

## REVIEW

# Complex ventricular septal defects. Update on percutaneous closure

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## Abstract

Ventricular septal defects (VSDs) are the most common congenital heart diseases. Sometimes they can be complex because of anatomy, age of the patients or associated diseases. Surgery has been performed for many years and is considered as the gold standard for the treatment of VSD. However, it is associated with morbidity and mortality. Less invasive techniques have been developed in last 15 years. Two types of devices from the Amplatzer family are currently used to close percutaneously muscular and perimembranous VSD. *Methods:* Comparative data and technical aspects of percutaneous closure in complex congenital defects (muscular and perimembranous VSDs) and in acquired defects (residual post-surgery, traumatic and postinfarction) are presented and discussed in this review. Hybrid approach to VSD closure is another complex situation and it is presented, too. *Results:* Successful closure is obtained in around 95% with a rate of major complication of 5.3% for muscular VSD. For the perimembranous VSD, the complete and successful closure is reported in 97.5% of patients, while major acute complications occur in 1.2%. Occurrence of complete atrioventricular block is reported in 1.6% of subjects. Acquired VSD can occur as post-surgical residual leak, traumatic or postinfarction VSD. Procedures are usually complex and different techniques should be used. *Conclusions:* Percutaneous closure of complex VSDs is possible, safe and effective procedure in highly specialized centers. Appropriate patient selection is of paramount importance to the success of the procedure.

**Keywords:** congenital heart defects, transcatheter, treatment.

## Introduction

Isolated ventricular septal defects (VSD) are the most common congenital heart diseases, accounting for almost 20% of all of these defects [1]. The large part, around 70% are located in the area of the membranous septum with various extensions to the outlet septum or to the trabecular septum. These defects are defined as perimembranous. These defects are very close to the aortic valve and are also defined as subaortic or infracristal VSDs (type II Kirklın). Some perimembranous defects extend beneath the septal leaflet of the tricuspid valve towards the inlet septum and are defined type III Kirklın. Defects related to both the aortic and the pulmonary valves are defined as supracristal (type I Kirklın) with two subtypes: intracristal (muscular rim  $\geq 2$  mm below the pulmonary valve) and subpulmonary (rim  $< 2$  mm below the pulmonary valve) and are quite rare accounting for 5% of all VSDs in western countries. Finally, VSDs can be entirely located within the muscular portion of the septum in around 15% of cases.

Sometimes VSD may be complex because of patients' age and size, location, number of defects, association to other anatomical morphological variations, previous surgical procedure or other factors.

The first VSD repair was performed by Lillehei *et al.*, in 1954 [2]. Surgery has been performed for many years and has been advocated as the gold standard for the treatment of VSD. However, it is associated with morbidity and mortality [3–10], patient discomfort, sternotomy and skin scar. In fact, complications as redo surgery due to

significant residual leak is reported in around 1–6% of cases [3–7], complete atrioventricular block (cAVB) may occur in around 1 to 8% of cases according to statistics [3–9], reoperation due to indications other than residual leakage is needed in around 2% of subjects [3–7]. Furthermore, occurrence of post-pericardiotomy syndrome, arrhythmias, infections, respiratory or neurological complications are also reported [3–7]. Mortality may occur in 0.5–10% of patients [3–7]. The risk for these events is increased in patients with multiple defects, associated lesions or when redo surgery is performed in patients with residual VSD [3, 5]. Finally, negative long-term effects on developmental and neuro-cognitive functions are reported in children who underwent by-pass surgery [10]. These risks are increased in subjects with complex VSDs and in particular in subjects with redo surgical procedures.

Less invasive techniques have been developed in order to reduce the impact of morbidity, mortality and psychological stress. Since the first VSD closed percutaneously by Lock *et al.* [11], various devices have been used to close VSDs [12–15]. On a meta-analysis published by Yang *et al.* [16] on VSD closure on 4406 patients with different types of VSD, the successful device implantation was 96.6% (95% CI – confidence interval: 95.7–97.5). As complications were mentioned residual shunt (25.5%), valvular defects (4.9%), and arrhythmias (10.6%).

Indications to VSD closure are symptoms of heart failure and/or signs of left heart chambers overload. In patients, and in particular in children with left atrium and ventricle overload, VSD closure is needed in order

to prevent pulmonary arterial hypertension, ventricular dilation, arrhythmias, aortic regurgitation, development of double-chambered right ventricle. Finally, subjects with small VSDs with neither symptoms of cardiac failure nor overload need closure if they experience endocarditis.

In this review, we will report and discuss data and technical aspects of percutaneous closure in complex congenital defects (muscular and perimembranous VSDs) and in acquired defects (residual post-surgery, traumatic and postinfarction). Finally, we will report on the hybrid approach to VSD closure that is another complex situation.

## ☒ Congenital VSD percutaneous closure

### Muscular VSD

After the first percutaneous VSD closure by Lock *et al.*, in 1988 [11], various attempts have been made to close these defects by using the Rashkind umbrella, Clamshell,

**Table 1 – Muscular ventricular septal defect transcatheter closure. Data from literature**

	No. of points	Age at procedure [years]	Success rate [%]	Major complication [%]	Death [%]	Embolization [%]	Cardiac perforation [%]	Stroke [%]	cAVB [%]
Thanopoulos & Rigby [22]	30	4–16	93	3.3	0	0	0	0	3.3
Hijazi <i>et al.</i> [23]	8	2–10	100	0	0	0	0	0	0
Holzer <i>et al.</i> [25]	75	0.1–54	87	10.7	2.7	2.7	1.3	1.3	0
Arora <i>et al.</i> [26]	50	3–28	100	0	0	0	0	0	0
Carminati <i>et al.</i> [27]	30	0.5–45	100	0	0	3	0	0	0
Diab <i>et al.</i> [28]	20	3 days–1	95	20	0	5	5	0	0
Zartner <i>et al.</i> [29]	17	10 days–7.3	88	11.7	0	0	5.8	0	5.8
Koneti <i>et al.</i> [30]	9	0.3–1.5	100	12.5	0	0	0	0	0
Total or mean (95% CI)	213		95 (88–100)	5.3 (0–13)	0.5 (0–2)	1.7 (0–4)	1.6 (0–3)	0.2 (0–1)	0.5 (0–2)

cAVB: Complete atrioventricular block; CI: Confidence interval.

Complications can occur in device closure in 5.3% (95% CI: 0–13%). Holzer *et al.* [25] reported the results of device closure of muscular VSD of an United States (US) multicenter trial involving 14 tertiary referral centers: 75 patients were treated, with a total of 59 (45%) adverse events, with 8/75 (10.7%) major procedure related complications, including device embolization, cardiac perforation, stroke and two (2.7%) deaths. Diab *et al.* [28] reported a series of 20 subjects aged less than one year. Success rate was 95%, while rate of major complication was 20%.

Many of these problems are likely to be related to age and clinical status of subjects treated with the higher risks in younger subjects.

### Complex cases and technical challenges

Technical challenges may be related to the existence of a mal-alignment between the delivery system advanced from the right internal jugular vein and the apical VSDs. In these cases, the left ventricular disc may prolapse through the defect and it could be quite difficult to catch the muscular rims. We have developed a technique where the device is delivered over a guide wire that gives support to the system avoiding this problem.

Another important point is the risk of entanglement of the tricuspid valve with the right ventricular disc of the Amplatzer muscular VSD device. Usually, this problem is clearly seen soon after implantation because of the appearance of a newly developed tricuspid regurgitation. Sometimes, it can develop during follow-up because of progressive flattening of the right ventricular disc.

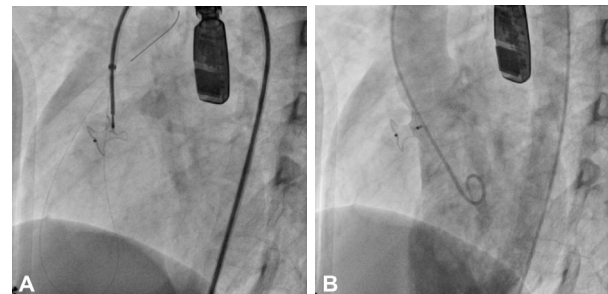
Cardioseal, Starflex, Sideris buttoned and Gianturco coils [12–14, 17–21]. The success rate was between 77 and 100% and the residual shunt was between 35 to 100% [12–14, 17–21]. Furthermore, the procedure was difficult and complications quite frequent with these devices [12–14, 17–21]. The introduction of the Amplatzer device [15] has enlarged the application of percutaneous techniques to these kinds of defects. Device and procedure have been previously reported in literature [15, 22–27].

### Results and complications

In our series, 26 of 30 patients with muscular VSD, the procedure was successfully performed in all, confirming the encouraging results reported in the preliminary papers of the literature [15, 22–26]. A mean success rate of 95% (95% CI: 88–100%) is obtained pooling data from reported in literature (Table 1) [22, 23, 25–30].

Complex situations are related to the presence of multiple defects or the treatment of high muscular VSDs.

Treatment of high muscular VSD has been reported in literature [31]. In these cases, it is possible to avoid the creation of an arterio-venous circuit. The defect is entered from the left ventricular side and the guide wire is left in the apex of the right ventricle. The delivery system is advanced from the femoral artery up to the left ventricle and through the defect in the apex of the right ventricle. The device is placed in a trans-aortic retrograde way paying attention to avoid the tricuspid valve chordae on the right side and the aortic valve on the left side (Figure 1).



**Figure 1 – High muscular VSD percutaneous closure. Cineangiograms in the left anterior oblique projection showing retrograde transaortic device implantation. The device is still attached to the delivery cable (A). Left ventricular angiography showing the device in place and a tiny residual shunting across the device (B). VSD: Ventricular septal defect.**

A second arterial access may be needed in order to perform angiographic tests during and after deployment. Trans-esophageal monitoring is also mandatory during the procedure.

This technique can be also very useful in cases when there is interruption of the inferior vena cava.

Multiple defects may be treated by using the standard technique implanting multiple devices.

Multiple VSDs closure is a great surgical challenge in which mortality is quite high ranging up to 10% [3, 5, 32, 33]. In our series [27], we closed successfully multiple VSD in three subjects by using two devices in each patient.

Similar good results were reported by Holzer *et al.* [25], Diab *et al.* [28] and Zartner *et al.* [29], by Waight *et al.* [34]. In particular, Zartner *et al.* reported 10 cases of multiple VSD in a series of 17 muscular VSDs in infants and small children (mean age 1.9 years, mean weight 8.5 kg).

In a study published by Koneti *et al.* [30], a transcatheter trans-septal antegrade closure of muscular ventricular septal defects in young children was reported. Nine patients were included (mean age six months, average weight 4.8 kg), presenting with heart failure, failure to thrive and respiratory infections. After femoral venous access, authors crossed the interatrial septum through a patent foramen oval or by performing a trans-septal puncture. Then authors positioned an angled glide wire into the left atrium, then into the left ventricle, the ventricular septal defect up to the right ventricle and pulmonary artery. No complications related to the procedure were reported, but a moderate mitral regurgitation, which led to surgical removal of the occluder [30].

### Perimembranous VSD

Experience in percutaneous closure of perimembranous (pm) VSD is more challenging. In fact, due to the proximity of the aortic valve and the atrioventricular valves, devices designed for other applications when used in the setting of a pmVSD do not fit perfectly to close these defects [13]. With the introduction of a specially designed Amplatzer eccentric device, closure of these defects became possible.

Patients with large size pmVSD present early in life with signs of congestive heart failure and undergo to surgical closure. Otherwise, subjects with moderate sized pmVSD can be managed medically and can be considered suitable candidates to device closure once their weight is >10 kg. Device and procedure have been widely described in literature [27, 35–42].

### Results and complications

In our experience [43] on percutaneous closure of perimembranous VSD using the Amplatzer membranous device, among the 104 patients who had the successful device implantation complete closure rate was excellent (96.2%), as in previous reports [36–46]. In fact, pooling data from literature the mean rate of successful closure is 97.5% (95% CI: 94–100%). An aneurysm of ventricular septum was found in 27 (32%) cases; we used membra-

nous occluder in 22 and muscular occluder in five cases, attempting to close the true anatomical hole with the more appropriate device, as judged from case to case. Device embolization occurred in two cases, but we could retrieve the device and successfully implant a second device in both. Transient hemolysis occurred in 2/25 in the U.S. phase I trial [41] and in 2/104 in our series [43]. Device related trivial aortic and tricuspid regurgitation only occurred in three cases. Complete heart block was the most important complication we encountered. It occurred in an early phase in two and late in four subjects; therefore, pacemaker (PM) implantation was required in 6/104 (5.7%). No cAVB was reported by Hijazi *et al.* [36] in six cases, Bass *et al.* [37] in 25 cases, Thanouopoulos *et al.* [38] in 10 children and Bentham *et al.* [44] in 23 cases. Complete atrioventricular block was reported in 1/25 (4%) by Fu *et al.* [41] and 1/12 (8%) during catheter manipulation leading to abandon the procedure by Pedra *et al.* [40]. However, follow-up was short in all these reports (up to three months) except in the paper by Bentham *et al.* [44] where follow-up was up to 41.7 months.

The most extended study on cAVB in pmVSD was published by Bai *et al.* [45], on 1046 patients in 13 years using a modified double disk occluder. They reported cAVB in 1.63% of the patients, from which 0.8% needed permanent PM implantation.

Zuo *et al.* [46] studied 301 subjects (mean age 9.8 years). The procedure was successful in 294 (97.6%) patients. No death occurred. Complications included aortic regurgitation in 11 (3.7%) patients (two requiring occluder retrieving), tricuspid regurgitation in 16 (5.4%) patients, hemolysis in two (0.7%) patients, and cAVB in 17 patients (15 early cAVBs, three late cAVBs, one patient had early and late cAVBs). Among the 15 early cAVBs, 12 were transient and three were considered prolonged cAVBs (persisted >2 weeks). The three (1%) patients underwent surgery and obtained stable sinus rhythm. PM implantation was needed in all three (1%) patients with late cAVB. Univariate analysis showed that risk factors were age ( $p<0.01$ ) and weight ( $p<0.021$ ). No risk factors were found in multi-variate analysis.

The proximity of the conducting tissue to the rims of the defects explains how, sometimes, a simple catheter or wire manipulation across the defect may cause heart block. If heart block occurs after device placement, it is highly probable that expansion of the device against the conducting tissue plays a major role; therefore, the use of oversized devices should be avoided. However, cAVB may also occur when the discs appear nicely flat on both sides [47]. The experience using Nit-Occlud® Lê VSD coil in a retrospective study published by Odemis *et al.* [48] on 20 patients showed no case of cAVB but an important number of hemolysis cases which led to removal of the device and surgical closure.

Pooling data from literature major acute complications occurred in 1% (95% CI: 0–2.1%), while the incidence of complete atrioventricular block needing PM implantation is 1.6% (95% CI: 0–4%) (Table 2) [37–40, 42–44, 46, 49].

**Table 2 – Perimembranous ventricular septal defect percutaneous closure. Data from literature**

	No. of points	Age at procedure [years]	Success rate [%]	Major acute complications [%]	Description	Follow-up [months]	Complication at follow-up [%]	cAVB/PM implantation
Bass <i>et al.</i> [37]	27	1.25–32	93	3.7	1 pt: acute AR	N.A.	/	0
Thanopoulos <i>et al.</i> [38]	10	1.5–12	100	0		3 months	0	0
Hijazi [39]	6	3.5–19	100	0		N.A.	/	0
Pedra <i>et al.</i> [40]	10	5–32	100	0		3 months	0	0
Arora <i>et al.</i> [42]	91	3–33	95	2.2	2 pts cAVB	N.A.		2.2
Butera <i>et al.</i> [43]	104	0.6–63	96.2	1.7	2 pts cAVB	38	4% 4 pts: cAVB	5.7
Bentham <i>et al.</i> [44]	25	2–19	91.3	4.3	1 pt: DE	2–71	1pt: H and DE	0
Zuo <i>et al.</i> [46]	301	1.2–50	97.6	0.3	2 pts: H 2 pts: acute AR 3 pts: cAVB	36.7	1% 3 pts: cAVB	2
El Said <i>et al.</i> [49]	21	1.25–30	90.5	4.7	1 pt: H	22.8	0	0
Total or mean (95% CI)	231		97.5 (94–100)	1.2 (0–2.8)		18 (0–38)	0.8 (0–4)	1.6 (0–4)

cAVB: Complete atrioventricular block; BBB: Bundle branch block; N.A.: Not available; AR: Aortic regurgitation; H: Hemolysis; DE: Device embolization; PM: Pacemaker; CI: Confidence interval.

### Perimembranous VSD closure using off-label devices

Amplatzer Duct Occluder (ADO) type I was used in perimembranous VSD with aneurismal tissue “wind-sock” type by El Said *et al.* [49] on 21 patients with a success rate of 90.5%. Hemolysis occurred in one patient that needed surgical removal and closure. No atrioventricular block was reported after the procedure and during follow-up.

ADO type II was used by Kanaan *et al.* [50] in 31 cases. Twenty subjects had a pmVSD, 10 subjects had a muscular VSD and one had ruptured sinus Valsalva. Success rate was 93.5% without any significant complications.

A case report using the ADO type II in an iatrogenic pmVSD in a 71-year-old man with a prior tricuspid valve ring annuloplasty and 3-vessel coronary artery bypass

graft surgery using retrograde approach was described by Retzer *et al.* [51].

### Other ventricular septal defect devices in perimembranous (or other types) ventricular septal defects

We found 10 studies reported in the medical literature for perimembranous and intracristal VSD closure using devices different from Amplatzer devices (Table 3) [52–62]. Those devices usually are similar with the Amplatzer occluder but they have small differences. The devices reported are the Shenzhen Lifetech Scientific devices, the Shanghai Shape Memory Alloy devices, the Huayishengjie Medical Corp. Device, the Shanghai pmVSD occluder (Lepu Corp., Beijing) and the CERA VR device (Lifetech) used by Esteves *et al.* [62]. All these devices were used in children over the age of two years.

**Table 3 – Chinese or other new devices used for VSD percutaneous closure. Data from literature**

	Center	No. of points	Age at procedure [years]	VSD type	Device used	Success rate [%]	Major acute complications [%]	Description	Follow-up [months]	Complication at follow-up [%]	cAVB/PM implantation
Li <i>et al.</i> [52]	Zhengzhou	78	2.5–44	Pm	VSD-O, HMC, Beijing	94.9	10.3	5 pts: cAVB 2 pts: AVF 1 pt: DE	40.5	1 pt: cAVB (1.3)	0
Zhou <i>et al.</i> [53]	Zhongshan Hospital, Shanghai	395	3–64 4–55	348 Pm 47 IC	SHSMA, Shanghai	97.4 78.7	2.3	3 pt: AVF 1 pt: DE 1 pt: PT (RVOT perforation) 2 pts: TE (renal, cerebral) 2 pts: pseudo-aneurysm	38.4	1 pt: cAVB (0.3)	1
Li <i>et al.</i> [54]	Changhai Hospital, Shanghai	79	15.7±13.5	Pm	MDVO (SHSMA), Shanghai	97	3.8	3 pt: cAVB (temporary)	10–76	0	0
Wang <i>et al.</i> [55]	Xijing Hospital; Xijing Cardiovascular Hospital, Xi'an; Xi Ning	525	2–12	Pm	Shanghai pmVSD occluder, Beijing (Lepu)	95.6	0.6	1 pt: TR 1 pt: AR 1 pt: cAVB	45	0	1
Wu <i>et al.</i> [56]	Changhai Hospital, Shanghai	64	2–56	Multihole Pm	SHSMA, Shanghai	98	7.8	4 pts: cAVB 1 pt: hemolysis	6–37	0	1
Qin <i>et al.</i> [57]	Shanghai; Shanxi; Shandong; Henan	412	3–65	Pm	MDVO (SHSMA), Shanghai	96.6	3.6	6 pts: VT 6 pts: cAVB (temporary) 3 pts: DE	24	0	0

	Center	No. of points	Age at procedure [years]	VSD type	Device used	Success rate [%]	Major acute complications [%]	Description	Follow-up [months]	Complication at follow-up [%]	cAVB/PM implantation
Esteves <i>et al.</i> [58]	Brazil	55	1.1–51.2	Pm	CERA VR (Lifetech)	91	10.8	1 pt: cAVB 1 pt: AR 4 pt: LRS	4.2–12.7	0	1
Yang <i>et al.</i> [59]	Xijing Hospital, Xi'an Children's Hospital, Xi'an; Hanzhong	114	5.5±2.6	Pm	Shanghai pmVSD occluder, Beijing (Lepu)	100	0	0	2–40	0	0
Gu <i>et al.</i> [60]	Shanghai	49 49	18.7±9.8 18.5±9.3	Pm IC	SHSMA, Shanghai	98 94	2 6.1	1 pt: AR 2 pt: AR 1 pt: PR	10–46	0	0
Yang <i>et al.</i> [61]	Nanjing	78	7.3±3.3	Pm	SVSDO, Shenzhen, Guangdong	94.9	2.5	1 pt: cAVB (temporary) 1 pt: AR	12–60	0	0
Chen <i>et al.</i> [62]	Shanghai	38	25.3±14	IC with aortic cusp prolapse	SHSMA, Shanghai	92.1	7.9	2 pt: AR 1 pt: DD	3–24	0	0

VSD: Ventricular septal defect; Pm: Perimembranous; IC: Intracristal; m: Muscular; HMC: Huayishengjie Medical Corp.; SHSMA: Shanghai Shape Memory Alloy; MDVO: Modified double-disk occluders; cAVB: Complete atrioventricular block; AVF: Arteriovenous fistula; DE: Device embolization; DD: Device dislodgement, PT: Pericardial tamponade; RVOT: Right ventricle outflow tract; TE: Thromboembolism; VT: Ventricular tachycardia; LRS: Large residual shunt; PM: Pacemaker.

The characteristics of the Shenzhen Lifetech Scientific devices used by Yang *et al.* [61] are quite similar to those of the Amplatzer devices in term of material, thickness of nitinol wires. Success rate was 94.9% and complication rate 2.5%.

In the studies published by Zhou *et al.* [53], Li *et al.* [54], Wu *et al.* [56], by Qin *et al.* [57] and Gu *et al.* [60], they used a modified two discs occluder, Shape Memory Alloy Shanghai (SHSMA). There are two models used to close perimembranous and infracristal ventricular septal defects: the symmetrical and the asymmetrical model.

By using this device, in literature there are cumulative data on 999 cases of perimembranous VSD and 96 patients with intracristal VSD. Regarding the pmVSD closed with this device the success rate was between 96.6–98%, with complication rates 2.3–7.8%. The occurrence of cAVB was 0.5% for permanent cAVB and 1.4% including the transitory form.

Gu *et al.* [60] reported a comparative study including 49 cases of perimembranous and 49 cases of intracristal VSD. They described only four failures (three in the intracristal group and one in the perimembranous group due to aortic, tricuspid and pulmonary moderate-severe regurgitation). No subject experienced complete heart block [60]. Another study that used the SHSMA device published by Chen *et al.* [62] refers only to intracristal VSD. They reported a 92.1% success rate with two cases of severe aortic regurgitation and one case of device dislodgement.

Using the Huayishengjie Medical Corporation device, Li *et al.* [52] reported a success rate in perimembranous VSD closure of 94.9% with a complication rate of 10.3%. The cAVB rate in this group was 7.6%.

The results regarding the device produced by the Shanghai pmVSD occluder (Lepu Corp., Beijing) were reported by Wang *et al.* [55] and Yang *et al.* [59]. They treated a total of 639 patients with a success rate of 98–100%, and a complication rate of 0–7.8%. Complete atrioventricular block occurred in 0.6%.

Finally, in the study that used the CERA<sup>®</sup> VR devices (Lifetech), Esteves *et al.* [58] reported a success rate of

91%, with a complication rate of 10.8% and a cAVB rate of 1.8%.

### Complications

The occurrence of cAVB after surgery is reported in around 1 to 5% of cases according to statistics [4, 5, 8, 9]. However, in the current era, the rate of cAVB is probably at the lowest limit of the range [58].

However, compared to surgery in which cAVB usually appears early after the operation, in patients treated percutaneously, the occurrence of cAVB is quite unpredictable and it is usually a late problem. This complication is related to the proximity of the conduction system to the margins of the pmVSD. Various mechanisms may be considered as causative. Probably, it may occur as a result of mechanical rubbing of the left and right ventricular retention disks on the proximal conduction system, resulting in a localized area of edema and inflammation. The use of steroids has been reported to be successful for treatment of atrioventricular block in postoperative heart block. Interventional cardiologists have also reported the successful use of steroids for treatment of cAVB after percutaneous pmVSD closure [63–66].

Yip *et al.* [65] reported about on two cases. In the first patient, the use of high-dose steroid and aspirin reversed completely the atrioventricular block while in the second one an inadequate dose resulted in recurrence of atrioventricular block after initial conversion. Therefore, their hypothesis is that despite severe atrioventricular block and prolonged ventricular pauses of up to 14 seconds, combination of high-dose steroid and aspirin appears to be effective in reversing the inflammatory process and normal atrioventricular conduction can recover in less than 24 hours [62]. Walsh *et al.* [66] reported on three cases of atrioventricular block after percutaneous pmVSD closure. In all cases, a temporary pacemaker was implanted and high-dose steroid and aspirin were used with success.

In our report [47, 67], high dose of steroid and aspirin showed to be effective in reversing early post-procedural cAVB showing that probably the inflammatory process has a significant role in the early phase.

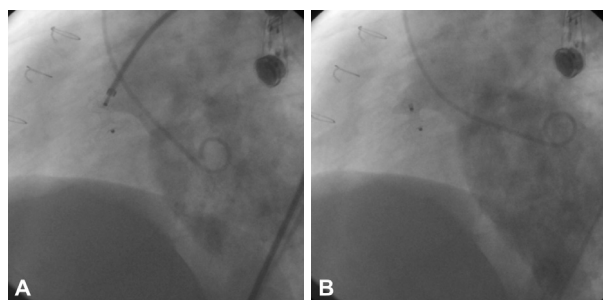
However, our patient showed us that we cannot be sure about efficacy of steroids and aspirin in the long-term. Furthermore, it gives us some insight about the mechanism of cAVB after device closure. In fact, probably the result of mechanical rubbing of the left and right ventricular retention disks on the proximal conduction system gives not only a localized area of edema and inflammation, but also a direct damage and scar formation not responding to anti-inflammatory therapy.

Finally, in order to reduce the risk of cAVB, a new device from Amplatzer group will be soon available with reduced wires thickness, increased central waist diameter and lower radial pressure on the defect and clamp forces on the ventricular septum. The new Amplatzer device has some important changes: the shape of the left disk became elliptical and concave, for a higher stability in the left ventricle outflow tract (LVOT), the nitinol wire is thinner, in dual layers, which decrease rigidity, the waist length increased from 1.5 to 3 mm and it has polyester patches sewn into the disks for rapid occlusion. This new device was experienced in several cases [68, 69] and in a prospective multicenter cohort study [70] of 19 patients from four centers with good results, but in one case difficulties with the orientation of the device in optimal position were noted and the device was removed [69]. No AVB were noted, nor severe valvular regurgitations. The success rate in the cohort study was 95%.

Finally, the devices developed by Chinese industry looks to have a lower incidence of cAVB at a rate of around 1%.

#### **Complex cases and technical challenges**

An aneurysm of ventricular septum was found in 27 (32%) cases; we used membranous occluder in 22 and muscular occluder in five cases, attempting to close the true anatomical hole with the more appropriate device, as judged from case to case. Sometimes, the device could cover the hole and the aneurysm, when the redundant tissue of the aneurysm was relatively small; in cases of very large aneurysms, the device was implanted within the aneurysm itself (Figure 2).



**Figure 2 – Perimembranous VSD percutaneous closure. Cineangiograms in the hepatoclavicular projection. Showing a perimembranous VSD with associated septal aneurysm before (A) and after (B) device implantation. The device is placed inside the aneurysm. VSD: Ventricular septal defect.**

The latter is our preferred choice, because in these cases the device is placed far from the conduction system. No complete AV block has been reported in these cases in our experience.

Sometimes, patients may have multiple congenital

heart diseases that can benefit from a percutaneous approach. Subjects with associated defects needing longer bypass time can be at higher risk for surgery and sometimes could need multiple surgical procedures.

In our series [27, 67], the following associated procedures were performed in the same session: three balloon pulmonary valvuloplasty, two device closure of atrial septal defect, one coil occlusion of patent arterial duct, one stent implantation in the aortic arch, one stent implantation in the right pulmonary artery. In all subjects, a fully successful result was obtained.

#### **Hybrid approach to the treatment of VSDs**

A hybrid approach (surgery + transcatheter) is emerging in order to reduce or eliminate bypass time. In our series, hybrid procedures were performed in three patients. Patients underwent VSD closure in the catheterization laboratory immediately before surgery. A 1-year-old girl (4.5 kg) with a large apical VSD has had previous pulmonary artery banding at the age of two months. The defect was closed using a 10 mm muscular Amplatzer VSD occluder. She went to the operating theatre for removal of the pulmonary artery band and did not need plasty of the pulmonary artery. A 7-month-old boy (5.5 kg) underwent percutaneous VSD closure of a muscular defect using a 10 mm muscular Amplatzer VSD device before surgical repair of an aortic coarctation. Finally, an 11-month-old boy (8.5 kg) had undergone pulmonary artery banding at the age of two months for large multiple VSD. These defects were closed with 6 and 8 mm muscular Amplatzer VSD occluders before surgical de-banding and plasty of the pulmonary artery.

In literature, there are few series reporting a hybrid approach performed in the operating theatre. Amin *et al.* [71] and Bacha *et al.* [72] have proposed the so-called perventricular approach. This method of closure can be done in small infants. After, the chest and the pericardium are opened, under transesophageal echocardiogram (TEE) control, a needle is used to puncture the right ventricle free wall, and then a short guidewire is passed through the needle and the VSD. Over the wire, a short sheath is advanced to the left ventricle cavity. Finally, the proper-size Amplatzer muscular VSD device is delivered in the usual way. Bacha *et al.* [72] have reported a series of 12 infants in whom this approach has been used successfully. More recently, a multicenter retrospective study from the German association of pediatric cardiology [73] reported a rate of success in 88% of cases (23 out of 26 procedures). Only one case of pericardial effusion was reported.

Another report on hybrid approach in VSD was published by Haponiuk *et al.* [74] on six muscular VSD cases, 2.7 to 17.8 months old using Amplatzer VSD Occluder and Amplatzer Duct Occluder II with success rate 100%. No complications were reported.

Kang *et al.* [75] also published a retrospective study on perventricular closure in 10 cases of muscular VSD using the Amplatzer Muscular VSD Occluder. All of them had a moderate to large muscular VSD, and three had at least two VSDs. 4/10 had previously coarctation repair and 5/10 cases had previous pulmonary artery (PA) banding. Only one patient needed the occluder removal due to entrapment of the tricuspid valve and progressive

tricuspid regurgitation, with final good surgical result. On a following period of 6.5 years, 5/9 had complete closure and 4/9 cases had a non-significant residual shunt.

## ☒ Acquired VSDs

### Post-surgical residual VSD

Significant residual VSD due to patch dehiscence may occur in 1–5% [76, 77]. Rarely, dehiscence of a patch for VSD closure may occur in 1–6% of cases [9, 40, 76]. Rarely suture disruption, incomplete closure of the defect or bacterial endocarditis may appear [78]. If it is hemodynamically significant redo surgery could be necessary. In these cases, risk of mortality or morbidity are increased [9, 39, 76]. Closing these residual shunts surgically is usually not an attractive option because it involves another open-heart surgery with another run of cardiopulmonary by-pass, sternotomy, bleeding and infection. Also, the residual VSD position may not be optimum for surgical closure or the myocardium may not be completely healthy. Hence, percutaneous device closure offers another option for these residual VSDs.

### Efficacy of transcatheter closure of residual VSDs

We have published data from 23 patients who underwent transcatheter closure of residual VSDs in our unit over an eight-year period [79]. All 23 patients had successful closure. Three (13.6%) patients had small residual shunts at discharge from hospital and at follow-up no patient has any residual shunt, currently. One patient had recurrent VSD due to patch dehiscence and required two transcatheter closures two years apart. After the second recurrence, she needed redo surgery which was complicated by a prolonged post-operative course and she developed hepato-renal insufficiency and paraplegia. Currently, she is under cardiac and physiotherapy follow-up. The VSD size varied from 4.3 to 16 mm and the VSD location also varied and included perimembranous, muscular and apical VSDs. The muscular or apical VSDs are frequently difficult to close surgically and may involve a ventriculotomy [9, 76, 80]. We did not find any significant relationship between the location of the VSD and outcome. These findings suggest that residual small to large VSDs, in different location; can be equally well closed with a transcatheter approach.

There are few results for transcatheter closure of post-surgical residual VSD [21, 77, 81]. Pedra *et al.* [81] reported a series of three transcatheter closures of VSD patients: two residual post-surgical VSDs, one post-infarct VSD, with 100% success rate. The data from Walsh *et al.* [77] consisted of nine patients with a residual post-surgical VSD. They used Amplatzer VSD devices. The procedural success rate was 100%; six patients had complete closure while three had residual shunts. Zhang *et al.* [78] reported 21 cases from a single center, 1.9 to 54 years (mean age 8.7 years) with residual ventricular septal defect surgery, interventional closed over a seven years period. Eighteen (18/21) defects were perimembranous while three were post tetralogy of Fallot. Residual VSD diameter was 7.8 mm (4–16 mm). No deaths were recorded. One case of intravascular hemolysis was reported

as an adverse event, which lasted seven days and other two cases of left anterior hemiblocks recovered spontaneously within the first week.

Rare cases of recurrent VSD after surgical patch dehiscence for postinfarction VSD (at three year distance [82] or closer to the infarct and VSD surgery [83] at four months distance and interventional VSD closure using percutaneous left ventricle access are described in the literature.

### Adverse events

There were only three (13.6%) transient early complications in the form of intra-procedural transient rhythm problems with no sequelae. Statistical analysis showed no variable predicted the occurrence of early complications. There were neither major adverse events nor deaths.

In our series, there were no procedure related deaths. However, one patient died five years after the device implantation, at home, presumably secondary to arrhythmia. In a series from Boston [80], 14 patients died during the follow-up period, in seven of these the cause of death was cardiovascular but in only one patient the cause of death was directly attributable to the device/catheterization procedure when the device was placed. In another publication from the same group, they determined that intracardiac implants were unlikely to cause sudden cardiac death [84].

No significant valve regurgitation occurred in our series and the incidence of residual shunting, which was 13.6% at discharge, decreased to 4.5% during the follow-up. In all cases, the residual shunts were graded as trivial except the above patient, who developed a patch dehiscence after implantation of the device.

The only reported significant concern for percutaneous pmVSD closure is the occurrence of cAVB. Various mechanisms may be involved including direct compression trauma, inflammatory reaction or scar formation in the conduction tissue. The reported rates for early and late cAVB vary between 0% and 5.7%. Although, we had no such complication, longer follow-up is required. Possibly, the presence of patch and scar tissue probably confers some protection against the mechanical/compressive effect of the device.

### Technical challenges

#### Anterograde approach

In some cases, it was impossible to direct the sheath towards the apex of the left ventricle. Therefore, the sheath was placed in the ascending aorta and the left ventricular disc opened coming back from the ascending aorta and through the aortic valve paying close attention to avoid any interference with the valve.

#### TEE and angiography

It is essential to have expert TEE guidance in addition to fluoroscopy and angiography throughout the procedure. These modalities complement each other.

#### Aortic retrograde approach

As majority of these VSDs are located in the muscular septum, there is a potential risk of the sheath passing through or under a trabeculation of the right ventricle

(RV). Crossing the VSD from the left ventricle (LV) side may prove easier in these cases. In addition, we have found that using the standard anterograde approach, it can be difficult to advance the sheath tip to the LV apex. This is probably related to the presence of the surgical patch. Secondly, there is less space in the sub-aortic region to deploy the LV disc and increased risk of complications. Thirdly, to overcome this, if the LV disc is deployed in the ascending aorta, it is more difficult to retrieve it back in the sheath, if required, with increased risk of damaging the aortic valve. Hence, we have employed a retrograde approach to overcome these issues. If the disc/device needs retrieval back into the sheath, it is relatively straightforward and less risky.

#### *Balloon sizing of the defect*

Due to the varied anatomy of the substrate, it may be difficult to accurately assess the exact size and site of the shunt on TEE and angiography. The presence of patches and patch leaks are other confounding factors. We have found that balloon occlusion of the shunt and assessment with TEE and angiography provides significantly better understanding of the shunt size and site.

#### **Traumatic VSDs**

Blunt chest trauma, which may cause cardiac injury, especially isolated injury, is very rare. Only anecdotic cases have been reported in the medical literature. Isolated traumatic VSD has an incidence of 1% in autopsy studies [85].

Kasem *et al.* reported the case of a 7-year-old boy run over by a truck of with traumatic VSD resulting from blunt chest injury in which the VSD was closed percutaneously with a 25-mm cribriform Amplatzer PFO device. The residual shunt was closed six months after with a 6 mm duct occluder device (ADO II) [85].

#### **Postinfarction VSDs**

The ventricular septal defect postinfarction is one of the most serious complications of myocardial infarction, associated with increased death. In the pre-reperfusion era, the mortality in these patients was 1–3%, and decreased to 0.2–0.5% with the development of percutaneous coronary intervention and thrombolysis [86].

Xu *et al.* [86] reported a multicentric study, performed in seven centers in China, with 42 patients enrolled over a period of four years, mean age 65 years with VSD post-myocardial infarction. They used two types of device the Amplatzer occluder and the domestic SHSMA (Shanghai Shape Memory Alloy Ltd., Shanghai, China) occluders. Device deployment was done in 39/42 patients and 34 survived until discharge. Device success rate was 89.6% (43/48) and the procedure success rate was 92.9% (39/42). A residual shunt was found in 32 patients (26 mild degrees, four moderate). Hemolysis developed in one patient, 10 hours after. There were eight death reported. Three patients died during the intervention for procedure related complications – two suffered left ventricular wall rupture related to the manipulation of the VSD positioning and one suffered unresponsive ventricular fibrillation). Five

patients died in intensive care unit after trans-catheter therapy. The in-hospital mortality (8/42) was higher in the trans-catheter urgent cases. The mortality rate in emergent closure is higher comparative with mortality in elective closure (66.7% vs. 6.1%) [86].

Another report about closure in acquired VSD, from Mayo Clinic [87], reported 27 cases, from which 18 were postinfarction VSD, mean age 69±11 years and follow-up 7.3±7 years. Adverse events occurred in 8/18 (44%) patients including three cases of death, one case of device embolization, one case of hemolysis, two cases of surgical VSD closure and one case reintervention. The survival free of any event was 70% at one month and 61% at five years.

#### **Conclusions**

In summary, the currently available data shows that percutaneous closure of complex VSDs is possible, safe and effective procedure in highly specialized centers. Appropriate patient selection is of paramount importance to the success of the procedure.

#### **Conflict of interests**

The authors declare that they have no conflict of interests.

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