A Large Institutional Study on Outcomes and Complications after Transcatheter Closure of a Perimembranous-Type Ventricular Septal Defect in 890 Cases

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Purpose: To investigate the incidence, cause, and prevention of complications associated with interventional therapy for perimembranous ventricular septal defects (pmVSDs).

Methods: A retrospective analysis was performed on 890 patients with pmVSDs after interventional therapy. The complications were then analyzed by electrocardiography and echocardiography during or after interventional therapy. During the follow-up period of 12-52 (mean of 26.9 ± 21.6) months, the technical success rate was 97.9% (871/890).

Results: The incidence of serious complication was 1.12% (10/890), including five cases of third-degree atrioventricular block, two of severe tricuspid valve regurgitation, one of cerebral infarction in the basal ganglia area, and two of femoral artery thrombosis. No death was reported during patient follow-up.

Conclusions: Transcatheter closure of pmVSDs in selected patients was found to be effective and safe.

Key Words: Complication • Interventional therapy • Ventricular septal defect

INTRODUCTION

Perimembranous ventricular septal defects (pmVSD) are common congenital heart defects in both children and adults.[1] Patients with a volume overload of the left chamber due to a pmVSD require closure of the defect to prevent ventricular dilatation and dysfunction, arrhythmias, aortic regurgitation, pulmonary arterial hypertension, endocarditis, and double-chambered right ventricle.[2] The standard treatment for pmVSD is open surgery, which is widely performed with minimal operative mortality. However, there are still the risks of

complete atrioventricular block (cAVB), residual shunt, postpericardiotomy syndrome, wound infection, etc.[1] Given its efficacy, minimal trauma, and rapid post-surgery recovery, transcatheter interventional therapy for VSD can be an alternative to surgical closure with acceptable mortality and morbidity, with encouraging results.[3-16] However, available reports on this treatment modality have been limited to studies with small samples and insufficient follow-up.[17-21] Both large-scale and long-term follow-up data for this technique are rare. In the present study, we analyzed 890 cases of pmVSDs in our hospital and performed transcatheter interventional therapy to determine the effective prevention and management of the complications of this therapy.

MATERIALS AND METHODS

Study population

This study was conducted in accordance with the

declaration of Helsinki, and with approval from the Ethics Committee of the First Affiliated Hospital of Hebei Medical University. Written informed consent was obtained from all participants. From March 2004 to November 2010, 890 patients with pmVSDs (410 males, mean age of 6.10 ± 3.16 years, range of 3.0 to 42 years) were enrolled in this research. All patients showed evidence of left ventricular and/or left atrial enlargement as documented by transthoracic echocardiography (TTE) (iE33, Philips Medical Systems, Andover, Massachusetts). Only patients with significant defects [pulmonary to systemic flow ratio (Qp/Qs) exceeding 1.5] were qualified for the procedures. There were 84 cases of complex lesions, including 33 with atrial septal defect, 16 with patent ductus arteriosus, 6 with pulmonary stenosis, and 1 with atrial septal defect combined with patent ductus arteriosus.

The exclusion criteria were as follows: 1) presence of thrombus at the intended site of implant, or documented evidence of venous thrombosis of the vessels to be catheterized; 2) active endocarditis or bacteremia; 3) anatomical abnormalities in which the occluder would interfere with the aortic or atrioventricular valves; 4) coagulation disorders wherein antiplatelet or anticoagulant therapy is contraindicated; and 5) intra-cardiac mass or vegetation. All varieties of occluders and delivery systems used in this research were provided by Lifetech Scientific (Shenzhen) Co., Ltd. Written informed consent was obtained from all patients or their parents (if children) prior to the procedure.

Procedure

Chloramine ketone was used as the general anaesthetic without tracheal intubation for patients < 7 years of age, whereas 1% lidocaine was used as the local anaesthetic for patients > 7 years of age. Surgical access was accomplished through the right femoral vein and right femoral artery. Angiography in the left ventricle at a 56°/20° left anterior oblique/cranial projection was used to profile the pmVSD. The location, size of the pmVSD, and its relationship with the aortic valve were assessed. The diameter of the pmVSD was measured at the largest diastolic phase, and an occluder was selected based on this measurement. The defect was then passed from the left ventricle by a 5 Fr partly cut pigtail catheter or a right Judkins catheter. An arteriovenous

circuit was set up via a femoral vein approach on the same side. A long sheath (6-12 Fr) was advanced to the left ventricle through the arteriovenous circuit and positioned beneath the aortic valve. Through the long sheath, the pmVSD occluder was deployed under fluoroscopic control and echocardiographic guidance. Angiography in the left ventricle and ascending aorta was performed again to verify complete occlusion and identify any new-onset valve regurgitation. During the procedure, heparin (100 U/kg) was injected intravenously. After the procedure, the patients underwent electrocardiography (ECG) monitoring for 5 days. Antibiotics and dexamethasone (200 µg/kg·d) were injected intravenously for 3 to 5 days, and aspirin (3-5 mg/kg·d) was administered orally for 6 months.

Follow-up

All subjects underwent clinical examination, ECG, chest X-rays, and TTE before discharge 1, 3, 6, and 12 months after the procedure, as well as yearly thereafter. New-onset arrhythmia was defined as a third-degree atrioventricular block, second-degree atrioventricular block, paroxysmal supraventricular tachycardia, left bundle branch block, or right bundle branch block after the transcatheter closure of the pmVSD. The residual shunt was defined as a left-to-right shunt beam ≥ 2 mm as detected by TTE.

Continuous variables were expressed as means $\pm$ standard deviations and categorical variables were expressed as percentages.

RESULTS

The defect diameter of the pmVSDs was 5.21 ± 8.15 mm (ranging from 2.01 mm to 13.1 mm) as detected by ventricular angiography before the interventional therapy. The occluder diameter was 9.46 ± 6.18 mm (ranging from 8 mm to 16 mm). The mean Qp/Qs was 2.06 ± 1.01 (ranging from 1.50 to 4.68).

In the 12-52 (mean of 26.9 ± 21.6) month duration of the follow-up period, 871 cases with pmVSDs were completely closed without residual shunts, with a success rate of 97.9%. Complications occurred in 129 cases, with a total complications rate of 14.49%. Cardiac complications occurred in 120 cases, including five

cases of third-degree atrioventricular block, 1 of emerging second-degree atrioventricular block, 32 of accelerated junctional arrhythmia, 10 of complete left bundle branch block, 39 of complete right bundle branch block, 12 of aortic insufficiency, 5 of tricuspid insufficiency, and 16 of residual shunt. Vascular complications occurred in 9 cases, including 1 case of femoral artery pseudoaneurysm, 5 of femoral arteriovenous fistula, 2 of femoral artery thrombosis, and 1 of cerebral infarction in the basal ganglia area.

The incidence of serious complication was 1.12% (10/890), including 5 cases of third-degree atrioventricular block (all of them occurred during the 3 to 5 days after the procedure), 2 of severe tricuspid valve regurgitation, 1 of cerebral infarction in the basal ganglia area, and 2 of femoral artery thrombosis. No death was reported during the follow-ups.

By the continual application of drug treatments such as dexamethasone and isoproterenol, and if necessary, combined with temporary cardiac pacing, all the 5 cases of third-degree atrioventricular block resumed normal conduction within 10 days. For one patient (a 15-year-old boy), the third-degree atrioventricular block associated with syncope returned 15 months after discharge, and he was then implanted with a permanent pacemaker.

In this research, 12 cases of aortic insufficiency developed after the transcatheter occlusion of pmVSD. Among these cases, 9 were mild regurgitation and 3 were moderate regurgitation. All cases occurred immediately after the release of the occluder by TTE monitoring. The parameters of TTE had no significant change during the follow-up period (the longest follow-up period was 52 months).

Five cases of tricuspid insufficiency were found after the pmVSD occlusion. Among them, 3 cases were mild to moderate tricuspid insufficiency that were stabilized via periodic TTE without special treatment, and 2 cases were severe tricuspid regurgitation whose occluders were removed by surgery. Among the cases of tricuspid regurgitation, 4 were found 3-5 days after transcatheter occlusion and 1 at the sixth month of follow-up by TTE.

Femoral artery thrombosis, a severe complication of interventional treatment, appeared in 2 cases (a 3.0-year-old boy and a 4.5-year-old girl). Both rapidly recovered by local or intravenous thrombolysis therapy

with a recombinant tissue plasminogen activator. Cerebral infarction in the basal ganglia area occurred after pmVSD closure in one case (a 7-year-old boy), who was also cured by intravenous thrombolysis therapy with a recombinant tissue plasminogen activator. The reason was the combination of congenital cerebral vascular malformation with the stenosis of the descending aorta and left pulmonary artery, as demonstrated by an angiogram. These subjects were treated very early in the study and there may have been a deficiency in operator experience. However, no death was reported.

DISCUSSION

Some major medical centers have shown that both open surgery and the transcatheter technique can yield extraordinarily good results for VSDs.[22-24] Transcatheter closure has the advantages of reduced psychological impact, minimal invasion, and short hospital stay.[1,14,20] Different devices have been used to close pmVSDs,[25-27] among which the Amplatzer pmVSD occluder and similar devices have been shown to cause few complications and produce good results.[13,16,17,19,28] The pmVSD occluder is a self-expandable, double disc device made from a Nitinol wire mesh. The two discs are connected by a short cylindrical waist which corresponds to the defect size. In order to increase its closing ability, the device is sewn with expanded polytetrafluoroethylene patches (Figure 1). Strengthening the early identification and treatment of the complications to avoid or reduce them during or after the transcatheter closure of pmVSDs has a high clinical significance.
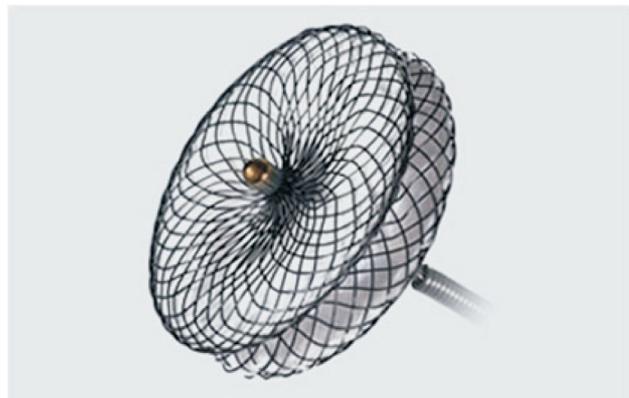

Figure 1. *Perimembranous ventricular septal defect occluder.*

Five patients experienced cAVB, among whom one patient was implanted with a permanent pacemaker (a 15-year-old boy) 15 months after discharge. The other four patients recovered to normal rhythm after effective treatment with dexamethasone and isoproterenol. cAVB has been reported to be the most significant complication both early in the treatment and during the follow-up period, with an incidence ranging from 3.5% to 8.6%. In the present study, the cAVB rate was 0.56%. The underlying mechanism may be related to the modification of domestic symmetric devices by enlarging the thickness of the waist from 2 mm to 3 mm and using soft nitinol wire mesh to braid the occluder. One large series reported by Andersen et al.,[22] comprising 2079 open VSD repair patients has shown a comparable cAVB rate of < 1%. The occurrence of cAVB is related to the proximity of the conduction system to the margins of the pmVSD. Therefore, both surgery and device implantation may interfere with atrioventricular conduction. The device may cause direct compression trauma, or provoke an inflammatory reaction or scar formation in the conduction tissue. In our opinion, the patients with the larger VSD (≥ 10 mm), who had a transient cAVB during the operation, should be paid close attention to persistent arrhythmia. Some authors[7,13,29] have suggested that a course of steroids should be used in an effort to avoid pacemaker implantation. We used this approach successfully in all of the subjects. Nonetheless, careful monitoring of the heart rhythm remains mandatory throughout follow-up due to the severe impact and characteristically late onset of cAVB. Identification of risk factors of cAVB will require further studies on larger cohorts of pmVSD patients.

The incidence of residual shunt immediately after VSD closure was 5.8% to 7.3%, but it was found to be gradually reduced in the follow-up. In this research, residual shunt was found in 16 cases with little influence on the hemodynamics of patients, and disappeared in 12 cases between the third to sixth month of follow-up. This finding may be related to the small micro-displacement of the occluder and the insufficiently covered irregular defect.

Aortic insufficiency is one of the severe complications that may occur after surgical repair and transcatheter closure of pmVSDs.[30,31] This condition is mainly due to defects on the proximal edge of the right coronary valve and the impact of an occluder on aortic valve closure, or the establishment of a femoral artery-ventricular septal defect-femoral vein track damaging the aortic valve. A pmVSD occluder shift after the occlusion may also be one of the reasons for aortic insufficiency. In this research, aortic insufficiency developed in 12 cases after the transcatheter occlusion of pmVSD, among which 9 cases were mild regurgitation and 3 were moderate regurgitation. Although the occluders were close to the aortic valve, no effect was found on the valve via TTE and angiography before their release. This result may be due to the occluder rotating and shifting in an instant of its separation from the push-pole after its release. A large occluder may get too close to the aortic valve, and the memory alloy of an occluder gradually orthokeratology may be the cause of the delayed aortic insufficiency. Therefore, to avoid aortic insufficiency, for a patient with a defect too close to the aortic valve, the pmVSD occluder should not be too large. The location or angle change of the occluder as affected by the push-pole should also be taken into account before its release. If the distance from the border of the pmVSD to the right coronary valve is less than 2 mm, the eccentric-type occluder should be chosen. If one edge of the defect is so soft that the eccentric-type occluder cannot be used successfully, the occluder can be implanted in the membranous aneurysm for the patient, ensuring the formation and firm adhesion of the membranous aneurysm to reduce its impact on the aortic valve.

Tricuspid regurgitation is another major consideration in the transcatheter closure of pmVSDs (incidence rate of < 2.0%).[32] The impingement of the occluder on the valve leaflets may cause instant tricuspid regurgitation by interfering with the chordae tendineae. Thus, TTE and angiography are crucial for confirming correct device deployment. In this study, there were 5 cases of tricuspid insufficiency after the pmVSD occlusion, 3 of mild to moderate tricuspid insufficiency that were stabilized via periodic TTE without special treatment, and 2 of severe tricuspid regurgitation whose occluders were removed by surgery. The mechanism may be associated with the improper placement of the occluder on the tricuspid septal leaflets, migration of the occluder, shape memory of nithinol wires, or rupture of the chordae tendineae.

Therefore, transcatheter interventional treatment for pmVSD can be further improved by reviewing cases involving advanced intervention technology and using modern equipment to reduce the incidence of complications.

ACKNOWLEDGEMENTS

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