Clinical Insights

SUMMARY OF CLINICAL DATA

AMPLATZER™ SEPTAL OCCLUDER

AMPLATZER™ SEPTAL OCCLUDER SAFETY

KEY MESSAGES

- The Amplatzer™ Septal Occluder (ASO) is a safe, effective, and reliable treatment option for the transcatheter closure of the secundum atrial septal defect (ASD).
- It is supported by over 20-years of clinical experience and has the largest body of safety and effectiveness data than any other transcatheter device occluder.
- Adoption of ASO is wide despite rare adverse events.

PERSPECTIVE

The ASO was the first transcatheter ASD occlusion device commercially available as a safe and effective treatment alternative to surgical ASD closure, receiving CE mark approval in 1998 and FDA approval in 2001. It is the most widely used transcatheter ASD occlusion device, amassing 750 peer reviewed articles, supporting its safety and effectiveness.[1] Consequently, transcatheter device closure has become the current standard of care for secundum ASD closure of appropriate anatomy.[2,3]

ASO SAFETY & EFFECTIVENESS

With over 20 years of commercialization and over 430,000 devices implanted, the ASO has the longest history and largest body of clinical evidence compared to any other device occluder.[4] Compared to much smaller data sets from other device occluders, safety and effectiveness data for the ASO device remains unmatched and allows for more robust assessment of complication rates.

After decades of clinical and commercial use, transcatheter device occluders, in particular the ASO, have become as effective and safer than traditional surgical closure of the ASD. European guidelines state that transcatheter device closure is the method of choice for secundum ASD closure of appropriate anatomies.[3] Surgery and transcatheter intervention have reported comparable success rates and mortality, however morbidity was lower and hospital stay shorter with catheter intervention.[3] The US AHA/ACC guidelines hold both therapeutic approaches at parity for adults with isolated ASD accompanied by clinically impaired functional capacity, right heart enlargement, and shunting[2] [Table 1].

TABLE 1: ASD TREATMENT GUIDELINES

AUTHORS	CLASS OF RECOMMENDATION	LEVEL OF EVIDENCE	RECOMMENDATIONS
2010 ESC Guidelines[3]	I	B	**Patients with significant shunt (signs of RV volume overload) and PVR <5 WU should undergo ASD closure regardless of symptom**
	I	C	**Device closure is the treatment of choice when applicable.**
2018 ACHD Guidelines[2]	I	B-NR	In **adults with isolated secundum ASD causing impaired functional capacity**, right atrial and/or RV enlargement, and net left-to-right shunt sufficiently large to cause physiological sequelae (e.g., pulmonary–systemic blood flow ratio [Qp:Qs] ≥1.5:1) without cyanosis at rest or during exercise, **transcatheter or surgical closure to reduce RV volume and improve exercise tolerance is recommended**, provided that systolic PA pressure is less than 50% of systolic systemic pressure and pulmonary vascular resistance is less than one third of the systemic vascular resistance.

NR: Non-Randomized

Indications for Use: The Amplatzer™ Septal Occluder is a percutaneous, transcatheter, atrial septal defect closure device intended for the occlusion of atrial septal defects (ASD) in secundum position or patients who have undergone a fenestrated Fontan procedure and who now require closure of the fenestration.

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The guidelines reflect acceptance of transcatheter intervention compared to surgery. Further, a meta-analysis of 13 studies summarizing ASD closure by surgery (1,270 patients) or transcatheter device (1,812) reported lower post-procedural and major complications rates compared to the surgical group (6.6% vs. 31.0% and 1.9% vs. 6.8% respectively).[5] The ASO was the main device used in 12 of the 13 studies. Patients treated surgically had a 5.4x and 3.8x higher risk of total and major complications respectively relative to transcatheter treatment [Figure 1].

ASD closure outcomes are best when repair is done at an age less than 25.[3] Studies have attested to the ASO as an ideal treatment for this important patient group. An observational study from pediatric cardiology databases in 375 patients, showed no difference in outcomes between transcatheter and surgery cohorts with regard to survival, functional capacity, arrhythmias or neurological events (follow up 5-20 yrs, median 10 yrs).[6] Despite better outcomes at younger ages, patients benefit from closure at any age with regard to morbidity (exercise capactiy, shortness of breath, right heart failure), particularly when performed with a transcatheter device.[3]

A retrospective multicenter study of 1,395 children implanted with the ASO reported a procedure success rate was 95.3%, with failed implantations were most often to unsuitable anatomy.[7] No deaths were reported during follow up (median 3.5yrs) and the complication rate was low at 1.04%. Overall, probability of complication free survival at 12, 60, and 120 months was 99.2 ± 0.2%, 99.1 ± 0.2%, and 98.6 ± 0.6%, respectively.

FIGURE 1: MAJOR COMPLICATIONS OF ASD CLOSURE: SURGICAL V TRANSCATHETER APPROACHES[5]

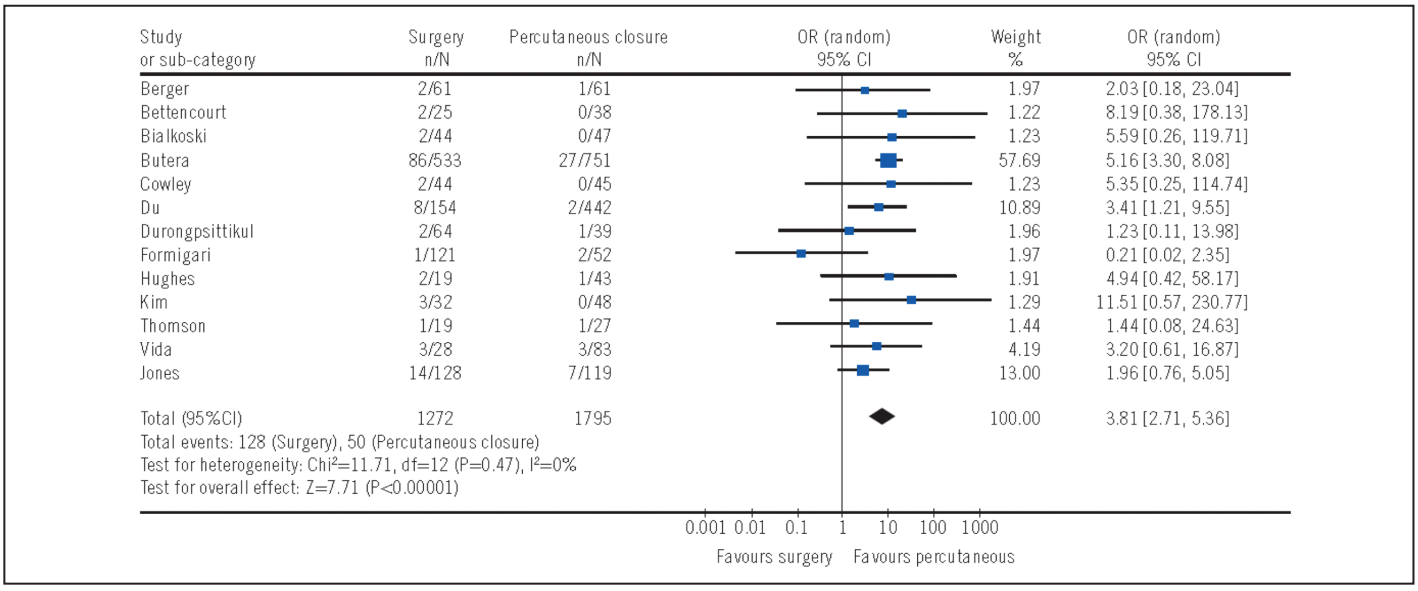

TABLE 2: SUMMARY OF PEDIATRIC ARTICLES

	PATIENTS (N)	TECHNICAL SUCCESS RATE	COMPLETE CLOSURE RATE	MINOR COMPLICATIONS*	SERIOUS COMPLICATIONS*
Omeish A, Hijazi ZM, 2001 [8]	3535	98%	100%	2.8%	0.3%
Everett AD, Jennings J, Sibinga E, et al 2009 [9]	478	96%	99%	4.8%	1.1%
Latiff HA, Alwi M, Samion H, et al. 2002 [10]	190	100%	99%	2.1%	0%
Faella HJ, Sciegata AM, Alonso JL, et al. 2003 [11]	109	94%	100%	3.9%	1.0%
Masura J, Gavora P, Podnar T, 2005 [12]	151	100%	100%	NA	0%
El-Said H, Hegde S, Foerster S, et al 2015 [13]	688	NA	95%	6.8%	4.7%
Nir-David Y, Mainzer G, Tal R, et al 2017 [14]	110	100%	97.2%	0	0
Putra ST, Djer MM, Idris NS, et al 2015 [15]	152	99.1%	100%	6.0%	1.3%

TABLE 3: SUMMARY OF ADULT ARTICLES

	PATIENTS (N)	TECHNICAL SUCCESS RATE	COMPLETE CLOSURE RATE	MINOR COMPLICATIONS*	SERIOUS COMPLICATIONS*
Omeish A, Hijazi ZM, 2001 [8]	3535	98%	100%	2.8%	0.3%
Majunke N, Bialkowski J, Wilson N, et al 2009 [16]	650	99%	96%	NA	NA
Patel A, Lopez K, Banerjee A, et al 2007 [17]	113	99%	90%	2.7%	0.9%
Faella HJ, Sciegata AM, Alonso JL, et al. 2003 [11]	109	94%	100%	3.9%	1.0%
Spies C, Timmermanns I, Schrader R 2007 [18]	166	98%	98%	6.5%	0%
Turner DR, Owada CY, Sang CJ Jr, et al 2017 [19]	1,000	NA	97.9%	5.4%	0.65%
Astarcioglu MA, Kalcik M, Sen T, et al 2015 [20]	125	100%	100%	15.2%	0
Godart F, Houeijeh A, Recher M, et al 2015 [21]	131	87.8%	89%	8.4%	1.5%
Kijima Y, Akagi T, Takaya T, et al 2016 [22]	463	98%	88%	5.6%	6%
Snijder RJ, Suttorp MJ, Berg JM, et al 2015 [23]	104	98.1%	NA	8.7%	NA

*Minor and serious complications are not defined the same way across all referenced studies
NOTE: Results from clinical trials are not directly comparable. Information provided for educational purposes only.

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ASO ADVANTAGE AND RISKS

The body of evidence associated with the ASO has allowed rare adverse events to be detected because of the extensive volume of treated cases. Permanent cardiac implants, such as the ASO, can be associated with long term arrhythmias, thrombo-embolism and cardiac tissue injuries.[24] These rates associated with the ASO are very low, and consistent across multiple studies.

Device embolization The ASO is easily retrieved until its release from the delivery cable, minimizing malpositioning or embolization.[8] A survey of ASO proctors reported an ASO-embolization rate of 0.55% (21/3,842) with no embolization-related deaths.[25] All 21 embolized devices were successfully retrieved by transcatheter means (15) or by surgery (6).

Rhythm disturbances A study in 650 adult patients reported new onset atrial fibrillation of 4.5%.[16] However, a long term study showed similar incidence of late arrythmias among transcatheter occlusion devices and surgical occlusion, implicating the act of defect closure itself rather than closure method.[5]

Cardiac erosion is a rare, serious complication, resulting from device abrasion through the atrial wall into the aorta and/or pericardial space. Reported ASO erosion rates are low at 0.043% - 0.3%.[25,26] Analyses of adjudicated ASO erosion cases identified rim deficiency, device oversizing, and low patient weight to device size ratio as possible risk factors.[25] Conclusive determination of root causes of cardiac erosion remains challenging due to patient heterogeneity and infrequent occurrence.

There have been recent erosion cases reported with the Figulla Flex II (Occlutech) device.[28] However, incidence rates for this and other occluders are not yet precise given shorter overall clinical and commercial experiences compared to the ASO.

With its extensive commercial coverage, Abbott works with regulatory agencies to ensure the latest safety data is being reported and reflected in product guidance. While there have been other device occluders commercialized, the ASO is the only device that has remained in the market for over 20 years with wide adoption, attesting to the safety and effectiveness of the product and therapy.

CONCLUSION

Clinical practice guidelines indicate that device closure is the treatment of choice for the repair of the ASD. As the device occluder with the largest body of evidence and the most extensive clinical and commercial experience, the Amplatzer™ Septal Occluder is the ideal treatment option for the closure of the secundum ASD.

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AMPLATZER™ SEPTAL OCCLUDER AND DELIVERY SYSTEM

IMPORTANT SAFETY INFORMATION

℞ ONLY

INDICATIONS FOR USE

The AMPLATZER™ Septal Occluder is a percutaneous, transcatheter, atrial septal defect closure device intended for the occlusion of atrial septal defects (ASD) in secundum position or patients who have undergone a fenestrated Fontan procedure and who now require closure of the fenestration.

Patients indicated for ASD closure have echocardiographic evidence of ostium secundum atrial septal defect and clinical evidence of right ventricular volume overload (such as, 1.5:1 degree of left-to-right shunt or RV enlargement).

CONTRAINDICATIONS

The AMPLATZER™ Septal Occluder is contraindicated for the following:

- Any patient known to have extensive congenital cardiac anomaly which can only be adequately repaired by way of cardiac surgery.
- Any patient known to have sepsis within 1 month prior to implantation, or any systemic infection that cannot be successfully treated prior to device placement.
- Any patient known to have a bleeding disorder, untreated ulcer, or any other contraindications to aspirin therapy, unless another antiplatelet agent can be administered for 6 months.
- Any patient known to have a demonstrated intracardiac thrombi on echocardiography (especially left atrial or left atrial appendage thrombi).
- Any patient whose size (such as, too small for transesophageal echocardiography probe, catheter size) or condition (active infection, etc.) would cause the patient to be a poor candidate for cardiac catheterization.
- Any patient where the margins of the defect are less than 5 mm to the coronary sinus, inferior vena cava rim, AV valves, or right upper lobe pulmonary vein.

WARNINGS

- Patients who are allergic to nickel may have an allergic reaction to this device.
- Physicians must be prepared to deal with urgent situations, such as device embolization, which require removal of the device. This includes the availability of an on-site surgeon.
- Embolized devices must be removed as they may disrupt critical cardiac functions. Embolized devices should not be withdrawn through intracardiac structures unless they have been adequately collapsed within the sheath.
- Use on or before the expiration date noted on the product packaging.
- This device is sterilized using ethylene oxide and is for single use only. Do not reuse or resterilize. Attempts to resterilize the device may result in device malfunction, inadequate sterilization, or patient harm.
- Do not use the device if the packaging sterile barrier is open or damaged.
- Do not release the AMPLATZER™ Septal Occluder from the delivery cable if the device does not conform to its original configuration, or if the device position is unstable or if the device interferes with any adjacent cardiac structure (such as Superior Vena Cava (SVC), Pulmonary Vein (PV), Mitral Valve (MV), Coronary Sinus (CS), aorta (AO)). Recapture the device and redeploy. If still unsatisfactory, recapture the device and either replace with a new device or refer the patient for alternative treatment.
- Implantation of this device may not supplant the need for Coumadin™ in patients with ASD and paradoxical emboli.
- The use of echocardiographic imaging (TTE, TEE, or ICE) is required.
- Balloon sizing should be used to size the atrial septal defect using a stop-flow technique. Do not inflate the balloon beyond the cessation of the shunt (such as, stop-flow). DO NOT OVERINFLATE.
- Patients with a retro-aortic rim of less than 5 mm in any echocardiographic plane, or patients in whom the device physically impinges on (i.e. indents or distorts) the aortic root, may be at increased risk of erosion.
- Do not select a device size greater than 1.5 times the echocardiographic-derived ASD diameter prior to balloon sizing.

PRECAUTIONS

- The use of this device has not been studied in patients with patent foramen ovale.
- Use standard interventional cardiac catheterization techniques to place this device.
- Placement of the AMPLATZER™ Septal Occluder may impact future cardiac interventions, for example transeptal puncture and mitral valve repair.

MR Conditional to 3.0 Tesla

Caution should be used if an MRI is performed with a magnetic field of >3.0 tesla.

Through non-clinical testing, the AMPLATZER™ device has been known to be MR Conditional at field strengths of 3.0 tesla or less with a maximum whole-body-averaged specific absorption rate (SAR) of 3.83 W/kg at 1.5 tesla and 5.57 W/kg at 5.0 tesla for a 20-minute exposure to a B1 of 118 μT. The AMPLATZER™device should not migrate in this MR environment. Non-clinical testing has not been performed to rule out the possibility of migration at field strengths higher than 3.0 tesla.

In this testing, the device produced a temperature rise of 1.1°C at 1.5 tesla and 1.6°C at 5.0 tesla.

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the device.

POTENTIAL ADVERSE EVENTS

Potential adverse events may occur during or after a procedure placing this device may include, but are not limited to:

Air embolus; Allergic dye reaction; Anesthesia reactions; Apnea; Arrhythmia; Cardiac tamponade; Death; Embolization; Fever Hypertension/hypotension; Infection including endocarditis; Need for surgery; Pericardial effusion; Perforation of vessel or myocardium; Pseudoaneurysm including blood loss requiring transfusion; Stroke; Tissue erosion; Thrombus formation on discs; Valvular regurgitation

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