NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME
Interventional procedure overview of endovascular closure of atrial 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 previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by Specialist Advisors and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

Date prepared
This overview was originally prepared by Bazian Ltd in March 2003 and was revised by NICE March 2004.

Procedure name
Endovascular closure of atrial septal defect

Specialty society
British Cardiac Society
British Cardiovascular Intervention Society
British Paediatric Cardiac Association

Indication(s)
Atrial septal defect

An atrial septal defect is the persistence of a hole in the wall (septum) between the two upper chambers of the heart, the right atrium and left atrium. Before birth the foetal heart has a structural communication between the two atria called the foramen ovale. This normal passage allows blood to bypass the lungs and be directed straight to the left side of the circulation, supplying blood to the brain and body before it returns to the placenta. After birth, blood flows directly to the lungs, returns back to the left side of the heart to then be pumped to the brain and body. The foreman ovale should close spontaneously. An atrial septal defect arises when this closure does not happen, which may occur for several reasons. In the most common type, an ostium secundum atrial septal defect, the septum between the atria fails to form properly during foetal development resulting in a permanent hole.

An atrial septal defect, therefore, allows blood to flow from the left atrium through to the right atrium increasing the flow of blood to the lungs. This is known as a shunt. Patients with atrial septal defects are usually asymptomatic through infancy and childhood but increasing age carries an increasing risk of stroke. Symptoms such as exertional dyspnoea, fatigue, palpitations, syncope can occur with congestive heart failure a possibility. Although not all atrial septal defects require treatment, it is generally agreed that larger defects and those associated with either symptoms or significant cardiomegaly should be electively closed.

Atrial septal defect requiring surgery is relatively rare. In 2000/2001, there were 503 operations to close a defect of interatrial septum in England (Source: Hospital Episode Statistics, ungrossed for missing data, Department of Health).

Current treatments and alternatives

Conventional surgery for atrial septal defect is performed through an incision in the front of the chest. After establishing cardiopulmonary bypass, the right atrium is opened to gain access to the interatrial septum. The defect is then repaired using a patch or stitches. People usually stay in hospital for several days after the operation.

What the procedure involves

Endovascular closure of an atrial septal defect involves making a small incision in the groin to introduce a guidewire and delivery sheath into the femoral vein. A balloon may be used to establish the stretched diameter of the defect. An occluder device is then pushed through the delivery sheath on a semi-rigid cable and expanded in the atrial septal defect to close it. Echocardiography and fluoroscopic guidance are used to determine the size and position of the defect and to place the occluder device. People can usually go home the next day. Small residual shunts after the procedure often resolve as endothelial tissue grows over and around the device.

The claimed advantages are shorter hospital stay, earlier return to normal activities and fewer complications than conventional surgery.

Efficacy

The three non-randomised controlled studies reported successful closure rates immediately after the endovascular procedure of 98%, 98% and 97% compared with rates of 100%, 98% and 100% for conventional surgery. A large case series of 3460 patients reported that 97% of atrial septal defects were successfully closed immediately after the procedure. Of the 4% (147/3460) of patients followed up for two years in this study, 100% had a successful closure. A further case series reported that 1% (4/314) of patients had a significant residual shunt immediately after the procedure and 92% (99/107) of patients had a successful closure one year after the procedure.

The Specialist Advisors stated that a small proportion of patients may be left with a residual shunt.

Safety

The reported complication rates were low. The most commonly reported complications included malposition requiring endovascular or surgical retrieval 1% (6/417) to 5% (16/334); arrhythmia 0.4% (2/459) to 5% (3/61); embolisation of the device 0.4% (14/3460) to 4% (14/334); thrombus formation 0.4% (1/258) to 3% (1/37); brachial plexus injury 3% (1/39); right iliac vein dissection 0.6% (1/159); stroke 0.1% (5/3460) to 0.3% (1/334); cardiac tamponade 0.1% (2/3460); cardiac perforation 0.03% (1/3460); and endocarditis 0.03% (1/3460)..

The Specialist Advisors agreed that arrhythmias, stroke, device embolisation and cardiac tamponade are potential adverse effects of the procedure. The device arm may fracture but this usually has no clinical sequelae.

Literature review

Appraisal criteria

We included studies of the Amplatzer®, Cardioseal®, Starflex® and Helex® devices for the endovascular closure of atrial septal defect.

List of studies found

We found no randomised controlled trials.

We found five non-randomised controlled studies, all relating to the Amplatzer device. The three largest are described in the table.[1-3] The largest case series for each of the devices are described in the table.[4] The annex gives the references to smaller studies identified.

Summary of key efficacy and safety findings (1)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Du[1] Non-randomised controlled study Multicentre study, USA 1998 to 2000 614 people with atrial septal defect (ASD): • 459 Amplatzer device; median age 10 (range: less than 1 to 82) • 155 conventional surgery; median age 4 (range: less than 1 to 38) Inclusion criteria: • large left to right shunt or symptomatic small shunt Inclusion criteria for Amplatzer: • ASD ≤38mm diameter • >5mm from ASD margin to coronary sinus, valves, and right upper pulmonary vein Exclusion criteria: • other cardiac abnormalities • primum or sinus venosus ASD • pulmonary hypertension • oxygen saturation <94% • current symptoms from ischaemic heart disease • heart failure Follow-up 12 months	Immediate successful closure (minimal residual shunt): • Amplatzer: 96% (423/442) • surgical: 100% (154/154) p=0.07 Intention to treat: • Amplatzer: 90% • surgical: 99% 12 month successful closure (minimal residual shunt): • Amplatzer: 99% • surgical: 100% p=0.33 Intention to treat: • Amplatzer: 71% • surgical: 61% Average procedure time: • Amplatzer: 106 minutes • surgical: 160 minutes p<0.001 Average length of hospital stay: • Amplatzer: 1 day • surgical: 3 days p<0.001 (Intention to treat results calculated by Bazian)	Cardiac arrhythmias requiring major treatment: • Amplatzer: 2 people • surgical: none Amplatzer embolism with surgical removal: • Amplatzer: 3 people • surgical: none Stroke • Amplatzer: 1 person • surgical: none Cardiac tamponade: • Amplatzer: none • surgical: 3 people Pulmonary oedema: • Amplatzer: none • surgical: 1 person Repeat surgery: • Amplatzer: none • surgical: 2 people Surgical wound complications: • Amplatzer: none • surgical: 2 people	Surgery or Amplatzer chosen by patients/guardians and physicians No reported attempt to adjust for confounding Amplatzer device group older, taller and heavier, more multiple ASDs, more respiratory infections Outcomes appropriate Loss to follow-up • Amplatzer: 25% • surgical: 29% No intention to treat analysis reported

Summary of key efficacy and safety findings (2)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Berger[2] Non-randomised controlled study Germany 1997 to 1998 122 people with secundum atrial septal defect: • 61 Amplatzer; median age 12 (range less than 1 to 78). • 61 conventional surgery; median age 20 (range: less than 1 to 74). Exclusion criteria: • partial anomalous pulmonary venous drainage • atrioventricular valve abnormalities • patent foramen ovale with history of stroke and transient ischaemic attacks Median follow-up: • 7 months (Amplatzer) • 8 months (surgery)	Echocardiographic successful closure rates: • Amplatzer: 98% • surgical: 98% Length of hospital stay: • Amplatzer: 3 days • surgical: 8 days p<0.001	Atrial flutter or fibrillation: • Amplatzer: 2 people • surgical: 7 people Intermittent supraventricular tachycardia: • Amplatzer: 1 person • surgical: none Pericardial effusion: • surgical: 2 people Wound infection: • surgical: 1 person Perforation of duodenal ulcer • surgical: 1 person Embolism of entire device: • Amplatzer: 1 person	Allocation to Amplatzer or surgery according to clinical characteristics Outcomes appropriate

Summary of key efficacy and safety findings (3)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Durongpisitkul[3] Non-randomised controlled study Bangkok, Thailand 1999 to 2000 103 people with secundum atrial septal defect: • 39 Amplatzer; median age 12 (range: 2-69) • 64 conventional surgery; median age 25 (range: 2-64) Inclusion criteria: • no other defect • atrial septal defect diameter <34mm for Amplatzer group • >5mm from atrial septal defect margin to coronary sinus, atrioventricular valves and right upper pulmonary vein for Amplatzer group Follow-up length for Amplatzer device closure was 12 months	Echocardiographic immediate successful closure: • Amplatzer: 28/29 (97%) • surgical: 64/64 (100%) Average hospital stay: • Amplatzer: 1 day • surgical: 8 days p<0.001	Hypotension requiring inotropic drugs: • Amplatzer: none • surgical: 4 people Bleeding: • Amplatzer: none • surgical: 4 people Supraventricular tachycardia: • Amplatzer: 1 person • surgical: 3 people Respiratory failure: • Amplatzer: none • surgical: 1 person Cardiopulmonary arrest: • Amplatzer: none • surgical: 1 person Pneumothorax: • Amplatzer: none • surgical: 1 person Brachial plexus injury: • Amplatzer: 1 person • surgical: none Post-pericardiotomy syndrome: • Amplatzer: none • surgical: 1 person Embolisation of Amplatzer device: 1 person	Allocated to surgery or Amplatzer by surgeon Amplatzer patients were younger, lighter, with smaller atrial septal defects Outcomes appropriate

Summary of key efficacy and safety findings (4)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Omeish[4] Case series Worldwide survey Published 2000 3460 people with secundum atrial septal defects; median age 12 (range: infant to 88) Inclusion criteria: • diameter of atrial septal defect <35mm • distance from defect to coronary sinus, atrioventricular valves, right pulmonary vein ≥ 5mm Follow up: • immediate: 3391 people • 6 months: 431 people • 1 year: 921 people • 2 years: 147 people	Echocardiographic successful closure: • immediate: 97% • 6 months: 98% • 1 year: 99% • 2 years: 100%	• Tamponade: 2 people • Cardiac perforation: 1 person • stroke or transient ischaemic attack: 5 people • Endocarditis: 1 person • Large haematoma: 1 person • Embolisation of Amplatzer: 0.4% • Rhythm disturbance: 1.3%	Uncontrolled case series Method of identifying people who had received Amplatzer not described Method of collecting information on follow up not described Follow-up data not complete

Summary of key efficacy and safety findings (5)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Carminati[5] Case series Multi-centre (Western Europe) 1996-1999 334 people with secundum atrial septal defect (68/334 had patent foramen ovale or persisting right to left shunt across previously performed fenestrated Fontan procedure) median age: 12 years (range 0.5 – 77) All received Cardioseal or Starflex device Exclusion criteria not described Follow up 12 months	Device successfully implanted in 94% (314/334) Immediately after procedure: • Complete closure: 59% (185/314) • Trivial residual shunt: 31% (96/314) • Small residual shunt: 9% (29/314) • Significant residual shunt: 1% (4/314) At 1 year: Successful closure: 93% (99/107)	• Malposition requiring endovascular retrieval: 4% (13/334) • Malposition requiring surgical retrieval: 1% (3/334) • Embolisation: 4% (14/334) • Distal arm caught requiring surgical removal: 0.3% (1/334) • Stroke: 0.3% (1/334) – after closure of fenestrated Fontan procedure	Uncontrolled case series Exclusion criteria not described Some patients had patent foramen ovale or persisting right to left shunting across a previously performed fenestrated Fontan procedure 12 month follow up data available for 32% (107/334) Limited description of data collection methods

Summary of key efficacy and safety findings (6)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Chessa[6] Case series Italy 1996-2001 417 people with secundum atrial septal defect; mean age 27 years 159 received Cardioseal/Starflex device 258 received Amplatzer device Exclusion criteria not described Follow up 12 months	None provided	Cardioseal/Starflex complications: • Embolisation requiring surgical retrieval: 2.5% (4/159) • Embolisation requiring endovascular retrieval: 0.6% (1/159) • Malposition requiring surgical treatment: 0.6% (1/159) • Malposition requiring endovascular retrieval: 1.9% (3/159) • Arrhythmia: 0.6% (1/159) • Right iliac vein dissection: 0.6% (1/159) Amplatzer complications: • Embolisation requiring surgical retrieval: 1.2% (3/258) • Malposition requiring surgical treatment: 0.8% (2/258) • Arrhythmia: 3.9% (10/258) • Pericardial effusion: 0.8% (2/258) • Thrombus formation: 0.4% (1/258) • Groin haematoma: 0.4% (1/258) • Haemorrhage in the retropharynx: 0.4% (1/258) • Rupture of sizing balloon: 0.4% (1/258) • Peripheral embolisation after 1 year: 0.4% (1/258) One patient died suddenly aged 34 years, 1.5 years after implant – unknown if death was related to procedure.	Uncontrolled case series Exclusion criteria not described Limited description of data collection methods Detailed information about procedural complications Follow up rate not clear

Summary of key efficacy and safety findings (7)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Sievert[7] Case series Germany 1994-2000 127 patients with patent foramen ovale and presumed paradoxical embolism 37 received a Cardioseal or Starflex 57 received an Amplatzer device 33 received a Helex device Mean follow up: 12 months	Complete closure at 6 months or earlier: • Cardioseal or Starflex: 94% • Amplatzer: 97% • Helex: 100%	Cardioseal or Starflex: • Thrombus formation: 3% (1/37) • Device frame fracture: 3% (1/37)	Consecutive recruitment Patients had patent foramen ovale
Vincent[8] Case series USA 2001 14 patients with atrial septal defects; all received the Helex device Median age 5.0 years (range 2.6 – 13.0) Follow-up: 6 months	Device implanted in 93% (13/14) Immediately after procedure: • Successful closure: 100% (13/13) At 6 months: • Complete closure: 85% (11/13) • Insignificant shunts: 15% (2/13)	"No procedural complications" One device had to be removed due to possible allergic reaction to nickel	Uncontrolled case series (Part of FDA phase II multicentre trial – data on control group not yet available) Small study Short follow-up

Validity and generalisability of the studies

Most studies were carried out in settings appropriate to the UK, though one was carried out in Thailand.[3]

The three non-randomised studies comparing the Amplatzer device and surgery are large, but may be susceptible to confounding. In all studies the eligibility criteria for Amplatzer device were stricter than for surgery. [1-3]

The largest case series was a worldwide survey.[4] However, the method of identifying people who had received the Amplatzer device and collecting follow up data were not described. The reliability of the survey may be compromised by selection and reporting bias.

Only two small case series including more than ten people were found for the Helex device.[7,8]

Specialist advisor's opinion / advisors' opinions

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

- The long-term safety and effectiveness of the devices need to be monitored.
- The procedure requires training and should be performed by an interventional cardiologist with cardiac surgical facilities.
- There is a Swiss trial in progress comparing Amplatzer device closure with medical treatment in patients with a patent foramen ovale.

Issues for consideration by IPAC

None other than those discussed above.

References

1. Du, Z. D., Hijazi, Z. M., Kleinman, C. S., Silverman, N. H., Larntz, K., and Amplatzer, Investigators. Comparison between transcatheter and surgical closure of secundum atrial septal defect in children and adults: results of a multicenter nonrandomized trial. Journal of the American College of Cardiology 2002; 39: 1836-1844

2. Berger, F., Vogel, M., Alexi-Meskishvili, V., and Lange, P. E. Comparison of results and complications of surgical and Amplatzer device closure of atrial septal defects. Journal of Thoracic & Cardiovascular Surgery 1999; 118: 674-678

3. Durongpisitkul, K., Soongswang, J., Laohaprasitiporn, D., Nana, A., Sriyoschati, S., Ponvilawan, S., Subtaweesin, T., and Kangkagate, C. Comparison of atrial septal defect closure using amplatzer septal occluder with surgery. Pediatric Cardiology 2002; 23: 36-40

4. Omeish, A. and Hijazi, Z. M. Transcatheter closure of atrial septal defects in children & adults using the Amplatzer Septal Occluder. Journal of Interventional Cardiology 2001; 14: 37-44

5. Carminati M, Giusti S, Hausdorf G, Qureshi S, Tynan M, Witsenberg M, et al. A European multicentric experience using the CardioSEAL® and Starflex double umbrella devices to close interatrial communications holes within the oval fossa. Cardiology in the Young 2000; 10: 519-526

6. Chessa M, Carminati M, Butera G, Margherita R, Drago M, Rosti L, et al. Early and late complications associated with transcatheter occlusion of secundum atrial septal defect. Journal of the American College of Cardiology 2002; 39: 1061-1065

7. Sievert, H., Horvath, K., Zadan, E., Krumsdorf, U., Fach, A., Merle, H., Scherer, D., Schrader, R., Spies, H., Nowak, B., and Limann-Jensen, H. Patent foramen ovale closure in patients with transient ischemia attack/stroke. Journal of Interventional Cardiology 2001; 14: 261-266

8. Vincent, R.N., Raviele, A.A., and Diehl, H.J. Single-center experience with the Helex septal occluder for closure of atrial septal defects in children. Journal of Interventional Cardiology 2003; 16: 79-82

Annex: References to studies not described in the table

Reference	Number of study participants
Non-randomised controlled study	
Walsh, K. P., Tofeig, M., Kitchiner, D. J., Peart, I., and Arnold, R. Comparison of the Sideris and Amplatzer septal occlusion devices. American Journal of Cardiology 1999; 83: 933-936	Comparison of two devices: Sideris (n=33) and Amplatzer (n=39)
Hughes, M. L., Maskell, G., Goh, T. H., and Wilkinson, J. L. Prospective comparison of costs and short term health outcomes of surgical versus device closure of atrial septal defect in children. Heart (British Cardiac Society) 2002; 88: 67-70	Comparison of Amplatzer (n=43) and surgery (n=19)
Case series	
Berger, F., Ewert, P., Dahnert, I., Stiller, B., Nurnberg, J. H., Vogel, M., von der, Beek J., Kretschmar, O., and Lange, P. E. Interventional occlusion of atrial septum defects larger than 20 mm in diameter. [German] Zeitschrift fur Kardiologie 2000; 89: 1119-1125	352 Amplatzer
Beitzke, A., Schuchlenz, H., Beitzke, M., Gamillscheg, A., Stein, H. I., and Zartner, P. Interventional closure of patent foramen ovale and atrial septal defects after paradoxical embolic events. Zeitschrift fur Kardiologie 2002; 91: 693-700	251 Mainly patent foramen ovale. Cardioseal or Starflex
Berger, F., Ewert, P., Bjornstad, P. G., Dahnert, I., Krings, G., Brilla-Austenat, I., Vogel, M., and Lange, P. E. Transcatheter closure as standard treatment for most interatrial defects: experience in 200 patients treated with the Amplatzer Septal Occluder. Cardiology in the Young 1999; 9: 468-473	200 (people may be included in Berger study above) Amplatzer
Beitzke, A.., Schuchlenz, H., Gamillscheg, A., Stein, J. I., and Wendelin, G. Catheter closure of the persistent foramen ovale: mid-term results in 162 patients. Journal of Interventional Cardiology 2001; 14: 223-229	162 All patent foramen ovale Amplatzer or Cardioseal or Starflex
Walsh, K. P. and Maadi, I. M. The Amplatzer septal occluder. Cardiology in the Young 2000; 10: 493-501	137 Amplatzer
Carminati, M., Chessa, M., Butera, G., Bini, R. M., Giusti, S., Festa, P., Spadoni, I., Redaelli, S., and Hausdorf, G. Transcatheter closure of atrial septal defects with the STARflex device: early results and follow-up. Journal of Interventional Cardiology 2001; 14: 319-324.	117 Cardioseal or Starflex
Chan, K. C., Godman, M. J., Walsh, K., Wilson, N., Redington, A., and Gibbs, J. L. Transcatheter closure of atrial septal defect and interatrial communications with a new self expanding nitinol double disc device (Amplatzer septal occluder): multicentre UK experience. Heart (British Cardiac Society) 1999; 82: 300-306	100 Amplatzer
Transcatheter closure of atrial septal defects in adults. Practicality and safety of four different closure systems used in 102 patients]. [German] La Rosee, K., Krause, D., Becker, M., Beuckelmann, D. J., Deutsch, H. J., and Hopp, H. W. Deutsche Medizinische Wochenschrift 20001; 126:1030-1036	<100 Amplatzer
Fischer, G., Masura, J., Kramer, H. H., and Gavora, P. Transcatheter occlusion of secundum atrial septal defects with the self- centering Amplatzer Septal Occluder. Progress in Pediatric Cardiology 1998; 9: 119-124	98 Amplatzer
Demkow, M., Ruzyllo, W., Konka, M., Kepka, C., Wilczynski, J., Jakubowska, E., Kowalski, M., and Rydlewska-Sadowska, W. Transcatheter closure of secundum atrial septal defects with the Amplatzer septal occluder. Kardiologia Polska 2001; 54: 205-209	69 Amplatzer
Arora, R., Kalra, G. S., Singh, S., Passey, R., Sinha, S., and Nigam, M. Transcatheter closure of atrial septal defect using self-expandable septal occluder. Indian Heart Journal 1999; 51: 289-293	63 Amplatzer
Sievert, H., Horvath, K., Zadan, E., Krumsdorf, U., Fach, A., Merle, H., Scherer, D., Schrader, R., Spies, H., Nowak, B., and Lissmann-Jensen, H. Patent foramen ovale closure in patients with transient ischemia attack/stroke. Journal of Interventional Cardiology 2001; 14: 261-266	57 Amplatzer 37 Cardioseal or Starflex
Fischer, G., Kramer, H. H., Stieh, J., Harding, P., and Jung, O. Transcatheter closure of secundum atrial septal defects with the new self-centering Amplatzer Septal Occluder. European Heart Journal 1999; 20: 541-549.	52 Amplatzer
Bialkowski, J., Szkutnik, M., Wilczek, K., Chodor, B., Zeifert, B., Sikora, J., Szatkowski, K., Haponiuk, I., and Zembala, M. Transcatheter closure of atrial septal defects in adults with the Amplatzer atrial septal occluder. [Polish] Polskie Archiwum Medycyny Wewnetrznej 2001; 105: 303-309	51 Amplatzer
Demkow, M., Ruzyllo, W., Konka, M., Kepka, C., Kowalski, M., Wilczynski, J., and Rydlewska-Sadowska, W. Transvenous closure of moderate and large secundum atrial septal defects in adults using the Amplatzer septal occluder. Catheterization & Cardiovascular Interventions 2001; 52: 188-193	50 Amplatzer