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Transcatheter closure of congenital ventricular septal defects: results of the European Registry

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Transcatheter

Aim To report the experience of 23 tertiary referral European Centres on transcatheter closure of congenital ventricular septal defects (VSD).

Methods and results Implantation of transcatheter devices was attempted in 430 patients (pts) with congenital VSDs until July 2005. The following anatomic types were present: 119 muscular, 250 perimembranous, 16 multiple, 45 residual post-surgery. Median VSD size was 7 mm (range 3–22), fluoroscopy time 33 min (range 3–146). Devices implanted were Amplatzer muscular or membranous devices in 364, PDA devices in 12, ASD devices in seven, Starflex in seven, and coils in nine patients. Procedure was successful in 410 cases (95%). Complications: device embolization in five cases (surgery in two, catheter retrieval in three), aortic regurgitation in 14 cases (two of which requiring surgery), tricuspid regurgitation in 27 cases (no surgery was necessary), minor rhythm disturbances in 10 pts, death in one patient, complete heart block (cAVB) in 16 pts [perimembranous 12 of 250 (5%), muscular one of 119 (0.8%), residual post-surgery VSD three of 45 (6.7%)]. CAVB was transient in six patients, requiring permanent pace-makers in 10 cases (3.8%) (six early, four late). In the multivariate analysis, the only variable associated with a risk of the occurrence of complication was age ($P = 0.012$) and weight ($P = 0.0035$). In the univariate analysis, risk factors for the development of cAVB were, device type ($P = 0.03$) and VSD location ($P = 0.05$). After the multivariable Cox proportional hazards analysis, no risk factor was found.

Conclusion Transcatheter closure of congenital VSDs offers encouraging results. Complications are limited; the most relevant one seems to be the device related to cAVB in perimembranous VSD. More experience and long-term follow-up are mandatory to assess safety and effectiveness of this procedure as an alternative to conventional surgery.

Introduction

Ventricular septal defects (VSDs) are a common congenital heart disease (approximately 20%).[1] According to their location within the septum, defects can be classified as: muscular, perimembranous, and supracrystal. The most common are the perimembranous VSD (around 70%), while completely muscular VSD may occur in around 15% of the cases. Supracrystal defects are quite rare in Western countries accounting for 5% of all VSD. Rarely, multiple VSDs may be present in a single patient (so called swiss cheese VSDs). Indications to VSD closure are symptoms of heart failure, signs of left heart chambers overload, and history of endocarditis. In patients with an overload of left heart chambers, closure is necessary in order to prevent pulmonary arterial hypertension, ventricular dysfunction, arrhythmias, aortic regurgitation, and development of double-chambered right ventricle.

The traditional treatment is surgical repair, which was performed for the first time by Lillehei *et al.*[2] in 1954. The surgical approach is considered to be the gold standard, but it is associated with morbidity and mortality,[3–14] patient discomfort, sternotomy, and skin scar.

Percutaneous techniques have been developed in order to reduce the impact of such drawback of surgery.

Since the first VSD closed by a transcatheter approach by Lock *et al.*[15] various devices and techniques have been used. However, large delivery sheaths were required, complex

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implantation techniques were needed, and interference with aortic and tricuspid valves and significant residual shunting were quite frequent.[15–23]

Recently, with the introduction of devices of the Amplatzer family (AGA Medical Corp., Golden Valley, MN, USA), this approach appears to be more promising for a routine use.[24–35]

The aim of this study is to report data from a European Registry about the percutaneous closure of VSDs performed in 430 patients in 23 European centres.

Methods

The study was conducted as a retrospective study on an intention-to-treat basis. The data was collected from an on-line registry (www.vsdeurope.com) involving 23 European tertiary referral centres (see appendix for list of the centres involved) and it was collected from patients treated until July 2005.

Inclusion and exclusion criteria

The following inclusion criteria were used: (i) isolated defects; (ii) congenital VSD; (iii) residual VSD post-surgical repair of a congenital VSD; (iv) muscular or perimembranous position within the septum; (v) haemodynamically significant VSD (demonstrated by clinical data and echocardiography and/or haemodynamic study and/or angiography); (vi) history of infective endocarditis.

The exclusion criteria were as follows: (i) defects associated with other cardiac lesions needing a surgical approach; (ii) irreversible pulmonary vascular disease (>7 U/m^2); (iii) contraindication to antiplatelet therapy; (iv) sepsis; (v) the presence of perimembranous VSD, a subaortic rim as shown by echocardiography in the long axis view <2 mm.

Four hundred and thirty patients [median age 8 years (range 0.4–70 years), 226 males] underwent an attempt at transcatheter device closure until July 2005. The baseline data are reported in *Table 1*.

Data collection

The data was collected prospectively at each participating centre at the time of the procedure by the responsible investigator and it was submitted to a central database at the following website: www.vsdeurope.com.

The data collected included demographic details (date of procedure, age, gender, weight, height), echocardiographic data (VSD position, associated anomalies, aortic, mitral or tricuspid valve regurgitation, subaortic rim in patients with perimembranous VSD), procedural details (access route, sheath size, pulmonary pressures, Qp/Qs, VSD size on angiography, type and measure of device implanted, associated procedures, residual shunting, fluoroscopic, and procedural times). Furthermore, when closure failed, reasons for failure were recorded.

A major complication was defined as an event that resulted in death, long-term sequelae, need for immediate surgery, potentially life-threatening events, persistent arrhythmias needing long-term therapy (>6 months) or pacemaker placement, ongoing haemolysis requiring blood transfusion, thrombosis that required thrombolytic therapy, and increased valvar regurgitation needing device removal or drug therapy.

A minor complication was defined as an event that required drug therapy but was not life-threatening, with no long-term (>6 months) sequelae, and which did not require long-term therapy. The following were also included in this group: device embolization with transcatheter retrieval, haematoma of the groin, cardiac arrhythmias that required cardioversion of drug therapy during the procedure, minor degree atrio-ventricular blocks, and transient loss of peripheral pulse needing only heparin therapy.

Table 1 General characteristics

Number of patient	430
Median age and age distribution	8 years (0.4–70 years)
<2 years	77 pts (18%)
2–6 years	105 pts (24%)
7–14 years	103 pts (24%)
>14 years	145 pts (34%)
Weight	28 (4–124 kg)
VSD size	
Echo size	7 (3–22 mm)
Angio size	7 (2.5–18 mm)
QP/Qs	2.1 (1.1–8)
Fluoro time	33 (4–149 min)
Procedure time	120 (30–300 min)
Defect types (muscular, pm, residual post-operative)	
Perimembranous	250
Muscular	119
(mid muscular 83, apical 20, high/outlet 16)	
Multiple	16
Residual post-surgery	45
Defect measure (by TEE)	
Median	7 (range 3–22)
Device used	
Membranous Amplatzer	213
Muscular Amplatzer	151
PDA Amplatzer	12
ASD Amplatzer	7
Starflex	7
Coil	9
Ratio defect/device	130 ± 37
Combined procedures	
ASD closure	5 pts
PDA closure	9 pts
Pulmonary valvuloplasty	7 pts
Stenting pulmonary branches	3 pts
Aortic coarctation	3 pts
Aortic valvuloplasty	1 pt

Total complications were defined as the sum of minor and major complications.

We defined a complication as early when it occurred during the first month after procedure.

Definition of outcomes

Procedural success

Procedural success was defined by device implantation in the appropriate position with no need for surgery (for example due to significant residual shunt or significant valve regurgitation).

Residual shunt

A residual shunt was considered to be present if colour-Doppler flow mapping showed a left to right shunt across the interventricular septum. It was classified as follows; trivial (<1 mm colour jet width), small (1–2 mm colour jet width), moderate (2–4 mm colour jet width), or large (>4 mm colour jet width).

Devices used

The following devices were used: muscular Amplatzer VSD occluder, membranous Amplatzer VSD occluder, PDA Amplatzer occluder, ASD Amplatzer occluder, Starflex device, coil. The details of these devices were previously reported.[15–35]

Closure protocol

Closure protocols for Amplatzer VSD occluders, for Starflex device, and for coil implantation have already been reported.[15–35] Closure with other device was related to device availability in the centre.

Post-operative care and follow-up

All subjects underwent clinical examination, electrocardiography, chest X-rays, and TTE before discharge and at 1, 6, and 12 months after the procedure and yearly thereafter. Platelet anti-aggregation therapy with aspirin 5 mg/kg/day po and endocarditis prophylaxis were prescribed for 6 months.

Statistical analysis

Data were expressed as a frequency or percentage for nominal variables, as the median (range) for categorical variables and as mean $\pm$ SD or median (range) for continuous variables. The STATISTIX package version 8 was used for the statistical computations.

The following dependent outcome variables were analysed: total complications, complete atrioventricular block (cAVB), embolization, and vascular complications. The following independent variables were included in the analysis: age at procedure, weight at procedure, gender, defect type (congenital, residual post-surgery), defect position (perimembranous, muscular), device type (muscular Amplatzer device, eccentric Amplatzer device, other device), device diameter, complex procedures (yes, no), multiple defects (yes, no), ventricular septal aneurysm (yes, no), device diameter/defect diameter measured on TTE, device diameter/patient weight.

Univariate analysis was performed using the χ^2 test, Fisher's exact test, unpaired Student's *t*-test, Wilcoxon rank sum test, one-way ANOVA, the Kruskall–Wallis test, log-rank test, Cox regression analysis, logistic regression analysis as appropriate.

Multivariable analysis to study risk factors for the occurrence of early complications was performed using multiple logistic regression analysis. Independent variables with a *P*-value <0.2 in the univariate analysis were included in the multivariable model. Odds ratios and their 95% confidence intervals were calculated for independent variables included in the multivariable model.

Multivariable analysis using Cox proportional hazard regression analysis was performed to study the role of independent variables on the occurrence of cAVB in the early period and during the follow-up. Evaluation of proportional hazards assumption was performed using the goodness-of-fit testing approach.[36] All tests were two-sided. A probability value of $P < 0.05$ was considered statistically significant.

Results

Procedural data

Baseline, procedural data, and devices used are reported in *Table 1*.

The procedure was successfully performed in 410 pts (95.3%). The procedure failed in 20 subjects due to the following reasons: technical difficulty in six patients, immediate death in one, need for early surgery in 13 subjects (*Table 2*).

Complex procedures

Combined procedures were performed in 28 subjects (6.5%) (*Table 1*). Post-operative residual defects were treated in 45 patients (10.5%), multiple defects in 16 subjects (3.7%).

Complications

A total of 55 early complications occurred (12.7%). However, significant complication occurred in 28 subjects (6.5%) and are reported in detail below.

Death

Death occurred in one patient during procedure (0.2%). A 6-year-old boy (weight 16 kg) with corrected transposition of the great vessels, dextrocardia, multiple VSD treated with pulmonary artery bending was sent to surgery for double switch, pulmonary artery debanding, and VSD closure. Significant residual VSDs were seen in the post-operative period residual and the patient was sent to the catheterization laboratory to close the residual defects percutaneously. Two muscular Amplatzer devices were implanted (6 and 8 mm). After implantation of the second device the patient experienced fatal cardiac arrest.

Vascular complications

Vascular problems occurred in three subjects (0.7%). All these patients were treated to close a perimembranous VSD using an Amplatzer membranous occluder. They were 3, 3, and 14 years of age, respectively. Two out of three had arterial thrombosis that resolved after r-TPA infusion. Finally, one subject developed aneurysm of the femoral artery needing vascular surgery.

Table 2 Need for early surgery

Patient	Age (years)	Weight (kgs)	Sex	Defect type	Device type	Measure (mm)	Problem
1	1.8	10	M	High-mVSD	A-mVSD	14	LVOT gradient
2	2	16	M	Residual p-op	A-mVSD	14	Haemothorax
3	0.9	7	F	pmVSD	pmVSD	8	cAVB
4	1.3	10	F	Apical VSD	A-mVSD	10	Perforation RVAW
5	68	70	M	pmVSD	A-pmVSD	16	Residual shunt
6	0.4	4	F	mVSD	A-mVSD	10	Malposition
7	1.3	9	M	mVSD	A-PDA	10–8	Residual shunt
8	5	20	M	pmVSD	A-mVSD	4	Embolization
9	3.7	16	F	pmVSD	SF	17	AOR
10	4	18	M	pmVSD	A-ASD	4	cAVB
11	56	48	M	pmVSD	A-pmVSD	14	Massive haemolysis
12	4.2	15	F	pmVSD	A-pmVSD	8	AOR
13	3.5	17	M	Residual p-op	A-ASD	4	Residual shunt

A-mVSD, Amplatzer muscular VSD occluder; A-pm VSD, Amplatzer perimembranous VSD occluder; A-ASD, Amplatzer atrial septal defect occluder; A-PDA, Amplatzer PDA occluder; SF, starflex occluder; cAVB, complete atrioventricular block; AOR, aortic regurgitation; RVAW, right ventricular anterior wall.

Haemolysis (1.2%) and need for blood transfusion

Massive haemolysis needing surgical retrieval of the device occurred in a 56-year-old man treated with a 12 mm membranous Amplatzer device. Transient haemolysis needing blood transfusion occurred in two patients (one treated with an 8 mm membranous and one treated with a 10 mm muscular Amplatzer device). In these two subjects, haemolysis resolved spontaneously after 1 and 2 weeks, respectively. Finally in two subjects very mild haemolysis occurred, needing no therapy and resolved spontaneously within the first two days after implantation.

No other subjects needed blood transfusion.

Infection

Infections after procedure occurred in two subjects (0.5%). Post-procedural sepsis occurred in a 3-year-old boy treated for a residual post-surgical VSD with a 10 mm Amplatzer VSD occluder. Endocarditis of the pulmonary valve was evident some days after the procedure in a 2-year-old boy who received the implantation of two muscular Amplatzer VSD occluders for multiple VSDs. In both cases, medical therapy was successfully achieved.

Device embolization

This complication occurred in four cases (0.9%). In three cases it was possible to retrieve the device percutaneously and to implant a larger device. In one case the patient was sent to surgery to retrieve the device and to close the defect.

Arrhythmic complications

Tachyarrhythmias

They occurred in three subjects (0.7%). All these patients had a post-operative residual VSD and were adults (32, 56, and 60 years). Two out of these three experienced ventricular tachycardia while one had atrial fibrillation. All subjects were treated by external cardioversion.

Bradyarrhythmias

A total of 12 subjects experienced early cAVB (2.8%).

Two subjects were sent to surgery because of the occurrence of complete atrioventricular block during implantation of a device in order to close a pmVSD (*Table 3*). In both subjects removal of the device during procedure resulted in restoration of the sinus rhythm. Therefore, operators decided to definitively retrieve the device and to send patients to surgery.

Transient cAVB occurred in four subjects during procedure. Finally, the device was implanted and no rhythmic abnormalities recurred.

In six subjects, cAVB needing PM, implantation occurred within 1 week after implantation. All subjects but two experienced syncope due to asystolia or severe bradycardia.

Analysis of risk factors for the occurrence of complications

Logistic univariate analysis demonstrated that age and weight, were significantly associated with the occurrence of total early complications. In the multivariable logistic regression model, the measure/weight ratio was also included. Multiple logistic regression analysis showed that the only variables associated with a risk of the occurrence of complication were age and weight (*Table 4*).

Valve regurgitation and residual shunt

Complete VSD closure was obtained in 40% at procedure, 65% at discharge, and 83% of patients at follow-up. Residual shunt was defined as trivial in 15% and as mild in 2% of subjects. As previously reported, residual shunt was severe needing surgery in only three cases (0.7%).

In the post-operative period, tricuspid regurgitation was shown in 27 pts (6%) but it was defined as trivial to mild and no treatment was needed. Aortic regurgitation was present in 14 subjects (3.3%), but surgery was needed to remove the device and close the defect in only two patients.

Table 3 Characteristics of patients with complete atrio-ventricular block

Patient	Age (years)	Defect type	Post-surgical defect (yes/no)	Device type	Measure (mm)	Transient (Yes/No)	Therapy	Timing of occurrence post-procedure
1	4	pmVSD	No	A-ASD	4	No	Stop kt—surgery	
2	2	pmVSD	No	A-pmVSD	12	No	PM	1 day
3	11	pmVSD	No	A-pmVSD	8	No	PM	5 days
4	55	mVSD	Yes	A-mVSD	10	Yes		
5	3.4	pmVSD	No	A-pmVSD	8	Yes		
6	4.2	pmVSD	No	A-pmVSD	8	No	PM	5 days
7	8.1	pmVSD	No	A-pmVSD	6	No	PM	4 days
8	11.6	mVSD	Yes	A-pmVSD	10	Yes		
9	5.2	pmVSD	No	A-pmVSD	10	No	PM	3 days
10	1.5	mVSD	Yes	A-PDA	5/4	No	PM	5 days
11	1.2	mVSD	No	A-PDA	8/6	Yes		
12	1	pmVSD	no	A-pmVSD	8	Yes	Stop kt—surgery	
13	36	pmVSD	no	A-pmVSD	16	No	PM	7 months
14	1.2	pmVSD	No	A-pmVSD	8	No	PM	18 months
15	2.7	pmVSD	No	A-pmVSD	12	No	PM	12 months
16	2.6	pmVSD	No	A-pmVSD	8	No	PM	4 months

A-mVSD, Amplatzer muscular VSD occluder; A-pmVSD, Amplatzer perimembranous VSD occluder; A-ASD, Amplatzer atrial septal defect occluder; A-PDA, Amplatzer PDA occluder; PM, pace-maker implantation.

Table 4 Analysis of risk factors for the occurrence of total early complications

	Age (years)	Weight (kg)	Device measure/weight
Univariate logistic regression analysis			
No complications	8.7 (0.2–83)	30 (4–124)	0.35 ± 0.37
Complications	4.1 (2–68)	20 (8–102)	0.48 ± 0.29
Coefficient	−0.012	−0.017	0.7
P-value	0.04	0.02	0.12
Multivariate logistic regression analysis			
Coefficient	0.06	−0.069	0.66
P-value	0.012	0.0035	0.12
OR	1.07 (1.01–1.12)	0.93 (0.89–0.98)	

Follow-up data

The median follow-up was 2 years with a range between 6 months and 10 years. The following complications occurred: sudden death in a patient (1.3 years, 8 kg) 6 weeks after percutaneous muscular VSD closure (10 mm muscular Amplatzer VSD occluder) and surgical pulmonary debanding.

Finally in four subjects, cAVB occurred late (respectively 4, 7, 12, and 18 months after procedure) and they needed PM implantation.

Two patients experienced syncope while two were completely asymptomatic. All these patients were treated for a perimembranous VSD using an Amplatzer perimembranous VSD occluder and were 18-, 31-, 32-months-old, and 36 years, respectively.

Analysis of risk factors for the occurrence of complete AV block

A total of 16 patients experienced cAVB during the period of the study (3.7%) (*Table 3*). All of them but four had a pmVSD. Two subjects had a muscular VSD, while two more patients had a residual post-surgical defect. This rhythm abnormality occurred early in 12 patients, while in four it was a late event. Pacemaker implantation was needed in 50% of the cases of early cAVB (six of 12) and in 100% of the cases of late cAVB (four of four). Regarding the VSD position, all PM implantations but one were needed in subjects with a perimembranous defect. Infact one patient (1.5 years) had a residual post-surgical VSD. He was previously treated for a perimembranous VSD and the residual defect was located in the higher part of the septum. Finally, all subject needing PM implantation but one were children. Univariate analysis showed that the following variables were significantly associated with the occurrence of cAVB: device type ($P = 0.03$) and VSD location ($P = 0.05$).

In the Cox proportional hazard regression analysis, we included age, device type, and VSD location. However, no variable was significantly associated with the occurrence of cAVB.

Discussion

This series reports the largest cohort of patients with congenital VSD who underwent device closure. In fact, 430 subjects were sent to the catheterization laboratory with the intention-to-treat a congenital or residual post-operative congenital VSD.

Success rate was very high because closure was successfully achieved in 95.3% of subjects. This confirms the data reported in literature where the success rate ranges between 87 and 100% of the cases. However, there are some differences between the devices of the Amplatzer family and the Starflex-type devices. In fact, in the latter devices, even if a very high success rate is reported to be up to 99%,[15] surgical explantation of the device is required in around 10% of subjects while with the Amplatzer devices in the European experience it occurs in around 3% of the cases.

Early mortality was very low (0.2%) and it occurred in one patient with a very complex clinical situation. This death rate compares well with the surgical results in which it is between 1 and 5%[4,5,8,9] and to the data reported in literature regarding percutaneous VSD closure.[27]

In our report, the total complication rate was 12.5%, however, significant problems occurred in 6.5% of the cases. In the multivariable analysis, the factors associated with the occurrence of complications were age and weight at the time of the procedure.

Percutaneous VSD closure has been reported in literature in around 820 subjects and major complications were described in 0–15% of subjects (*Table 5*). A higher rate of complications was reported in the American trials about percutaneous VSD closure[27] and in subjects treated with the Starflex-type devices.[21] Probably, device-type and the involvement of centres with low experience, may account for the higher rates of severe complications.

Surgery is generally considered a safe procedure for VSD closure, however, it does have some potential risks of complications, including cAVB in 1–5% of the cases,[4,5,8,9] significant residual VSD in 1–10% of the subjects,[5,11–13] the necessity for re-operation in 2% of the patients,[5] and even death in 0.6–5% of the cases.[5,8,12–14] Furthermore, infections, tachyarrhythmias, and neurological complications may occur[5] after surgery.

In our experience, the most significant complications were related to conduction abnormalities and in particular to the occurrence of cAVB.

In literature, cAVBs needing pace-maker implantation are reported to occur in 0–8% of subjects (*Table 5*). However, the highest rate of occurrence of cAVB occurred in patients treated with the Starflex-type device;[21] and

Table 5 Ventricular septal defect transcatheter closure

	Type of defect	*N* of patients	Devices	Age at procedure (years)	Success rate (%)	Major complication (%)	Description	cAVB needing PM (%)	Follow-up (months)
Hijazi *et al.*[30]	pmVSD	6	ASO	3.5–19	100	0	/	0	/
Bass *et al.*[31]	pmVSD	27	ASO	1.25–32	93	3.7	Acute aortic regurgitation: one patient	0	/
Thanopoulos *et al.*[34]	pmVSD	10	ASO	1.5–12	100	0	/	0	Up to three
Thanopoulos and Rigby[24]	mVSD	30	ASO	4–16	93	3.3	cAVB: one patient	3.3	/
Arora *et al.*[28]	mVSD and pmVSD	137		3–33	95	1.9	cAVB: two patients	1.9	/
Masura *et al.*[33]	pmVSD	186		3–51	100	1.07	Transient cAVB: two patients	0	/
Holzer *et al.*[27]	mVSD	75	ASO	0.1–54	87	10.7	Death, two patients; stroke, one patient; device embolization, two patients; cardiac perforation, one patient	0	/
Carminati *et al.*[29]	MVSD and pmVSD	122	ASO	0.5–64	97.5	1	Early cAVB, one patient; late cAVB, two patients	2.5	Median 12
Hijazi *et al.*[25]	mVSD	8	ASO	2–10	100	0	/	0	/
Pedra *et al.*[32]	pmVSD	10	ASO	5–32	100	0	/	0	Up to three
Knauth *et al.*[21]	mVSD	170	STARFlex-type	0.3–73	99	15	See reference	8	Median 24
Fu *et al.*[35]	pmVSD	35	ASO	1.2–54.4	91	11.4	Early cAVB, one patient; Late cAVB, one patient; peri-hepatic bleeding, one patient; Rupture of tricuspid valve chordae tendinae: one patient	5.7	Up to 16

Data from literature. mVSD, muscular ventricular septal defect; pmVSD, perimembranous ventricular septal defect; cAVB, complete atrioventricular block; ASO, Amplatzer septal occluder.

also, this data should to be analysed critically because in most studies, follow-up was not reported. In our experience, cAVB occurred in 16 patients (3.7%). Pace-maker implantations were necessary in 10 subjects (2.3%). Finally in four out of 10 patients this occurred as a late event. Therefore, with a median follow-up of 24 months, cAVB needing PM implantation occurred in 2.3% of the patients treated. Subjects treated with the eccentric Amplatzer device or with other devices (Starflex, coil, ASD Amplatzer, PDA Amplatzer) were at higher risk for this complication.

Some authors have suggested that the presence of an aneurysm of ventricular septum or of an oversized device are associated with a higher risk of cAVB. However, our data did not support these statements at all.

Also the occurrence of cAVB after surgery is reported in around 1–5% of cases according to statistics.[4,5,8,9] However, in the current era, even if recently published data is not available, the rate of cAVB is probably at the lowest limit of the range.

However, compared with 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. Therefore, both surgery and device implantation may interfere with atrioventricular conduction. Various mechanisms may be considered as causative. It is possible that the presence of the device may disturb atrioventricular conduction by direct traumatic compression. Furthermore, the device may give rise to an inflammatory reaction or scar formation in the conduction tissue. However, there are is no specific data about the mechanisms involved in the occurrence of cAVB after percutaneous

closure of a pmVSD. Large studies are needed to clarify the real impact of arrhythmic problems in these patients and the mechanism of the events.

Conclusions

In the current era and in experienced centres, percutaneous VSD closure provides a valuable alternative to surgery even in cases with complex morphology and in very young children.

Finally, due to the late occurrence of cAVB, careful monitoring of rhythm and atrioventricular conduction is essential during follow-up, especially in the case of subjects treated for a perimembranous VSD.

Conflict of interest: Dr De Giovanni is proctor and lecturer for AGA. Other authors have nothing to declare.

Appendix

Physician and centres involved in the European VSD Registry

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References

1. Rudolph AM. Ventricular septal defect. In: Rudolph AM, ed. *Congenital Diseases of the Heart: Clinical–Physiological Considerations*. 2nd ed. Armonk, NY: Futura Publishing Company; 2001. p197–244.
2. Lillehei CW, Cohen M, Warden HE, Varco RL. The results of direct vision closure of ventricular septal defects in eight patients by means of controlled cross circulation. *Urg Gynecol Obstet* 1955;**101**:447.
3. Kouchoukos NT, Blackstone EH, Doty DB, Hanley FL, Karp RB. Ventricular septal defect. In: *Kirklin/Barrat-Boyes*, 3rd ed. USA: Elsevier Science; 2003. p850–910.
4. Ross-Hesselink JW, Mejiboom FJ, Spitaels SEC, Van Domberg R, Van Rijen EH, Utens EM, Bogers AJ, Simons ML. Outcome of patients after surgical closure of ventricular septal defect at a young age: longitudinal follow-up of 22–34 years. *Eur Heart J* 2004;**25**:1057–1062.
5. Mavroudis C, Backer CL, Jacobs JP. Ventricular septal defect. In: Mavroudis C, Backer CL (ed.) *Pediatric Cardiac Surgery*, 3rd ed. Mosby, Inc.; 2003. p298–320.
6. Nygren A, Sunnegard J, Berggren H. Preoperative evaluation and surgery in isolated ventricular septal defects: a 21 years perspective. *Heart* 2005; **83**:198–204.
7. Monro JL, Alexiou C, Salmon AP, Keeton B. Follow-up and survival after primary repair if congenital heart defects in children. *J Thorac Cardiovasc Surg* 2003;**126**:511–520.
8. Hobbins SM, Izukawa T, Radford DJ, Williams WG, Trusler GA. Conduction disturbances after surgical correction of ventricular septal defect by the atrial approach. *Br Heart J* 1979;**41**:289–293.
9. Bol-Raap G, Weerheim J, Kappetein AP, Witsenburg M, Bogers AJ. Follow-up after surgical closure of congenital ventricular septal defect. *Eur J Cardiothorac Surg* 2003;**24**:511–515.
10. Visconti KJ, Bichell DP, Jonas RA, Newburger JW, Bellinger DC. Developmental outcome after surgical versus interventional closure of secundum atrial septal defect in children. *Circulation* 1999;**100**(Suppl. II): II-145–II-150.
11. Kitagawa T, Durham LA, Mosca RS, Bove EL. Techniques and results in the management of multiple ventricular septal defects. *J Thorac Cardiovasc Surg* 1998;**115**:848–856.
12. Wollenek G, Wyse R, Sullivan I, Elliot M, de Leval M, Stark J. Closure of muscular ventricular septal defects through a left ventriculotomy. *Eur J Cardiothorac Surg* 1996;**10**:595–598.
13. Serraf A, Lacour-Gayet F, Bruniaux J, Ouaknine R, Losay J, Petit J, Binet JP, Planche C. Surgical management of isolated multiple ventricular septal defects: logical approach in 130 cases. *J Thorac Cardiovasc Surg* 1992;**103**:347–342.
14. Backer CL, Winters RC, Zales VR, Takami H, Muster AJ, Benson DW, Mavroudis C. The restrictive muscular ventricular septal defect: how small is too small to close? *Ann Thorac Surg* 1993;**56**:1014.
15. Lock JE, Block PC, McKay RG, Baim DS, Keane JF. Transcatheter closure of ventricular septal defects. *Circulation* 1988;**78**:361–368.
16. Janorkar S, Goh T, Wilkinson J. Transcatheter closure of ventricular septal defects using the Rashkind device: initial experience. *Catheter Cardiovasc Interv* 1999;**46**:43–48.
17. Kalra GS, Verma PK, Dhall A, Singh S, Arora R. Transcatheter device closure of ventricular septal defects: immediate results and intermediate follow-up. *Am Heart J* 1999;**138**:339–344.
18. Sideris EB, Walsh KP, Haddad JL Chen C, Ren SG, Kulkarni H. Occlusion of congenital ventricular septal defects by the buttoned device'Buttoned device' Clinical Trials International Register. *Heart* 1997;**77**:276–279.
19. Kalra GS, Verma PK, Singh S, Arora R. Transcatheter device closure of ventricular septal defects: using detachable steel coil. *Heart* 1999;**82**: 395–396.
20. Bridges ND, Perry SB, Keane JF, Goldstein SA, Mandell V, Mayes JE, Jonas RA, Castaneda AR, Lock JE. Preoperative transcatheter closure of congenital muscular ventricular septal defects. *N Engl J Med* 1991;**324**: 1312–1317.
21. Knauth AL, Lock JE, Perry SB, McElhinney DB, Gauvreau K, Landzberg MJ, Rome JJ, Hellenbrand WE, Ruiz CE, Jenkins KJ. Transcatheter device closure of congenital and post-operative residual ventricular septal defect. *Circulation* 2004;**110**:501–507.
22. Rigby ML, Redington AN. Primary transcatheter umbrella closure of ventricular septal defects. *Br Heart J* 1994;**72**:368–371.
23. Vogel M, Rigby ML, Shore D. Perforation of the right aortic valve cusp: complication of ventricular septal defect closure with a modified Rashkind umbrella. *Pediatr Cardiol* 1996;**17**:416–418.2.
24. Thanopoulos BD, Rigby ML. Outcome of transcatheter closure of muscular ventricular septal defects with the Amplatzer ventricular septal defect occluder. *Heart* 2005;**91**:513–516.
25. Hijazi ZM, Hakim F, Al Fadley F, Abdelhamid J, Cao QL. Transcatheter closure of single muscular ventricular septal defects using the Amplatzer muscular VSD occluder: initial results and technical considerations. *Catheter Cardiovasc Interv* 2000;**49**:167–172.

26. Chessa M, Carminati M, Cao QL, Butera G, Giusti S, Bini RM, Hijazi Z. Transcatheter closure of congenital and acquired muscular ventricular septal defects using the Amplatzer device. *J Invasive Cardiol* 2002;**14**:322–327.
27. Holzer R, Balzer D, Lock Qi-Ling Cao K, Hijazi ZM for the Amplatzer Muscular Ventricular Septal Defect Investigators. Device closure of muscular ventricular septal defects using the Amplatzer muscular ventricular septal defect occluder. *J Am Coll Cardiol* 2004;**43**:1257–1263.
28. Arora R, Trehan V, Thakur AK, Mehta V, Sengupta PP, Nigam N. Transcatheter closure of congenital muscular ventricular septal defect. *J Interv Cardiol* 2004;**17**:109–115.
29. Carminati M, Butera G, Chessa M, Drago M, Negra D, Piazza L. Transcatheter closure of congenital ventricular septal defects with Amplatzer occluders. *Am J Cardiol* 2005;**96**(suppl.):52L–58L.
30. Hijazi Z, Hakim F, Haweleh AA, Madani A, Tarawna H, Hiari A, Cao QL. Catheter closure of perimembranous ventricular septal defects using the new Amplatzer membranous VSD occluder: initial clinical experience. *Catheter Cardiovasc Interv* 2002;**56**:508–515.
31. Bass JL, Kalra GS, Arora R, Masura J, Gavora P, Thanoupoulos B, Torres W, Sievert H, Carminati M, Fisher G, Ewert P. Initial human experience with the Amplatzer perimembranous ventricular septal occluder device. *Catheter Cardiovasc Interv* 2003;**58**:238–245.
32. Pedra AC, Pedra SRF, Esteves CA, Pontes SC, Braga SL, Arrieta SR, Santana MV, Fontes VF, Masura J. Percutaneous closure of perimembranous ventricular septal defects with the Amplatzer device: technical and morphological considerations. *Catheter Cardiovasc Interv* 2004;**61**:403–410.
33. Masura J, Gao W, Gavora P, Sun K, Zhan AO, Jiang S, Tiang-Liang C, Wang Y. Percutaneous closure of perimembranous ventricular septal defects with the eccentric Amplatzer device: multicenter follow-up study. *Pediatr Cardiol* 2005;**26**:216–219.
34. Thanopoulos BD, Tsaousis GS, Karanasios E, Eleftherakis NG, Paphitis C. Transcatheter closure of perimembranous ventricular septal defects with the Amplatzer asymmetric ventricular septal defect occluder: preliminary experience in children. *Heart* 2003;**89**:918–922.
35. Fu YC, Bass J, Amin Z, Radtke W, Cheatham JP, Hellenbrand WE, Balzer D, Cao QL, Hijazi ZM. Transcatheter closure of perimembranous ventricular septal defects using the new Amplatzer membranous VSD occluder. Results of the U.S. phase I trial. *J Am Coll Cardiol* 2006;**47**:319–325.
36. Kleinbaum DG, Klein M. Chapter IV: Evaluating the proportional hazards assumption. In: Kleinbaum DG, Klein M (eds), 2nd ed. New York, Springer-Verlag Publishers; 2005. p131–171.