Clinical Insights

SUMMARY OF CLINICAL DATA

RECENT INSIGHTS INTO A RARE COMPLICATION

CARDIAC EROSION AFTER ASD CLOSURE WITH THE ASO DEVICE: OVERVIEW OF RECENT LITERATURE

KEY MESSAGES

- Risk factors for erosion may be anatomical (severely deficient or absent aortic rim), technical (device oversizing) or device related (device stiffness, especially with an oversized device).
- Cardiac erosion after ASD closure is a rare complication, with a current estimated incidence between 0.1% – 0.3%. Addressing various anatomical and technical risk factors can further reduce occurrence, however if event does occur and if treated promptly, virtually all erosion cases have a favorable outcome after surgery.
- The risk of cardiac erosion is mitigated by using intraprocedural echocardiography and detailed defect evaluation. Appropriate device sizing, facilitated by the large number of different ASO device sizes, is crucial for risk reduction.
- Currently, physicians are well aware of the risk of cardiac erosion after ASD closure and the importance of prompt surgical treatment.

PURPOSE

Cardiac erosion is a rare complication after closure of a secundum atrial septal defect (ASD). The purpose of this review is to present the current knowledge and status regarding this complication with the Amplatzer Septal Occluder (ASO) device, based on data recently published in the scientific literature (i.e., 2010 – 2020). It will discuss the incidence and outcomes of cardiac erosion after ASD closure, as well as the current awareness among physicians of this complication and its prompt, surgical treatment. The review will also provide a summary of risk factors and suggested mitigations reported in the literature. While this review is aimed at providing a representative and unbiased overview of the recent literature on the key aspects of cardiac erosion after ASD closure, it should not be considered an exhaustive discussion of all specific details and aspects of this complication.

INTRODUCTION

Percutaneous, catheter-based closure is an established first-line treatment for secundum atrial septal defects (ASD) in adult and pediatric patients. Benefits of percutaneous ASD closure over surgery include elimination of the need for cardiopulmonary bypass and sternotomy, shorter hospitalization and potentially lower incidence of postprocedural complications[1]. Currently, cardiac erosion is a rare complication after ASD closure with usually favorable outcome if treated promptly. Based on increased experience and widespread clinical application with ASD closure, physicians are well aware of the low, but clinically relevant risk of cardiac erosion. Potential risk factors for this complication have been identified and the importance of prompt surgical treatment is emphasized in the literature.

INCIDENCE AND OUTCOMES

Early reports

While not observed in the approval study for the Amplatzer Septal Occluder (ASO) device (442 patients undergoing ASD closure followed up to 24 months)[2], cardiac erosion was reported as a rare complication during the ASO post-approval study (1000 patients followed up to 2 years)[3] and subsequently from widespread device application and increasing clinical experience. A comprehensive report on cardiac erosion associated with the ASO device was published by Amin et al. in 2004[4]. Of the 28 cases reported to the manufacturer, 9 confirmed cases occurred in the United States, representing an estimated incidence in the US of 0.1% of the total number of implanted devices. Other publications[5,6,7] prior to 2010 and reporting on events recorded in the FDA MAUDE database indicated incidence rates of cardiac perforation or erosion ranging between 0.05% and 0.28%. Early cases of cardiac erosion were associated with a relatively high risk of mortality, with death rates reported to be as high as almost 20%[7]. Most cases occurred early after device implantation (68% within 72 hrs[4], 61% within 1 month[7]) although some events (4% – 6%) were reported to occur at more

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than 1 year post-implant[4,7]. FDA MAUDE data[8] and pooled data from the ASO post-approval study, product surveillance complaints and events identified from the literature[9] indicated that approximately 7% – 8% of documented cases of erosion had a fatal outcome, while in more than 90% of cases a favorable clinical outcome occurred following surgical intervention. Of note, while these reports were published starting in 2010, most of the included data were collected between 2002 and 2010. In addition, it should be noted that early reports utilized variable terminology including terms like perforation, hemopericardium and fistula formation, which may be related to acute events (e.g., intraprocedural perforation by the device delivery system or guidewires) which were incorrectly classified as erosion events[10]. Recent reports Table 1 provides an overview of recent publications (2010 – 2020) explicitly referring to cardiac erosion after ASD closure with the ASO device. While not claiming to provide a full, comprehensive overview of the literature, these publications were identified by a systematic, literature search and are considered to provide a cross-section of the literature on this topic.

TABLE 1: LITERATURE OVERVIEW: RELATIVELY LARGE STUDIES ON ASO DEVICE PUBLISHED BETWEEN 2010 AND 2020 AND EXPLICITLY REPORTING ON CARDIAC EROSION

STUDY	PATIENTS*	FOLLOW-UP**	DETAILS ON EROSION
Almanla[11] 2019	219	23.5 ± 28.4 months	No case of erosion.
Dalvi[12] 2017***	87	44 ± 15.7 months	No case of erosion.
Jalal[13] 2018	1,326	Median: 3.5 yrs (0.5 – 18 years)	No observation of acute or delayed cardiac erosion.
Kadirogullari[14] 2020	245	22.1 ± 2.5 months	No cases of aortic root erosion.
Kijima[15] 2016	474	25 ± 19 months	1 case of erosion at 3 days post-implant. Emergency surgery for device removal and ASD closure. Uncomplicated hospital discharge.
Kim[16] 2019	98	Median: 29 months (15 – 37 months)	No case of erosion.
Knepp[17] 2010	94	Median: 73 months (63 – 120 months)	No confirmed cases of erosion. 1 patient had hemorrhagic pericarditis 9 months after implantation with no signs of erosion. Drainage with device left in place, patient recovered completely.
Mitchelson[18] 2017	517	≥12 months	1 case of erosion at 8 days post-implant. Surgery for device retrieval, repair of perforation and ASD closure. Unremarkable recovery without long-term sequelae.
O'Byrne[19] 2014	271	Median: 5.8 years (12 days – 12.6 years)	No case of erosion.
Rigatelli[20] 2019	251	10.3 ± 3 years	No aortic or atrial free wall erosions occurred.
Sadiq[21] 2012	205	Median: 5.8 years (0.5 – 10.3 years)	No case of erosion. In 1 patient, echocardiography after the procedure showed a small pericardial effusion, but transesophageal echocardiography confirmed no evidence of perforation or erosion.
Saritas[22] 2013	166	40 ± 15 months	No erosion into aortic wall.
Takaya[23] 2020	103	Not reported	No case of erosion.
Turner[3] 2017****	1000	2 years	3 cases of erosion at 12, 67 and 171 days post-implant. No erosion events resulted in death.
Ueda[24] 2012	203	2.4 ± 1.3 years	No cases of erosion.

Notes:
* Implanted (or implant attempted) with ASO device. Studies may have used several devices, only data from the ASO device are included.
** Mean ± standard deviation, unless indicated otherwise
*** Closure of large ASDs using the 40 mm ASO device
**** Post-approval study for the ASO device.

Overall, these studies reported 5 cases of cardiac erosion from a total of 5,259 patients (0.1%). As far as reported, erosion involved protrusion into the aortic wall[15] with perforation of the posterior aortic wall and/or the anterior roof of the left atrium[18]. Two of the 5 patients showing erosion were reported to have a deficient aortic rim. Events were resolved by urgent or emergency surgery to remove the device, repair the perforation and close the septal defect. No fatalities or permanent neurologic consequences were reported among the 5 erosion cases. Many other studies enrolling cohorts ranging between approximately 100 and 250 patients and with follow-up of 6 months to 10 years reported that no cases of cardiac erosion were observed[11,12,14,16,17,19-25]. On the other hand, cardiac erosion after ASD closure with the ASO device is reported by several case reports. Reported cases occurred during implantation as well as at various intervals after ASD closure, up to 15 years post-implantation[26]. In addition, Kitano et al.[27] reported on 12 cases of cardiac erosion associated with the ASO device that occurred in Japan between 2005 and 2016. In almost all reported cases, surgery was performed to resolve the event, typically with acceptable outcome.

An analysis of reports submitted to the FDA MAUDE database between 2012 and 2018 identified 83 erosion events associated with the ASO device[10], of which 4 cases were associated with a patient death. The absolute number of annually reported cases declined to 5 cases reported in 2015, followed by an increase to 16 in 2018. Device sizes most frequently associated with erosion included the 18 mm, 20 mm, 24 mm, 26 mm and 28 mm devices, which in total accounted for 60% (n = 50) of the cases. As noted by the authors, the number of erosion events could not be related to the total number of device implantations. This prevents further interpretation of temporal trends and estimation of the actual risk. Nevertheless, considering that ASD closure with the ASO device is standard of care and widely available worldwide, it was concluded that the absolute number of events during the 7-year review period was relatively low. All erosions described in the literature occurred at the same location, i.e., the anterior-superior region of the free wall of the left and/or right atrium. This area is in proximity of the ascending aorta or aortic sinus. The aorta is separated from the free wall of the left and right atrium by the transverse sinus which is a free space contiguous with the pericardial cavity. In susceptible cases, the edge of the device tents the free wall of either the left or right or both atria and it protrudes into the transverse sinus. If the edge of the device and atrial free wall are immediately adjacent to the ascending aorta, the protruded edge may rub on the aorta and cause injury. Pericardial effusion without tamponade is reflective of atrial free wall tear. Tamponade is reflective of aortic tear in addition to atrial free wall tear. Rarely, an atrial free wall tear occurs below the pericardial reflection. When this happens, the device edge injures the aorta directly and creates a fistulous connection between the respective atria and the aorta. In such cases, as expected, there is no pericardial effusion.

Summary

Based on the totality of available clinical data, cardiac erosion associated with the ASO device occurs at an estimated rate between 0.1% and 0.3%. Cardiac erosion is most frequently seen within days or months after implantation, but may occur at many years after ASD closure. While early data sets showed a 7% – 8% mortality rate among patients with cardiac erosion, more recent literature indicates that with increased physician's awareness and prompt treatment, virtually all erosion cases have a favorable outcome after surgery.

RISK FACTORS

Erosion after ASD closure is a multifactorial process and the identification of individual risk factors is impeded by the low incidence rate of this complication. Nevertheless, several risk factors have been described in the literature. Table 2 lists potential risk factors that are frequently mentioned in the literature.

TABLE 2: POTENTIAL RISK FACTORS FOR CARDIAC EROSION[9,28,29]

RISK FACTOR	DESCRIPTION
Anatomical risk factors: • Deficient aortic and/or superior rim • Thin, flimsy, flailing posterior rim (if aortic rim absent) • SVC rim deficiency (if aortic rim absent)	Severely deficient or absent aortic rim, in multiple views of short axis rim interrogation. Nearly all erosions have been in patients with a deficient aortic rim, which is present in ~25% – 50% of patients undergoing ASD closure. The absolute risk of erosion in patients with a deficient aortic rim is 2–4–fold higher than in the general ASD population, although still <1% and potentially <0.1%[9].
Technical risk factors: • Aggressive balloon sizing • Insertion of an oversized device	A device size >5 mm larger than the static ASD diameter was significantly associated with cardiac erosion (p=0.036)[9]. An oversized device may protrude into vulnerable tissue and eventually cause erosion.
Device-related risk factors • Certain devices may have a higher risk of erosion[1,8]	Device stiffness may increase the risk of erosion, especially when the device is oversized.
Other factors possibly increasing the risk of erosion include: - Rotation of the device and dynamic defect: abrasion effect of the device exerted onto the adjacent cardiac tissue. An associated factor may be an ASD that changes in size with the cardiac cycle. - Septal malalignment[30] - Flaring of the device around the aortic root[1] - Valsalva sinus wall deformation perpendicularly pressed by the edge of the disc of the occluder[31] - Procedure-related aspects, such as multiple attempts to deploy the device[28]. This may cause atrial trauma related to multiple catheter manipulations, rather than to the occluder itself. - Patient age: Not completely understood. The incidence of erosion and associated mortality appear to be higher in adults compared to pediatric patients. Tissue rigidity may be a factor.	

Rim deficiency is a predominant anatomic aspect associated with erosion after ASD closure[4,9]. Atrial septal defects are frequently associated with rim deficiencies, with a prevalence up to 70% – 80% for relatively large ASDs[28]. While deficiency of the aortic rim is a frequent finding in erosion cases[9,31], deficiency of any rim (i.e., aortic, superior or inferior vena cava) was also significantly associated with erosion[9]. On the other hand, the presence of rim deficiency alone does not seem to be a sufficient condition to cause

erosion. For instance, in the study reported by Kijima et al.[15], 68% of the 474 patients had a retro-aortic rim deficiency while erosion occurred in only one of these patients. A deficient rim smaller than 5 mm is included in the contraindications of the ASO device[32]. Device oversizing is another potential risk factor for erosion[9], underlining the importance of appropriate device sizing.
As recommended by Abbott, the appropriate device size should be determined intraprocedurally, based on echocardiographic measurements and balloon sizing, using the stop-flow technique (i.e., inflation of a sizing balloon until left-to-right shunting ceases)[32]. In a relatively small cohort[33], measurement of the ASD diameter by color flow Doppler echocardiography was shown to be safe and feasible, resulting in appropriate device sizing consistent with balloon sizing.

MITIGATIONS

Several measures to mitigate the risk of erosion have been proposed in the literature [see Table 3].

TABLE 3: EROSION RISK MITIGATION MEASURES PROPOSED IN THE LITERATURE[1,28,33,34]

Pre-implantation echocardiography	Thorough and accurate delineation of the relevant anatomy. Main pre-implantation echocardiographic risk factors include the absence of the aortic rim in multiple views, a poor posterior rim consistency, a septal malalignment, and a dynamic ASD (defined as at least 50% decrease in size of the ASD during atrial systole).
Device sizing	Echocardiographic measurements and balloon sizing, using the stop-flow technique. Avoid enlarging / stretching of the defect during balloon sizing, as this may lead to device oversizing. The ASO device is available in many sizes (4 – 40 mm waist diameter, with 1 or 2 mm increments), allowing for precise device sizing.
Echocardiography after device placement (to inform decision to release the device)	Echocardiographic predictors of erosion after device placement include tenting of the atrial free wall into the transverse sinus caused by the edge of the device, wedging of the discs into the posterior wall of the aorta, and early pericardial effusion. Establish that the device is not unduly affecting the natural anatomy of the heart, e.g., exerting repetitive compressive force on the aorta.
Follow-up	Frequent follow-up after ASD closure during the first year (1 day, 1 week, 1 month, 6 months, 1 year) and life-long regular follow-up thereafter.
Patient education	Ensure that patients are informed of risks and benefits of the procedure. Educate patients with regard to symptoms that may represent early signs of erosion and/or require emergent treatment.

These protective measures underline the importance of intraprocedural echocardiography and appropriate device sizing (using the large variation in ASO device sizes) as crucial factors to reduce the risk of cardiac erosion after ASD closure. Early detection of erosion and prompt resolution relies on regular follow-up and patient awareness.

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