Transcatheter Closure of Intracristal Ventricular Septal Defect With Mild Aortic Cusp Prolapse Using Zero Eccentricity Ventricular Septal Defect Occluder

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Background: Transcatheter closure is a well-established therapy for patients with perimembranous ventricular septal defects (VSDs), but with limited experience in intracristal VSDs (IVSDs) with aortic cusp prolapse (ACP).

Methods and Results: From 2012 to 2014, we reviewed 38 patients with IVSDs complicated with mild ACP who underwent device closure, and, in light of the findings, assessed the effect of transcatheter intervention on preoperative mild ACP. The zero eccentric VSD occluder was chosen for closure (Shanghai Shape Memory Alloy Ltd, Shanghai, China). The mean defect was 4.8±1.6 mm (range, 2–8) as measured by transthoracic echocardiography and the mean device size was 10.1±2.1 mm (range, 4–14). Placement of the device was successful in 35 patients (92.1%). In the remaining 3 patients (7.9%), major complications occurred and they were converted to surgical intervention: severe aortic regurgitation (AR) in 2 patients and occluder dislodgement in 1 patient. During the follow-up (median 14.2 months; range, 3–24), no deaths, residual shunt, late-onset AR, heart block, or device failure occurred.

Conclusions: The mid-term prognostic results of high success rate and low complications rate in this study are inspiring. Transcatheter closure of IVSD with mild ACP can be performed safely and effectively as an alternative to surgery in selected patients. (Circ J 2015; 79: 2162–2168)

Key Words: Cardiac catheterization/intervention; Congenital; Coronary cusp prolapse; Heart defects; Intracristal ventricular septal defect

Subarterial ventricular septal defect (SVSD), also known as an infundibular, conal, or supracristal defect, has been reported as more common in Eastern countries than western countries. Intracristal VSD (IVSD), a subtype of SVSD, is located within the infundibular septum adjacent to the aortic and pulmonary valves. Early surgical patch closure has been the mainstay of therapy for IVSD, but with long recovery times. With the introduction of a specifically designed, Chinese-made zero eccentric VSD occluder, transcatheter closure of pure IVSD has been reported in recent studies from China with high closure rate, low mortality, and acceptable complication rates. However, IVSD is often associated with aortic cusp prolapse (ACP), which can eventually lead to progression of aortic regurgitation (AR). So far, whether IVSD complicated by ACP is suitable for interventional therapy is still controversial and there is limited reportage. Thus, this study retrospectively reviewed our experience of transcatheter closure of IVSD complicated by mild ACP using the zero eccentricity VSD occluder and is the first data available for assessing the therapeutic value of transcatheter device closure.

Methods

Patient Enrollment

Between March 2012 to March 2014, 75 consecutive patients with IVSD were screened for transcatheter closure at Changzheng Hospital. Among them, mild ACP was observed in 38 patients and no ACP in 29; 12 others were referred for surgical correction because of moderate or severe ACP in 8 and large defects in 4. Data of the 38 IVSD patients (mean age 25.3±14.0, range 3–59 years) with mild ACP (all in the right cusp) who underwent transcatheter closure were retrospectively reviewed. Mild AR was found in 11 of 38 patients.

The Ethics Committee of Changzheng Hospital approved the
Transcatheter Closure of Intracristal VSD

The diagnosis of IVSD with mild ACP was mainly based on transthoracic echocardiography (TTE) (Philips, Best, The Netherlands) and the degree of ACP was graded according to a 3-point scale.\textsuperscript{14,15} The inclusion criteria included: (1) age $\geq$ 3 years old and body weight $\geq$ 10 kg; (2) the maximum diameter of defect $\leq$ 15 mm as observed by TTE; (4) defect position on an analog clockface in the short-axis parasternal view on TTE (12:00 to 1:30 o’clock for the IVSD); (5) distance $\geq$ 2 mm from the pulmonary valve annulus to the upper edge of the IVSD; (6) left-to-right shunt. Patients with moderate or severe AR, right to left shunt, pulmonary pressure $>70$ mmHg, cardiac function class IV, or accompanied by fever with suspected infective endocarditis <1 month before the procedure were excluded.

Occluder Device

The occluder used in the study was the zero eccentricity VSD occluder designed by the Shanghai Shape Memory Alloy Corporation. A full description of the occluder and its delivery system has been reported previously.\textsuperscript{7,8,14} In brief, the diameter of the left disk is 6 mm larger than that of the waist and the left disk extends towards the apex while no superior margin extends towards the aorta, which is specifically designed to close defects with a rim $<2$ mm under the aortic valve (Figures 1A, B). The zero eccentricity VSD occluder was approved by the State Food and Drug Administration of China in 2003 and received CE mark in 2008.

Catheterization and Device Implantation

The catheterization procedure was performed under local anesthesia with 2% lidocaine for adult patients and general anesthesia for children (≤10 years). Heparin (100 IU/kg) was injected intravenously during the procedure. The location, shape, and size of the VSD and its relationship with the aortic valve were confirmed by left ventricular angiography and TTE in all standard views. The implantation of the VSD occluder was performed as described previously.\textsuperscript{7,8,16,17} A device size 1–2 mm larger than the measured VSD diameter was chosen. In patients with IVSD diameter $\geq 5$ mm, the device was 3–5 mm larger than the size of the defect. When using the zero eccentricity occluder, the platinum marker on the left disk was positioned towards the apex. The device was deployed until its proper position was obtained and residual shunts and AR had been excluded. The patients were monitored with TTE, chest radiography and ECG monitoring for 5 days before discharge. After the proce-
dure, patients were treated with daily oral aspirin (3 mg/kg) for 6 consecutive months to prevent thrombotic events.

Follow-up Protocol
After discharge, clinical symptoms, physical examination, ECG, chest radiography and TTE were routinely performed for all patients at 1, 3, 6, and 12 months postoperatively and yearly thereafter. The shape and orientation, valve regurgitation, device thrombosis, and residual shunts were evaluated.

Results
Success Rate of Transcatheter Closure
The general and procedural characteristics are presented in Table 1. Of the 38 patients, 35 (92.1%) were successfully treated using zero eccentricity VSD occluders, including 31 (88.6%) with complete closure and 4 (11.4%) with trivial-small residual shunt immediately after the occluder was released. The procedure failed in 3 patients: severe AR in 2 patients before release of the occluder (the device impinged on the aortic valve) and dislodgment of the device (a smaller VSD occluder used; Figure 2) in 1 patient the day after the procedure. These patients were converted to surgical repair. No deaths, vascular complications, hemolysis, or pericardial tamponade occurred during the procedure. All patients were successfully discharged after a median hospital stay of 7 days (range, 4–22 days).

Valvular Regurgitation
In the 12 patients with mild preoperative AR (Table 2), AR disappeared in 5 (Figure 3) and remained unchanged in 6 after operation, but progressed to severe in 1 patient before release of the occluder. In the 26 patients without AR before closure, no AR was observed in 21 patients (Figure 4) and new-onset mild AR in 4 postoperatively, whereas significant AR was detected in 1 (Figure 5) before occluder release. In the 2 patients in whom severe AR occurred during the procedure, the procedure was discontinued and the occluder was retrieved.

Table 2. Presence of AR After Transcatheter Closure of Intracristal Ventricular Septal Defect

<table>
<thead>
<tr>
<th>Postoperative AR</th>
<th>Mild preoperative AR n=12 (31.6%)</th>
<th>No preoperative AR n=26 (68.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>5 (13.2%)</td>
<td>21 (55.3%)</td>
</tr>
<tr>
<td>Mild</td>
<td>6 (15.8%)</td>
<td>4 (10.5%)</td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>1 (2.6%)</td>
<td>1 (2.6%)</td>
</tr>
</tbody>
</table>

AR, aortic regurgitation.

Arrhythmic/Conduction Complications
New-occurrence arrhythmias developed in 13 patients (34.2%) after closure (Table 3). All recovered within 2 weeks, except for 1 patient with right bundle-branch block who recovered 1 month later. Complete atrioventricular block (cAVB) requiring temporary pacemaker implantation treatment occurred in a 21-year-old man. That patient, in whom a 14-mm zero eccentricity VSD occluder was used, was found to have cAVB by ECG monitoring at 4 days after implantation. A temporary cardiac pacemaker was implanted (Medtronic, Minneapolis, MN, USA) and he was also administered 10 mg dexamethasone IM once daily. He resumed normal sinus rhythm 5 days after pacemaker implantation and dexamethasone treatment.

Follow-up
Follow-up data were available for all patients. The median period was 14.2 months (range, 3–24 months) with ECG, TTE and chest X-ray monitoring. No deaths, late-onset AR, morphologic change in the aortic or pulmonary valve, clinical hemolysis, thrombosis, late complete heart block, infective endocarditis, vascular complications, or pericardial tamponade occurred during the follow-up. The 4 patients who had trivial-small residual shunt immediately after the procedure achieved complete closure at 3 months follow-up. All devices kept their optimal shape and stable position as shown by TTE. The 6 patients with mild AR during the operation continue to show regurgitation in the late period, but it did not progress to moderate or severe.

A total of 8 cases of complications occurred during the follow-up period: 2 patients experienced a transient junctional tachycardia on ECG at 1.5 and 2.5 months, respectively, after the intervention, and no immediate treatment was required; minor complications occurred in 6 patients, including nasal bleeding in 1 patient, premature ventricular beats in 2 patients and new-onset incomplete right bundle-branch block in 3 patients.

Discussion
With the advances in interventional techniques and occluder devices, transcatheter closure has been performed at many institutions with high success rates and low cost.15–20 Previous studies have reported on the safety and efficacy of transcatheter closure of pure IVSD.2,7,8 Nonetheless, there are no other reports of device closure of IVSD with ACP until now. The novel finding of this study is that, in the selected patients, most cases of IVSD complicated with mild ACP (92.1%) can be safely and successfully closed by the zero eccentricity occluder, which was previously considered not to be suitable for use in transcatheter closure.

Of the 3 patients referred to open heart surgery, severe AR during the procedure was observed in 2 patients. AR was the major consideration in transcatheter closure of IVSD with...
which, cardiac arrhythmia was the most common (76.5%). The most frequent arrhythmia was a transient, well-tolerated episode of junctional tachycardia 61.5% (8/13), and all converted to sinus rhythm without any intervention within 2 weeks. Complete atrioventricular block is a serious complication during and after device closure of VSD, and occurred in 0.23–5% of patients with perimembranous VSD.21,22,23,24–27

Because the subarterial defect is located distant to the conduction tissue, there is a small chance of conduction system injury. ACP. The reported incidence of AR after surgical repair in the literature ranges between 0% and 6.452%.21,22 In our study, the rate of moderate to severe AR was 5.3% (2/38). Significant AR following device occlusion may be related to defect size and position not being estimated accurately because of prolapse of the aortic valve into the defect, and the left disc of the larger size occluder may interfere with the right coronary cusp and lead to AR.

Most postoperative complications were minor (85.0%), among which, cardiac arrhythmia was the most common (76.5%). The most frequent arrhythmia was a transient, well-tolerated episode of junctional tachycardia 61.5% (8/13), and all converted to sinus rhythm without any intervention within 2 weeks. Complete atrioventricular block is a serious complication during and after device closure of VSD, and occurred in 0.23–5% of patients with perimembranous VSD.21,22,23,24–27

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**Figure 4.** Angiographic images of device closure of intracristal ventricular septal defect (VSD) with mild aortic cusp prolapse (ACP) without aortic regurgitation (AR) in a 36-year-old woman. (A) Left ventriculography shows a left-to-right shunt, indicating a VSD in close proximity to the aortic valve. (B) Aortic angiogram shows mild, preoperative right ACP without AR, and a 7-mm zero eccentricity VSD occluder was selected. (C) No residual shunt before occluder release is shown left ventriculography. (D) Aortic angiography shows right ACP has disappeared and the occluder was released with optimal shape and position.

**Figure 5.** An 18-year-old woman in whom severe aortic regurgitation (AR) was found during transcatheter closure of intracristal ventricular septal defect. (A) Left ventriculography shows a left-to-right shunt located close to the aortic valve. (B) Mild, preoperative right aortic cusp prolapse without AR demonstrated on aortic angiogram and an 11-mm asymmetric occluder was selected. (C) Aortic angiography shows severe AR (red arrow) before occluder release, so the procedure was stopped and the occluder was retrieved. The patient was transferred for surgical repair.
from mechanical trauma compression by the delivery system or device. In our study, no cases of permanent cAVB occurred and transient cAVB occurred in only 1 patient (2.6%). The most likely reason is that the inferior end of the left disk of a larger sized occluder injures the conduction bundles. In addition, no severe events were observed during the mid-term follow-up period after discharge.

Several reasons can account for the high success closure rate with low AR rate in this study. First of all, unlike the Amplatzer occluder (0.5-mm superior rim of the left ventricular disk), the zero eccentricity occluder does not have a superior margin towards the aorta, which avoids contact with the aortic valve, and the larger apical side of the left disk can lean on the muscular septum more stably to avoid dislodgement of the device. In addition, the device may support pre-existing mild ACP without significant dysmorphism of aortic valve, and thus prevent possible progressive deterioration of AR in some cases. Second, the distance between the upper edge of the defect and the pulmonary valve was used in the present study to assess suitability for interventional therapy. The upper edge of the right disk of the zero eccentricity occluder was 2 mm and defects with a rim <2 mm under the pulmonary valve were excluded from transcatheter intervention, preventing potential interference with the pulmonary valve. Finally, patients with moderate or severe AR were excluded from transcatheter intervention according to TTE and aortic angiography, and the device was deployed until its proper position was obtained. During the outpatient follow-up, no interference with adjacent cardiac valves was found by TTE assessments.

Technical issues were important to the overall success of transcatheter closure of IVSD with mild ACP. Accurate assessment of the location and size of the defect was critical. The routine projection position of left ventriculography (45–60°left anterior oblique+10–25°cranial projection) could show perimembranous defects clearly, but the size and shape of IVSDs could not be clearly visualized in that projection. In our study, during interventional therapy, the relationship between the defect and aortic valve was shown well on left ventriculography in the 60–80°left anterior oblique+20–30°cranial projection. When the defect size is unclear, TTE is helpful. In our study, during interventional therapy, the relationship between the defect and aortic valve was shown well on left ventriculography in the 60–80°left anterior oblique+20–30°cranial projection. When the defect size is unclear, TTE is helpful. In our experience, unconventional parasternal long axes views of the left ventricle on TTE were the best for measuring the distance from the VSD to the aortic valve, and the size of the VSD on the short-axis aortic and parasternal 5-chamber views. Furthermore, either the color width of the VSD shunt on TTE or the diameter of the delivery sheath is also useful for identifying the size of the defect. Moreover, an appropriately sized occluder will avoid dislodgement of the device and interference with valve function. In general, the device chosen for closure was 1–2 mm larger than the defect diameter measured by TTE. However, for large IVSD, the actual defect size or shunt amount was frequently underestimated to some extent because of the prolapsing aortic valve into the defect.

Thus, in our study, in patients with IVSD ≥5 mm, a device that was 3–5 mm larger than the maximum size of the defect measured by TTE was chosen.

Study Limitations

This was a single-center study and limited by the small number of patients and short duration of postoperative follow-up; therefore, larger trials with long-term follow-up are needed to fully evaluate the adequacy and usefulness of this method. Also, transesophageal echocardiography (TEE) was not used during the transcatheter procedure because it extends the procedural time and may cause patient discomfort. Thus, TTE combined with angiography was used to guide device closure in our study, which was helpful for accurate sizing of the defect and device choice.

Our findings indicate that transcatheter device closure of IVSD with mild ACP is associated with excellent success and closure rates, no mortality and low morbidity, suggesting that transcatheter closure is a minimally invasive alternative treatment for appropriately selected patients.

Acknowledgments

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