NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endovascular closure of perimembranous ventricular septal defect

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in September 2005.

Procedure name

- Endovascular closure of perimembranous ventricular septal defect
- Transcatheter closure of perimembranous ventricular septal defect

Specialty societies

- British Cardiac Society
- Society of Cardiothoracic Surgeons of Great Britain and Ireland
- British Cardiovascular Interventional Society
- British Society of Interventional Radiology
- British Paediatric Cardiac Association

Description

Indications

Perimembranous ventricular septal defect (VSD).

A VSD is the persistence of one or more holes in the muscular wall (septum) that separates the two lower chambers of the heart; the left and right ventricles. VSD is the most common heart defect present from birth (congenital). Development of the ventricular septum in the foetus is usually complete after the seventh week of gestation. If the ventricular septum does not form completely, a hole or VSD remains. The cause of a congenital VSD is unknown and the defect may occur in association with other congenital heart defects. The most common type of VSD is perimembranous (or membranous) VSD which is located in the membranous septum

close to the tricuspid and aortic heart valves. Muscular (or trabecular) VSDs are less common and can be located anywhere in the muscular ventricular septum.

A VSD allows blood to leak from the left ventricle through to the right ventricle, thereby increasing the flow of blood to the lungs (known as shunting). This may have several consequences including congestive heart failure, pulmonary vascular disease (particularly from large defects) and an increase in the risk of infective endocarditis (particularly from small defects).

In adults, a VSD may be acquired as a complication of a heart attack (myocardial infarction) or trauma. This type of VSD has not been addressed in this overview.

Current treatment and alternatives

Most infants have small VSDs that are not associated with symptoms and usually close spontaneously after birth. Patients with symptoms of congestive heart failure may be treated conservatively with medication; if the defect is large, surgical closure is usually recommended. Conventional surgery for VSD is performed through an incision in the front of the chest. After establishing cardiopulmonary bypass, the defect is usually closed with a patch or occasionally by direct suture if the defect is small. Patients usually stay in hospital for several days after the operation and will have a scar in the chest.

What the procedure involves

Endovascular closure of a VSD involves making a small incision in the groin to introduce a guidewire into the femoral artery and also into the femoral or jugular vein in order to establish an arteriovenous wire loop. A delivery sheath is advanced over the wire across the defect, usually through the right heart system. Echocardiographic and fluoroscopic guidance are used to determine the size, position and number of defects, their relation to adjacent structures and to place an occluder device. A balloon may be used to establish the stretched diameter of the defect. The occluder device is advanced through the delivery sheath and expanded so as to close the defect. Patients can usually go home the next day. Small residual shunts after the procedure often resolve as endothelial tissue grows over and around the device. Among endovascular closure procedures, perimembranous VSDs may be technically more challenging due to the close proximity of the defect to the tricuspid and aortic valves.

The Amplatzer perimembranous (membranous, asymmetric or eccentric) VSD occluder device is the only device currently available that is specifically designed for closure of perimembranous VSDs. Devices designed for other types of defects have also been used, including the Amplatzer muscular VSD occluder device, Rashkind double umbrella device and detachable steel coil.

Claimed advantages of endovascular closure of VSDs over conventional surgery include a smaller incision, shorter hospital stay, earlier return to normal activities, and fewer complications, particularly those associated with cardiopulmonary bypass.

Efficacy

In a large case series[1] of 137 patients, of which 91 patients had a perimembranous VSD, the results of patients with perimembranous and muscular VSDs were reported together according to the type of device implanted. Of the 107 patients implanted with Amplatzer ventricular septal occluder (AVSO) devices (17 perimembranous and 90 muscular VSD occluders), successful implantation of the device was reported in

97% (104/107) of patients. Complete closure of the defect was achieved in 99% (103/104) of patients immediately after the procedure and 100% (104/104) at follow-up (1–48 months). Of the 29 patients implanted with a Rashkind umbrella device in the same study, 86%(25/29) were successfully implanted with complete closure rates of 68% (17/25) immediately after the procedure and 96% (24/25) at follow-up (32–46 months).

In the largest case series[2] of 186 patients using the Amplatzer perimembranous VSD occluder device, patients were divided into three groups: single defects without aneurysm; single defects with aneurysm; and multiple defects with aneurysm. Immediate closure rates in the three groups were 90%, 98% and 89%, respectively, and complete closure rates at 1-year follow-up were 100%, 98% and 89%, respectively.

Two other case series[3,4] using the Amplatzer perimembranous VSD occluder device reported successful device implantation rates of 93% (25/27) and 100% (13/13). Immediate closure rates were reported in 85% (11/13) to 88% (22/25) of patients. Complete closure rates at follow-up were 92% (23/25) at 1 week and 92% (12/13) at 3 months.

In one cases series[5] using the Rashkind double umbrella device (RUD), successful device implantation was achieved in 86% (24/28) of patients with perimembranous VSDs. Complete closure of the defect was achieved in 67% (16/24) of patients immediately after the procedure and at mean follow-up of 17.1 months. This included one patient who was implanted with a detachable coil device after RUD placement failed.

The success rates for device implantation and defect closure using the Amplatzer device appears to be higher than those using other occluder devices. However, no randomised controlled trials directly comparing different devices have been performed. Comparisons between devices should therefore be made with caution as patient selection, patient numbers and follow-up durations vary in different studies.

The Specialist Advisors stated that some patients with unsuccessful device implantations required surgical repair. There is a risk of residual shunting following successful device implantation, which is usually higher for defects with aneurysms, especially if the defects are fenestrated, compared with defects without aneurysms.

Safety

During implantation of the Amplatzer perimembranous VSD occluder device, transient ventricular arrhythmias were reported as being common in one case series[4] and occurring in all patients (27/27) in another case series[3]. In these two case series, misplacement of the device was reported in 0% (0/27) and 15% (2/13) of patients, and aortic regurgitation in 0% (0/13) and 4% (1/27) of patients.

Complications reported after the procedure[1,3,4] using Amplatzer occluder devices (perimembranous and muscular) included left bundle branch block 0% (0/13) to 4% (1/25), complete heart block 0% (0/25) to 1.9% (2/107), aortic regurgitation 0% (0/13) to 4% (1/25), tricuspid regurgitation 0% (0/13) to 8% (2/25), tricuspid stenosis 0% (0/25) to 0.9% (1/107) and device embolisation 0% (0/107) to 7.7% (1/13). No new complications were reported at 3 months in one case series[4] and up to 48 months in another case series[1].

In a case series[2] that focused on ECG findings, complete heart block 1.07% (2/186) was reported immediately after the procedure, and left anterior hemiblock 4.8%

(9/186), complete right bundle branch block 4.3% (8/186) and incomplete right bundle branch block 3.8% (7/186), were reported at least 3 months after the procedure.

Other devices have been used for closure of perimembranous VSDs including the Rashkind double umbrella device and detachable steel coil. There may be variations in the safety between different devices, however most safety data have been reported for the Amplatzer devices.

The Specialist Advisors stated that the risk of complications is potentially much greater in infants than in older patients. Complications involving the aortic valve, the tricuspid valve and the atrioventricular node may potentially arise during and after device implantation due to their close proximity to the membranous septum. The incidence of heart block is small but varies between institutions and appears to be higher than for surgical repair. It is also uncertain whether closure of the defect with a device will eliminate or reduce the risk of endocarditis.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endovascular closure of perimembranous ventricular septal defect. Searches were conducted via the following databases, covering the period from their commencement to September 2005: Medline, PreMedline, EMBASE, Cochrane Library and other database. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See Appendix B for details of the search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1. Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with perimembranous ventricular septal defects. Adults with ventricular septal defects acquired as a complication of heart attacks or other trauma were excluded.
Intervention/test	Endovascular closure using occluder devices
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English language articles were excluded unless they were thought to add substantively to the English language evidence base.

List of studies included in the overview

No systematic reviews, randomised controlled trials or non-randomised controlled trials were found.

The five largest[1-5] case series published in English have been included in this overview. Most of the case series (4/5) used the Amplatzer perimembranous VSD occluder device.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (Table 2) have been listed in Appendix A.

Existing reviews on this procedure

Interventional procedures guidance documents have been previously issued for the endovascular closure of other heart defects including atrial septal defect (IPG096), patent ductus arteriosus (IPG097) and patent foramen ovale for the prevention of cerebral embolic stroke (IPG109).

Table 2. Summary of key efficacy and safety findings on endovascular closure of perimembranous ventricular septal defect.

Abbreviations used: AVSO, Amplatzer ventricular septal occluder; PMVSD, perimembranous ventricular septal defect; MVSD, muscular ventricular septal defect; RUD, Rashkind umbrella device.

Study Details	Key efficacy findings	Key safety findings	Comments
Arora R et al (2003)[1] Prospective case series (Aug 1995 to Apr 2002) India Devices: • 107 Amplatzer ventricular septal occluder (AVSO) (90 muscular, 17 perimembranous AVSO) • 29 Rashkind umbrella device (RUD) • 1 detachable steel coil 137 patients with congenital VSD (91 PMVSD, 46 MVSD); 64 males, 73 females Mean age 12.2 ±5.6 (range 3–33) years, median 11.5 years Mean VSD diameter 6.5 ±2.1 mm, median 6.1 mm (range 3–12mm) measured by echocardiography Aneurysm of septum (35 membranous, 2 muscular) Left ventricular/right atrial communications (n = 7) Inclusion criteria: • infracristally located perimembranous defects with at least 5 mm rim from the aortic valve (for perimembranous Amplatzer device, defects < 5mm rim were also included) • distance from centre of defect to the insertion of right coronary aortic valve leaflet is more than 50% of the size of the required device • defects with aneurysm formation • preference for isolated muscular defects, mid-muscular and anterior in location. (High apical and posterior defects were not excluded.) Exclusion criteria: • defects mainly supracristal in position, with malalignment of outlet septum, atrioventricular canal type and defects associated with aortic valve prolapse/aortic regurgitation • post-infarction or post-operative residual VSD Follow-up: mean 35.2 ±10.7 (range 1–66) months • AVSO (1 to 48 months) • RUD (≥ 45 months for 25 patients) • Coil (duration not specified) Disclosure of interest: not specified.	**Device implantation** Successful: 94.8% (130/137) • AVSO 97.1% (104/107) (muscular AVSO 100%, perimembranous AVSO 92.3%) (the latter appears incorrect and should probably be 82.4% (14/17)) • RUD 86.2% (25/29) • Coil 100% (1/1) for a PMVSD Unsuccessful: 5.1% (7/137) • AVSO 2.8% (3/107) All three patients had PMVSD with superior margin of defect < 3mm to the aortic valve. The perimembranous AVSO was retrieved due to significant acute aortic regurgitation. • RUD 13.8% (4/29) Unsuccessful due to chordae tendinae of tricuspid valve attached to rim of VSD (2 patients), undersized RUD (1 patient), and communication on right ventricular side on superior aspect of aneurysm prevented passage of delivery sheath (1 patient). **Immediately after procedure (at 24 hours)** Complete closure: (Calculated from figures for residual shunts.) • AVSO: 99% (103/104) • RUD: 68% (17/25) • Coil: 100% (1/1) All seven patients with left ventricular/right atrial communications (5 AVSO, 2 RUD) had complete occlusion. Residual shunt: (Based on successfully implanted patients) • AVSO: 0.9% (1/104) • RUD: 32% (8/25) (30% was also reported in the article) • Coil: 0% (0/1) **At follow-up** Complete closure: 99.2% (129/130) Residual shunt: • RUD: 1 patient – AVSO was implanted as second device for a perimembranous VSD • AVSO and coil: no residual shunts	**Immediately after procedure** Left bundle branch block: • AVSO: 2.8% (3/107) (reverted spontaneously within 48 hours) • RUD: 0% (0/29) • Coil: 0% (0/1) Complete heart block: • AVSO: 1.9% (2/107) (reverted to sinus rhythm after 24 hours in 1 patient and 5 days in 1 patient) • RUD: 0% (0/29) • Coil: 0% (0/1) Acute aortic regurgitation: • AVSO: 2.8% (3/107), PMVSD • RUD: 0% (0/29) • Coil: 0% (0/1) Tricuspid stenosis: • AVSO: 0.9% (1/107), PMVSD • RUD: 0% (0/29) • Coil: 0% (0/1) New tricuspid regurgitation: • AVSO: 0.9% (1/107) • RUD: 0% (0/29) • Coil: 0% (0/1) **At follow-up** No patients developed intravascular haemolysis, infective endocarditis, aortic regurgitation, or conduction defects Tricuspid stenosis unchanged at 9 months for AVSO: 0.9% (1/107)	Prospective case series using four different types of devices for closure of PMVSDs and MVSDs. Study included children and adults. Patient selection for different devices was not described. The number of PMVSD and MVSD cases implanted with AVSO devices and RUD were not specified. Both perimembranous and muscular AVSO devices were used to close PMVSDs, but the numbers were not specified. A relatively small number of perimembranous AVSO devices (17) were used compared to the total number of PMVSD patients (91). Distance from defect rim to aortic valve was not reported, except in 3 patients with failed AVSO placement. Discrepancies were found in the percentages reported for some of the efficacy outcomes. Intention to treat analysis was not performed for efficacy outcomes, even though the figures for all treated patients may have been stated as the denominator. Drop-out rate was not reported. The authors concluded that successful device implantation is higher for AVSO compared with previously used devices. However, comparisons should be made with caution as patient selection and patient numbers varied between different devices.

Abbreviations used: AVSO, Amplatzer ventricular septal occluder; PMVSD, perimembranous ventricular septal defect; MVSD, muscular ventricular septal defect; RUD, Rashkind umbrella device.

Study Details	Key efficacy findings	Key safety findings	Comments
Masura J et al (2005)[2] Case series (Time period of study not specified) Multicentre, multinational study Slovak Republic, China Device: Amplatzer membranous eccentric occluder 186 patients with PMVSD (102 male, 84 female) Divided into 3 groups: Group 1: 106 single PMVSD Group 2: 63 single PMVSD with aneurysmatic formation Group 3: 17 multiple VSD with aneurysmatic formation Mean age 15.9 (range 3–51) years Mean VSD diameter 5.1 mm (range 2.5–12 mm) assessed by angiography for groups 1 and 2. (Table 1 of the article shows range of 2.8–12.8 mm.) VSD size was not measured for group 3. Device was selected according to size of entry to aneurysm. Study method was not specified, including inclusion and exclusion criteria. Up to 2 years of follow-up Number of patients at follow-up: **Time** / **24 hrs** / **3 mths** / **1 yr** / **2 yrs** Group 1 / 106 / 106 / 106 / 31 Group 2 / 63 / 63 / 55 / 16 Group 3 / 17 / 17 / 17 / Disclosure of interest: not specified	Successful device implantation: 100% (186/186) Immediate closure: Group 1: 90% (Table 3 of the article also reports 100%) Group 2: 98% Group 3: 89% Closure rate at 1 month: Group 1: 100% Not reported for groups 2 and 3. Closure rate at 3 months and 1 year: Group 1: 100% Group 2: 98% Group 3: 89% Closure rate at 2 years: Group 1: 100% Group 2: 98% Group 3: no data	Before procedure, all patients showed normal ECG or left ventricle enlargement. **Immediately after procedure** • Complete heart block (CHB): 1.07% (2/186) o 1 patient developed left anterior hemiblock (LAH) immediately after closure and CHB within 24 hours. After steroid and atropine treatment, CHB changed to sinus rhythm with LAH within 2 months. LAH remained after 1 year. o 1 patient developed CHB immediately after procedure and on temporary pacing for 1 week. After 1 month returned to sinus rhythm and ECG showed LAH. No patients in group 3 developed CHB. **At least 3 months after procedure** • Left anterior hemiblock: 4.8% (9/186) • Complete right bundle branch block: 4.3% (8/186) • Incomplete right bundle branch block: 3.8% (7/186) **After procedure (time not specified)** • No haemolysis • No device embolisation • No bacterial endocarditis	Case series – uncertain if retrospective or prospective. Study included children and adults. No methodology was described. It is uncertain if bias has been introduced from selection of centres and patients into the study. Only centres with proven follow-up data were included in the study – the criteria for this were not specified. Centres considered for inclusion but excluded from the study were not specified. It is uncertain if only patients with successful device implantation were included in the study. Discrepancies were found in the reported range of VSD size and immediate closure rates (for group 1). Raw figures for closure rates were not reported. 2-year follow-up data should be interpreted with caution as few patients were available for analysis. The study did not specify which group of patients developed the reported heart block findings. Reported safety findings appear to be incomplete as the focus of the study was on ECG changes after device implantation.

Abbreviations used: AVSO, Amplatzer ventricular septal occluder; PMVSD, perimembranous ventricular septal defect; MVSD, muscular ventricular septal defect; RUD, Rashkind umbrella device.

Study Details	Key efficacy findings	Key safety findings	Comments

Bass JL et al (2003)[3]
Prospective case series (time period not specified)
Multicentre, multinational study
(8 centres, 6 countries- not including UK)
 	
Device: Amplatzer perimembranous ventricular septal occluder
 	
27 patients with PMVSD
Mean age 13.8 (range 1.25–32) years
Mean VSD diameter 6.9 mm (range 1.6–8 mm) measured by echocardiography
Mean distance from aortic valve to ventricular septal rim 5.3 mm (range 1–11mm)
 	
Ventricular septal aneurysm (n = 14)
Left ventricular/right atrial communications (n = 0)
 	
There was trivial tricuspid regurgitation and no aortic insufficiency before device placement – number of patients not specified.
 	
Inclusion criteria:
• clinical or echocardiographical evidence of significant left-to-right shunt through an isolated PMVSD
• at least 1 mm rim separating the aortic valve from the VSD
 	
Exclusion criteria: not described
 	
Follow-up: 1 week
 	
Disclosure of interest: The author disclosed a financial or other interest in the subject discussed in the article.
	Device implantation
	• Successful 93% (25/27)
	• Unsuccessful 7% (2/27) due to:
	  • device-related aortic insufficiency requiring device removal (n = 1)
	  • inability to position the delivery sheath in the left ventricle (n = 1)
	
	Immediately after procedure (at 24 hours)
	• Complete closure: 88% (22/25)
	
	At 1 week
	• Complete closure: 92% (23/25)
	• Residual shunt: 8% (2/25)
		During procedure
		• Transient ventricular arrhythmias during sheath manipulation: 100% (27/27)
		• Aortic insufficiency: 3.7% (1/27)
		• Device embolisation: 0% (0/27)
		• Atrioventricular block: 0% (0/27)
		
		Immediately after procedure
		• Transient progression of trivial tricuspid regurgitation: 8% (2/25)
		(unchanged the following day)
		• Trivial aortic insufficiency: 4% (1/25)
		• Mitral regurgitation: 0% (0/25)
		• Atrioventricular block: 0% (0/25)
		
		At 1 week
		• Transient left bundle branch block: 4% (1/25) - resolved 3 weeks later
			Prospective case series.
			First experience with the Amplatzer perimembranous ventricular septal occluder device in humans.
			
			Study included children and adults
			
			Number of patients in each centre was not specified.
			
			Patient series was small and follow-up very short.
			
			Intention to treat analysis was not performed.
			
			The article states that the device and delivery system underwent small modifications during the study period to overcome procedural difficulties – the modifications and procedural difficulties were not specified.
			
			Some of the defects treated may be considered as high muscular rather than true perimembranous as the separation between the aortic valve and superior defect rim was large in some patients.

Abbreviations used: AVSO, Amplatzer ventricular septal occluder; PMVSD, perimembranous ventricular septal defect; MVSD, muscular ventricular septal defect; RUD, Rashkind umbrella device.

Study Details	Key efficacy findings	Key safety findings	Comments
Thanopoulos BD et al (2003)[4] Prospective case series (Since 1997 for MVSD, not specified for PMVSD) Greece Devices: Amplatzer muscular VSD occluder (AMVSDO) for MVSDs Amplatzer asymmetric VSD occluder (AAVSDO) for PMVSDs 35 patients with VSD (13 PMVSD, 22 congenital or acquired MVSD) PMVSD: • Mean age 6.2 ±3.5 (range 1.5–14) years (the article actually states median age, not mean) • Mean VSD diameter 4.9 ±2 mm (range 2–8 mm) • Associated ventricular septal aneurysm (n = 6) • Distance from aortic valve to ventricular septal rim 2–5 mm MVSD: • Age range 8 months to 14 years (mean or median not reported) Inclusion criteria: For PMVSDs: Maximal VSD diameter < 12 mm; at least 2 mm from margin of defect to the aortic valve; left to right shunt across defect with left ventricular enlargement (end diastolic diameter > 95% for age) For MVSDs: VSD diameter > 4mm; more than 5 mm from margin of defect to aortic, mitral and tricuspid valves; single or main central (for multiple Swiss cheese type defects) opening into right ventricle; left to right shunt across defect with left ventricular enlargement (end diastolic diameter > 95% for age) Exclusion criteria: Not specified for either PMVSD or MVSD cases. Follow-up • PMVSD: 3 months • MVSD: median 2 years (range 0.25–4 years) Disclosure of interest: not specified	**For PMVSD** Immediately after procedure: • successful closure: 84.6% (11/13) • trivial residual shunt: 15.4% (2/13) At 1 and 3 months' follow-up: • complete closure: 92.3% (12/13) • trivial residual shunt: 7.7% (1/13) **For MVSD** Location of MVSD: • 12 midmuscular • 5 apical • 3 anterior • 2 outlet Immediately after procedure: • complete closure: 91% (20/22) • trivial or small residual shunt: 9% (2/22) At follow-up (median 2 years): • Complete closure: 95.5% (21/22) • Small residual shunt: 4.5% (1/22), at 6 months There were 10/22 patients at 2-year follow-up.	**For PMVSD** During procedure: • Transient ventricular arrythmias were described as 'common' • Device misplacement: 15.4% (2/13) (required recapturing and redeploying device) Immediately after procedure: • Device embolisation: 7.7% (1/13) (required device retrieval and implantation of another AAVSDO) At 3 months' follow-up: • 'No complications' were reported, such as 'metal fatigue fractures, aortic or atrioventricular valve damage'. **For MVSD** During procedure: • Transient ventricular arrythmias in all patients during sheath manipulation • Device misplacement: 9.1% (2/22) (required repositioning and redeploying device) • Left bundle branch block: 13.6% (3/22) (resolved within 12 hours) At follow-up (median 2 years): • 'No early or late complications' were reported, such as 'atrioventricular or semilunar valve regurgitation, device embolisation, thromboembolic events, wire fracture or endocarditis'. Also 'metal fatigue fractures, aortic or atrioventricular valve damage were not encountered'.	Prospective case series Early experience with Amplatzer devices for PMVSDs and MVSDs. Infants and children were included, but no infants with PMVSDs were included. Patients with PMVSD were implanted with the AAVSDO device, while patients with MVSD were implanted with the AMVSDO device Number of patients with PMVSD was small and follow-up short. Drop out rate for PMVSD patients was not reported. Successful device placement was reported in all patients, but device embolisation occurred in one patient with PMVSD. The device was successfully retrieved and another AAVSDO device implanted. Four patients (2 PMVSD, 2 MVSD) had misplacement of the device, which required recapturing/repositioning and redeploying it.

Abbreviations used: AVSO, Amplatzer ventricular septal occluder; PMVSD, perimembranous ventricular septal defect; MVSD, muscular ventricular septal defect; RUD, Rashkind umbrella device.

Study Details	Key efficacy findings	Key safety findings	Comments
Kalra GS et al (1999)[5] Prospective case series Over 2-year period (dates not specified) India Devices: RUD (Placement of detachable steel coil was attempted in two cases where RUD placement failed.) 30 patients with VSD (28 PMVSD, 2 MVSD) 17 male and 13 female Mean age 12.9 ±5.7 years, median 12.2 (range 5.5–33) years Mean diameter of VSD 4.7 ±1.3mm, median 4.5 mm (range 3–8mm) • PMVSD with aneurysm of membranous septum 43% (12/28) • PMVSD with left ventricular/right atrial communications 7% (2/28) Inclusion criteria: • septal tissue of at least 6 or 8mm between the aortic valve and VSD with 12 mm or 17 mm RUD, respectively. Exclusion criteria: • patients with postinfarction or postoperative residual VSD • patients with malalignment of the outlet septum, atrioventricular canal type, apical or posterior muscular VSD, aortic valve prolapse and aortic regurgitation. Mean follow-up 17.1 ±6.4 (5–28) months Disclosure of interest: not specified	**Device implantation:** • Successful: 87% (26/30) o PMVSD: 86% (24/28) – includes 1 coil o MVSD: 100% (2/2) • Unsuccessful: 13% (4/30) o PMVSD: 14% (4/28) – includes 1 coil o MVSD: 0% (0/2) Reasons for unsuccessful device implantation: • RUD undersized (n = 1) • Anatomic distortion of septal aneurysm; RUD and coil attempted (n = 1) • Tricuspid valve chordae tendinae attached to VSD; RUD attempted (n = 2) **Immediately after procedure (at 24 hours):** • Complete closure: 69% (18/26) o PMVSD: 67%(16/24) – includes 1 coil (includes 2 patients with left ventricular/right atrial communications) o MVSD: 100% (2/2) • Minimal (trivial or small) residual shunt: 31% (8/26) o PMVSD: 33% (8/24) o MVSD: 0% (0/2) **At follow-up:** • Complete closure: 69% (18/26) • Minimal residual shunt: 31% (8/26) Note: Complete closure and minimal residual shunt rates reported in the article were 70% and 30%, respectively.	**During procedure** • Embolisation of coil device: 1 patient • RUD slipped into right ventricle: 6 patients (taken from Table 1 of the article) **Immediately after procedure (at 24 hours)** • No new aortic or tricuspid regurgitation • No intravascular haemolysis • 2 patients with pre-existing moderate tricuspid regurgitation decreased in severity **At follow-up** • No intravascular haemolysis, infective endocarditis, bundle branch block or valvular insufficiency • No evidence of arm fracture in device	Prospective case series using the Rashkind double umbrella device primarily for PMVSDs. Study included children and adults. Detachable steel coil was used in some patients in whom RUD placement failed – patient selection for coil placement was not specified. Number of patients with PMVSD was small. Drop-out rate was not reported. Intention to treat analysis was not performed. Repeat device placement was performed in 20% (6/30) patients and was successful in four cases. Detachable steel coil was implanted in two patients: one was successfully implanted while the other failed (device embolised). The authors concluded that “the RUD is not an ideal device for VSD closure” and that although the procedure is moderately difficult, “it can be performed with reasonable safety in small perimembranous VSDs that are not in the immediate vicinity of either the aortic or tricuspid valve.”

Validity and generalisability of the studies

- This overview is based on five case series. No randomised controlled trials or non-randomised controlled trials were found.
- None of the studies in this overview included infants with perimembranous VSDs.
- None of the studies included in this overview were conducted in the UK.
- Most of the case series reported early clinical experience with the Amplatzer devices for endovascular closure of perimembranous VSDs. Improvements in the device and technique may have been made since these early case series.
- Intention to treat analysis was not usually performed for efficacy outcomes, except in those studies that reported successful device placement in all patients.
- Efficacy and safety findings were, in general, poorly reported. Reporting of adverse events immediately after the procedure appeared to be better than during later follow-ups.
- Some studies allowed successfully repeated implantation of another device (either the same or a different type of device) to be included in the overall success rate for device implantation. This should be taken into consideration when comparing between studies as other studies considered such repeat device placement as failures.
- The reliability of the largest case series[2] was questionable as selected centres were included in the study based on the availability of follow-up data, and no methodology was described. Furthermore, closure rates at 2 years of follow-up should be interpreted with caution as a significant number of patients had either dropped out or had data missing for analysis.
- A large case series[1] combined the results of patients with perimembranous and muscular VSDs according to the type of device used, which makes it impossible to determine the efficacy and safety of the procedure for patients with only perimembranous VSDs.
- Patient selection for closure with different occluder devices varied within and between studies. Many factors may affect the success of device implantation and defect closure including the number, size and location of the defects, proximity of the defect to the aortic and tricuspid valves, degree of shunting (pulmonary to systemic flow ratio), presence of membranous septal aneurysms and presence of left ventricular to right atrial communications. These factors should be taken into consideration when comparing results of different devices and studies.
- The success rates for device implantation and defect closure using the Amplatzer devices (muscular and perimembranous) appear to be higher than those using other occluder devices. However, no randomised controlled trials have been performed comparing different devices. Comparisons between devices should therefore be made with caution as patient selection, patient numbers and follow-up durations vary in different studies.
- The procedure for endovascular closure varied within and between studies, including the route of delivery of the device (usually via the femoral or jugular vein, and occasionally via the femoral artery), type of catheter used, and use of transthoracic and/or transoesophageal echocardiography. These may need to be taken into consideration when comparing different devices and studies.

Specialist advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Dr. J Gibbs, Dr JD Giovanni, Professor M Rees, Dr A Salmon, Mr B Sethia, Dr P Wilde.

- The Amplatzer perimembranous VSD occluder is the only device specifically designed to close perimembranous VSDs.
- Most device implants are carried out in children. However, some implants are carried out in adults.
- The procedure is highly dependent on the expertise of the operator. Specific training is important as the procedure is more challenging than closing other heart defects such as atrial septal defects, due to the close proximity of the defect to the tricuspid and aortic valves.
- Patches that can be deployed through a catheter are being researched and are not yet commercially available.
- A potential concern is that small defects that may be treated conservatively are closed by the endovascular route because of the relatively non-invasive nature of the procedure.
- Patient selection for the procedure is controversial.
- Long-term outcomes of the procedure are unknown.
- There are registries for VSD closures in Europe (available from www.vsdeurope.com) and in the USA (run by the University of Chicago Children's Hospital). The Central Cardiac Audit Database (CCAD) collects data on VSD closure in the UK.

Issues for consideration by IPAC

None other than those described above.

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4. Thanopoulos BD, Karanassios E, Tsaousis G et al. (2003) Catheter closure of congenital/acquired muscular VSDs and perimembranous VSDs using the Amplatzer devices. *Journal of Interventional Cardiology* 16(5):399–407.

5. Kalra GS, Verma PK, Dhall A et al. (1999) Transcatheter device closure of ventricular septal defects: immediate results and intermediate-term follow-up. *American Heart Journal* 138(2 Pt 1):339–344.

Appendix A: Additional papers on endovascular closure of perimembranous ventricular septal defects not included in summary Table 2.

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table. It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non inclusion in Table 2
Durongpisitkul K, Soongswang J, Laohaprasitiporn D et al. (2003) Transcatheter closure of perimembranous ventricular septal defect with immediate follow-up. *Journal of the Medical Association of Thailand* 86(10):911–917.	4 PMVSD patients 1-month follow-up Median age 4 years (2, 3, 4 and 22 years)	Amplatzer membranous VSD occluder device Successful device placement and complete closure in all 4 patients at 1-month follow-up	Small case series
Ewert P, Kretschmar O, Peters B et al. (2004). [Transcatheter closure of congenital ventricular septal defects]. [German] *Zeitschrift fur Kardiologie* 93(2):147–155.	26 VSD patients (21 PMVSD, 5 MVSD) 7 months follow-up (range 1–12 months) Median age 8 years (5 months to 59 years)	28 devices implanted: Amplatzer occluder device (16/28) and Nit-occlud coil systems (12/28) At 7 months: • 13 complete closure • 9 minimal residual shunts • 2 small residual shunts	Non-English
Hijazi ZM, Hakim F, Haweleh AA et al. (2002) Catheter closure of perimembranous ventricular septal defects using the new Amplatzer membranous VSD occluder: initial clinical experience. *Catheterization and Cardiovascular Interventions* 56(4):508–515.	6 PMVSD patients Immediate (24 hours) follow-up Median age 10.5 (3.5–19) years	Amplatzer membranous VSD occluder device All patients achieved immediate complete closure	Small case series
Hu HB, Jiang SL, Xu ZY et al. (2004) [Transcatheter closure of perimembranous ventricular septal defects using the new Amplatzer membranous VSD occluder: a short-term evaluation.]. *Chung-Hua i Hsueh Tsa Chih [Chinese Medical Journal] [Chinese]* 84(19):1592–1596.	48 PMVSD patients Mean follow-up 3.8 (1–12) months Mean age 17 ±12 (3–48) years	Amplatzer membranous VSD occluder device Successful device placement 94% (45/48) Immediate complete closure 80% (36/45)	Non-English

Hu HB, Jiang SL, Xu ZY, et al. (2004) [Transcatheter closure of perimembranous ventricular septal defects: a clinical application in children]. [Chinese]. *Zhonghua Erke Zazhi*.42(11):808–812.	50 PMVSD children Mean follow-up 7 (1–18) months Mean age 9.1 ±4.8 (2–17) years	Amplatzer perimembranous VSD occluder device Successful device placement 94% (47/50) Immediate complete closure 96% (45/47) Complete closure at 6 months 98% (46/47) Significant decrease in left ventricle end diastolic dimension at mean follow-up 7 (1–18) months	Non-English
Huang G-Y, Ma X-J, Sheng F et al. (2005) Transthoracic echocardiographic monitoring and evaluation in transcatheter closure of perimembranous ventricular septal defects in children. *Acta Academiae Medicinae Shanghai*.32(3):337–339.	15 PMVSD children Mean follow-up 7.9 months (1 month to 1 year) Mean age 5.5 (3–14) years	Amplatzer perimembranous VSD occluder device Successful device placement 93.3% (14/15) Complete closure at follow-up 100% (14/14)	Small case series
Michel-Behnke I, Le TP, Waldecker B, et al. (2005) Percutaneous closure of congenital and acquired ventricular septal defects-considerations on selection of the occlusion device. *Journal of Interventional Cardiology* 18(2):89–99	12 congenital and acquired VSD patients Follow-up not specified in abstract 7 PMVSD, 5 MVSD Mean age 13 (0.2–74 years)	Placement and short term follow-up of Amplatzer VSD devices are superior to other devices Devices: • 4 Amplatzer muscular VSD occluder • 2 Amplatzer membranous VSD occluder • 2 Amplatzer septal occluder • 1 Amplatzer duct occluder • 2 Nit-Occlud coil • 1 Cook detachable coil Successful device placement in 9 patients Immediate complete closure in 8 patients	Small case series
Pawelec-Wojtalik M, Masura J, Siwinska A et al. (2004) Transcatheter closure of perimembranous ventricular septal defect using an Amplatzer occluder-early results. *Kardiologia Polska* 61(7):31–40	9 PMVSD patients Mean follow-up 11.5 (3–22) months Mean age 11 (1.5–19) years	First experience with Amplatzer membranous VSD occluder (AMVSDO) in Poland Successful device placement and complete closure in all patients at follow-up	Small case series

Pedra CA, Pedra SR, Esteves CA et al. (2004) Transcatheter closure of perimembranous ventricular septal defects. *Expert Review of Cardiovascular Therapy* ;2(2):253–264	18 PMVSD patients 3–6 months follow-up Median age 8 (3–32) years	Amplatzer membranous septal occluder device Successful device placement 94%(17/18) Complete closure at 3–6 months 100% (17/17)	Small case series
Rigby ML, Redington AN. (1994) Primary transcatheter umbrella closure of perimembranous ventricular septal defect. British Heart Journal 72(4):368–71	13 PMVSD patients No follow-up Age 3 weeks to 16 years	Transcatheter closure with a modified Rashkind ductal double umbrella device is feasible but moderately difficult to perform Successful device placement and complete or partial immediate defect closure 77% (10/13)	Small case series
Sideris EB, Macuil B, Varvarenko V et al. (2005) Transcatheter patch occlusion of perimembranous ventricular septal defects. *American Journal of Cardiology* 95(12):1518–1521	16 PMVSD patients Follow-up range 0–4 years Median age 7 years (range 2–35 years)	Transcatheter patch closure of PMVSD Success device placement 87.5% (14/16) Complete closure 86% (12/14) at follow-up	Small case series; unlicensed product
Thanopoulos BD, Tsaousis GS, Karanasios E et al. (2003) Transcatheter closure of perimembranous ventricular septal defects with the Amplatzer asymmetric ventricular septal defect occluder: preliminary experience in children. *Heart (British Cardiac Society)* 89(8):918–922.	10 PMVSD children 3 months follow-up Age range 1.5–12 years	Preliminary experience with Amplatzer asymmetric VSD occluder Results of study have been included in Thanopoulos BD et al, J Interv Cardiol 2003[4]	Small case series

Abbreviations: PMVSD, -perimembranous ventricular septal defect; MVSD, muscular ventricular septal defect.

Appendix B: Literature search for endovascular closure of perimembranous ventricular septal defect

Databases	Version searched (if applicable)	Date searched
The Cochrane Library	2005 Issue 3	6.9.2005
CRD	2004	6.12.2004
Embase	1980 – 2005 week 36	6.9.2005
Medline	1966 – August week 4 2005	6.9.2005
Premedline	1966 – August week 4 2005	6.9.2005
National Research Register	2004	6.12.2004
Controlled Trials Registry	N/A	6.12.2004

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

```
1. (Perimembranous adj3 sept$ adj3 (lesion$ or defect$)).tw.
2. (membranous adj3 sept$ adj3 (lesion$ or defect$)).tw.
3. (ventricular adj3 sept$ adj3 open$).tw.
4. vsd.tw.
5. exp heart septal defects, ventricular/
6. (ventricular adj3 sept$ adj3 (defect$ or lesion$)).tw.
7. (interventricular sept$ adj3 (lesion$ or defect$)).tw.
8. or/1-7
9. exp *heart catheterization/
10. amplatzer.tw.
11. (percutaneous adj3 (clos$ or interven$)).tw.
12. (endovascular adj3 (clos$ or interven$)).tw.
13. ((transcatheter$ or catheter$) adj3 (clos$ or interven$)).tw.
14. or/9-13
15. 8 and 14
16. animal/
17. human/
18. 16 not 17
19. 15 not 18
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