

Echocardiographic Assessment and Guidance in Minimally Invasive Surgical Device Closure of Perimembranous Ventricular Septal Defects

Yifeng Yang, MD, PhD,² Lei Gao, MD,¹ Xinhua Xu, MD,¹ Tianli Zhao, MD,² Jinfu Yang, MD,² Zibo Gao, MD,² Ni Yin, MD,² Lian Xiong, MD,² Li Xie, MD,² Can Huang, MD,² Wancun Jin, MD,¹ Qin Wu, MD¹

Departments of ¹Echocardiography and ²Cardiac Surgery, Cardiovascular Research Institute, The Second Xiangya Hospital, Central South University, Changsha, Hunan, 410011, China

ABSTRACT

Background: The primary aim of this study was to explore the safety and feasibility of minimally invasive surgical device closure of perimembranous ventricular septal defects (PMVSDs) in children using echocardiography for preoperative assessment and intraoperative guidance.

Methods: We enrolled 942 children diagnosed with PMVSDs from April 2010 to October 2013. All children underwent full evaluation by transthoracic echocardiography (TTE) and multiplane transesophageal echocardiography (MTEE) to determine the sizes, types and spatial positions of defects and their proximity to the adjacent tissues. The PMVSDs were surgically occluded using MTEE for guidance.

Results: Eight hundred eighty-nine (94.37%) of 942 children underwent successful closure of PMVSDs. Symmetric devices were used in 741 children (including 38 A₄B₂ occluders) and asymmetric devices were used in the other 148. All patients received follow-ups at regular intervals after successful occlusion. The occluders remained firmly in place. No noticeable residual shunt or valvular regurgitation was discovered, with the exception of one child whose original mild aortic regurgitation progressed to moderate by the 18 month follow-up. Overall there were no significant arrhythmias with the exception of 3 children, all of whom experienced postsurgical acute attacks of Adams-Stokes syndrome.

Conclusions: Minimally invasive surgical device closure of PMVSDs is safe and feasible. TTE and MTEE play vital roles in all stages of treatment of PMVSDs.

INTRODUCTION

Ventricular septal defects (VSDs) are among the most common congenital heart defects; of these, the perimembranous ventricular septal defects (PMVSDs) comprise the majority. A significant proportion of PMVSDs requires closure [Tynan 2002]. At present, there are two methods used for closure of PMVSDs: open-heart surgery with

cardiopulmonary bypass (CPB), and percutaneous transcatheter closure. Both of these treatment interventions have risks and limitations. Surgical closure with CPB is a reliable and successful treatment method but the drawbacks include a relatively large wound and prolonged hospital stay. Percutaneous transcatheter closure has a short recovery time and small wound but has limited indications, especially in infants with low weight and in those with complex defects. In recent years an alternative technique employing minimally invasive surgery (off pump) and intraoperative device closure is being used for the closure of PMVSDs. Minimally invasive surgery is a relatively low risk procedure which has also been shown to have higher patient acceptance [Quansheng 2009; Chen 2010].

PMVSDs have varied shapes. The key to successful closure is accurate assessment and guidance by echocardiography – transthoracic echocardiography (TTE) and multiplane transesophageal echocardiography (MTEE) – TTE is used in preoperative screening and postoperative follow-ups, while MTEE is used for intraoperative guidance for implantation of the device. The aim of this study was to evaluate the safety and feasibility of minimally invasive surgery for closure of various types of PMVSDs under the guidance of MTEE.

METHODS

This study was approved by the ethics committee of our hospital. Written informed consent was obtained from the parents or guardians of the children. Parents were informed that minimally invasive surgery for closure of PMVSD is a novel procedure at our institution.

Patients

From April 2010 to October 2013, 942 children (501 males and 441 females) diagnosed with various PMVSDs underwent minimally invasive surgical closure at our hospital. The age range was 2 months to 14 years (mean 4.61 ± 3.37), and weights ranged from 4.0 kg to 65.5kg (18.01 ± 7.25). A few of these cases presented with mild valvular regurgitation and pulmonary hypertension. A standard electrocardiogram showed normal sinus rhythm, and chest X-rays and blood tests showed no severe disease.

Equipment and Devices

For echocardiography, we used the GE Vivid 7 Dimension echocardiographic system (GE USA) with 6T (for adults) and 9T (for children) MTEE transducers and

Received March 9, 2014; received in revised form June 22, 2014; accepted July 20, 2014.

Correspondence: Qin Wu, Department of Echocardiography, Cardiovascular Research Institute, The Second Xiangya Hospital, Central South University, No. 139 Renmin Road, Changsha, Hunan 410011, China; 86-731-85292025; fax: 86-731- 85292133; (e-mail: wq_211@163.com).

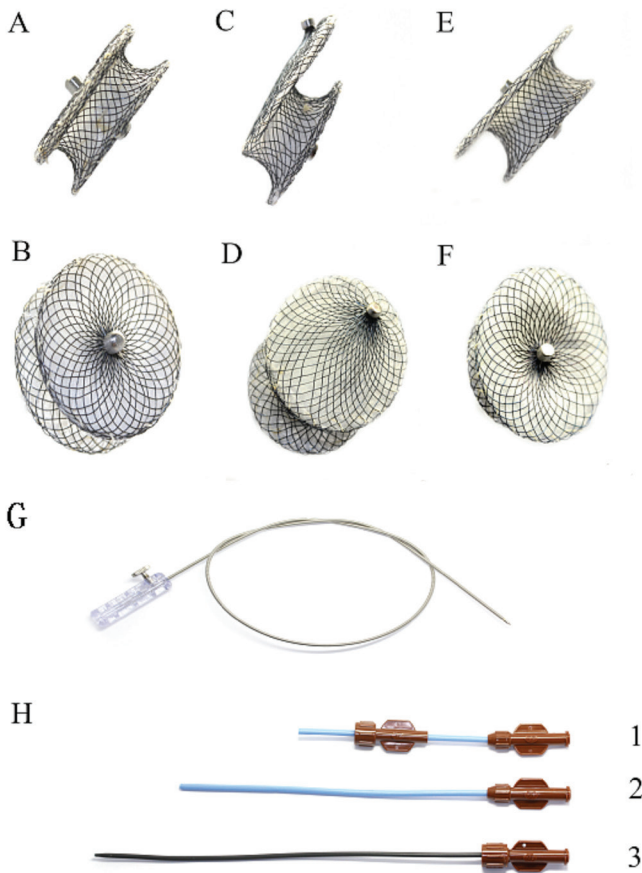


Figure 1. A, B: Symmetric occluder (A: top view, B: side view); C, D: Asymmetric occluder (C: top view, D: side view); E, F: A_4B_2 occluder (E: top view, F: side view); G, H: delivery system (G: push wire, H.1: loading sheath and butt joint, H.2: delivery sheath, H.3: internal dilator sheath).

3.5 - 10 MHz TTE transducers. We used Shanghai Shape Memory Alloy Co. Ltd (Shanghai, PRC) for the occluders and the delivery system. The devices were double-disks devices with a connecting waist. We used several types of VSD occluders, which included ordinary symmetric occluders (the two disks are both 2 mm larger than the waist) (Figure 1 A, B), asymmetric occluders with a marker on the longer side (the right disk is 2 mm larger than the waist, while the left disk is asymmetric, with the longer edge 5 mm wider than the waist and the other side ending with waist nearly without edge) (Figure 1 C, D) and A_4B_2 occluders (the right disk is 2 mm larger than the waist; the left is 4 mm larger) (Figure 1 E, F). All occluders were self-expandable and made of 0.004 inch woven mesh nitinol wire, with 3 to 5 layers of polyester mesh inside. The sizes of the PMVSD occluders, denoted by the diameters of the waists, ranged from 4 mm to 16 mm. The delivery system consisted of a guide wire, a push wire (Figure 1 G), an internal dilator sheath, a delivery sheath and a loading sheath with a butt joint (Figure 1 H).

Echocardiography

Before surgery, a TTE examination was performed to determine appropriate indications for the procedure. Multiple sections (including parasternal left heart long axis view, parasternal main pulmonary artery long axis view, apical 4-chamber and 5-chamber view, parasternal right ventricular outflow tract long axis view, etc.) showed the sizes, positions, shapes and relationship with adjacent tissues. Measurements of cavity size, left ventricular function and valvular function were taken. Patients with any one of the following were excluded:

- severe pulmonary hypertension (low velocity and dim color shunt – often against our judgement of residual shunt)
- overlarge defects (diameter of right outlet > 14 mm)
- moderate to severe aortic valve (AV) prolapse and/or aortic regurgitation
- VSDs complicated with other complex cardiac abnormalities

Surgical procedures

General anesthesia was administered and patients were placed in a supine position. Antibiotic prophylaxis and full heparinization (1 mg/kg) were administered per routine protocol. A 2-5 cm incision was made in the subxiphoid and lower partial sternotomy was performed. The pericardium was suspended and the right ventricle exposed. The RV free wall was palpated to locate the area for puncture and a purse string suture was placed at this location. The puncture area had to be large enough to establish a delivery pathway. A trocar was introduced into the RV and a guidewire passed through the trocar. A delivery sheath (7-9 F) was fed over the wire and manipulated into the left ventricular (LV) cavity and across the VSD under the guidance of MTEE. The wire was removed and the loading sheath (with an occluder and push wire) was screwed to the delivery cable at the end by a butt joint. The LV disk was deployed into the interventricular septum by pushing the occluder forward and retracting the sheath. The RV disk was then deployed with continuous traction on the sheath and push wire. The occluder was then pulled and pushed to test its steadiness and, the device was released. The sheath and the push wire were then pulled out together. A chest tube was placed and the chest closed. Dexamethasone was administered for the first 3 days to prevent arrhythmia and aspirin was administered for the first 3-6 months to prevent clot formation.

Surgical evaluation and guidance using MTEE

After induction of general anesthesia the MTEE transducer was inserted down the esophagus. A series of planes (long-axis view, short-axis view, and 4 or 5-chamber view, etc.) were scanned to reassess the VSD size (we measured the maximal dimension of both left and right ventricular defects) shape and spatial position, and the length of the margin adjacent to the aortic and tricuspid valves and valvular function. The size and type of occluder was then selected based on the MTEE findings. The MTEE evaluation was essential for

confirmation of the presence of a defect and in the choice of the appropriate occlusion device [Bai 2012]. The size for the occluder was initially calculated by considering the maximal dimension of the defect and adding 1-2 mm. Further adjustment of size or type was made as necessary.

It is important to take the time to choose an appropriate puncture area and direction under the guidance of MTEE. The image in Figure 2A shows a strong echoed protrusion into the RV cavity by forceps. This procedure will help to establish a clear delivery pathway for the occluder and prevent a prolonged surgical procedure. We used a three plane method to accurately determine the puncture area. The three planes were: 0° for 4 or 5 chamber view from left to right; 45° for short axis view from upper left to lower right and 135° for long axis view from upper right to lower left. This permits display of the defect clearly in each plane. Through the 3-plane positioning, we could generally determine an accurate puncture area and direction.

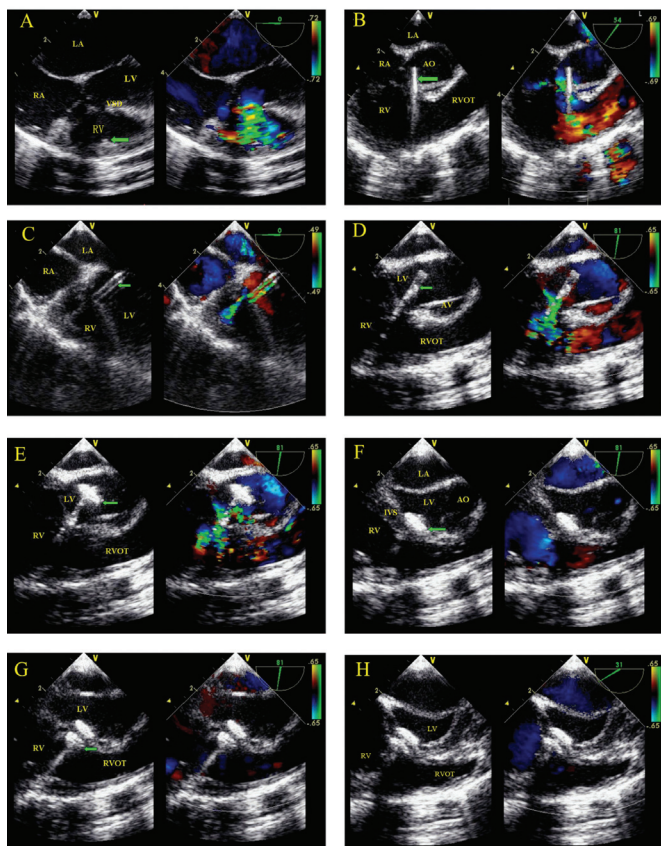


Figure 2. A: guide wire inserted into right ventricular cavity, B: bilateral image of delivery sheath, C: the compressed occluder (arrow) with strong echo being pushed forward slowly by the push wire inside the sheath, D: the left disk and central waist were deployed in sequence in the LV by pushing the occluder forward and retracting the sheath, E: the LV disk clings to the interventricular septum with continuous retreat of the sheath and push wire. F: the right disk was deployed (arrow) in RV cavity, G: TEE showing the symmetric occluder H: TEE showed the symmetric occluder as an “H”-shaped image.

After the RV anterior wall was punctured, a strong echoed guide wire was inserted into the RV cavity. MTEE was then used to direct the guide wire through the VSD to the LV cavity (Figure 2 B). With the guide wire through VSD successfully, a delivery sheath was introduced from the RV to LV, then through the VSD. Next, the guide wire was removed and a bilateral image was taken (Figure 2 C). Then a loading sheath was screwed to the delivery cable and the loaded occluder was pushed forward. We could then visualize the compressed occluder with strong echo being pushed forward slowly by the push wire inside the sheath (Figure 2 D). As we moved to the end of the sheath, the left disk and central waist were deployed in sequence in the LV (Figure 2 E, F). Next, the right disk (Figure 2 G), then an H-shaped image was seen (Figure 2 H). Finally, an MTEE guided push-and-pull test was made to test for stability.

A complete MTEE examination was performed to confirm device placement and to assess residual shunting and valvular incompetence. Electrocardiography was employed in the meantime to ensure there was no severe conduction defect. If the examination was satisfactory, that is – there was no significant residual shunt (width < 2 mm, velocity < 3 m/s) and significant aortic regurgitation (vena contracta width < 0.3 cm) or TV regurgitation (central jet area < 5 cm²) [Petros 2009], the device was released and the sheath pulled out. If the exam showed otherwise, the occluder was changed.

PMVSD size and correlation with occluder sizes

The measurement of PMVSDs sizes by TTE ranged from 2 to 11 mm (4.22 ± 1.59 mm), and the sizes measured by MTEE ranged from 2 to 12 mm (4.43 ± 1.76 mm). The sizes of the occluders used were 4 to 14 mm (6.43 ± 1.81 mm). In evaluating the correlations between two methods of measurement (TTE and MTEE) and occluder size, we obtained robust results in favor of MTEE ($r^2 = 0.542$ and $r^2 = 0.772$ for TTE and MTEE, respectively) ($P < .001$). Symmetric devices were used in 741 children (including 38 cases of A₄B₂ occluders), and asymmetric devices were used in the other 148 children.

Closure of aneurysm-like VSDs

Aneurysm-like VSDs are a unique type of PMVSDs. Of the 942 children, 357 presented with aneurysm-like VSDs, of which 329 were successfully closed (253 common symmetric, 36 A₄B₂ and 40 asymmetric). The remaining 28 children underwent open-heart surgery. Aneurysm-like VSDs have an inlet and single or multiple outlets. Two hundred twenty-one of the 329 successfully closed presented as single outlet, and the other 108 with multiple outlets. One hundred seventy-eight cases were closed by placing the occluders at the right outlet of the defects with the right disks in the pseudoaneurysm, and another 151 were closed by placing the occluders at the left inlet of VSDs. Eighteen of the 28 unsuccessfully closed presented with multiple outlets.

The relationship between PMVSDs and valves

The defects of 137 cases were very close to the aortic valves (AVs) and their distances from the border of the defect

(left side) to the AV were less than 2 mm. The closest was only 0.8mm; this case was closed successfully with an asymmetric device. Twelve of 53 unsuccessful cases subsequently underwent surgical treatment due to AV prolapse and the interference with valvular function by the occluders. Nearly all of these types of defects were successfully closed by asymmetric occluders, except those which were closed by placing the occluders at the right outlets with the right disks in the pseudoaneurysm. One hundred-two cases were very close to tricuspid valves (TVs) and their distances from the border of the defect (left ventricular side) to the tricuspid annulus were less than 2 mm. Most of these were aneurysm-like VSDs with large left inlets and the shortest distance was zero mm. Seventeen of these cases subsequently underwent open-heart surgery for repair of the defects.

Follow-up utilizing TTE

Routine postoperative follow-ups were done by TTE. The follow-ups included the position and shape of the occluder, the influence on valvular function by occluder, the residual shunt and routine assessments. Regular follow-ups were done at 4 and 15 days, and at 1, 3, 6, 12, 24 and 30 months after surgery.

Statistical Analysis

Continuous data were presented as mean \pm standard deviation and range. The SPSS 15.0 software (IBM Corporation; Somers, NY) was used for statistical analysis. Correlation analysis of various measurements was performed. A value of $P < .05$ was considered statistically significant.

RESULTS

Of a total of 942 children, 889 underwent minimally invasive surgical device closure successfully, with a success rate

of 94.37%. TTE showed resolution of the ventricular shunt with two disks presenting as two parallel strong echo bands. Fifty-three patients underwent surgical repair with CPB after a failed attempt at closure.

Follow-up

All children were followed-up on a regular basis. The duration of follow-up ranged from 1 to 43 months (21.32 ± 8.67 mos). There were no deaths. During TTE follow-ups, the occluders echoed clear without movement (Figure 3). Residual shunts were observed immediately after closure in 53 successful cases. The peak velocities of the shunts were less than 3m/sec and the width less than 2 mm. Follow ups revealed that the majority of the shunts had been resolved successively. Only 5 cases, all within 6 months after surgery, showed residual mild shunts (no evidence of change in hemodynamics) and no hemolysis. In thirty-nine children mild tricuspid regurgitation was detected. Ten children had mild aortic regurgitation immediately after closure, and only one (with an aneurysm-like VSD with a 7 mm inlet and multiple outlets) required additional treatment on follow-up. This patient had been implanted with an asymmetric occluder with the longer side of the left disk pointing to the AV in order to cover the upper micropores. At that time, MTEE showed the distance between the disk edge and the AV annulus was 1mm and it was thought to be safe. Follow-ups within the first year in this patient showed mild aortic regurgitation, and at the 18 month follow-up showed moderate aortic regurgitation. However, the regurgitation has not progressed since that time.

Thirty-six children presented with late onset mild pericardial effusion, with the exception of 5 children who presented with moderate to severe pericardial effusion and who received percutaneous aspiration. None of the effusions reoccurred.

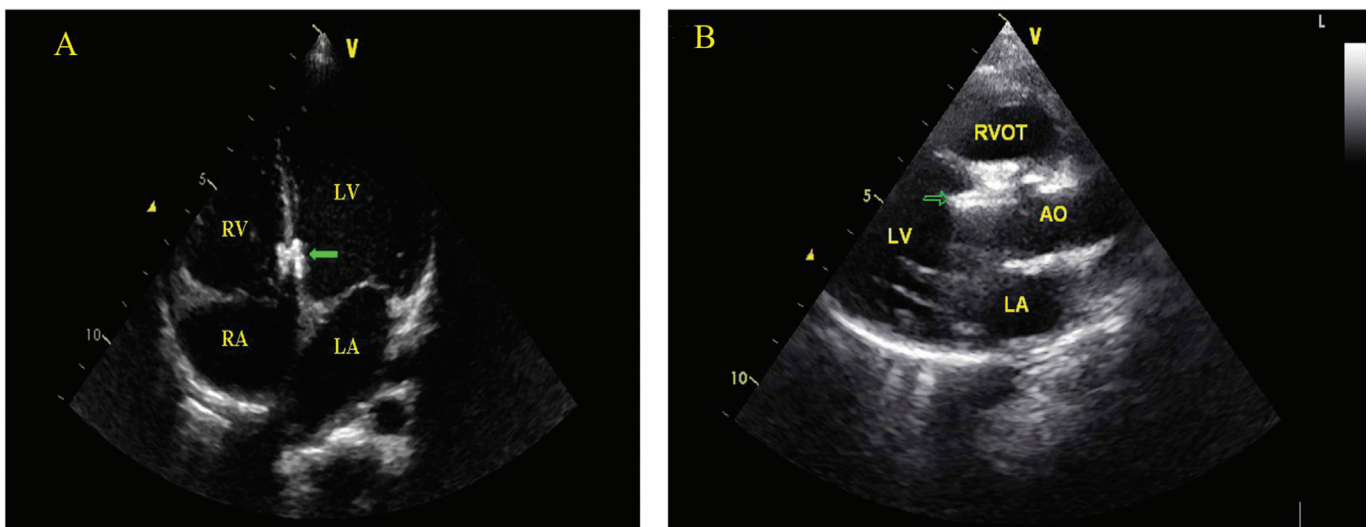


Figure 3. A: TTE showing the symmetric occluder, B: TTE showed the asymmetric occluder
LA=Left Atrium, RA=Right Atrium, LV=Left Ventricular, RV=Right Ventricular,
RVOT=Right Ventricular Outflow Tract, AO=Aorta, VSD=Ventricular Septal Defect,
IVS=Interventricular Septum

ECGs showed no significant conduction defects on follow-up with the exception of 3 children all of whom experienced acute attacks of Adams-Stokes syndrome within 2-6 days after surgery. One was implanted with a 7 mm A_4B_2 occluder in the inlet of the aneurysm-like defect, one was implanted a 6 mm asymmetric occluder and the other was implanted a 6 mm symmetric occluder. These 3 patients all underwent emergency open-heart surgery to remove the occluders and repair the VSDs. Two of these reverted to normal sinus rhythm within one to two days after surgery.

DISCUSSION

Although it has been established that both surgical and percutaneous transcatheter closure of VSDs are safe, with negligible mortality rates [Bol-Raap 2003; Yang 2011], both have drawbacks and limitations. In the early stages of development, this technology showed initial successful results in animals and subsequently in humans [Bacha 2003; Amin 2004; Amin 2006].

Recently, a new hybrid method has been developed and applied to clinical treatment [Quansheng 2009]. This new technique has multiple advantages: it requires no CPB and the echocardiography guidance is in real-time and without radiation exposure. The operating pathway won't damage the vascular intima and occluders can be easily controlled. There are no age and weight limitations, and open-heart surgery can be used as a backup as a last resort.

Echocardiography (TTE), used as a non-invasive image guidance, plays a vital role in the safety and feasibility of this minimally-invasive procedure. TTE is routinely used for pre-operative screening, and for postsurgical follow-ups, while MTEE is used intraoperatively to guide the implantation of occluders. MTEE has the advantage of multiple sections and less interference, providing a more detailed evaluation that does not interfere with the operative field. PMVSDs are of multiple shapes and are situated in areas wedged between the tricuspid and aortic valve [Cao 2011]. Although minimally invasive surgical closure has relatively wide applications, not all PMVSDs can be closed by this method. The key is the distance between the defect and the aortic and tricuspid valves in addition to the size and shapes of the defects. It has been reported that the safe distance between the defect and the closest valve is 2 mm [Bai 2012]. In our study, a 5 mm PMVSD with a rim of 0.8 mm from the AV was successfully closed by an asymmetric occluder and the follow-ups showed the occluder and valve function were satisfactory. In our experience we found:

- If an AV prolapse or regurgitation is detected, the patient should be eliminated as a candidate for the procedure.
- If a large PMVSD has a rim <1 mm from the AV, we should exercise caution not to injure the valve during the operation.
- A PMVSD with a rim > 1mm and < 2mm from an AV implanted with an asymmetric occluder will not likely interfere with the valvular function.
- A PMVSD with a rim > 2mm from an AV implanted

with a symmetric occluder can likely be closed successfully.

- If the longer side was used to point in the direction of the AV, the distance between the longer edge of the disk and the AV annulus should be > 2mm.
- The influence of the spatial relationship between the TV and defect on choosing the occluder is similar to that of the AV and defect.
- Follow-ups showed that it should be generally safe when vena contracta width of aortic regurgitation <0.3cm and central jet area of tricuspid regurgitation is <5cm².

Some PMVSDs, such as tunnel-shaped and aneurysm-like defects, often have an inlet and one or more outlets. The key to successful closure in these cases is finding the best position to embed the occluder. The pseudoaneurysm is a specific type of PMVSD and the key stage of the spontaneous closure of PMVSDs [Freedom 1974; Vidne 1976]. Due to the complex morphologic characteristics, it is difficult to cover aneurysm-like VSDs with large inlet and multiple outlets completely [Hu 2004; Anil 2005; Cao 2005; Holzer 2006; Fischer 2007]. Our evaluation of aneurysm-like VSDs includes:

- the size of the left inlet and its distance from valves
- the size of each outlet and the space between them
- the thickness of the pseudoaneurysm wall
- the distance of the pseudoaneurysm to adjacent tissues

From the above evaluation, we can assess two important elements about choosing the appropriate occluders. The first is determination of the optimal implant position, whether at the inlet or the outlet. The inlet provides closure by blocking the source of shunt, but it could affect adjacent tissues. The outlet might be relatively safer due to left disk placement in the pseudoaneurysm, but it may not close all outlets and has the potential for instability because of the thin pseudoaneurysm wall. The other element is determining an appropriate occluder type –symmetric, A_4B_2 or asymmetric. Unlike the asymmetric occluder, the symmetric and A_4B_2 both have better stability but are less advantageous for avoiding adjacent tissues.

With aneurysm-like VSDs with large inlet and multiple outlets, occluding the outlet is the safest approach. A larger outlet should be chosen for establishing the delivering pathway. An occluder is chosen that will cover all outlets to the greatest extent. With adjacent outlets, if the largest outlet is in the center, we use an A_4B_2 occluder to cover surrounding small outlets by the large left disk; if the largest outlet is at the side, we use an asymmetric occluder to cover surrounding outlets by the longer edge of left disk, which is determined by the marker on the longer edge towards surrounding outlets. The A_4B_2 occluder is used primarily in aneurysm-like VSDs with large inlet and multiple outlets. It is difficult to cover all outlets when they are far apart from each other, especially when the distance is more than 4-5 mm (determined by the shape of the occluder).

The main complications of minimally invasive surgical device closure are residual shunt, valvular regurgitation and conduction defects. In most instances, the former two can be avoided by monitoring with MTEE during surgery, while the

latter is difficult to avoid completely. There were 3 children in this study who had sudden attacks of Adams-Stokes syndrome in 2, 3 and 6 days after operation respectively. Their ECGs had been normal up to the date of the sudden attacks. We think the sizes of the occluders used were too large and the subsequent edema impinged on the conduction system. After taking out the occluders, normal sinus rhythm was gradually regained. Therefore, we believe that choosing an appropriate occluder is the key to a successful procedure. Oversized occluders are prone to causing valvular regurgitation and atrioventricular block, while smaller ones tend to cause residual shunting and occluder displacement [Bai 2012]. However, the duration of follow-ups in this study to date are not long enough for an accurate assessment of the causes of the conduction defects, so subsequent follow-ups should further elucidate the possible causes of these complications.

CONCLUSION

Echocardiography-guided minimally invasive surgical closure is a safe and feasible treatment option for PMVSDs. It is particularly suitable for those complex defects which are difficult to close using the percutaneous transcatheter procedure, and has broad applications, such as hybrid surgery of complex congenital heart disease. Precise and detailed preoperative assessment using echocardiography can aid in patient screening, selecting occluders of appropriate size and type, and in avoiding potential complications from procedures. The preoperative, intraoperative and postoperative application of echocardiography (TTE and MTEE) effectively increases success rates and the safety of procedures. Long term follow-ups of this study and further clinical studies are needed for assessment of this new hybrid technology for closure of perimembranous ventricular septal defects.

ACKNOWLEDGEMENT

This work was supported by the fund from the Bureau of Science and Technology of Hunan Province, P.R.China. Grant No.2013SK3038.

REFERENCES

- Amin Z, Danford DA, Lof J, Duncan KF, Froemming S. 2004. Intraoperative device closure of perimembranous ventricular septal defects without cardiopulmonary bypass: preliminary results with the perventricular technique. *J Thorac Cardiovasc Surg* 127:234-41.
- Amin Z, Woo R, Danford DA, et al. 2006. Robotically assisted perventricular closure of perimembranous ventricular septal defects: Preliminary results in yucatan pigs. *J Thorac Cardiovasc Surg* 131:427-32.
- Anil SR, Sreekanth R, Bhalerao S, et al. 2005. Transcatheter closure of perimembranous ventricular septal defect with amplatzer membranous occluder. *Indian Heart J* 57:698-703.
- Bacha EA, Cao QL, Starr JP, et al. 2003. Perventricular device closure of muscular ventricular septal defects on the beating heart: Technique and results. *J Thorac Cardiovasc Surg* 126:1718-23.
- Bai W, An Q, Tang H. 2012. Application of transesophageal echocardiography in minimally invasive surgical closure of ventricular septal defects. *Tex Heart Inst J* 39:211-4.
- Bol-Raap G, Weerheim J, Kappetein AP, Witsenburg M, Bogers AJ. 2003. Follow-up after surgical closure of congenital ventricular septal defect. *Eur J Cardiothorac Surg* 24:511-15.
- Cao H, Chen Q, Zhang GC, et al. 2011. Intraoperative device closure of perimembranous ventricular septal defects in the young children under transthoracic echocardiographic guidance; initial experience. *J Cardiothorac Surg* 6:166.
- Cao QL, Zabal C, Koenig P, Sandhu S, Hijazi ZM. 2005. Initial clinical experience with intracardiac echocardiography in guiding transcatheter closure of perimembranous ventricular septal defects: Feasibility and comparison with transesophageal echocardiography. *Catheter Cardiovasc Interv* 66:258-67.
- Chen Q, Chen LW, Wang QM, et al. 2010. Intraoperative device closure of doubly committed subarterial ventricular septal defects: initial experience. *Ann Thorac Surg* 90:869-73.
- Fischer G, Apostolopoulou SC, Rammos S, et al. 2007. The amplatzer membranous VSD occluder and the vulnerability of the atrioventricular conduction system. *Cardiol Young* 17:499-504.
- Freedom RM, White RD, Pieroni DR, et al. 1974. The natural history of the so-called aneurysm of the membranous ventricular septum in childhood. *Circulation* 49:375-84.
- Holzer R, de Giovanni J, Walsh KP, et al. 2006. Transcatheter closure of perimembranous ventricular septal defects using the amplatzer membranous VSD occluder: immediate and midterm results of an international registry. *Catheter Cardiovasc Interv* 68:620-28.
- Hu HB, Jiang SL, Xu ZY, et al. 2004. Transcatheter closure of perimembranous ventricular septal defects using the new amplatzer membranous VSD occluder: A short-term evaluation. *Zhonghua Yi Xue Za Zhi* 84:1592-96.
- Nihoyannopoulos P. Aortic Valve Disease: A. Aortic Stenosis. In: *Echocardiography*. Nihoyannopoulos P, Kisslo J, eds. London New York: Springer Dordrecht Heidelberg, 2009:117-227.
- Quansheng X, Silin P, Zhongyun Z, et al. 2009. Minimally invasive perventricular device closure of an isolated perimembranous ventricular septal defect with a newly designed delivery system: preliminary experience. *J Thorac Cardiovasc Surg* 137:556-9.
- Tynan M, Anderson RH, Baker EJ, et al. Ventricular septal defects. In: *Paediatric Cardiology* 2nd ed. Anderson RH, Baker EJ, Macartney FJ, Rigby ML, Shinebourne EA, Tynan M, eds. London: Churchill Livingstone; 2002:983-1014.
- Vidne BA, Chiariello L, Wagner H, Subramanian S. 1976. Aneurysm of the membranous ventricular septum. Surgical consideration and experience in 29 cases. *J Thorac Cardiovasc Surg* 71:402-9.
- Yang R, Sheng Y, Cao K, et al. 2011. Transcatheter closure of perimembranous ventricular septal defect in children: Safety and efficiency with symmetric and asymmetric occluders. *Catheter Cardiovasc Interv* 77:84-90.