Prognostic Implications of Initial Echocardiographic Findings in Adolescents and Adults with Supracristal Ventricular Septal Defects

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Background: Although surgery is recommended for pediatric patients with supracristal ventricular septal defects (sVSDs) to prevent progression of aortic regurgitation (AR), outcomes in adolescents and adults with sVSDs are not known.

Methods: In this retrospective observational study, clinical data without surgery were obtained in 60 patients with sVSDs (group 1; mean age, 36 ± 13 years), 120 age- and defect size–matched patients with perimembranous ventricular septal defects (group 2), and 52 patients with sVSDs who underwent surgery (group 3; mean age, 32 ± 11 years).

Results: Aortic sinus wall prolapse (38% vs 3%, $P < .0001$) and moderate to severe AR (7% vs 0%, $P = .012$) were more frequently observed in group 1 than in group 2. Five, three, and two patients in group 1 had surgery during follow-up because of rupture of the aneurysm of the sinus of Valsalva, endocarditis, and heart failure, respectively. Group 1 had a lower 12-year clinical event-free (surgery and endocarditis) rate (76 ± 9% vs 94 ± 4%, $P = .031$) but an equivalent overall survival rate (100% vs 94 ± 3%, $P = .143$) compared with group 2. Patients with maximal prolapsing aortic sinus wall length > 7 mm showed a higher frequency of aneurysm of the sinus of Valsalva rupture than those with no prolapse or maximal prolapsing length ≤ 7 mm (80% [four of five] vs 2% [one of 55], $P < .001$). The event-free and overall survival rates were comparable between groups 1 and 3, with equivalent 10-year AR progression–free survival rates (94 ± 5% vs 91 ± 5%, $P = .301$).

Conclusions: Aneurysm of the sinus of Valsalva rupture, rather than AR progression, was the main clinical event. Watchful monitoring of patients with high-risk echocardiographic features may be a rational option. (J Am Soc Echocardiogr 2014;27:965-71.)

Keywords: Subarterial ventricular septal defect, Aortic regurgitation, Aneurysm of sinus of Valsalva, Echocardiography

The association between ventricular septal defect (VSD) and aortic regurgitation (AR) was recognized as an important disease entity many years ago. Supracristal VSD (sVSD) is strongly associated with this disease entity, which is characterized by a totally deficient infundibular septum[1] and a lack of continuity between the aortic media, annulus, and ventricular septum.[2] Aortic valve prolapse that results in AR and aneurysm of the sinus of Valsalva (ASV) are common aortic complications of sVSD and are reported to progress once they develop.[3-6] Therefore, it has been recommended to repair the defect surgically as soon as these aortic complications are detected.[2,7-9] However, this recommendation is based on observational studies of young pediatric patients (mean age < 10 years),[5,8,9] and the natural history of patients with sVSDs who have reached adolescence or adulthood is poorly understood. Given that the aorta and cardiac chambers grow only during childhood and stop expanding significantly after 15 years of age,[10] it is possible that the progression or pattern of these aortic complications in adult patients with sVSDs may differ from those in children, and even in young pediatric patients, the role of prophylactic surgery for patients without aortic complications remains controversial.[11,12] We aimed to evaluate the natural histories of adolescents and adults with sVSDs and to determine factors associated with the development of aortic complications, including AR progression and ASV rupture. The clinical outcomes of those adolescent or adult patients with sVSDs, who were followed conservatively and treated surgically only when necessary, were compared with those of adult patients with perimembranous VSDs (pmVSDs), for whom the same watchful monitoring strategy has been accepted as the standard approach, and those of patients with sVSDs who underwent initial surgery.

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Abbreviations
AR = Aortic regurgitation
ASV = Aneurysm of the sinus of Valsalva
pmVSD = Perimembranous ventricular septal defect
sVSD = Supracristal ventricular septal defect
VSD = Ventricular septal defect

METHODS

Study Population

Between January 1990 and November 2009, 134 patients >16 years of age were confirmed to have isolated sVSDs without complex congenital lesions in our institution. The routine evaluation included transthoracic echocardiography and a single-pass heart scan using ^{99m}Tc-diethylenetriamene penta-acetate to measure Qp/Qs. Patients were excluded if they had Eisenmenger syndrome ($n = 2$) or were not followed up after the initial visit ($n = 20$). The subjects thus consisted of the remaining 60 patients with sVSDs who were followed conservatively and whose follow-up data were available (group 1) and 52 who underwent initial surgery (group 3). In group 3, the development of complications (ASV rupture [$n = 11$] and infective endocarditis [$n = 6$]) or heart failure ($n = 5$) was main indication for surgery, and the remaining 30 stable patients without symptoms underwent surgery under attending physicians' discretion. As a control group, 120 age- and defect size–matched patients with pmVSDs who were also followed conservatively for the development of symptoms or complications before surgical intervention were selected from the database of our echocardiography laboratory (group 2). This retrospective study conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by our institutional review board. The requirement for informed consent was waived by the board for this study.

Echocardiography

The diagnoses of sVSD and pmVSD were based on the echocardiographic observations,[13,14] and transesophageal echocardiography was generally recommended for detailed evaluation of sVSDs and associated anatomic abnormalities, which was performed in >70% of patients. The echocardiographic images were reviewed to determine whether significant aortic sinus wall prolapse was present because of herniation of the aortic wall through the VSD (Figures 1A–1D). The size of the remnant VSD showing flow communication through the defect was measured at mid-systole in the magnified view (Figure 1). In patients with aortic sinus wall prolapse, the maximal length of the prolapsed wall was measured at diastole; the maximal distance between the crest of interventricular septum and beginning of the aortic sinus wall prolapse at systole was defined as presumptive true VSD size (Figures 1E–1H). Parasternal long-axis images on transthoracic echocardiography were used for VSD size measurement; in patients with poor resolution, the long-axis image on transesophageal echocardiography was used. The degree of AR was assessed by comprehensive Doppler echocardiographic measurements using jet width, jet cross-sectional area in the left ventricular outflow tract, and Doppler tracing of the aortic flow and classified as mild, moderate, or severe.[15] Cardiac chamber dimensions and left ventricular ejection fraction were measured according to the recommendations of the American Society of Echocardiography.[16]

Data Collection and Analysis

A chart review was performed, and the data were collected by using a standardized form that recorded the information regarding patient demographics, medical history, clinical presentation, result of imaging studies, and adverse clinical events. Adverse clinical events included a composite of open-heart surgery for any cause, including reoperation after the initial surgery in group 3, cardiac death, and the development of infective endocarditis.[9] Follow-up data were collected by a direct telephone interview and a detailed review of all medical records. The causes and dates of any deaths were confirmed by information gathered from the National Population Registry of the Korean National Statistical Office, together with a review of all available clinical records at the time of death. The median follow-up durations were 78 months in the sVSD group (interquartile range, 37–137 months) and 71 months in the pmVSD group (interquartile range, 39–115 months).

Statistical Analysis

All statistical analyses were performed by using SPSS version 18.0 (SPSS, Inc, Chicago, IL). Summary statistics are presented as frequencies and percentages or as mean ± SD. Differences between two groups in terms of continuous variables were tested by using unpaired Student t tests and the Mann-Whitney U test and differences among three groups by using analysis of variance and the Tukey method for post hoc analysis. The χ^2 test or Fisher exact test was used to compare the frequencies of categorical variables between groups. Bonferroni correction was used for multiple comparisons. The Spearman rank correlation test was performed to evaluate an association between AR severity and the maximal length of the prolapsing aortic wall. To determine the cutoff value of the maximal length of the prolapsing aortic wall for predicting the development of ASV rupture, a receiver operating characteristic curve was used. To identify factors that were associated with the development of clinical events in groups 1 and 2, univariate and multivariate Cox proportional-hazard models were used. In multivariate analysis, VSD type, left atrial size, and left ventricular size were used in the backward linear regression method. Cumulative survival and event-free survival rate curves were generated with the Kaplan-Meier method and compared by using the log-rank test. All P values were two sided, and P values $< .05$ were considered significant. Intraobserver and interobserver variability for the measurement of VSD size were assessed by Bland-Altman analysis, with interobserver variability by intraclass correlation coefficients between two independent observers for 20 randomly selected patients. The two independent observers achieved interobserver variability of 0.92 to 0.98 and intraobserver variability of 0.94 to 0.98.

RESULTS

The baseline characteristics of the patients are summarized in Table 1. Groups 1 and 2 did not differ with regard to age at initial diagnosis, mean size of the remnant VSD, left ventricular size, or Qp/Qs. Compared with group 2, group 1 had a significantly higher prevalence of aortic sinus wall prolapse ($P < .0001$) and moderate to severe AR ($P = .012$). Moderate to severe AR was observed only in the sVSD group. There was no significant association between AR severity and the maximal length of the prolapsing aortic sinus wall in the group 1 ($r = -0.115$, $P = .603$). The presumptive true VSD size (6.1 ± 4.1 vs 8.7 ± 5.6 mm, $P = .010$) and remnant VSD size (3.5 ± 0.9 vs 5.1 ± 3.3 mm, $P < .001$) were larger in group 3 compared with group 1. This trend was also observed in patients