Favorable mid-term performance of fully biodegradable implantable device for ventricular septal defect closure

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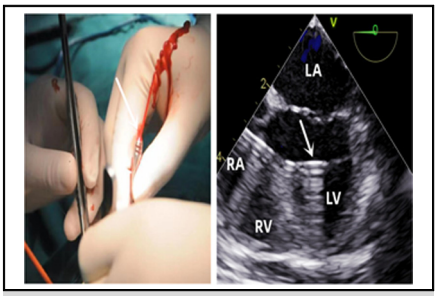
ABSTRACT

Objectives: To assess the mid-term safety and efficacy of transthoracic perimembranous ventricular septal defect (Pm-VSD) closure using a new biodegradable device. Implantation entailed right subaxillary minithoracotomy under transesophageal echocardiography guidance.

Methods: Between October 2019 and January 2020, 13 patients (males, 5; mean age, 3.6 ± 2.5 years) with Pm-VSDs underwent transthoracic device closures at Zhengzhou University Central China Fuwai Hospital as described previously. Delivery pathways were established by manipulating a hollow probe from right atrium through tricuspid valve to right ventricle and then through VSDs to left ventricle, whereupon installation took place.

Results: All occluder implantations were successfully executed. Mean defect size was 4.1 ± 1.0 mm, and mean device waist size was 5.2 ± 1.1 mm. One patient (7.7%) with 1.5-mm residual shunt showed complete closure at discharge. There was 1 instance of postoperative incomplete right bundle branch block, which converted to complete right bundle branch block at month 1. During patient follow-up (mean, 24.6 ± 0.8 months), no device dislocations, new residual shunts, new valvular regurgitation, or detectable atrioventricular block ensued.

Conclusions: Closure of Pm-VSDs using a novel, fully biodegradable occluder in the manner described has proven safe and effective at mid-term follow-up. Long-term safety and efficacy of this device must be further corroborated in a large patient cohort going forward. (JTCVS Techniques 2023;17:133-7)



Establishing the delivery pathway from right atrium to left ventricle using hollow probe.

CENTRAL MESSAGE

Mid-term analysis of a novel, fully degradable VSD occluder has proven quite satisfactory, a transaxillary approach providing greater technical advantage in this regard.

PERSPECTIVE

Development of a fully biodegradable occluder to overcome shortcomings of metal VSD closure device has been an ongoing research focus. Use of a novel, fully biodegradable occluder for this purpose has now proven safe and effective at mid-term patient follow-up. Implantations were achieved under TEE guidance via small right subaxillary incisions, a more technically advantageous approach in this setting.

Perimembranous (Pm) ventricular septal defects (VSDs) account for the majority of VSDs and may involve both membranous and adjacent muscular portions of septum. Surgical closure remains the remedy of choice, especially if defects in question are sizeable. Catheter-based interventions, as opposed to open surgical correction, have shown promising results since reporting of the first case in 1988.[1] At present, most clinically used occluders have skeletons of nickel–titanium shape memory alloy and feature biostable membranes.[2-5] However, metal occluders carry potential complications, such as metal allergy or corrosion, friction damage, and late atrioventricular block

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Abbreviations and Acronyms

AVB = atrioventricular block
LBBB = left bundle branch block
Pm-VSD = perimembranous ventricular septal defect
RBBB = right bundle branch block
TEE = transesophageal echocardiography

(AVB). Thus, the development of a novel, fully biodegradable occluder to address shortcomings of existing metal devices has been an ongoing focus of research.

In 2020, Chen and colleagues[2] published initial results of a fully bioabsorbable occluder (Shanghai Shape Memory Alloy). Herein, we report mid-term safety and efficacy data for this same fully biodegradable device used in transthoracic Pm-VSD closures. Implantations were achieved via right subaxillary route and under transesophageal echocardiography (TEE) guidance only.

PATIENTS AND METHODS

Patient Selection

Between October 2019 and January 2020, 13 patients with Pm-VSDs were recruited at Zhengzhou University Central China Fuwai Hospital to undergo transthoracic device closure using the aforementioned fully biodegradable occluder (Shanghai Shape Memory Alloy). Mean age was 3.6 ± 2.5 years (range, 1.2-10.1 years), and mean weight was 14.9 ± 4.1 kg (range, 10.1-22.7 kg). In all patients, comprehensive preprocedural evaluations, including laboratory testing, radiographs, electrocardiograms, and transthoracic echocardiograms, were conducted (institutional review board approval date: August 5, 2019, #2019-Q009-01).

Inclusion criteria were as follows: (1) isolated Pm-VSD; (2) age ≥1 year; (3) body weight ≥10 kg; (4) right-sided opening diameter of 3.0 to 8.0 mm; (5) subaortic rim ≥3 mm, as shown by echocardiography in long-axis view; and (6) left-to-right hemodynamic shunt. The following were grounds for exclusion: (1) multiple VSDs; (2) defect diameter >8 mm or margin prohibiting device closure; (3) confirmed severe pulmonary hypertension; (4) aortic valve prolapse; (5) contraindications to antiplatelet therapy; (6) infective endocarditis; and (7) other associated congenital heart disease requiring open repair.

Written informed consent was obtained from the parents or legal guardians of each patient. The hospital's medical ethics committee granted approval for this study.

Occluder Device and Delivery System

Each fully biodegradable VSD occluder incorporates a polydioxanone framework, with 2 poly-L-lactic acid fabric inserts (Figure 1, *red arrow*). The framework is woven from polydioxanone monofilament and thermoformed into 2 flat disks and a connecting waist. Both disks are identically sized (ie, same diameters), each harboring a piece of nonwoven poly-L-lactic acid fabric to enhance thrombogenicity. Flanges at the disks exceed those at the waist (diameter range, 4-16 mm) by 2-3 mm.

The occluder has a flexible loop at disk center on right ventricular side for delivery cable attachment. The cable is made of stainless-steel spring tubing that is clamped at the tip (Figure 1, *yellow arrow*). Release or engagement is achieved by rotating a threaded pipe attached to the handle.

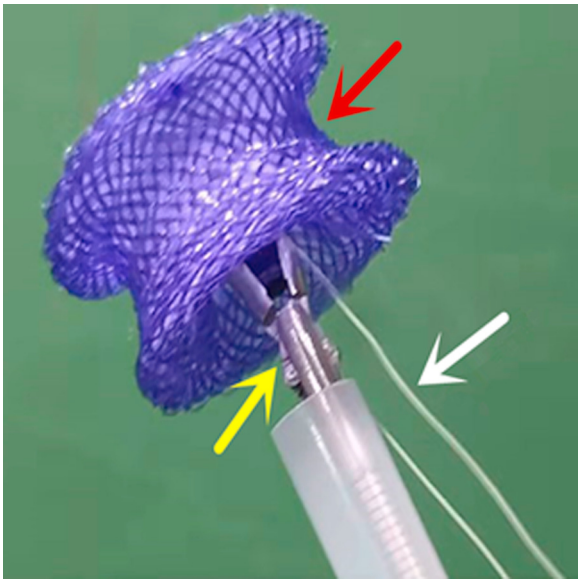

FIGURE 1. Device image: fully biodegradable ventricular septal defect occluder device (*red arrow*), showing clamp on tip of delivery cable (*yellow arrow*) and shaping line (*white arrow*).

Thus, the occluder is either secured to or released from the delivery cable through clamp manipulation. Because the polydioxanone framework is less elastic than one of metal, the occluder configuration is controlled by a shaping line aside the left disk (Figure 1, *white arrow*).

Operative Procedure

Although this technique has a learning curve, all operations performed were undertaken by experienced specialists.

Step 1. All procedures were performed with the patient under general anesthesia, and prophylactic intravenous antibiotics were administered 30 to 60 minutes in advance. TEE served to assess Pm-VSDs in terms of size and position. Devices selected were 1 to 2 mm larger than measured VSD diameters.

Step 2. Patient positioning was switched from supine to left lateral, and a 3-cm incision was made along right midaxillary line vertically between superior border of third rib and inferior border of fifth rib (Figure 2, *A*). The thoracic cavity was entered through fourth intercostal space, and intravenous heparin (100 μ/kg) was given for systemic anticoagulation. The pericardium was opened 2 cm anterior to phrenic nerve and suspended to elevate the heart, placing a 5-0 PROLENE purse-string suture (Ethicon) on the free right atrial wall.

Step 3. Under continuous TEE guidance, a right atrial puncture was made between the purse-string sutures. The hollow probe was then inserted into right atrium (Figure 2, *B*), advancing it through tricuspid valve into right ventricle. Next, the probe tip was adjusted to cross or point to the defect (Figure 3, *A*), spurting forth arterial blood (Figure 4).

Step 4. A flexible guidewire was inserted through the hollow probe into the left ventricle (Figure 3, *B*), then removing the hollow probe and introducing the dilator and the delivery sheath over the guidewire into left ventricle cavity. Both dilator and guidewire were subsequently removed, thus establishing a delivery pathway (Figure 3, *C*).

Step 5. The selected occluder was attached to the delivery cable tip by clamping the loop of the disk on right ventricular side. Once clamped tightly closed, by screwing the threaded pipe on the handle, the occluder was withdrawn into the loader sheath, flushed with saline, and transferred into the delivery sheath.

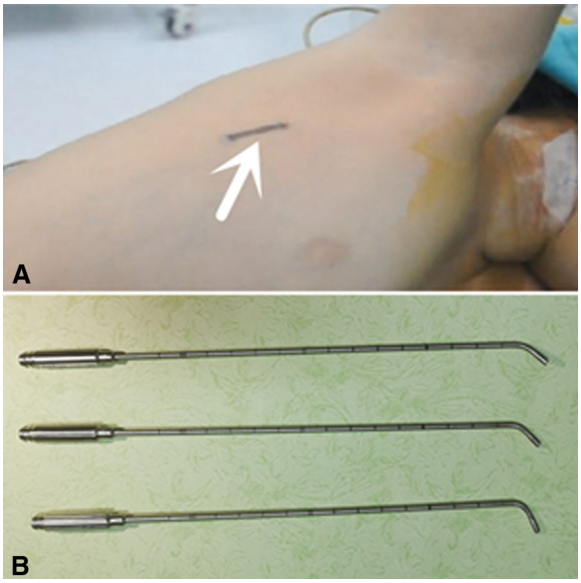

FIGURE 2. Incision and hollow probe: A, Subaxillary entry point (*arrow*). B, Array of hollow probes.

We finally deployed the biodegradable occluder under TEE guidance. Upon ventricular release, the occluder disk has a spindle shape. Its "double-umbrella" configuration is produced by pulling back on the shaping line while pushing the delivery cable forward (Figure 3, *D*).

To release the device from the delivery cable, the clamp was disengaged, and the entire delivery system was withdrawn (Figure 3, *E* and *F*). We then tied the purse-string suture of free right atrial wall, placed a drainage tube in right chest, and closed the chest wall in routine manner.

Follow-up Protocol

All patients underwent laboratory examinations, radiographs of the chest, transthoracic echocardiogram, and electrocardiograms before discharge; at postoperative months 1, 6, and 12; and yearly thereafter. Aspirin (3-5 mg/kg) was regularly administered for 6 months after procedures.

Statistical Analysis

Data were expressed accordingly as frequencies or percentages (for nominal variables), as mean ± standard deviation values (for continuous variables), or as medians with ranges. All statistical analyses were driven by standard software (SPSS Statistics for Windows, version 17.0 [2011 release]; IBM Corp).

RESULTS

Perioperative Results

The fully biodegradable occluders were successfully implanted in all patients. Mean defect size was 4.1 ± 1.0 mm (range, 3.0-6.0 mm); mean waist size of implanted devices was 5.2 ± 1.1 mm (range, 4.0-7.0 mm); and mean delivery sheath size was 9.2 ± 0.9 Fr (range, 8.0-10.0 Fr). Mean operative time was 68.9 ± 22.6 minutes (range, 40.0-120.0 minutes).

One patient with a 1.5-mm residual shunt showed complete closure at discharge, and another patient developed incomplete right bundle branch block (RBBB) postoperatively. At preoperative baseline, tricuspid regurgitation was trivial in 11 patients and mild in 2. Postoperatively, degrees of tricuspid regurgitation were downgraded from mild to trivial in 2 patients (15.4%) and upgraded from trivial to mild in 2 others. No device-induced aortic regurgitation was encountered during this study. Pre- and postoperative levels of routinely tested hematologic indices and biochemical blood parameters did not differ significantly.

Follow-up Results

Median follow-up was 24.8 months. One patient with incomplete RBBB converted to complete RBBB at postoperative month 1 but later normalized at month 6. Two patients with mild preoperative tricuspid regurgitation were downgraded to trivial regurgitation. No new residual shunting was observed in the course of follow-up. Complete defect closure, with no residual shunting, was achieved before discharge. Ultrasound depictions of occluder remnants tended to gradually decline, indicating increasing absorption over time. During the follow-up period, there were no instances of death, device dislocation, new or aggravated aortic regurgitation, left bundle branch block (LBBB), AVB, thrombosis, or infective endocarditis.

DISCUSSION

Since release of the AMPLATZER Septal Occluder (Abbott Laboratories) in 1998, many centers have considered interventional occlusion a viable alternative treatment modality for patients with VSDs.[3,4] However, transcatheter Pm-VSD closure with the AMPLATZER Septal Occluder remains controversial, given the high AVB rate that is especially problematic long-term. This explains why the US Food and Drug Administration has not yet authorized its use for this purpose.[3,4] Consequently, devising a fully biodegradable VSD occluder to avoid such long-term complications has become one of the most pressing research issues in China and abroad.[2,5-10]

The fully biodegradable occluder we tested and its delivery system have certain design features that traditional counterparts lack. The polydioxanone (vs memory alloy) framework is comparatively less elastic, so occluder shaping is assisted by a line affixed to the left disk. The delivery cable is also a stainless-steel spring tube with a clamp on the tip, allowing the occluder to be secured or released through clamp manipulation.

Another important aspect is the device deployment route. It must be simple to traverse and of limited distance, ensuring that occluder elasticity is preserved. In 2017, we published our initial results for transthoracic device closure of Pm-VSDs via right subaxillary route under TEE guidance alone.[11] Advantages of this technology are its operative simplicity, the short delivery path entailed, an unobtrusive incision, and radiation-free execution. TEE in

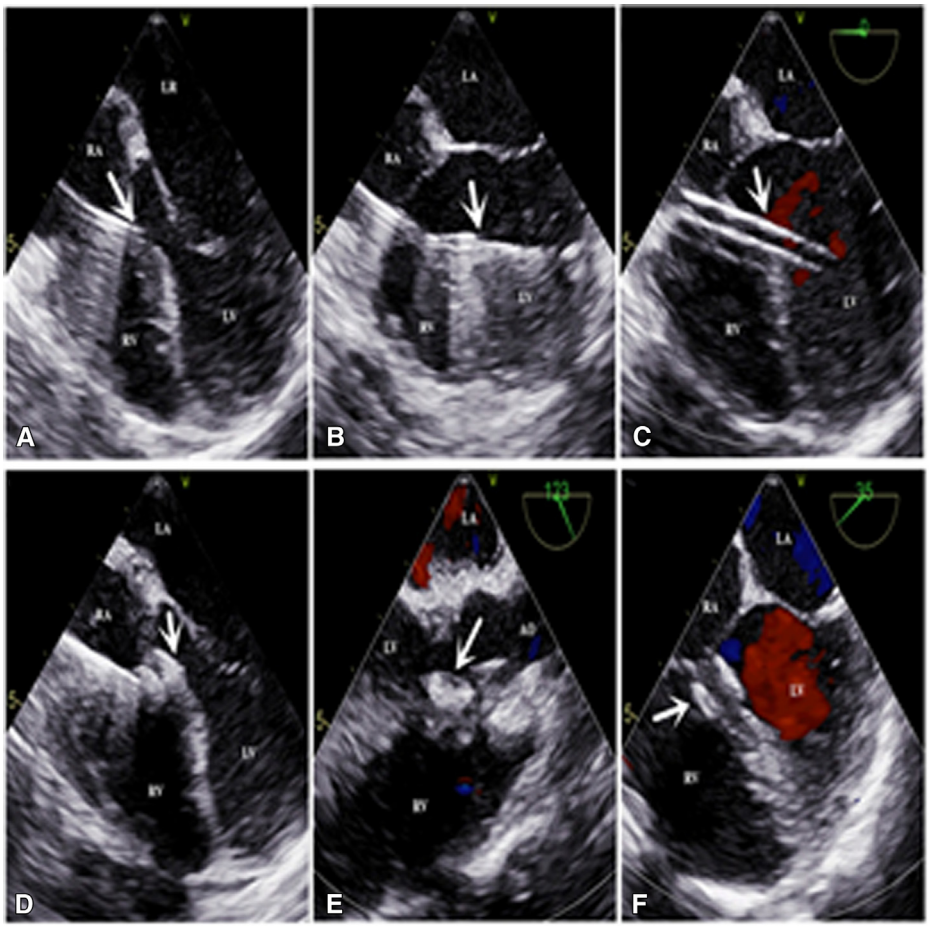

FIGURE 3. Operative steps. A, Hollow probe (*arrow*) passed across the defect. B, Flexible guidewire (*arrow*) passed to the left ventricle (LV) through hollow probe. C, Delivery sheath (*arrow*) introduced over the guidewire into the LV. D, Deployment of left and right occluder disks (*arrow*). E and F, Occluder (*arrows*) release from the delivery cable.

particular provides excellent occluder visualization and tracking performance during implantations, eliminating the need for fluoroscopic guidance.

In our hands, this novel, fully biodegradable device conferred a high rate of complete closure. Only 1 patient showed a residual postoperative shunt, which resolved before discharge. Suligoj and colleagues of the BioSTAR group[10] has described a patient with a new left-to-right peri-device shunt, demonstrated by color Doppler at month 6 of follow-up. It was suspected that a late residual shunt of this sort might reflect premature degradation of the BioSTAR matrix, before complete occluder endothelialization. To date, none of our study participants have registered newly emergent residual shunts during follow-up.

Complete AVB is one of the most serious complications of implantable Pm-VSD closure devices.[3,4,12] AVB occurrences during procedures may be directly tied to mechanical injury or compression by catheters or devices, whereas late-onset AVB is more likely attributable to chronic inflammation or fibrosis. In the present study, no instances of AVB were recorded during follow-up. We believe the risk of late-onset AVB is minimized by occluder degradation over time, leaving "native" tissue in its wake. Currently, the use of softer-shape memory alloy devices for Pm-VSD transcatheter closure has yielded substantial benefit. Unlike the AMPLATZER Membranous Occluder, the AMPLATZER Duct Occluder II (Abbott Laboratories) and the KONAR-MF multifunctional occluder (Lifetech Scientific) have shown less risk of AVB.[13,14] In our subjects, there were no reports of LBBB during follow-up, and 1 patient with complete RBBB at postoperative month 1 converted to normal status at month 6. If AVB or complete LBBB develop during or after procedures, we mandate occluder extraction as soon as feasible, especially in pediatric patients.

In summary, biodegradable occluders seem highly promising this setting, demonstrating favorable complication profiles and improved biocompatibility. Their degradation over time leaves only "native" tissue behind. Overall, this accounts for the considerable efforts expended thus far.

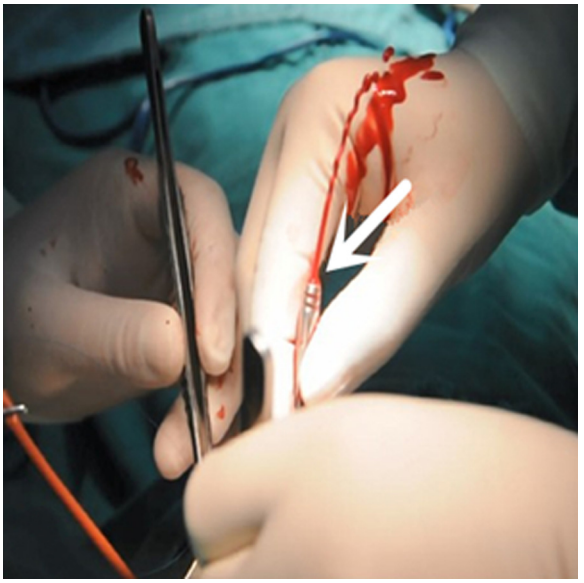

FIGURE 4. Hollow probe insertion: probe spurting arterial blood is shown (*arrow*).

However, there are still critical issues, such as enhanced elastic recovery, strategic locking structures, and implantation by percutaneous route, that await future pursuit.

Limitations

The chief limitation of this study is the small sample size. Clearly, a randomized controlled trial in a large patient population is warranted for validation. In addition, there were no provisions to assess degrees of in vivo occluder biodegradation at various time points during follow-up.

CONCLUSIONS

Closure of Pm-VSDs using a novel, fully biodegradable occluder under TEE guidance has proven safe and effective at mid-term follow-up. Transthoracic device closure of Pm-VSDs via right subaxillary route is also less traumatic than traditional surgery, offering better cosmetic results. We will continue our long-term follow-up, anticipating even more favorability with the passing of time.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: ventricular septal defect, biodegradable device, echocardiography, transthoracic intervention, minimally invasive surgery