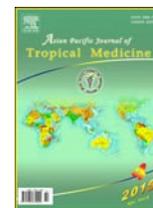


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## Transcatheter closure of ventricular septal defect in patients with aortic valve prolapse and mild aortic regurgitation: feasibility and preliminary outcome

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### ABSTRACT

**Objective:** To evaluate the feasibility, safety and efficacy of transcatheter closure of ventricular septal defect (VSD) in patients with aortic valve prolapse (AVP) and mild aortic regurgitation (AR). **Methods:** Between January 2008 and July 2014, transcatheter closure of VSD was attempted in 65 patients. **Results:** The total intermediate closure successful rate in all subjects was 96.9%. During the perioperative period, no death, major bleeding, pericardial tamponade, occluder dislodgement, residual shunt or hemolysis occurred. Two procedures had been forced to suspend due to significant aggregation of device related aortic regurgitation, three cases of transient complete left bundle branch block occurred but did not sustain. At 1-year follow-up, no patients had residual shunts and complications. Furthermore, grade of residual AR were relieved in 61.9% (39/63) cases and degree of AVP were ameliorated in 36.5% (23/63) patients; **Conclusions:** Transcatheter closure VSD in selected patients with AVP and mild AR is technically feasible and highly effective. Long term safety and efficacy needs to be assessed.

## 1. Introduction

Ventricular septal defect (VSD) is the most common (approximately 20%) congenital heart disease[1]. Long-term follow-up studies have shown that transcatheter closure of VSD, which as a feasible alternative to surgery, has been commonly recommended[2]. Taking into account the increasing of potential risk of AR aggravation, device closure of patients with VSD companied with AVP and AR still represents a challenging issue. Moreover, there

is little clinical data available in the literature about the feasibility and safety of this procedure for such patients. In this article, we summarize our experience of transcatheter closure technique and report initial follow-up outcome of feasibility, safety and efficacy in 65 patients.

## 2. Materials and methods

### 2.1. Device

The HeartR™ VSD Occluder (Lifetech Scientific (Shenzhen) Corporation, P.R.C) has been thoroughly described previously[3]. It is a self-expandable, double disc device made from a Nitinol wire mesh. The two discs are linked together by a short cylindrical waist corresponding to the size of the VSD. The discs and waist are filled with PTFE membranes eccentric sewn to the device by Nylon threads. The device is loaded into a 6-8F delivery sheath. Asymmetric occluder (Figure 1) was selected in accordance with

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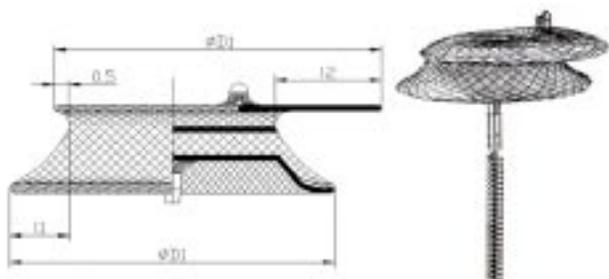
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the anatomical conditions and pathophysiological types in patients with valve prolapse (AVP) and aortic regurgitation (AR).



**Figure 1.** Schematic diagram of VSD membranous asymmetric occluder.

## 2.2. Patient population

Between January 2008 and July 2014, 65 patients underwent an attempt of transcatheter closure of VSDs. Subjects had indications for transcatheter closure of VSD associated AVP and mild AR were verified by transthoracic and transesophageal echocardiography (TTE) was included. Patients with infective endocarditis, right to left shunt, sepsis, complex heart lesions require surgery or contraindication to antiplatelet therapy were excluded. The patients ranged in age from 3 years to 14 years [(6.01±3.05) years] and in weight from 13.2 kg to 38.9 kg [(24.9±11.3) kg]. The mean subaortic rim was 3.7 mm, with a range of 3 mm to 5 mm. The mean VSD diameter was 4.9 mm, with a range of 4 mm to 7 mm. Perimembranous VSD (pmVSD) was present in 18 (27.7%) patients and intracristal VSD (icVSD) was noted in 47 (72.3%) patients respectively. Membranous aneurysms were present in 29 (44.6%) patients. The mean pulmonary to systemic flow ratio (Qp/Qs) was 1.9:1, with a range of 1.6:1 to 2.2:1. The VSD diameter evaluated by TTE was 4.9 mm, with a range of 4 mm to 7 mm. The Biomedical Research Ethics Committee of Hainan General Hospital had approved the study and all subjects or their guardians had signed a written informed consent to undergo the transcatheter procedures. The clinical characteristics of patients are summarized in Table 1.

## 2.3. Preprocedural echocardiography

All patients were evaluated by TTE in the apical five-chamber view and long axis parasternal view to evaluate the diameter of VSD and rim under the aortic valve, then in the short axis parasternal view the type of VSD and anatomical location were detected. Inclusion criteria of patients as follows: (i) pmVSD diameter < 12 mm or icVSD diameter < 10 mm; (ii) mild aortic regurgitation is confirmed by TTE.

## 2.4. Implantation procedures

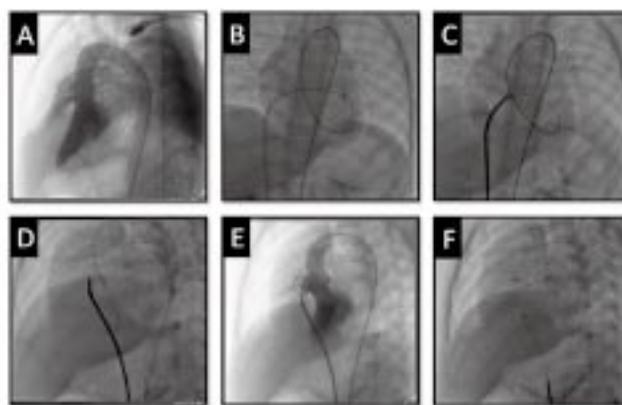
All patients were administered with 80-100 IU/kg heparin and antibiotics prophylaxis intravenously before the procedure. Procedures were performed under local anesthesia, while children aged < 10 years were under general anesthesia and guided under fluoroscopic (Figure 2) and TTE (Figure 3). The protocol used has been described in detail in previous reports[4]. Briefly, access was obtained through the right femoral artery and vein. Routine right and left cardiac catheterization and standard left ventricular angiography

were undergone in all cases to calculate again the diameter, pathophysiological type and anatomical location of the VSD. Then, a wire was positioned into the pulmonary artery followed by placing a sheath. Catheter was then positioned in the pulmonary artery through this sheath. The wire was snared from the pulmonary artery and forming a femoral artery- left ventricle-defect-femoral vein loop. Once this loop was established, the delivery sheath was advanced over this wire and positioned in the left ventricle. Once the sheath was confirmed in good position, device placement was performed as usual. The appropriate device size was chosen to be at least 1 mm to 2 mm larger than the defect size as measured. If significant residual shunts still existed or the device was easy to dislodge after attempted closure of the defect using the above size device, we further tried to close with a larger size device (2-4 mm larger than the defect). Oral aspirin 3-5 mg/kg daily was administered for patients was recommended.

**Table 1**

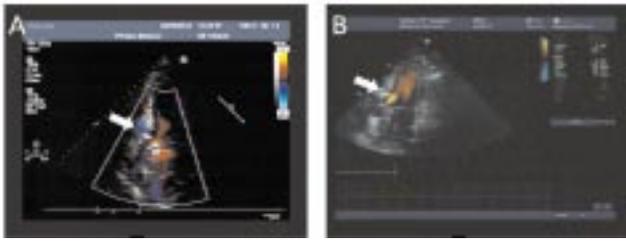
Clinical characteristics of patients.

Male/Female	38/27
Age (yrs)	6.01 (3-14)
Weight (kg)	24.9 (13.2 -38.9)
TTE	
pmVSD (n, %)	18 (27.7%)
icVSD (n, %)	47 (72.3%)
Subaortic rim (mm)	3.7 (3-5)
VSD diameter (mm)	4.9 (4-7)
Rim from the tricuspid to the defect (mm)	3.6 (2 -5)
Membranous aneurysms (n, %)	29 (44.6%)
Catheterization	
VSD diameter (mm)	5.2 (5 -7)
Qp/Qs	1.9 (1.6-2.2)
PA systolic pressure (mmHg)	33 (28-40)
PA mean pressure (mmHg)	17 (13-21)
Severity of AVP	
Grade I (n, %)	43 (66.2%)
Grade II (n, %)	20 (30.7%)
Grade III (n, %)	2 (3.0%)
Device diameter (mm)	7.3 (5-10)



**Figure 2.** Illustration of the various steps of closure by fluoroscopy, respectively.

(A) LV angiogram showing the mVSD. (B) Same view as (A) demonstrating showing the arteriovenous loop. (C) Left ventricular disk has been deployed. (D) Cine image immediately after the whole occluder has been deployed. (E) Left ventriculography showing no residual shunt. (F) Final LV angiogram same view as (A) showing good device position and complete closure.



**Figure 3.** Comparison of severity of AR that as seen on a modified apical five-chamber view in early diastole. (A) before procedure (arrow); (B) immediately after occluder retrieved (arrow).

### 2.5. Data collection and follow-up

Immediate procedure success was defined by device release and fixed in the appropriate position without residual shunt and aggravation of device-related aortic regurgitation. Perioperative data of complications were collected from the moment of procedure initialing to that of participant discharged. Any adverse event occurring during the time defined as severe procedure related complications as death, cerebral or pulmonary embolism, device dislocation that required surgical removal, persistent III Degree atrioventricular block (AVB) that required pacemaker placement and any event that required acute resuscitation. Any transient significant increase in AR and worsened cardiac dysfunction that required drug treatment was categorized into moderate procedure related complications. These events included peripheral hemorrhage (transient or required suspending anticoagulant therapy); transient complete left bundle branch block (CLBBB) and transient III Degree AVB that required medication and monitoring were defined as mild procedure related complications.

Patients were commonly discharged 3–4 days after the procedure. Clinical examination, echocardiography (for evaluating residual shunts, device position and relation to aortic and tricuspid valves, valvular regurgitation), chest radiography, and electrocardiography were performed before discharge, as well as 1, 3, 6, 12 months following the procedure. Until the time when performing this analysis, the 63 patients successfully undergoing the closure had been followed.

## 3. Results

### 3.1. Procedural data

Device placement was successful in 56 cases at the first attempt of closure. Another 7 patients required another interventional replacement of occluders due to inappropriate device size. Two participants quitted procedure due to significant aggravation of device-related aortic regurgitation when attempt with a total immediate success rate of 96.9%.

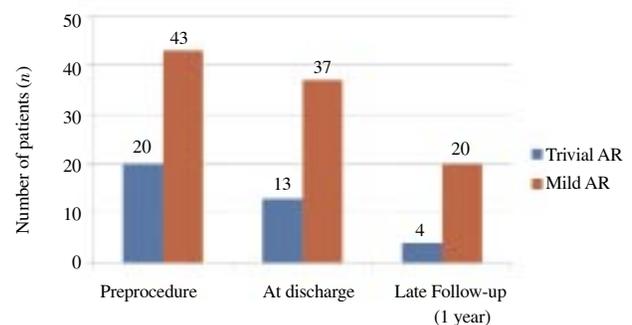
### 3.2. Data of perioperative complications

A total of 7 complications related to the procedure or device implantation occurred in 65 patients (10.8%). There was no death,

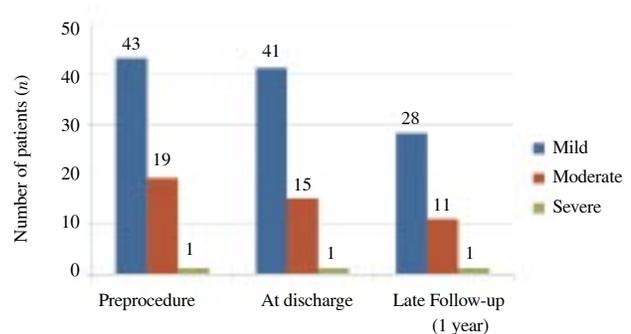
cerebral or pulmonary embolism, occluder dislocation or persistent III Degree AVB occurred. Moderate complications were encountered in 2 patients (3.0%) because of significant aggravation of device-related aortic regurgitation and finally their parents decided to quit transcatheter closure procedures. Mild complications occurred in 5/65 patients (7.7%). Those included postoperative peripheral hemorrhage in 3 patients and transient III degree AVB in 2 patients. The latter two patients remained in sinus rhythm and required a prolonged course of monitoring after procedure. None of patients required temporary and permanent pacemaker implantation.

### 3.3. Follow-up data

At discharge, no aggravation of aortic regurgitation was detected in patients. Of the 63 patients who have reached the 1-year postprocedural follow-up, none had trivial residual shunting cross defect. No cases of hemolysis, thromboembolic events, or endocarditis occurred. Furthermore, at one-year follow-up, grade of residual AR were relieved in 39 of 63 (61.9%) patients and there were 23 of 63 (36.5%) cases gained amelioration in grade of AVP (Figure 4 and 5).



**Figure 4.** Comparison of severity of AR preoperatively, at discharge, and at one year follow-up, respectively.



**Figure 5.** Comparison of severity of AVP assessed by echocardiography preoperatively, at discharge, and at one year follow-up, respectively.

## 4. Discussion

AVP and AR are well known to be linked with VSD[5]. Subaortic VSD will enhance progression of AR with the incidence of 18%[6]. There is few studies have focused on a subset of patients with

subaortic VSDs combined with AVP. The development of AVP is a risk factor for increasing AR was also confirmed[7]. Transcatheter closure such defects with devices as early as possible for avoiding deterioration of hemodynamic situation may prove to be a valuable alternative. However, there still are rare reports in the literature provide clinical information on device closure of VSDs in patients with AVP and mild AR. The main reason for it was contributed to that the diameter of defects and a limited aortic rim could present a significant challenge to operator. If the left ventricular disc of occluder impairs leaflets of aortic valve, patients may require abort procedure because of significant AR. This has been reported as high as 6.8% and tends to spontaneously resolve with time but not always. Therefore, whether perform the closure or not remains controversial[8]. ACC/AHA Guideline also reminded that patients with a small VSD and AVP may not recommended as the primary indication for closure and high possibility of developing progressive AR[9]. However, confronted with this obstacle, considering that transcatheter closure is less invasive than surgery and believing that early occlusion can prevent late hemodynamic disorder of AR and diminish the need for surgery, we still made attempt of transcatheter closure for these patients and manifested a satisfactory results.

The present study shows an excellent intermediate and perioperative outcome with a very high rate of success closure and a low incidence of complications. Here we demonstrate that when this procedure was successful in most of patients and only two patients exhibited aggravated AR. There were no severe complications related to the procedure. Moderate and mild complications occurred in 2 and 5 of the 65 patients, respectively. These results suggest that transcatheter closure can be performed feasibly and safely by selecting proper subjects and performing precisely even patients combined with AVP and mild AR. We have shown that the application of the device closure should not be limited on these patients if appropriate inclusion criteria were implemented. However, 2 cases with increasing AR imply that conventional left ventricular angiography and TTE sometimes may underestimate the movement of prolapsed aortic valve. Intraoperative cranial plus angulation projection and TTE in other view should be much better for showing anatomical and functional relationship between the retrieved occluder and prolapsed aortic valve, especially for patients with severe prolapsed aortic valve. Since the two unsuccessful percutaneous attempts occurred in patients, we conclude and emphasize that subaortic rim from VSD should be more than 3mm. Result of this series make us believe that preoperative elaborate evaluation of the anatomical and pathophysiological characteristic of defect plays a crucial role in avoiding unnecessary attempts in patients without proper indication. On the other hand, we also founded that two participants present with transient III degree AVB. The plausible explanation for it should be expansion of oversized VSD occluder transiently compress adjacent conduction tissues and induce the local edema.

Our series follow-up demonstrates other encouraging results with no progressive AR were detected in participants after hospital discharge. Furthermore, part of patient present gradual amelioration of AR or AVP. This also claim that direct closure actually improved degree of AVP and secondary AR. Base on general agreement of that prolapse of the aortic valve leaflet were the dominant factor of AR[10],

We postulated that the potential mechanism may be (i) occluders supply support and change original hemodynamic configuration like Venturi effect is created by the left-to-right shunting through the VSD during early systole, which make transseptal blood stream directly enhancing of the distribution of tension throughout the leaflet, aggravate the pressure burden of the diastolic pressure; (ii) The edge of device offer a commissural support from subaortic zone to prolapsed aortic valve leaflet and prevent tendency toward the imbalance of that and related progressive deterioration of AR. Therefore, correction and maintaining the integrity and stability of whole structure of aortic valve zone will be the key issue of success in this transcatheter study. We believe that with further experience in performing transcatheter closure in these patients, it will be less prone to complications and higher success rate.

### Conflict of interests statement

We declare that we have no conflict of interests.

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