Outcomes After Transcatheter ASD Closure

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KEYWORDS
- Atrial septal defect • Percutaneous device closure • Outcomes • Complications

KEY POINTS
- Surgical and interventional closure of an ostium secundum-type atrial septal defect (ASD-II) are equally effective.
- Percutaneous closure shows lower major and minor complication rates compared with surgical closure.
- Although rare, the most frequent complications described for device closure are embolization, erosion/perforations, and arrhythmias.
- Transcatheter closure has proved safe and effective, becoming the standard treatment of ASD-II.

INTRODUCTION
The ASD-II represents approximately 10% of all congenital heart disease and, with the exception of bicuspid aortic valve, is the most common congenital heart defect in adulthood.1 Although recognized as a benign form of heart lesion, if left untreated, it can eventually contribute to significant morbidity and mortality, as reported by the natural history studies.2,3 Over the past 4 decades, pediatric interventional cardiology has evolved enormously. The use of novel materials, technologies, and imaging modalities has opened new possibilities in the field and has had a significant impact on the outcomes of old and new procedures. As such, percutaneous closure of the ASD-II had evolved to become the standard treatment modality in lieu of cardiac surgery with cardiopulmonary bypass. Since the initial report by King and colleagues4 of nonoperative closure of secundum ASD during cardiac catheterization,4 several devices constructed in different shapes and materials have been introduced in the interventional arena. Some of these devices have undergone modifications and redesign and some have even disappeared from the market due to problems detected in the original models. This article presents the current clinical outcomes after ASD-II transcatheter closure as well as the complications encountered and future directions.

THERAPEUTIC OPTIONS AND/OR SURGICAL TECHNIQUES
Percutaneous device implantation has emerged as an attractive and effective alternative to surgical approach for ASD-II closure. Current devices have significantly improved the safety and success rate of the procedure, resulting in an expansion of the indications of the technique for more complex cases.5,6 Currently, it has been estimated that more than 85% to 90% of all ASD-II are amenable to transcatheter closure and include fenestrated defects (associated or not with an aneurysm of the interatrial septum), multiple distant defects, and

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large ASDs (Figs. 1–5).7–9 Device and surgical closures have low risks, equal effectiveness, and comparable cost. A recently published meta-analysis10 compared the 2 methods of closure for occurrence of death and major complications. Thirteen original nonrandomized studies, including 3082 patients, searched in electronic databases, journals, and major international conference proceedings were reviewed until December 2008. Only 1 death was reported in the surgical group. Analysis of post-procedural complications showed a 31% rate in surgical patients and a 6.8% rate in patients who received a device (odds ratio [OR] 5.4; 95% CI, 2.96–9.84; P < .0001). The postprocedural major

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**Fig. 1.** Very large ASD-II (33 mm) seen on 3-D transesophageal echocardiogram. (A) Right atrial view. (B) Left atrial view. (C) An Occlutech device still attached to the delivery cable (right atrial view). Final aspect after device release with adequate device position and no residual defect seen from right atrial (D) and left atrial aspects (E). AO, aorta; ASD, atrial septal defect; IVC, inferior vena cava; MV, mitral valve; SVC, superior vena cava.
complication rate was 6.8% in the surgical group and 1.9% for catheter-based closure (OR 3.81; 95% CI, 2.7–5.36; \( P = .006 \)), again favoring percutaneous closure.

Another cohort of patients comparing both methods, including 1268 consecutive patients with isolated ASD-II, was published by the same group, with emphasis on mortality, morbidity, hospital stay, and efficacy.\(^{11} \) There were no postoperative deaths. The overall rate of complications was higher in the surgical group than in the interventional group: 44% (95% CI, 39.8%–48.2%) versus 6.9% (95% CI, 5.6%–8.7%) (\( P < .0001 \)). Major complications were also more frequent among surgical patients: 16% (95% CI, 13%–19%) versus 3.6% (95% CI, 2.2%–5.0%) (\( P = .002 \)). Multiple logistic regression analysis showed that surgery was independently strongly related to the occurrence of total complications (OR 8.13; 95% CI, 5.75–12.20) and of major complications (OR 4.03; 95% CI, 2.38–7.35). The occurrence of minor complications was also independently related to surgery. Hospital stay was shorter in the interventional group (3.2 ± 0.9 vs 8.0 ± 2.8 days, \( P < .0001 \)).

A multicenter, nonrandomized concurrent study comparing both techniques with the purpose of looking for differences in safety, efficacy, and clinical utility was presented by Du and colleagues\(^{12} \) in 2002. Among 596 patients, the total complication rate was 7.2% for the device group and 24.0% for the surgical group (\( P < .001 \)). There were no deaths. The success rates for both groups were

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**Fig. 2.** Two close ASDs divided by a flimsy tongue of tissue seen on 3-D transesophageal echocardiogram (right atrial view). The catheter crossed through the superior hole (A). Both ASDs were closed with a single Occlutech device: final aspect after device release with a tiny residual leak (arrow) in the postero-inferior portion of the interatrial septum (left atrial view) (B). AO, aorta; IVC, inferior vena cava; SVC, superior vena cava.

**Fig. 3.** Two distant ASDs as seen by 3-D transesophageal echocardiogram (right atrial view). The largest is located in the anterosuperior portion of the interatrial septum and the smaller is located in the postero-inferior interatrial septum. The distance between the defects is 10–12 mm (A). Two Occlutech devices (P1 – P2) were used to close the holes and there is some interposition between the two. Despite that, there is a tiny residual leak (arrow) between the 2 disks (left atrial view) (B). AO, aorta; ASD I, atrial septal defect—inferior; ASD S, atrial septal defect—superior; CS, coronary sinus; IVC, inferior vena cava.
Fig. 4. Multifenestrated aneurismal septum seen on intracardiac echocardiography. On home view, the redundant and aneurismatic interatrial septum is seen (A). On short-axis view, color flow Doppler shows a multifenestrated interatrial septum with left-to-right shunt (right atrial, superior portion of the screen) (B). One single Amplatzer cribiform device was used to close the multifenestrations. It is seen still attached to the delivery cable (C).

not statistically different; however, the complication rate was lower and the length of hospital stay was shorter for device closure. This was a landmark study because it resulted in approval of the Amplatzer device for transcatheter closure of the ASD-II by the Food and Drug Administration (FDA).

In several other smaller studies, the overall safety and effectiveness of the percutaneous technique have compared favorably with surgical repair.11–14

CLINICAL OUTCOMES

In the proper assessment of outcomes after any interventional procedure, especially with insertion of a device in the heart, the definitions of clinical

Fig. 5. A moderate-sized ASD-II seen on a modified 91° transesophageal echocardiogram view in 2-D (A) and color Doppler (B). The defect was closed using a Nit-Occlud ASD-R device, which is seen after release in a correct position without residual shunting (C). V, a mark for orientation of the side of the echo image.
success and clinical efficacy are crucial. Among the multiple goals pursued during ASD-II closure, complete defect occlusion, right ventricular (RV) volume normalization, absence of late complications (erosion, perforation, and fractures), and no significant arrhythmias or deleterious ECG changes are the most important. Absence of additional interventions after closure and no infectious or thrombotic events are also key issues.

The success rate of implantation of devices depends on the experience of the operator and the anatomy of the defect (presence of large defects, multiple defects, inadequate rims of septal tissue, atrial septal aneurysm, or combination of those factors). Due to its design and easier-to-use system, the Amplatzer septal occluder results in higher rates of successful implantation, approaching 99% in experienced hands. Although this device can close a broad range of ASD dimensions, including the large ones, the Halex device is only recommended for small-to-moderate size defects (up to 18 mm of stretched diameter).

RV volume overload is a well-known cardiac consequence of ASD-II left-to-right shunt, accounting for most of its long-term complications. Thus, cardiac volumetric unloading is a major aim of percutaneous intervention. Transcatheter closure of ASD-II results in a rapid normalization of RV volume overload and improvement of RV function, as demonstrated by the decrease of RV end-diastolic and end-systolic volumes, the decrease of the RV myocardial performance index, and the increase of the RV ejection fraction after device insertion. Percutaneous closure leads to a progressive decrease in size of the RV, usually taking 6 to 12 months (or even more) to attain normal dimensions. In comorbid patients, however, especially those with higher pulmonary blood flow and operated at older ages, the RV remains enlarged. Although this residual dilatation has been termed, cardiomyopathy of volume loading, its clinical impact on exercise performance is limited. By the same token, the left ventricular volume increases due to the shift of the septum toward the decompressed RV and this plays a major role in the impaired exercise response. Echocardiography, CT, and functional studies have shown better RV improvement in younger than older patients and those undergoing closure by interventional catheterization rather than by surgery.

Complete closure of the defect depends on the type of device, size of the defect, and timing of evaluation. An immediate residual shunt may be seen in up to 10% to 30% of patients immediately after device release. With progressive endothelialization of the devices, closure rates reach 92% to 99% after a year of follow-up, higher for the Amplatzer device and smaller defects. Due to its non–self-centering mechanism, residual leaks are more frequently observed with the Halex device. The vast majority, if not all, of these residual leaks seen with either device, however, are trivial or small in size (<3–4 mm) and do not result in any hemodynamic burden to the RV. Therefore, clinical cure is achieved in virtually 100% of patients.

Several publications showing long-term outcomes after ASD-II closure in children and adults have confirmed the safety and effectiveness of the procedure. Successful interventions associated with high closure rate and improvement in both RV dilatation and supraventricular arrhythmias are commonly reported. Moreover, a recent analysis of the FDA Manufacturer and User Facility Device Experience (MAUDE database) revealed that there was no difference between clinical outcomes and overall mortality comparing surgical and device closure.

Device embolization was the most prevalent adverse event for the percutaneous procedure, with an estimated rate between 0.55% and 0.62%. A report showing long-term outcomes (5–20 years) after surgical or device ASD-II closure was recently published. Outcomes for either method were excellent and no significant differences were found with regards to survival, functional capacity, atrial arrhythmias, or embolic neurologic events. Age and pre-existing arrhythmia, but not surgery or percutaneous closure, were identified as independent risk factors for late arrhythmia.

Patients with ASD-II associated with pulmonary arterial hypertension constitute a challenging group to manage. The clinical outcomes in 54 patients with moderate or severe pulmonary arterial hypertension who underwent successful device implantation for ASD-II closure have been recently examined by the group in Toronto. During early follow-up, all patients were alive and the RV systolic pressure decreased significantly. At the late follow-up, 2 patients had died and the baseline RV systolic pressure continued to decrease significantly. Nevertheless, only 43.6% of patients had normalization (<40 mm Hg) of RV pressure during the last clinical visit. In patients showing severe pulmonary arterial hypertension with a partial fall of pressure after compliant balloon occlusion test, implantation of a homemade fenestrated Amplatzer septal occluder device has been reported to decrease the left-to-right shunt and promote further decrease of pulmonary arterial pressure in the long-term.
The diameter of the modified fenestration decreases significantly in size during follow-up, although applying this technique to the selected patients avoided acute decompensation and benefit from gradual diminution of RV volume overload. Additionally, the group in Mexico showed that the efficacy for ASD-II closure was similar in both a percutaneous and a surgical group, although a higher rate of events was significantly associated with age greater than 40 years, pulmonary arterial hypertension, and low oxygen saturations.

Perhaps the elderly patients with ASD-II are the ones who are at a higher risk of surgical complications and may benefit from the interventional procedure the most. In this regard, a group in Edmonton, Canada, has recently reported the clinical outcomes after device (81%) or surgical (19%) ASD-II closure in such groups of patients (older than 60 years). During follow-up (3.3 years), the quality of life was comparable to age-matched healthy controls, and RV and left ventricular end-diastolic dimensions, RV function, and New York Heart Association class showed significant improvement ($P<.001$) in both groups. The prevalence of atrial arrhythmias, however, was unchanged. Morbidity was higher for the surgical group (23% vs 7%).

Although chronic right heart volume overload and right heart failure are abolished over time after transcatheter closure of ASD-II, acute pulmonary venous congestion may be occasionally observed in older patients with large defects immediately after device closure. The main mechanism of this complication is probably an age-related left ventricular diastolic dysfunction, although other factors, such as left systolic dysfunction, ventricular wall and vascular stiffening, and increased incidence of comorbidities (diabetes, systemic hypertension, and coronary artery disease), may also play a role. The resultant effect of ASD closure is an acute volume loading of the noncompliant left chambers and subsequent pulmonary edema, which may require positive pressure ventilation for 24 to 48 hours until it subsides. Accurate assessment of preclosure diastolic function, especially after test ASD-II occlusion to unmask possible abnormalities, may help identify high-risk patients for postclosure pulmonary edema. Anticongestive therapy (dopamine, milrinone, and furosemide) for 48 to 72 hours before definitive device closure or the use of fenestrated device seems effective in preventing this complication in high-risk patients. Long-term outcome of such patients needs further studies.

In conclusion, excellent quality of life, functional class improvement, and ventricular remodeling are the rule after percutaneous ASD-II closure.

COMPLICATIONS AND CONCERNS

Both pivotal studies for the FDA-approved devices (Amplatz Septal Occluder and Helex Septal Occluder) showed that the rate of major adverse events was lower in the device group compared with the surgical group. The Mid-Atlantic Group of Interventional Cardiology (MAGIC) reported the results of unrestricted multiinstitution routine use of an ASD device in 478 patients from 2004 to 2007. This ASD study showed a major adverse event rate of only 1.1%. Although these complications are rare, they can be life threatening (discussed later).

MALPOSITION AND EMBOLIZATION

The major adverse events attributed to the transcatheter group in the pivotal Amplatz Septal Occluder study included device embolization requiring surgical (0.7%) or percutaneous retrieval (0.2%). In the pivotal Helex Septal Occluder study, device embolization also represents the most frequent major adverse events (1.7%). If an embolization does happen, devices can usually be retrieved from the heart using transcatheter techniques, with the exception of devices that are entangled with the tricuspid or mitral valve chordae. Surgical removal is recommended in such cases. The overall published embolization rate is approximately 0.55% and the mortality rate for surgical management of a device adverse event increases to 1.8% to 2.6%. Most embolizations occurred because of inadequate rim or undersized devices. Among the various causes of device embolization, the most common is the absence or inadequacy of an inferior vena cava rim. Large and eccentric defects, other rim deficiencies, and technical problems during the procedure (improper sizing of the defect and suboptimal placement of the device) are also risk factors related to embolization. More than 90% of these events occur within the first 24 hours of implantation, typically while the patients are being observed in the hospital setting, although late embolizations have been reported. Because of its design and configuration, the Helex device is, perhaps, the easiest device to be retrieved using snare and biotomes.

DEVICE MALFUNCTION (EROSION/PERFORATION AND FRACTURE)

Injury to either the atrial wall or the aorta has been described as a consequence of device implantation in the interatrial septum. The mechanisms of device erosion/perforation after ASD-II device implantation have not been established with
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certainty, but several clinical observations merit discussion. In 2002, AGA Medical Corporation focused on the issue of cardiac perforation and selected an expert panel to review all cases of hemodynamic compromise after device implantation with the objective of dictating recommendations to minimize its occurrence. The incidence of device erosion was 0.1%. Twenty-eight cases were reported to AGA Medical Corporation and all erosions occurred at the dome of the atria, near the aortic root (5 involved perforation of the roof of the left atrium and the aorta, 6 involved perforation of the roof of the right atrium and the aorta, both atria were involved in 1 case, no atrial perforation in were involved in 3 cases, and, in 3 cases with aortic perforations, a fistulous communication was noted). Deficient aortic rim was seen in 89% and the defect was described as a high ASD-II, suggesting deficient superior rim. Device to unstretched ASD ratio was significantly larger in the adverse event patients. The panel concluded that a deficient aortic rim and/or superior rim, an overstretching during balloon sizing, and use of oversized devices were all possible risks factors for erosion. Nevertheless, other poorly understood mechanisms of erosion may also play a role and may include older age, extensive device manipulation during prolonged procedures, and alternative techniques to anchor the device (coming from pulmonary veins).

A retrospective review of all adverse events reported to the FDA (MAUDE database) and Health Canada published in the literature, including a review presented by Divekar and colleagues, found 24 cardiac perforations occurring early in 20.8% and late in 66.6%. Five events occurred within 1 day, 10 within 3 days, and 6 after 3 days (3 weeks to 3 years). Cardiac perforation occurred predominantly in the anterosuperior atrial walls and/or adjacent aorta. The relationship of device size, patient size, or atrial dimensions have not been clearly associated with the occurrence of device erosion. What is unknown is the extent of rim deficiency that would result in an insecure placement and whether this contributes to erosion risks. The most important action to minimize future risks of this adverse event is to identify high-risk cases, alert for early recognition of complications, and prompt adequate intervention.

Alternatively, wire frame or wire wings/arms fractures are potential structural problems in other types of devices. This complication has been reported for the Clamshell family of devices, the Helix device, and the Solysafe device and has occurred even after some modifications were implemented to overcome this problem. The incidence of wire frame fracture for the more compliant and less rigid Helix device was approximately 6.4% and it was most commonly observed in larger devices. Although this is usually benign, mitral valve perforation by a fractured wire has been reported. Because wire fracture on the Solysafe device could lead to cardiac perforation and tamponade, this device was withdrawn from the market recently.

ARRHYTHMIAS

Conduction abnormalities and new-onset arrhythmias are some of the most important complications after device insertion, most frequent in the adult population, with an estimated incidence of approximately 1.5% of the patients. Whether conduction abnormalities and new-onset arrhythmias is caused or just triggered by the device in a subpopulation who already has an underlying anatomic substrate for this occurrence is debatable.

An acute increase in supraventricular ectopy and a small risk of atrioventricular conduction abnormalities, including complete heart block, has been rarely reported among patients undergoing ASD-II percutaneous closure. Occasionally, the use of larger devices in young patients may result in a higher than expected incidence of postprocedural heart block. The group at the Mayo Clinic, Rochester, Minnesota, has presented a study comparing ECGs registered before and after ASD-II or PFO device closure. Although uncommon, significant heart block episodes, changes in several markers of atrial conduction, and new-onset atrial tachyarrhythmias were found. Moreover, a low risk of clinically significant post-procedure arrhythmias suggesting an effect of device closure on intra-atrial conduction was encountered. It has been postulated that patients with prolonged PR interval before device closure are at a higher risk of developing complete heart block after the procedure.

In the majority of cases, the rhythm abnormality improves after the device is removed. It is recommended that a device should be electrically removed even if the heart block episode is intermittent. A large device related to the defect diameter seems associated to arrhythmias, suggesting mechanical compression of the disk as etiology of the complication.

THROMBOEMBOLISM

According to the published literature, the incidence of thrombus formation on closure devices is low, and if it does occur, usually resolves under anticoagulation therapy. In a major study presented by Krumsdorf and colleagues, a total of 1000
consecutive patients were investigated using transesophageal echocardiography after patent foramen ovale (PFO) or ASD-II closure at 1 and 6 months postprocedure. Thrombus formation was detected in 1.2% of the ASD-II patients and in 2.5% of the PFO patients \( (P = NS) \). The majority of the diagnoses were made after the first 4 weeks. The incidence distributed by device type was 7.1% in the CardioSEAL device (NMT Medical, Boston, Massachusetts); 5.7% in the StarFLEX device (NMT Medical); 6.6% in the PFO-Star device (Applied Biometrics, Burnsville, Minnesota); 3.6% in the ASDOS device (Dr Ing, Osypka Corp., Grenzach-Wyhlen, Germany); 0.8% in the Helex device (W.L. Gore and Associates, Flagstaff, Arizona); and 0% in the Amplatzer device (St Jude Medical, St Paul, Minnesota). A prethrombotic disorder as a possible cause of the thrombus was found in 2 PFO patients. Postprocedure atrial fibrillation and persistent atrial septal aneurysm were shown as significant predictors for thrombus formation \( (P<.05) \). In the vast majority of patients, the thrombus resolved under anticoagulation therapy using heparin or warfarin.

Also, periprocedural events with detection of acute thrombi formation in both the device and the sheath have been described, despite proper preprocedural anticoagulation.\(^{61,62}\) Meticulous flushing of catheters and sheaths is imperative to avoid this complication.

Finally, a routine and standard cardiac catheterization should be performed before devices are implanted. As such, it has the potential of causing some complications, including hematoma formation, vascular damage, air embolism, catheter-related arrhythmia, pericardial effusion, and/or tamponade and infection. The occurrence of these events is low and may need a specific treatment.\(^{63,64}\)

**FUTURE CONSIDERATIONS**

During past decades, there has been a great deal of effort to design and develop the "perfect" device for ASD-II closure. Ideally, this device should be easy to implant and retrieve, show 100% closure rate and no potential for erosion or embolization, require small-size sheath for implantation, and maintain a low profile in the atrial septum as well as be manufactured in biocompatible and bioabsorbable\(^{55-57}\) materials to optimize biologic response and mechanical integrity. Alternative methods of device fixation that do not rely on device dimensions exceeding the defect itself for closure would also be beneficial. The years to come will surely witness the application of new technologies for the imaging diagnosis and treatment of ASD-II. Evolving imaging technology will be applied not only for the accurate diagnosis of all types of ASDs but also mainly for the guidance of transcatheter closure. Real-time 3-D intracardiac echocardiography will probably be helpful in this regard. MRI-guided interventions is an exciting field that may have an impact on abolishing the need for radiation exposure in the catheterization laboratory for ASD-II closure. With the rapid development of new devices to close the left atrial appendage in high-risk elderly patients with atrial fibrillation and to repair functional mitral valve insufficiency percutaneously, the development of devices manufactured using bioabsorbable materials is of paramount importance to allow free transseptal access to the left atrium in the future.

**SUMMARY**

ASD-II closure has evolved from a surgical procedure requiring cardiopulmonary bypass to a percutaneous, catheter-based procedure usually requiring only an overnight hospital stay. The overall safety and effectiveness have compared favorably with surgical repair. Although rare, complications have been described, including device embolization, malfunction, and arrhythmias. The overall long-term clinical outcomes have been excellent: good quality of life, functional class improvement, and ventricular remodeling have been the rule after the procedure. It is mandatory to recommend indefinite follow-up of patients undergoing this procedure for potential long-term complications.

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