prolapse. Perimembranous outlet and muscular outlet type ventricular septal defect were frequently associated with infundibular hypertrophy and subaortic ridge, and perimembranous outlet type was associated with anterior septal malalignment. In juxta-arterial ventricular septal defect and ventricular septal defect with anterior malalignment, prolapsed cusp was always the right coronary cusp, but noncoronary cusp involvement was also common in perimembranous outlet type (17 of 103, 16.5%).**

Conclusions. **The association with anterior septal malalignment, infundibular stenosis and subaortic ridge is related to the location of the outlet ventricular septal defect. The age of onset of aortic valve prolapse in each type was quite similar, and a larger shunt may predict an earlier onset.**

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According to the classification by Soto and associates [1], Tynan and Anderson [2], and Gatzoulis and colleagues [3], outlet type ventricular septal defects (VSD) include doubly committed juxta-arterial, perimembranous outlet type, and muscular outlet type. With a relative high incidence in Asian countries [4, 5], the association of juxta-arterial type VSD with aortic valve prolapse (AVP), mainly right coronary cusp prolapse, and aortic regurgitation (AR) has been defined. According to previous reports, the incidence of AVP in juxta-arterial VSD was 36% to 79% [6–8]. The peak age for AVP was around 7 years, and that for AR was between 5 and 10 years [6, 7, 9]. To avoid irreversibility of AVP and AR after operation, early surgical intervention in juxta-arterial type VSD is suggested at most centers as long as significant AVP is detected either by echocardiography or by angiography [10–13]. In contrast, study about AVP and AR in perimembranous outlet and muscular outlet VSD is limited. This study based on a large cohort of patients was to compare the clinical manifestations of AVP and AR in the three types of outlet VSD.

Patients and Methods

Patients

From September 1987 to December 2002, 717 patients who had undergone surgical repair of VSD that extended to the outlet septum were retrospectively studied. Patients associated with complex cardiac lesions such as double outlet ventricle, tetralogy of Fallot, transposition of great artery, arch anomaly, and mitral valve anomaly were excluded. Forty patients were also excluded due to inadequate surgical information as type categorization. For the 677 remaining patients (male:female ratio, 424:253), AVP developed in 373 (57.2%). The medical records, echocardiographic recordings, and angiographic and surgical findings of these patients were reviewed.

Methods

The classification of VSD was according to the Soto and Anderson classification as illustrated in Figure 1 [1, 2]. For juxta-arterial type, the defect is immediately beneath both aortic and pulmonary valve, with aortic valve and

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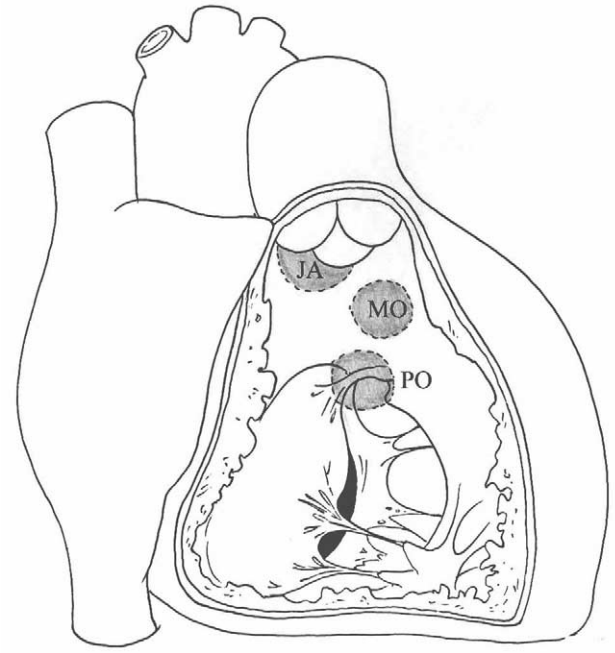

Fig 1. Schematic presentation of the location of three outlet types of ventricular septal defect from the right ventricular aspect. (JA = *doubly committed juxta-arterial;* PO = *perimembranous outlet;* MO = *muscular outlet.)*

pulmonary valve in fibrous continuity. Both the outlet septum and septal component of subpulmonary infundibulum are absent. For muscular outlet VSD, the defect is in muscular septum opening into outlet septum, with intact subpulmonary infundibulum between the pulmonary valve and defect. For perimembranous outlet VSD, the defect is in the membranous septum and extending toward the outlet. Classification of VSD was based on the surgical findings, as there may be controversial between echocardiography and cardiac catheterization diagnosis. The size of VSD was defined as the largest anatomical diameter measured during surgery to avoid underestimation at echocardiography or angiography due to AVP.

The diagnosis of AVP was made according to the echocardiographic findings that were confirmed by angiographic or surgical findings. The grading of AR by echocardiograms was based on the Omoto scale system as trivial (slight under aortic valve), mild (not reaching tip of mitral valve leaflet), moderate (reaching tip of mitral valve leaflet), and severe (beyond tip of mitral valve leaflet) [14, 15]. Only AR greater than mild degree will be considered as significant AR and used in statistical analysis.

The associated anomalies were defined either by echocardiography or during surgery. The anterior malaligument was defined as anterior deviation of the outlet septum relative to the muscular interventricular septum. The subaortic ridge was a fibrous subaortic ridge that may cause left ventricular outlet narrowing. The infundibular hypertrophy was either due to hypertrophy of anomalous muscle bundles of right ventricle or secondary to long-term jet effect of VSD over the infundibulum. For those defined as syndromic, it means patients have other associated syndromes in addition to ventricular septal defect, with most of them being Down syndrome. For the 446 patients receiving cardiac catheterization (all receiving catheterization within 1 month before surgery), Qp/Qs and mean pulmonary artery pressure were measured. The Qp/Qs was the ratio between flow of pulmonary circulation and systemic circulation. When the value was greater than 1.5, it indicated a significant left to right shunt.

Table 1. Comparisons of Clinical Characteristics in 677 Patients With Outlet Ventricular Septal Defect According to Presence of Aortic Valve Prolapse

	Non AVP	AVP	*p* Value
Sex	155 (55.6%)	254 (68.1%)	***0.001***
CHF symptom	194 (72.1%)	103 (28.9%)	***0.000***
Syndrome	13 (4.7%)	7 (1.9%)	***0.036***
Subacute bacterial endocarditis	6 (2.2%)	11 (2.9%)	0.355
VSD type			
Juxta-arterial	91 (32.6%)	209 (56.0%)	
Perimembranous outlet	161 (57.7%)	103 (27.6%)	***0.000***
Muscular outlet	27 (9.7%)	61 (16.4%)	
VSD size	8.8 ± 5.1	7.9 ± 4.6	***0.020***
Qp/Qs	2.6 ± 1.7	1.6 ± 0.8	***0.000***
Pulmonary artery pressure	27.9 ± 15.7	15.3 ± 7.3	***0.000***
Operation age	5.7 ± 8.7	10.7 ± 10.3	***0.000***
Operation mortality	8 (2.9%)	3 (0.8%)	***0.043***

Bold italics indicates *p* value less than 0.05.

AVP = aortic valve prolapse; CHF = congestive heart failure; VSD = ventricular septal defect.

Statistics

The statistics used in our study include χ^2 study, likelihood ratio, or Fisher's exact test for the comparisons of mean and frequency. One-way analysis of variance (ANOVA) was applied for numeric comparison. Linear multiple regression was used for multivariate analysis. The log-rank test was used for comparisons in Kaplan-Meier curves. Statistical significance was defined as a *p* value less than 0.05.

Results

The clinical characteristics of 677 patients with outlet VSD are summarized in Table 1. The surgical indications differed between the two groups as most of the patients with AVP underwent operation owing to valve prolapse and some because of heart failure symptoms. For those without AVP, most received an operation because of heart failure, and some because of associated lesions. So we can see more heart failure symptoms, younger age at operation, larger Qp/Qs, and higher pulmonary artery pressure in patients without AVP as compared with patients with AVP.