

Coexisting ventricular septal defect affects the features of ruptured sinus of Valsalva aneurysms

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ABSTRACT

الأهداف: تحديد العلاقة الموجودة بين خلل الحاجز البطيني VSD و RSVa.

الطريقة: خلال الفترة من سبتمبر 2013م وأبريل 2014م خضع 80 مريض RSVa للإصلاح الجراحي. تم تقييم هؤلاء المرضى بأثر رجعي إلى مجموعتين مجموعة VSD (38 حالة) ومجموعة ليست VSD (42 حالة).

النتائج: نشأت نقاط تمزق SVA بشكل متكرر أكثر في الجيب الأيمن التاجي (RCS) للمرضى في مجموعة VSD من تلك الموجودة في مجموعة غير VSD ($p=0.002$). في مجموعة VSD يميل أكثر من 92.1% إلى تمزق في تدفق مجرى البطين الأيمن. ونقاط التمزق متنوعة في مجموعة غير VSD. ظهر فرق كبير في نقاط تمزق RSVa بين المجموعتين ($p<0.001$). المرضى في المجموعة VSD ظهر لديهم مرض الصمام الأبهري أكثر من المرضى في مجموعة غير VSD ($p<0.001$). تم إصلاح جميع مجموعته 67 مريض في فتح RSVa. من بينهم، تم إصلاح جميع المرضى في مجموعة VSD و29 مريض في مجموعة غير VSD. تلقى 9 مريض ليسوا في مجموعة VSD إغلاق RSVa بطريق القسطار.

الخاتمة: وجود أو إختفاء VSD يؤثر على نقاط تمزق RSVa، ومرض الصمام الأبهري المعني، والجدول الزمني العلاجي. نوع RSVa يجب أن يتم تعديله سريريا على أساس وجود أو اختفاء VSD.

Objectives: To determine the correlation exists between ventricular septal defect (VSD) and ruptured sinus of Valsalva aneurysm (RSVA).

Methods: Between September 2003 and April 2014, 80 RSVa patients underwent surgical repair. These patients were retrospectively divided into two groups: the VSD group (38 cases) and the non-VSD group (42 cases).

Results: Rupture points of SVA originated more frequently in the right coronary sinus (RCS) of patients in the VSD group than those in the non-VSD group ($p=0.002$). In the VSD group, more than 92.1% tended to rupture into the right ventricular outflow tract. The rupture points are diverse in the non-VSD group. A significant difference was found in rupture points of RSVa between the two groups ($p<0.001$). Patients in the VSD group presented with aortic valve disease more often than those in the non-VSD group ($p<0.001$). A total of 67 patients were repaired with a patch at the opening of RSVa; of those, all patients in VSD group and 29 patients in non-VSD group were repaired with a patch. Nine patients in non-VSD group received transcatheter closure of RSVa.

Conclusion: The presence or absence of VSD affects the rupture points of SVA, aortic valve disease involved, and therapeutic schedule. Ruptured sinus of Valsalva aneurysm type should be clinically modified on the basis of presence or absence of VSD.

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Sinus of Valsalva aneurysm (SVA) refers to a deficiency of the elastic fibers in the aortic sinus middle wall and valve ring.¹ Rupturing of a SVA usually occurs in the young and middle-aged. Approximately 50% of ruptured SVAs (RSVAs) coexist with ventricular septal defect (VSD).^{2,3} However, among SVA patients with both ruptured and non-ruptured SVA,⁴ only 11.6% of them coexist with VSD. Therefore, we propose that RSVA patients with VSD should have some distinguishing features. Matsushita et al⁵ reported a rupture of SVA from the right coronary to the right ventricle in a patient whose VSD had closed 10 years prior. A similar case occurred in our study. Thus, SVA and VSD may undergo independent pathological changes respectively. The objective of our study was to determine whether a correlation exists between VSD and ruptured SVA in order to simplify the clinical classification and provide useful guidance to clinical practices.

Methods. Between September 2003 and April 2014, 11,535 cases of congenital heart disease were treated in the General Hospital of Shenyang Military Area Command, Shenyang, China. Among those cases, all RSVA patients were eligible for our retrospective case-control study. For patients with RSVA, there were no exclusion criteria. Eighty patients with RSVA were observed (80/11535, 0.7%), among which there were 38 cases of RSVA with coexisting VSD (38/80, 47.5%). Fifty-seven patients were male and 23 were female. The mean age was 37.8±12.0 years (range: 15-64 years). Patients included in the study were retrospectively divided into 2 groups: VSD group (n=38 cases) and a non-VSD group (n=42 cases). The patients were followed up at our outpatient department or through telephone calls, e-mails, and questionnaires. Follow-up time ranged from 6 months to 10.2 years, with a mean of 3.2±7.6 years. This study was conducted according to the ethical guidelines of the Declaration of Helsinki (1975) and approved by our hospital's ethics committee.

Echocardiography. All patients underwent a complete transthoracic 2D and Doppler echocardiographic examination using an ultrasound system (Philips IE 33, Andover, MA, USA) with a 5 MHz probe. The key planes included a parasternal long-axis view of the left ventricle, a short-axis view of the aortic root, a long-axis view of the right ventricular outflow tract (RVOT), an apical 5-chamber view, and some modified, non-standard views showing the aortic root. In particular, the following details were identified on review of the images: size, origin, and termination of the RSVA; continuity of the aneurismal wall; severity of any involved valvular insufficiency, especially of the aortic

valve; and the presence of associated cardiovascular anomalies (Figures 1A & 1B). These echocardiographic characteristics were then compared with the operative findings at surgery.

Operative procedure. Under moderate hypothermic (28°C) cardiopulmonary bypass, 67 patients were operated using median sternotomy. Cardioplegia was retroperfused through the coronary sinus via a right atriotomy. In patients with RSVA without VSD, the base of the fistula was repaired with an ellipsoidal packing piece closing in discontinuous sutures. In patients with RSVA and VSD, the base of the fistula and VSD was repaired with a dumbbell-shaped packing piece simultaneously closing in discontinuous sutures. The aneurismal wall should be reserved as a lining of packing piece for simultaneous closure. If aortic insufficiency in RSVA patients was found by preoperative echocardiography, the aortic valvuloplasty or valve replacement should be operated on via an aortotomy after the fistula and/or VSD are repaired with one packing piece. The aortic valve with calcification and contracture should be replaced.

Transcatheter closure. Transcatheter closure was performed on 9 patients with RSVA, all without VSD. The SVAs of those patients were delineated by aortic root angiography and occluded with 2-5 mm patented ductus arteriosus (PDA) occluder (Lifetech Ltd, Shenzhen, China) based on the narrowest opening of the RSVA. Methods were in accordance with Fang et al.⁶ Under the guidance of fluoroscopy and TTE, we confirmed that the RSVA was closed completely and no significant aortic regurgitation (AR) occurred.

Statistical analysis. Statistical analyses were performed using Statistical Package for Social Sciences Version 12.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are reported as the mean ± standard deviation. Comparisons in age, duration, and cardiac functional class between the 2 groups were performed using independent t-tests. Chi-square tests were performed to compare gender, co-existing cardiac abnormalities, the presence of aortic valve disease, and the origin and rupture points of RSVA between 2 groups. A p-value of 0.05 was used to deem statistical significance.

Results. Table 1 summarized the clinical data of 80 patients admitted in the General Hospital of Shenyang Military Area Command, Shenyang, China. There was one early death and 4 patients who were not operated on due to severely impaired left ventricular function. During the intraoperative phase, 3 patients (3/38, 7.9%) were found with co-existing VSD.

Comparison of the origin and rupture positions.

There was a significant difference in the origins of RSVA between the VSD and non-VSD groups ($n=80$, $\chi^2=9.175$, $p=0.002$). The origin of RSVA was primarily located in the right coronary sinus (RCS). The ruptured aneurysms originated in the RCS in all 38 VSD patients. In the non-VSD group, more than 78.6% (33/42) originated in the RCS. There was also a significant difference in the rupture points of SVA between these 2 groups ($n=80$, $\chi^2=55.98$, $p<0.001$). In the VSD group, more than 92.1% (35/38) tended to rupture into the right ventricular outflow tract (RVOT). In the non-VSD group, the rupture points of SVA are diverse (Table 2).

Treatment of aortic valve disease. In the VSD group, 18 patients (18/38) were complicated with aortic valve disease, and in the non-VSD group, only 3 patients (3/42) were complicated with aortic valve disease. Thus, a significant difference exists between these 2 groups ($p<0.001$). In the VSD group, 11 were operated with aortic valve replacement, 5 with aortic valvuloplasty, and 2 could not be operated due to severely impaired left ventricular function. Three patients had cardiac malformations, including 2 cases of subaortic stenosis and one case of quadricuspid aortic valve. In the non-VSD group, only 3 patients were complicated with the aortic valve disease, among them one patient with bicuspid aortic valve who was operated on using the Bentall procedure, one with aortic valvuloplasty, and one patient who could not be operated on due to severely impaired left ventricular function and severe pulmonary hypertension.

Table 2 - Distribution of rupture points of 80 patients admitted in the General Hospital of Shenyang Military Area Command, Shenyang, China.

Rupture points	VSD group (n=38)	Non-VSD group (n=42)
RCS rupture into RVOT	35 (92.1)	7 (16.7)
RCS rupture into RA	2 (5.3)	18 (42.9)
RCS rupture into RV body	1 (2.6)	7 (16.7)
RCS rupture into pericardium	0	1 (2.4)
Non-CS rupture into RA	0	8 (19.1)
LCS rupture into RA	0	1 (2.4)

Data were expressed as number and percentage (%).

VSD - ventricular septal defect, RCS - right coronary sinus, LCS - left coronary sinus, Non-CS - noncoronary sinus, RA - right atrial, RV - right ventricular, RVOT - right ventricular outflow tract

Comparison of operative methods. The operative methods selected were different for the 2 groups. Sixty-seven patients were repaired with a patch in the opening surgery of RSVA. All patients in VSD group (38 cases) underwent this procedure. Nine patients in the non-VSD underwent transcatheter closure of the opening of the RSVA; 3 originated from the RCS and ruptured into the RA, 3 originated from the RCS and ruptured into the RV, and 3 originated from the non-CS and ruptured into the RA. The aortic valve and heart function in 75 cases were in good condition during follow-up.

Discussion. In our study, RSVA patients were divided into 2 groups based the presence or absence of VSD. We found significant distinctions in the patients'

Table 1 - Clinical data of 80 patients admitted in the General Hospital of Shenyang Military Area Command, Shenyang, China.

Clinical data	VSD group (n=38)	Non-VSD group (n=42)	P-value
Gender (male,%)	30 (78.9)	27 (64.3)	0.132
Age (Y)	34.9±12.5	38.5±11.5	0.179
Duration of symptoms (Y)	5.9±11.3	0.6±1.3	0.004
Co-existing other cardiac abnormalities (n)	7 (quadricuspid aortic valve 1, ASD 2, subaortic stenosis, 2 RVOTS1, PDA 1)	1 (bicuspid aortic valve 1)	0.043
Cardiac functional class (NYHA)	2.37±0.58	3.12±0.52	0.0412
Aortic cross-clamp time (min)	56.2±16.5	31.7±18.2	0.0132
Cardiopulmonary bypass time (min)	86.2±22.5	54.16±19.2	0.0189
LVEDI (ml)	53.2±5.3	51.6±4.8	0.0819

VSD - ventricular septal defect, ASD - atrial septal defect, RVOTS - right ventricular outflow tract stenosis, PDA - patent ductus arteriosus, LVEDI - left ventricular end diastole internal diameter

presentation, pathological anatomy, treatment, and incidence of aortic valve disease between the 2 groups. Further, we found significant correlations between specific features of RSVA and whether the RSVA occurred with or without VSD. We propose that RSVA type should be clinically modified on the basis of presence or absence of VSD. This could be helpful in understanding the history and therapeutic schedule of RSVA.

Sinus of Valsalva aneurysm primarily originated in the right coronary sinus (RCS)^{7,8} followed by the non-coronary sinus (non-CS). Presently, classification of RSVA is based on the anatomical origin and rupture points of SVA.^{9,10} We found that the rupture points of SVA originated more frequently in the RCS of patients in the VSD group than those in the non-VSD group ($n=80$, $\chi^2=9.175$, $p=0.002$). We also found that the rupture points of SVA in the non-VSD group are diverse; in contrast, in the VSD group, rupture points are nearly all located in the RVOT. Thus, there is a significant difference in the rupture points of SVA between these 2 groups ($n=80$, $\chi^2=55.98$, $p<0.001$). Therefore, we propose that there is a correlation between the anatomical features of RSVA and the presence or absence of VSD.

While the origin and the rupture site of aortic sinus aneurysms are related to structural defects of the aortic sinus, they are more related to surrounding anatomical structures. The RCS is globally close to the RVOT, and the boundary between the RCS and the non-CS is situated in the perimembranous interventricular septum. Therefore, most SVAs with VSD ruptured into RVOT through the infundibular VSD and subpulmonary VSD instead of the perimembranous VSD. Most RSVA patients with origins in the non-CS and rupturing into the RA and RV body did not have co-existing VSD. Infundibular VSD increased the extent of right aortic sinus bulging, which means that a right aortic sinus aneurysm with ventricular septal defect is more likely to rupture. When the dilated aortic sinus aneurysm is embedded into the VSD, the shunting of blood caused by VSD is reduced; thus, the enlargement of the left atrium and left ventricle is not obvious, so it is prone to misdiagnosis and missed diagnosis of combined VSD. Three-D echocardiogram,^{11,12} CT, and MRI¹³ can improve the rate of correct diagnosis. We propose that the presence or absence of VSD affects the rupture points of SVA due to the anatomical relationships between VSD and the sinus of Valsalva.

Ventricular septal defect is a common congenital heart disease often associated with other cardiac malformations such as aortic abnormalities, subaortic

stenosis, patent ductus arteriosus, and coarctation of the aorta.¹⁴ This characteristic is also reflected in RSVA patients. In our study, patients in VSD group were more likely to suffer from other co-existing cardiac abnormalities than patients in non-VSD group ($p=0.043$). In RSVA patients with co-existing VSD, the aortic valve could be unsupported, increasing the likelihood of aortic insufficiency. Therefore, regardless of VSD size, VSD patients should receive regular check-ups to identify possible involvement of a SVA and the aortic valve.

The SVA patients in the VSD group were complicated with aortic valve disease significantly more than those in non-VSD group ($p<0.001$). Ruptured SVAs patients complicated with VSD should be operated on using special surgical methods. In order to design effective surgical methods, it is important that the severity and reason for aortic valve disease are provided by preoperative echocardiography. Aortic valves with calcification and contracture should be replaced. Aortic valvuloplasty should be considered if aortic valve leaflets are in good condition, there is a fine echo, and the missing aortic valve ring is supported. Leftover or progressive aortic regurgitation are often important factors affecting the postoperative short- and long-term efficacy. If a preoperative diagnosis of aortic regurgitation is confirmed, the 2-incision technique should be applied. For patients with SVA combined with aortic regurgitation, after repairing the opening of the SVA and VSD with the same dumbbell-shaped patch, the next step should be aortic valvuloplasty or valve replacement through the aortic incision.

Liu et al¹⁵ found that RSVA repaired with direct sutures was an independent risk factor for follow-up aortic insufficiency worsening. In our study, 67 RSVA patients with and without VSD were repaired with a patch simultaneously closing the base of the fistula and/or VSD in interrupted sutures, and the supportive effect of aortic valve rings were recovered and reinforced. During follow-up, the structure and function of aortic valves were in good condition. Therefore, RSVA surgical methods affect the long-term function of the aortic valve, and RSVA repaired with a patch in interrupted sutures is proposed.

The existence of combined VSD not only affects the opening of aortic sinus aneurysm, but also the shape and size of the ruptured SVA. For a few patients without VSD, intervention methods can be attempted to close the rupture. If the extent of the SVA rupture into the heart chamber is small, the edge of the rupture is even, and the opening's distance with respect to valve is greater than 7 mm, intervention can be considered.

In our study, 9 patients (9/42, 21.4%) in the non-VSD group received transcatheter closure of the opening of the RSVA. During follow-up, all cases were found in good condition. It is a relatively effective and safe therapy to close the opening of the RSVA without VSD using a transcatheter in a few patients.⁶ The points and shape of RSVA should be evaluated appropriately before the operation method is chosen.¹⁶ The bulging range and the opening of the sinus aneurysm in most patients are large and not suitable for intervention methods. Due to the presence of VSD, the aortic sinus aneurysm and its opening into the heart chamber are even larger, so interventional therapy is not an option.^{17,18} Surgical repair of RSVA and associated cardiac anomalies remains the most common method of SVA management. In our study, preoperative diagnosis of VSD was critical, so careful selection of interventional treatment was required.

Study limitation. Due to our small sample size, additional RSVA cases should be studied to determine whether RSVA classification should be modified based on the presence or absence of VSD.

In conclusions, the presence or absence of VSD in RSVA patients affect the origin and ruptured points of SVA, aortic valve disease involved, and therapeutic schedule. Ruptured SVAs type should be clinically modified on the basis of presence or absence of VSD.

References

1. Structure and anatomy of the aortic root. *Eur J Echocardiogr* 2011; 12: E40.
2. Cheng TO, Yang YL, Xie MX, Wang XF, Dong NG, Su W, et al. Echocardiographic diagnosis of sinus of Valsalva aneurysm: a 17-year (1995-2012) experience of 212 surgically treated patients from one single medical center in China. *Int J Cardiol* 2014; 173: 33-39.
3. Jonas RA, editor. Comprehensive surgical management of congenital heart disease. 2nd ed. Boca Raton (FL): CRC Press; 2002.
4. Yan F, Abudurehman M, Huo Q, Shabiti A, Zhu T, Liu Z. Surgery for sinus of Valsalva aneurysm: 33-year of a single center experience. *Chin Med J (Engl)* 2014; 127: 4066-4070.
5. Matsushita T, Masuda S, Inoue T, Okawa Y. Perforation of sinus Valsalva 10 years after repair of ventricular septal defect. *Asian Cardiovasc Thorac Ann* 2012; 20: 353.
6. Fang ZF, Huang YY, Tang L, Hu XQ, Shen XQ, Tang JJ, Zhou SH, et al. Long-term outcomes of transcatheter closure of ruptured sinus Valsalva aneurysms using patent ductus arteriosus occluders. *Circ J* 2014; 78: 2197-2202.
7. Peddinti KC, Gattu V, Samala KB, Karuturi M, Ramathoti P. Rupture of aortic sinus Valsalva aneurysm and its management. *J Clin Diagn Res* 2014; 8: GD05-GD06.
8. Sarikaya S, Adademir T, Elibol A, Büyükbayrak F, Onk A, Kirali K. Surgery for ruptured sinus of Valsalva aneurysm: 25-year experience with 55 patients. *Eur J Cardiothorac Surg* 2013; 43: 591-596.
9. Xin-Jin L, Xuan L, Bo P, Hong-Wei G, Wei W, Shou-Jun L, et al. Modified Sakakibara classification system for ruptured sinus of Valsalva aneurysm. *J Thorac Cardiovasc Surg* 2013; 146: 874-878.
10. Guo HW, Sun XG, Xu JP, Xiong H, Wang XQ, Su WJ, et al. A new and simple classification for the non-coronary sinus of Valsalva aneurysm. *Eur J Cardiothorac Surg* 2011; 40: 1047-1051.
11. Ahmed MI, Gok G, Yuzbas B, Burkhart J, Amado Escanuela MG, Alli OO, et al. Incremental value of three-dimensional echocardiography over the two-dimensional technique in the assessment of combined sinus of Valsalva rupture into the right ventricle and adjacent perimembranous ventricular septal defect. *Echocardiography* 2014; 31: 779-782.
12. Mahara K, Saito M, Fukumoto R, Tamura H, Kin H, Takanashi S. Visualization of perimembranous ventricular septal defect with ruptured sinus of Valsalva aneurysm by three-dimensional transesophageal echocardiography and multidetector three-dimensional computed tomography. *J Echocardiogr* 2016; Jun 3: [Epub ahead of print]
13. Barre E, Redheuil A, Ladouceur M, Mousseaux E, Iserin L. Definitive diagnosis of ruptured sinus of Valsalva in a patient with ventricular septal defect using cardiac magnetic resonance imaging. *Eur Heart J Cardiovasc Imaging* 2012; 13: 364.
14. Shi QY, Zhang JB, Mi YQ, Song Y, Ma J, Zhang YL. Congenital heart defects and maternal fever: systematic review and meta-analysis. *J Perinatol* 2014; 34: 677-682.
15. Liu YL, Liu AJ, Ling F, Wang D, Zhu YB, Wang Q, et al. Risk factors for preoperative and postoperative progression of aortic regurgitation in congenital ruptured sinus of Valsalva aneurysm. *Ann Thorac Surg* 2011; 91: 542-548.
16. Liu S, Xu X, Chen F, Zhao Z, Zhang Y, Wang C, et al. Angiographic features of ruptured sinus of Valsalva aneurysm: new classification. *J Cardiol* 2014; 64: 139-144.
17. Cao LB, Hannon D, Movahed A. Noncoronary sinus of Valsalva rupture into the right atrium with a coexisting perimembranous ventricular septal defect. *World J Clin Cases* 2013; 1: 146-148.
18. Kuriakose EM, Bhatla P, McElhinney DB. Comparison of reported outcomes with percutaneous versus surgical closure of ruptured sinus of Valsalva aneurysm. *Am J Cardiol* 2015; 115: 392-398.