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ORIGINAL ARTICLE

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Percutaneous closure of perimembranous ventricular septal defects utilizing almost ideal Amplatzer Duct Occluder II: Why limitation in sizes?

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Abstract

Aim: The purpose of this study is to describe the special aspects of perimembranous ventricular septal defects (pmVSD) closure by utilizing Amplatzer Duct Occluder II (ADO II) devices with a rational request for bigger ADO-II sizes, based on our experience in transcatheter device closure of pmVSD.

Methods and Results: At our institution, placement of an ADO II device was used in 15 patients with pmVSD; the patients' age ranged between 6 months and 20 years. The indications for closure were CHF (n = 4), hemodynamically significant shunt (n = 7), tricuspid regurgitation (n = 3), and high risk for infective endocarditis (n = 2), respectively. The location of the VSD was infracristal in 13 patients, supracristal in 1, and a postsurgical Gerbode VSD in another one. Implantation of the device was successfully performed without embolization, any evidence of an AV block, or other conductance abnormalities during implantation and follow-up in the mean of 2.5 years (range 2 months-6.5 years).

Conclusions: Transcatheter closure of a pmVSD with ADO II is feasible in all pediatric and young adult age groups, by considering the device diameter limitations. The off-label use of ADO II implantation seems to be safe for VSDs closure up to 6 mm of size and feasible for various locations including unusual morphology such as postsurgical Gerbode defect.

KEYWORDS

Amplatzer Duct Occluder II, pediatric, perimembranous ventricular septal defect, transcatheter closure

1 | INTRODUCTION

Ventricular septal defects (VSDs) are the most common congenital heart defects. VSD can occur in all areas of the interventricular septum. In 70% of the cases, the defects are located in the (para-)membranous part of the interventricular septum with various extensions toward the inlet and outlet septum.[1] Although the first interventional closure of VSD was already described in the late 1980s,[2] surgical closure remains the treatment of choice in most patients particularly in infancy.[3] The interventional approach of the perimembranous VSDs is occasionally difficult due to an unfavorable size and location caused by the close anatomic proximity to the aortic valve or by doubly committed lesions or Gerbode defects. Technical skills are required with limited device dimensions versus patient's size. Nevertheless, interventional closure is increasingly applied to isolated VSDs with a favorable device defect ratio.[3,4] In the past, the first designer of the pmVSD occluder believed in asymmetrically shaped perimembranous VSD occluders, which should have increased procedural success rate by

several technical improvements. However, the first of these designed, Amplatzer pmVSD occluders, were related to unacceptable high conductance disturbances,[5,6] in particular complete AV block (cAVB). The appearance of cAVB correlates especially with age less than 4 years[5] and weight less than 10 kg.[8] The risk for the occurrence of cAVB is reported in the European register at 3.6%[5]; further follow-up data described a risk of almost 5% by including late onset cAVB; in 25% of the cases, a cAVB occurred as a late event. Despite the fact that the AVB incidence was lower[4,9] than with the previously used STARFlex type device of an acute rate of 8%,[10] it was still too high in comparison to a surgical closure. Also, surgical VSD closures are recently performed as a minimally invasive procedure, with a less than 5-cm right anterior axial intercostal access causing a small scar in the later follow-up.[3,11]

An alternative VSD closure system is represented by the Amplatzer Duct Occluders II system (ADO II). ADO II is a modification of the ADO I, as produced by St. Jude Medical (St. Paul, Minnesota) for the purpose of small to moderate-sized PDA closure. An "off-label" use of ADO II for the closure of VSDs is already described in some small case numbers.[12,13] Due to the more flexible and finer meshwork of the ADO II device, the devices can advance through small 4F of 5F catheter systems, which from the technical point of view allow theoretically VSD closure even in young infants or newborns. Additionally, lower risk for the occurrence of cAVB is expected by the soft ADO II design.[12] Until today only one single case with a late onset of cAVB is described.[14]

We report our follow-up results of percutaneous closure of perimembranous VSDs in different ages and locations with ADO II supporting the requirement of larger sizes of ADO II devices.

2 | PATIENT SELECTION

Considering our criteria for VSD closure by an ADO II device, between January 2012 and August 2018, 15 patients were treated and five excluded.

The excluded patients had VSDs larger than 6 mm, one patient with an aortic valve prolapse and one patient with a 4-mm large Inlet-VSD and straddling of the tricuspid valve. All patients with other structural heart defects requiring cardiac surgery were also excluded. To prevent a mechanical touching of the aortic valve by the device, patients were also excluded if the defect was located with a distance less than 3 mm from the aortic valve.

Patient selection was made according to clinical and echocardiographic aspects. The patients showed clinical signs of congestive heart failure or echocardiographic signs for a volume overload of the left atrium and chamber or pressure overload of the pulmonary circulation. A 5-year-old boy was selected solely due to a supracristal position of the VSD. A young man 20 years of age was treated because of an iatrogenic Gerbode-type defect after surgical correction of a double outlet right ventricle (DORV) and further restoration of an obstructed right ventricle outflow tract by a transcatheter Melody stent valve (Medtronic Inc, Minneapolis, Minnesota) implantation.

3 | CLINICAL PROCEDURE AND IMPLANTATION TECHNIQUE

The initial indication for the intervention was made after morphological assessment and after measuring the VSD diameter by transesophageal (TEE) or transthoracic echocardiography (TTE) in several views.

After written informed consent by the caregivers and patients, all patients received 50 mg/kg of cefuroxime (maximum dose: 1500 mg) prior to catheter intervention. Immediately before the examination, 0.1 mg/kg midazolam was administered. Intravenous analgo-sedation was achieved with a combination of continuous infusion of propofol (2-3 mg/kg/h) and repetitive single iv applications of ketamine (0.2-0.5 mg/kg) or pethidine (0.5 mg/kg/dosage). Anesthesia with intubation and controlled ventilation was not necessary in any of the patients. Catheter procedures were carried out without TEE, but by fluoroscopy by a biplane Siemens catheter (Artis, Siemens AG Healthcare, Erlangen, Germany); transthoracic echocardiography was performed in all patients before and after device release. The interventions were performed after additional local anesthesia of the right groin via cannulation of the right femoral vein and the ipsilateral or contralateral femoral artery in which a 4Fr or 5Fr introducer sheath was placed. After arterial sheath placement, patients received 100 U/kg heparin as a single intravenous application.

Based on the echocardiographic data, pmVSD position was delineated by biplane (lateral 90° and LAO 30° angulation) left ventricular angiography utilizing a 4 or 5Fr pigtail catheter. Confirmation of supracristal VSD was performed by LV angiography in lateral 90° projection and in particular RAO 30°/cranial 20° angulation. The chosen device was usually 1-2 mm larger than the largest size of VSD, as determined by angiography.

After placement of an Amplatz GooseNeck Snare (10-25 mm) within the pulmonary artery or superior caval vein in one (previous DORV patient), VSD was crossed with a 4Fr JR together with a 0.035" Terumo GLIDEWIRE 260-cm-long (Terumo, Leuven, Belgium) exchange wire, which was snared in the pulmonary artery or caval vein, respectively. After snaring, an arteriovenous loop was performed. From the femoral vein, the Amplatzer delivery catheter (St. Jude Medical) was advanced in the "kissing position" to the JR. By pulling and simultaneous pushing, the ADO II delivery catheter was finally positioned through the VSD in the descending aorta. In two patients, kinking of the relative soft catheter required exchange in one and utilizing a Flexor glide sheath (Cook Medical, Limerick, Ireland) was required in the other. The JR catheter was exchanged to the previously used pigtail catheter, which was placed back in the left ventricle marking additionally the interventricular septum. Avoiding the entrapment of the tricuspid chordae by the double umbrella device, in some patients with dominant tricuspid valve regurgitation, the left-sided umbrella was opened together with the middle stent component still positioned within the left ventricular outflow tract. Subsequently, the entire

TABLE 1 Patient data and relevant procedural information

Nr	Age (year)	Weight (kg)	Defect size (mm)	ADO II size (mm)	FT (min)	RD (cGycm^2)	Residual shunt[a]	Complication	Follow-up (month)	Indication for closure
1	5.7	19.5	3	6 × 4	22.4	693	None	None	31.0	LA-dilatation
2	20.9	63.4	3	6 × 4	14.1	12 527	None	None	80.9	TR 2°
3	0.5	6.8	5	6 × 4	23.7	324	None	None	74.3	CHF
4	6.3	21.7	3	6 × 4	12.7	389	None	None	72.9	LA/ LV-dilatation
5	6.1	17.5	3	4 × 4	8.7	334	None	None	56.2	TR 2°
6	5.1	20	4	5 × 4	29.0	390	None	None	71.3	Supracristal VSD, IE
7	0.7	7.1	4	6 × 4	7.5	215	Trivial	None	23.3	CHF
8	4.0	16	5	5 × 6	9.9	296	None	None	19.7	LA-dilatation
9	2.8	14	6	6 × 6	15.6	258	None	None	33.5	LA-dilatation
10	0.6	6.3	4	6 × 4	21.0	211	Trivial	None	19.8	CHF
11	6.9	20.2	3	6 × 4	37.6	560	Trivial	None	16.9	TR 2°
12	1.5	9	3	6 × 4	9.0	160	None	None	14.8	LA-dilatation
13	0.4	5.7	4	6 × 4	15.,0	317	Trivial	None	12.7	CHF
14	10.9	36	5	6 × 4	19.2	1842.5	None	None	11.8	LA-dilatation
15	20	76	5	6 × 4	41	13 156	None	None	2.3	RA-dilatation, IE

Abbreviations: CHF, congestive heart failure; FT, fluoroscopy time; IE, infective endocarditis; LA, left atrium; LV, left ventricle; RA, right atrium; RD, radiation dose; TR, tricuspid regurgitation.
[a]Residual shunt immediately after the intervention.

device was pulled back into the defect. Only then the right-sided component was deployed.

During the ADO II placement within the VSD, angiographies with small amounts of contrast medium were performed as needed. In addition, a TTE was performed in order to ensure the regular function of the aortic and tricuspid valves before the occluder was released. The size of the ADO II occluder was determined by the ratio of the VSD diameter versus the stent size of the ADO II occluder. Importantly, the occluder size and even the length of 4 or 6 mm should fit the defect. The selected size of the device was usually 1-2 mm larger than the VSD, except in two patients with almost the same defect size as the device (6 mm).

Following the procedure, patients were observed in the hospital for 2 days. All patients received 300 U/kg/d of unfractionated heparin for the duration of 24 hours after the procedure. Subsequently, all patients were placed on about 2 mg/kg of acetylsalicylic acid (ASA) with a maximum dose of 100 mg once daily for 6 months. Follow-up visits were arranged for 1, 3, and 6 months, and yearly thereafter. Each follow-up visit includes a detailed physical examination, electrocardiogram, and a transthoracic echocardiography.

4 | RESULTS

The closure procedure was successfully performed in all patients. At the time of closure, the patient's median age was 5.1 years ranging from 4 months to 20.9 years. The median body weight consisted of 17.5 kg, ranging from 5.7 to 76 kg. As shown in Table 1, the weight of five children was less than 10 kg. The average size of the defect was 4 mm (range from 3 to 6 mm). Fluoroscopy lasted for a median of 15.3 minutes ranging from 7.5 to 41 minutes and the radiation dose was in the median 334 μGym^2 (ranging from 160 to 13 156 μGym^2). The position of VSD was infracristal in all but two patients. In a 5-year-old boy, a supracristal positioned VSD (Figure 1A) was also successfully closed by a 5 × 4-mm ADO II device. Percutaneous closure of a subpulmonary positioned VSD is shown on Figure 1B and C. For crossing a supracristal positioned VSD, a 4F Shepherd Hook Catheter (Cordis, Milpitas, California) became necessary for performing an arteriovenous loop and by exchanging to a right 4 Fr Judkins 2.5 curved coronary catheter, when the 260-cm-long 0.035 Terumo wire was snared. In two patients with a pmVSD and associated large septal aneurysm (Figure 2A), the device was placed within the aneurysm itself aiming to avoid the anatomic entrance with the need of an oversized device (Figure 2B).

At the end of the procedure, trivial residual shunts were still present in 4 of the 15 patients (26%). In the six-month follow-up, a complete closure in all patients could be demonstrated by auscultation and TTE (Table 1). Procedure or device-related tricuspid or aortic regurgitation was not observed. Three patients received VSD closure because of progressive tricuspid regurgitation; VSD occlusion improved tricuspid regurgitation to a trivial grade.

Follow-up data with a median of 23 months were achieved for all patients; echocardiography and in particular ECG did not show

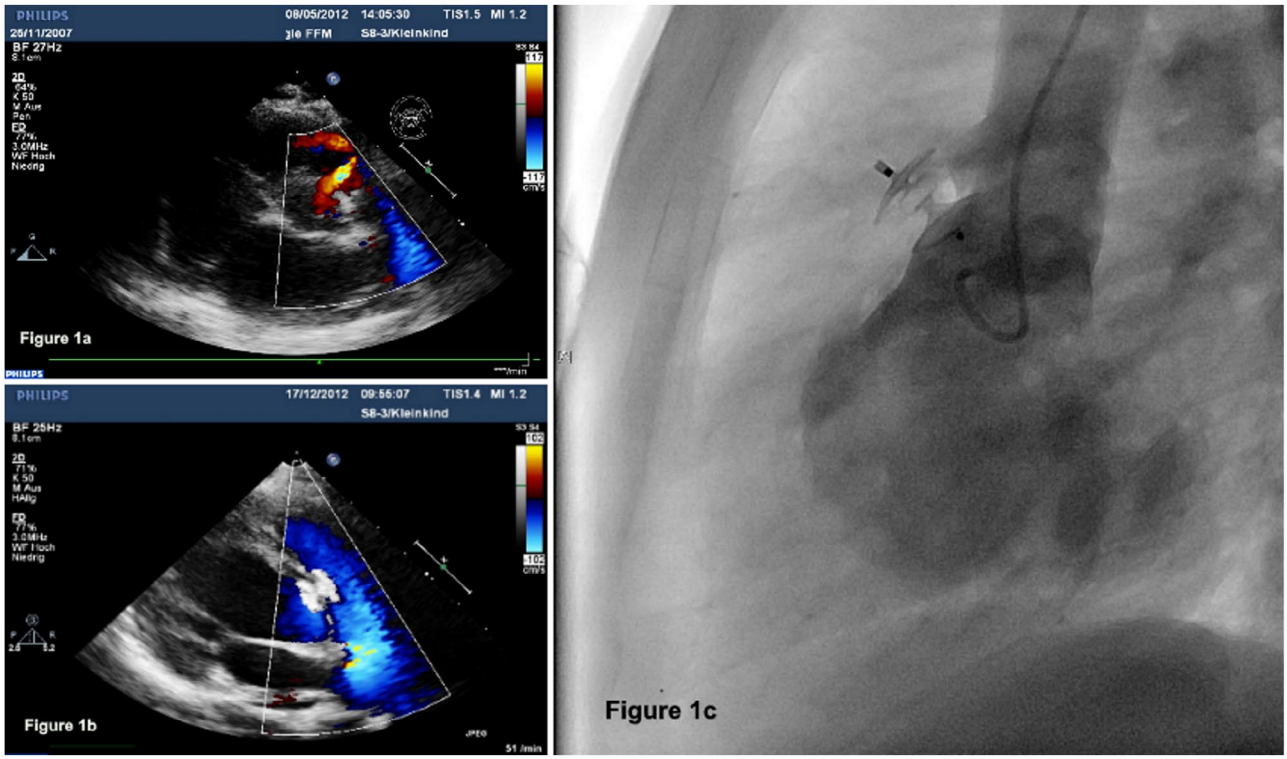

FIGURE 1 Shows an infundibular VSD before and after device closure in a 5-year-old boy (Patient 6) by echocardiography and cine-angiography. A, The colored jet flow from the left ventricle to the subpulmonary region, looking like an almost doubly committed VSD position. B, The ADOII (5 × 4 mm) is depicted with laminar subpulmonary flow without residual shunt across the device closed defect. C, The released device position during the final left ventricular angiography

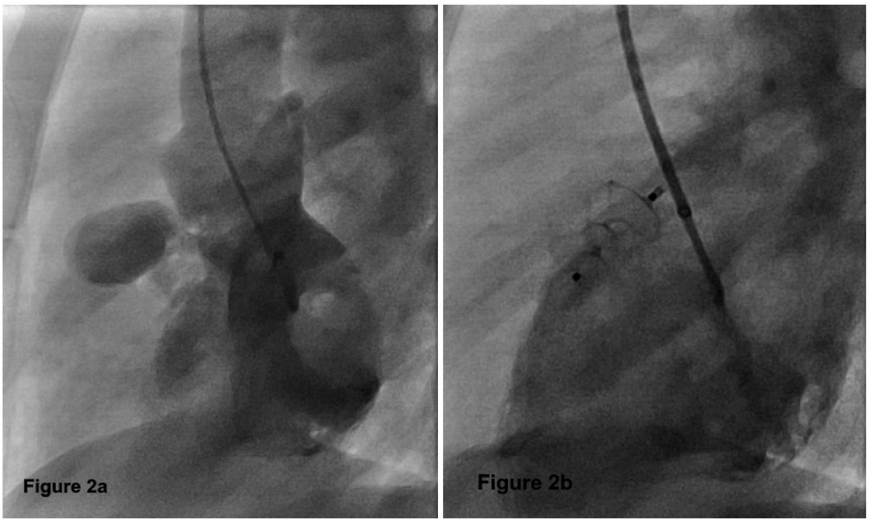

FIGURE 2 Depicts a huge aneurysmal perimembranous VSD (Patient 11) delineated by left ventricular angiography (2A); on 2B the device position after release

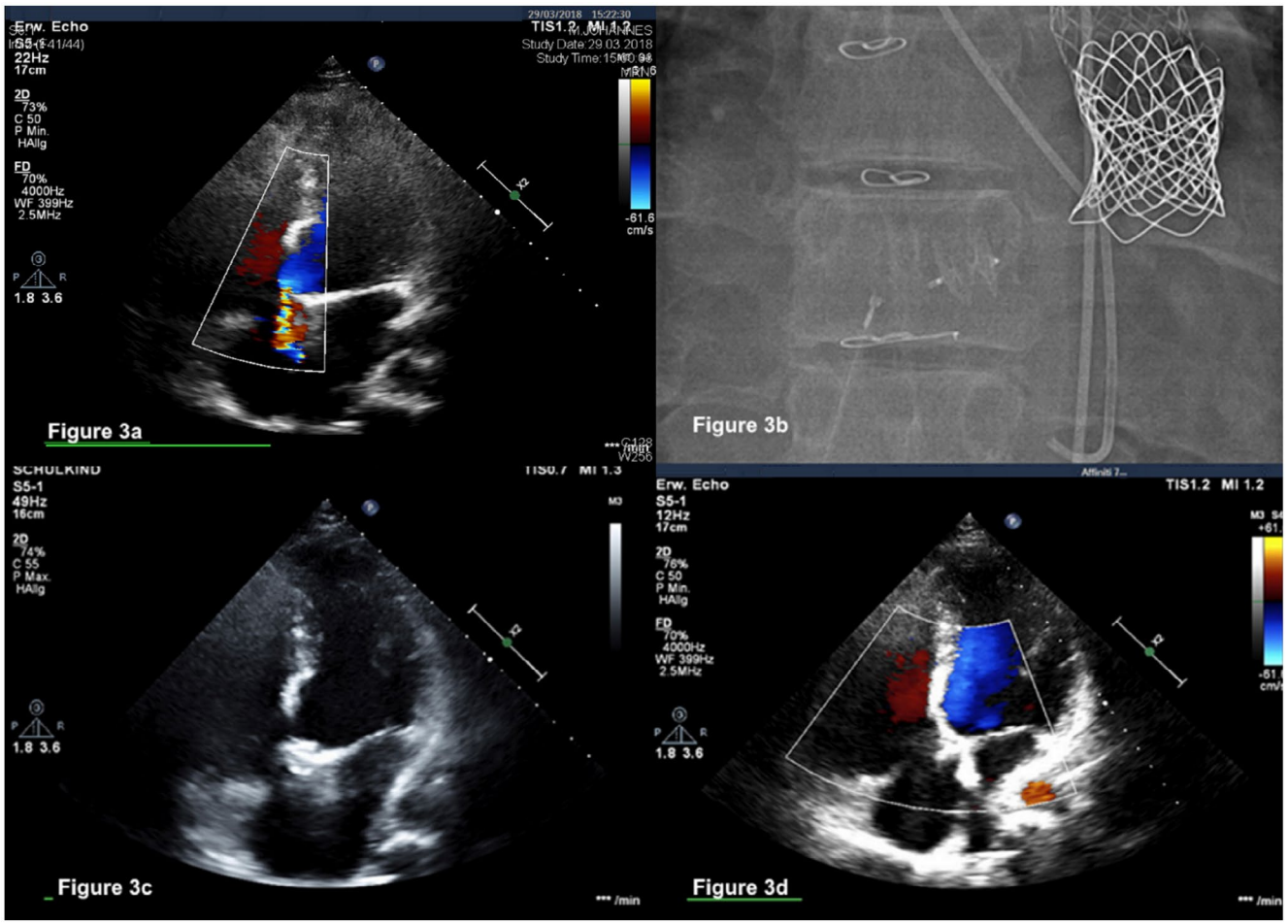

FIGURE 3 Demonstrates an iatrogenic Gerbode defect in a 20-year-old patient (Patient 15) after Rastelli surgery for repair of a double outlet right ventricle with transposition of the great arteries and subpulmonary obstruction. A, The echocardiographic 4-chamber view; the colored jet under the tricuspid valve to the right atrium assumes high endocarditis risk. B, The ADO II occluder within the left ventricular to right atrial shunt defect as well as the previous placed Melody 22 mm valve for reconstruction of the previously reobstructed right ventricular outflow tract. C, The ADO-II occluder positioned within the previous postsurgical Gerbode-like defect by echocardiography. D, Effective closure of the previous left ventricular to right atrial shunt by color Doppler

evidence of rhythm abnormalities, conductance abnormalities, or complete heart block.

VSD closure as an exclusive approach was performed in 12 patients.

Three patients had additional interventions prior to or during the same procedure of percutaneous VSD closure.

The first patient with neonatal aortic coarctation received an immediate balloon angioplasty at the age of 2 days. Re-coarctation did not occur at the age of 5 months, when the pmVSD was closed by utilizing a 6 × 4-mm ADO II, nor at the current age of 26 months.

A second patient, at age 6 months, with a combinded congenital heart defect consisting of a pmVSD and valvular pulmonary artery stenosis, was successfully treated in one single catheter session by closing the VSD followed by balloon valvuloplasty. The pmVSD was closed by a ADO II, 6 × 4 mm, and the associated pulmonary valve stenosis was treated by gradual ballooning utilizing a Sterling Ballon dilatation catheter (Boston Scientific, Natick, Massachusetts) with a balloon diameter of 6 × 20 mm.

The third patient, a 20-year-old male with the condition of Rastelli surgery and following Melody valve placement within the obstructed right ventricular outflow tract (RVOT), received a successful closure of a left ventricular-to-right atrial shunting defect, corresponding with an iatrogenic Gerbode-like defect. A 6 × 4-mm ADO II device was placed within a 5.7 mm measured intra-cardiac communication (Figure 3A-C). This patient was born with a double outlet right ventricle with transposition of the great arteries and an associated subpulmonary obstruction. A Rastelli procedure was carried out at an age of 3 years. The iatrogenic Gerbode-like defect was hemodynamically tolerated because of the obstructed RVOT, which was treated by implanting a 22-mm Melody valve when the patient was 18 years old. We decided for an additional interventional procedure for closing the iatrogenic VSD due to the enlarged right atrium and the additional endocarditis risk, despite the relatively high complex anatomy. Snaring the Terumo glide wire positioned in the pulmonary artery did not come without risk of damaging the Melody valve; therefore, we captured the wire just at the left ventricular to right atrial shunt connection within the right atrium.

5 | DISCUSSION

Our experience in percutaneous transcatheter VSD closure is still limited. At our Pediatric Heart Center, only 150 patients received Amplatzer membranous or muscular VSD occluders during a time period of more than 15 years. We here described our experience with the ADO II for perimembranous VSD closure, even treating some advanced morphological conditions, underlining the need for this favorable device in additional larger sizes. Comparing the excellent experience obtained in other centers utilizing the off-label use of the ADO II for VSD closure,[11,12] the self-expandable, double disc device with nitinol mesh wire less than 160 µm has multiple advantages, which provides new potentials and options for transcatheter VSD treatment. The delivery system needs only a 4F or 5F Amplatzer Delivery Catheter, which fits through a 4F or 5F venous or arterial introducer sheath. A very flexible nitinol wire mesh, lacking polyester fabric inside the occluder and with dual articulating discs, makes it easier to track the device through angulations. It seems to be an important technical factor to avoid or reduce the risk of conductance injuries by less tension and pressure to the ventricular septal conductance branches. cAVB requiring permanent pacemaker implantation and aortic valve regurgitation are the most serious events after VSD closure. However, for the cAVB, the exact cause in such cases is unclear. In the past when asymmetric pmVSD devices were used, the risk of cAVB increased significantly with young age, low body weight, and presence of ventricular septal aneurysm.[4,5,9] In our small study, we closed five VSDs in five infants with a body weight of less than 10 kg and two of them had a large ventricular septal aneurysm. There was no evidence of cAVB immediately after the procedure and during the follow-up, although single cases were recently reported by other authors.[14] Great flexibility of the system and the small size of the delivery catheters have also contributed to the essential advantage for closure of pmVSDs in young children and infants. However, the only limitation is the available size ratio of the ADO II to the ventricular septum defects with diameters of less than 6 mm, making the transcatheter closure less appropriate compared to the surgical open-heart approach. Additionally, the technical characteristics of the ADO II allow also the closure of VSDs in more difficult positions, as in congenital and acquired Gerbode-like defects and in lesions with large septal aneurysm formations.

Of note, if you consider VSD closure in patients with a thin aneurysmal tissue and therefore missing resistance during device pullback from the left ventricle to the septum, without general anesthesia and consecutive TEE, device displacement in the right ventricle can occur, as seen in one of our patients. The displacement in this case occurred before the release of the device. The whole procedure could be repeated, successfully.

Therefore, prompt and repetitive TTE is recommended. In addition, echocardiography is the only technique to recognize immediate adverse events as aortic regurgitation caused by the impingement of the device on the aortic valve leaflets as well as device-related mitral or tricuspid affections. Only if transthoracic echocardiography confirms optimal device positioning by fluoroscopy, the device should be released.

6 | CONCLUSION

In conclusion, percutaneous closure of VSDs utilizing Amplatzer Duct Occluder II devices with a maximal stent size of 6 mm can safely be implanted with high effectiveness. However, VSD closure with a size above a 6 mm dimension should be avoided in terms of effectiveness as well as embolization risk. Device characteristics allow implantation in infants and toddlers and even adult patients with a complex anatomy. Size limitation is mostly the reason that ADO II devices are not used more often in hemodynamically more relevant ventricular septum defects.

The main limitations of our study are the small number of enrolled patients and the relative short follow-up period. However, the main objective was to assess the feasibility and the safety of this strategy in VSDs with unusual locations. Despite our small number of patients, we clearly can argue for utilizing ADO II for closure of such defects if the ratio of the device size to the VSD diameter is larger than 1.

Considering the worldwide experience, especially in Asia,[11,15] transcatheter VSD closure can be performed with finally good results and low complication rates. However, effective devices are often used off-label; the ADO II is such an off-labelly used device, which is highly effective in treating perimembranous VSDs, but limited by its size. We hypothesize that even VSDs with diameters beyond 6 mm could be used with a favorable benefit-risk ratio, if appropriate ADO II devices with larger sizes would be available.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

Anoosh Esmaeili: performed transcatheter interventions.

Kachina Behnke-Hall: was responsible for patients' care and was intensively involved in preparing and correcting the manuscript, as a fluent English speaker.

Roland Schrewe: was responsible for patients' care and performed the echocardiographic examinations.

Dietmar Schranz: head of the department, made clinical decisions and performed catheter interventions.

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