Infective Endocarditis After Percutaneous Device Closure of Atrial Septal Defects: Incidence, Diagnosis, and Treatment. Case Report and Literature Review

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ABSTRACT

Infective endocarditis (IE) on atrial septal defect (ASD) closure devices, while extremely rare, has been reported to be more frequent early after the procedure. We describe a case of late IE after percutaneous closure of patent foramen ovale (PFO). We also performed a literature review on this subject.

We reviewed a total of 42,365 patients who were treated with percutaneous devices: 13,916 for ostium secundum (OS) (32%), 24,726 for PFO (58%) and 3,723 for OS+PFO (8%). Among these patients, we identified 50 cases of IE after atrial septal defect device closure (0.001%).

In contrast to previous reports, nearly 66% of IE in this setting occurred late, after at least 6 months from the procedure (33/50 patients). A statistical analysis clearly showed that the mean time from the procedure to IE increased in the last five years, probably associated with a change in antiplatelet therapy after ASD closure. Management of IE on an ASD occluder should always be discussed in the setting of a multidisciplinary heart team that includes a cardiologist, cardiac surgeon, and anesthetist. While surgical strategies gave excellent results, conservative management might be considered in cases of small IE vegetations and for patients in good general condition. However, in these cases, the patient must be closely observed with repeated blood and instrumental tests.

INTRODUCTION

Infective endocarditis (IE) is a relatively rare disease with an incidence of <10 cases/100,000 person-years. Despite early diagnosis and prompt treatment, IE is associated with high morbidity and mortality.[1-4] The causes and epidemiology of this disease have evolved in recent decades, with doubling of the average patient age and an increased incidence in patients with indwelling cardiac devices.[5] Among the major risk factors for IE, degenerative valve disease, diabetes, cancer, intravenous drug use and congenital heart disease have become more prevalent than rheumatic heart disease in high-income countries.[5] Furthermore, healthcare-acquired IE accounts for 25–30% of contemporary cohorts.[5] Transient bacteremia, which occurs in a wide variety of procedures and manipulations associated with mucous membrane trauma, as in the setting of poor oral hygiene and periodontal disease, or in the course of normal daily activities (e.g., tooth brushing), may play a role in some cases of IE.[6]

Although people who use injectable drugs are at higher risk for IE, this is only considered to be a "minor indicator" of disease by the modified Duke's criteria.[7]

Despite the increased prevalence in patients with all types of devices, IE on atrial septal defect (ASD) closure devices is extremely rare and is reported to be more frequent early after the procedure.[3,8]

We describe here a case of late IE after percutaneous closure of PFO. We also performed a literature review on this subject.

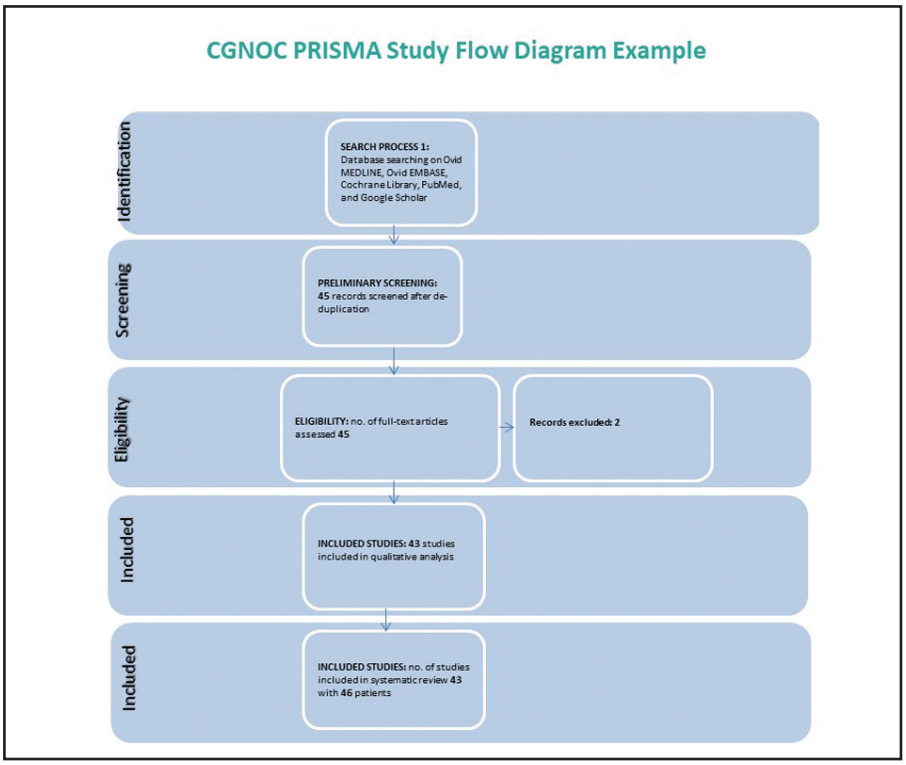


Figure 1. PRISMA Flowchart of case selection according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. A comprehensive systematic search was performed to identify studies on infective endocarditis on Amplatzer (IE). Ovid MEDLINE (in-process and other nonindexed citations and Ovid MEDLINE 1946 to present), Ovid EMBASE (1974 to present), as well as The Cochrane Library (Wiley), PubMed, and Google Scholar databases were searched from their inception to June 2021 using keywords and MESH terms "atrial septal defect", "endocarditis", "catheter device endocarditis", "device closure endocarditis", "patent foramen ovale endocarditis" or "PFO", "ASD", "Amplatzer", "ASO", "STARFlex", "CardioSEAL", "interventional catheterization" and "infective endocarditis". In total, 47 papers that included 50 patients and a total of 50 IE cases met the eligibility criteria.

MATERIALS AND METHODS

A systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-

Analyses (PRISMA) statement. We identified 49 eligible papers that included 51 patients with ostium secundum (OS)/patent foramen ovale (PFO) closure-related endocarditis. The following data were collected: patient sex and age at the time of diagnosis; time interval between ASD closure and endocarditis; eventual residual shunt, symptoms at presentation; diagnosis and germ involved; treatment and management strategy; peri-operative outcomes; and device endothelialization.

Search strategy

A comprehensive systematic search was performed to identify studies on IE. Ovid MEDLINE, Ovid EMBASE, as well as The Cochrane Library (Wiley), PubMed, and Google Scholar databases were searched from their inception to June 2021 using the following keywords and MESH terms: "atrial septal defect", "endocarditis", "catheter device endocarditis", "device closure endocarditis", "patent foramen ovale endocarditis" or "PFO", "ASD", "Amplatzer", "ASO", "STARFlex", "CardioSEAL", "interventional catheterization" and "infective endocarditis" in combination (Fig. 1).

Study selection and inclusion criteria

To eliminate data duplication, a comprehensive search was performed by 2 reviewers (WV and MDA) for the preliminary inclusion in the study. A third independent reviewer (ADL) confirmed the adequacy of abstracts based on predefined inclusion criteria. We did not set any restrictions on the study setting, year, place, or language on the first screening. We included pediatric and adult patients who were treated for OS and/or PFO closure, excluding other indications. Studies identified during title or abstract screening were included for full-text review.

A second round of eligibility screening was applied to the retrieved full text. In their meta-analysis and review, Butera et al.[9] reported 1,812 patients with OS/PFO treated with percutaneous devices and 1,270 treated surgically, and only identified a single case of IE in the surgical series, and was therefore not considered in our analysis. One case report was not included because it was written in Russian.[10]

Statistical analysis

All statistical analyses were performed using MedCalc Statistical Software version 15.8 (MedCalc Software bvba, Ostend, Belgium; 2015). We created a distribution plot to compare the range and distribution of numerical data in the different groups. A Kruskal-Wallis test was used to compare the time between the interventional procedure and endocarditis presentation.

CASE REPORT

A 31-year-old man presented with worsening fever and cough associated with left knee swelling that was not responsive to steroid therapy. He had a history of drug abuse and was on antiretroviral therapy for HIV. Three years previously he had undergone PFO closure with an Amplatzer device (Abbott Structural Heart, Plymouth, MN).

On physical examination, there was a widely harsh vesicular murmur with right basal hypophonesis, tachycardia and swelling of the right knee with functional impotence.

A methicillin-sensitive Staphylococcus aureus was isolated from blood cultures. Left leg magnetic resonance imaging (MRI), lumbar MRI and total body computed tomography (CT) showed spots of infective embolism disseminated throughout the body, the lung and multiple abscess collections with a necrotic core in the left leg. Transesophageal echocardiography showed multiple formations on the right side of the inter-atrial septum in an area corresponding to the previously implanted closure device and floating into the right atrium up to the tricuspid orifice (maximum size 5 x 0.6 cm); the left side of the inter-atrial septum appeared to be free from vegetation and completely covered by a thin layer (thickness about 3 mm) of tissue. He started a target antibiotic therapy with piperacillin/tazobactam and teicoplanin, which was switched to daptomycin and amikacin for persistent fever.

The patient underwent high-risk cardiac surgery for Amplatzer® removal and subsequent repair of the atrial defect. After median sternotomy and cardiopulmonary bypass, the right atrium was opened and an extensive vegetation of 3.5 mm was removed, including the previously implanted device (Fig. 2).

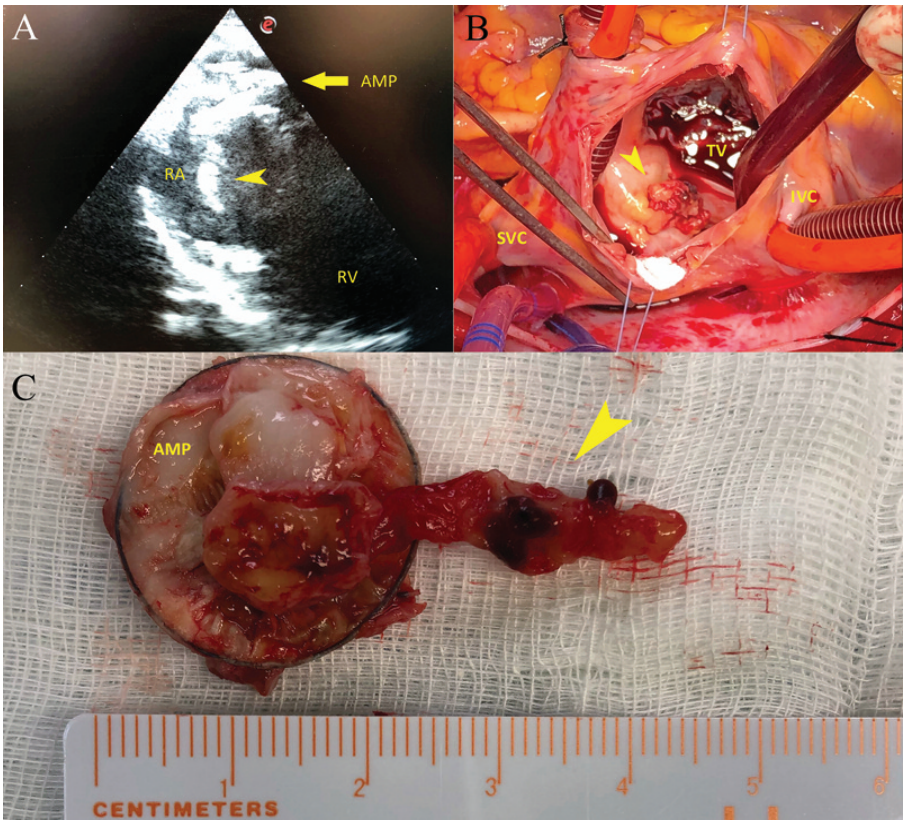


Figure 2. Echocardiographic and operative images. A) Pre-operative transesophageal echocardiographic findings, in TransGastric RV inflow, of infective endocarditis (arrowheads) adherent to the body of the Amplatzer (AMP) projecting into the right atrium. It commits the tricuspid valve in systolic movement without adhesion to it. RA, Right Atrium; RV, Right Ventricle. B) Surgical view of the endocarditis (arrowheads) from a right atrium approach in bicaval cannulation. SVC, Superior Vena Cava; ICV, Inferior Vena Cava; TV, Tricuspid Valve. C) Surgical sample of endocarditis (arrowheads) adherent to the removed Amplatzer (AMP).

Table I
Review of all cases of infective endocarditis

Author	Year	Study	N	CHD	Device	Time Interval	Residual Shunt	Principal Symptom at Presentation	Emboli	Treatment Patch	Endothelialization	Vegetation
Sievert[12]	1998	FUC	1/46	PFO	ASDOS	2 Weeks	No	Septic Embolism	Yes	Undetermined Patch	-	-
			1/154	OS	ASDOS	6 Months	Yes	Pneumonia, Pleural Effusion,	No	Homologous Patch		No
Wilkinson[16]	1998	CR	1	OS	ASO	2 Months	No	Septicaemia	---	Surgical Removal	-	---
Bullock[17]	1998	CR	1	OS	ASO	1 Month	No	Fever	No	Autologous Patch	----	
Goldstein[50]	2002	CR	1	PFO	CardioSEAL	10 Weeks	No	Fever, Fatigue	No	Autologous Patch		
Calachanis[18]	2004	CR	1	PFO	CardiaStar	2 Days	No	Low-Grade Fever	No	Antibiotic Therapy	Complete	LA
Balasuundaram[19]	2005	CR	1	OS	ASO	3 Months	No	Sepsis	No	Undetermined Patch	----	
Divchev[20]	2007	CR	1	PFO	STARFlex	6 Months	No	Paroxysmal Palpitations	No	Surgical Removal		
Slesnick[21]	2008	CR	1	OS	ASO	1 Year	---	Sepsis	Yes	Autologous Patch	Poorly	
Zahr[22]	2010	CR	1	OS	ASO	30 Months	---	Fever		Undetermined Patch		
Stöllberger[23]	2011	CR	1	OS	ASO	7 Years	---	Fever, Erysipelas	Yes	Antibiotic Therapy		---
Doguet[24]	2011	CR	1	PFO	ASO	3 Months	---	Fever	---	Autologous Patch		
Verma[14]	2011	FUC	1/13736	PFO	CardioSESAL		---	---		---	---	
Walpot[25]	2011	CR	1	PFO	Helex	9 Years	No	Fever, Malaise	Yes	Undetermined Patch		
Saguner[15]	2011	SCCC	1/40	PFO	Figulla	3 Months	---	Fever	No	Antibiotic Therapy		
Sadiq[13]	2012	FUC	1/205	OS	ASO	3 Months		Fever	No	Antibiotic Therapy		
Aruni[26]	2013	CR	1	OS	ASO	Late	---	Sepsis		Antibiotic Therapy	---	
Abaci[11]	2013	MA	3/28142	1 OS, 2 PFO	---	---	---	---	---	Autologous Patch	---	---
Krantz[27]	2014	CR	1	PFO	ASO	2 Years	---	Malaise + Low Grade Fever	Yes	Homologous Patch	Complete	
Iezzi[28]	2014	CR	1	OS	ASO	5 Years	---	Fever	No	Undetermined Patch	Incomplete	
Bialkowski[29]	2015	CR	1	OS	ASO	2 Years	---	Bacterial Meningitis	Yes	Pulmonary Homograft	Incomplete	LA
Jha[30]	2015	CR	1	OS	ASO	6 Years	---	Sepsis	Yes	Homologous Patch	Incomplete	

FUC, Follow-Up Cohort; CR, Case Report; SCCC, Single-Center Case-Control; MA, Meta-Analysis; ASDOS, atrial septal defect occluder system; RA, Right Atrium; LA, Left Atrium; OS, ostium secundum; PFO, patent foramen ovale; ASO, AMPLATZER Septal Occluder; CHD, congenital heart defect

Table I (cont)
Review of all cases of infective endocarditis

Author	Year	Study	N	CHD	Device	Time Interval	Residual Shunt	Principal Symptom at Presentation	Emboli	Treatment Patch	Endothelialization	Vegetation
Kim[51]	2015	CR	1	OS	ASO	4 Years	No	Fever, Janeway Lesions	Yes	Autologous Patch		LA, RA,
Thibodeau-Jarry[31]	2015	CR	1	OS	ASO	4 Years	---	Fever	Yes	Extracellular Matrix	Incomplete	Aorta
Nguyen[32]	2016	CR	1	OS	ASO	12 Years	---	Pharyngitis, Petechiae	No	Patch	Complete	
Toporcer[33]	2018	CR	1	OS	ASO	12 Years	---	Stenocardia, Fever	Yes	Autologous Patch	Incomplete	LA
Amedro[8]	2016	CR	1	OS	ASO	3 Years	---	Fever, Janeway Lesions	No	Undetermined Patch	---	
Sinning[34]	2016	CR	1	OS	---	15 Years	---	Spondylodiscitis, Fever	No	Antibiotic Therapy		LA
Kumar[35]	2017	CR	1	OS	Cocoon As	7 Months		Tachypnea, Tachycardia	No	Pulmonary Homograft	Complete	
Sharma[46]	2017	CR	1	PFO	CardioSEAL	11 Years	No	Fever	Yes	Autologous Patch		LA, RA,
Thiagarqaj	2017	CR	1	PFO	Helex	5 Years	---	Fever	No	Antibiotic Therapy	Incomplete	Mitral
Chien[49]	2018	CR	1	OS+Vsd	Figulla	1 Year	Yes	Fever	No	Undetermined Patch	Incomplete	
Yamaoka[47]	2018	CR	1	PFO	ASO	6 Years	---	Fever, Janeway Lesion	---	Undetermined Patch		
Morillo[36]	2019	CR	1	OS	ASO	6 Years	No	Recurrent Fever	No	Antibiotic Therapy		
Ng[37]	2019	CR	1	OS	ASO	9 Years	No	Fever	Yes	Antibiotic Therapy	---	LA
Alvi[38]	2020	CR	1	OS	Helex	7 Years	---	Respiratory Failure	---	Undetermined Patch	Incomplete	---
LA Sala[39]	2020	CR	1	OS	ASO	13 Years	No	Tachycardia	Yes	Device Preserved	Incomplete	
Tamura[40]	2021	CR	1	OS	Figulla	21 Months	No	Cerebral Infarction, Fever	No	Undetermined Patch		
Le Gloan[41]	2021	CR	1	OS	ASO	6 Months	Yes	Prolonged Fever	Yes	Antibiotic Therapy	Incomplete	
Naimi[42]	2021	CR	1	OS	ASO	2 Years	No	Fatigue, Intermittent Fever	No	Autologous Patch	Incomplete	LA, RA
Alvarez[43]	2021	CR	1	OS	ASO	15 Months	No	Fever, Atypical Chest Pain	No	Autologous Patch		---
Kitamura[44]	2021	CR	1	OS	ASO	3 Years	No	---	Yes	Homologous Patch	---	LA, RA
Sharma[45]	2021	CR	1	OS	ASO	7 Months	No	Fever, Janeway Lesions	No	Autologous Patch		RA
Gaibazzi[54]	2022	CR	1	PFO	ASO	11 years	No	--	No	Undetermined Patch	Incomplete	
Toyoshima[55]	2022	CR	1	OS	Figulla	3 months	No	Fever	Yes	Undetermined Patch	--	
Sanjuanelo[52]	2022	CR	1	OS	ASO	3 years	--	Right-sided weakness, Fever, Tachycardia	Yes	Antibiotic Therapy	Incomplete	--
Parekh[53]	2023	CR	1	OS	ASO	4 weeks	--	Fever, Janeway lesions	Yes	Undetermined Patch		
This paper	2023	CR	1	PFO	ASO	9 Years	No	Fever, Knee Swelling		Autologous Patch	Complete	LA

FUC, Follow-Up Cohort; CR, Case Report; SCCC, Single-Center Case-Control; MA, Meta-Analysis; ASDOS, atrial septal defect occluder system; RA, Right Atrium; LA, Left Atrium; OS, ostium secundum; PFO, patent foramen ovale; ASO, AMPLATZER Septal Occluder; CHD, congenital heart defect

Table II
Summary of data collected

Clinical data		
CHD	Ostium secundum ASD Patent Foramen Ovale	34/50 16/50
Age		10 months – 76 years
Sex	Male Female XXY	23 18 1
Device	Amplatzer CardioSEAL Figulla Flex II Helex ASDOS CardiaStar STARFlex Cocoon AS Device	31 3 4 3 2 1 1 1
	CardiaStar	1
Time interval (from procedure to endocarditis)		2 days – 15 years
Residual shunt	Yes No	4 23
Diagnosis	Culture (blood, urine, emboli) TEE TTE other (angiography, TC, serology test)	42 34 25 5
Emboli	Yes No	18 21
Surgical removal	Yes No	35 11
Endothelialization	Complete Incomplete	6 17
Vegetation	Yes No	42 4
Survival	Yes No	40 4

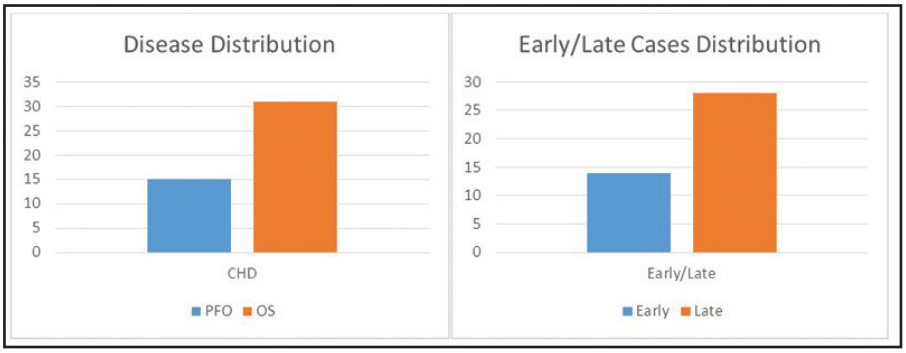


Figure 3. Distribution Plot. A) Congenital heart disease distribution in 15/46 (32%) cases following PFO closure and 31/46 (68%) following ASD closure; B) Early/late case distribution in 14/42 (33%) early cases and 28/42 (66%) late cases.

The remaining inter-atrial defect was repaired with an autologous pericardial patch.

The postoperative course was uneventful, with regression of symptoms and progressive reduction of the disseminated abscess collections. He completed his course of antibiotic therapy and was discharged home on day 40. At 6 months after the operation, he was free from symptoms and echocardiography signs.

RESULTS

We selected 47 studies on ASD device implantation, including a meta-analysis,[11] two follow-up studies,[12,13] a database review,[14] a single-center case–control study,[15] 41 case reports[8,16-55] and our patient.

Eventually, a total of 42,365 patients who had been treated with percutaneous devices, 13,916 for OS (32%), 24,726 for PFO (58%) and 3,723 for OS+PFO (8%), were included in our review. Among these patients, we identified 50 cases of infective endocarditis after atrial septal defect device closure (0.001%) (Tables I,II). Of the 50 cases identified, 16 (32%) were following PFO closure and 34 (68%) were following OS closure (Fig. 3A).

In their meta-analysis, Abaci et al.[11] reported 3 cases of IE among 28,142 patients (0.0001%), consisting of 2 PFOs and one OS closure. Sievert et al.[12] and Sadiq et al.[13] analyzed 200 and 205 patients, respectively, and together reported only 3 cases of IE: two after OS and one after PFO closure. Verma et al.[14] reviewed databases of patients treated for PFO at 18 western institutions and found one case of IE among 13,736 patients. Saguner et al.[15] compared two groups of 20 patients each who had been treated for PFO, and found one case of IE. The remaining cases were described as case reports: 31 cases of IE following OS and 11 following PFO closure. Among all of the patients, 16 cases occurred within 6 months from the implantation and 30 cases occurred after that period; IE was not reported in the remaining cases (Fig. 3B). The time from the procedure to diagnosis ranged from 2 days to 15 years. The patient age at diagnosis ranged from 10 months to 76 years. The indication for the initial procedure was specified in a total of 19 patients. The indication was for cerebral disease in 11 patients (11/19), moderate dimension of OS in 4, dyspnea in 2, poor weight gain and

recurrent lower respiratory tract infections in one, and moderate shunt in one. The presence of residual shunt as a risk factor for IE was reported in just four patients; it was not specified in 21 patients, and not present in the rest. The types of devices used were the Amplatzer® (AGA Medical, Golden Valley, MN, USA) in 31, CardioSEAL (NMT Medical, Boston, MA) in 3, Figulla Flex II ASD occluder (FPO, Occlutech, Jena, Germany) in 4, Helex (W.L. Gore & Associates, Flagstaff, AZ, USA) in 3, ASDOS (Sulzer, Winterthur, Switzerland) in 2, CardiaStar (Cardia, Burnsville, MN, USA) in one, STARFlex (NMT Medical, Boston, MA) in one, and a Cocoon AS device (Vascular Innovations Co., Nonthaburi, Thailand) in one; the device was not specified in 4 cases. Vegetations were detected echocardiographically on the left side of the device in 19 cases, on the right side in 5, and bilaterally in 9. In 2 patients they involved the mitral valve, tricuspid valve, and the septum bilaterally. The vegetation was near the tricuspid valve in one patient. It involved the left side, right side and outflow tract in one case, the left side and mitral valve in one, the left side, right side and aortic root in one, and both the left side and aortic valve in one. Vegetations were not present in 2 cases and their presence was not specified in 8 patients. The process of endothelization was described in 23 patients; endothelialization was absent or incomplete in 17 and complete in 6. Two patients were described as injectable drug users. Most patients (n= 35/50) underwent surgical procedures to remove the device after antibiotic treatment, 11 were only treated with antibiotics, and treatment was not specified in 4. Surgical treatment was always preceded by targeted antibiotic therapy, allowing a reduction of the infective process, unless the surgical indication was urgent. In 11 patients, an associated procedure was performed: coronary artery bypass grafting in 2 patients, isolated mitral valve repair in 2, aortic valve replacement in 2, mitral repair and Ebstein anomaly repair in one, mitral valve replacement in one, and aortic noncoronary sinus repair in one. Regarding complications, 16 cases of embolism were described, one patient required a thoracoscopic decortication for pleural effusion, pacemaker implantation was necessary in one patient, two patients died after surgery, and one patient died of septicemia and multi-organ failure before surgery.

Table III
Infective data

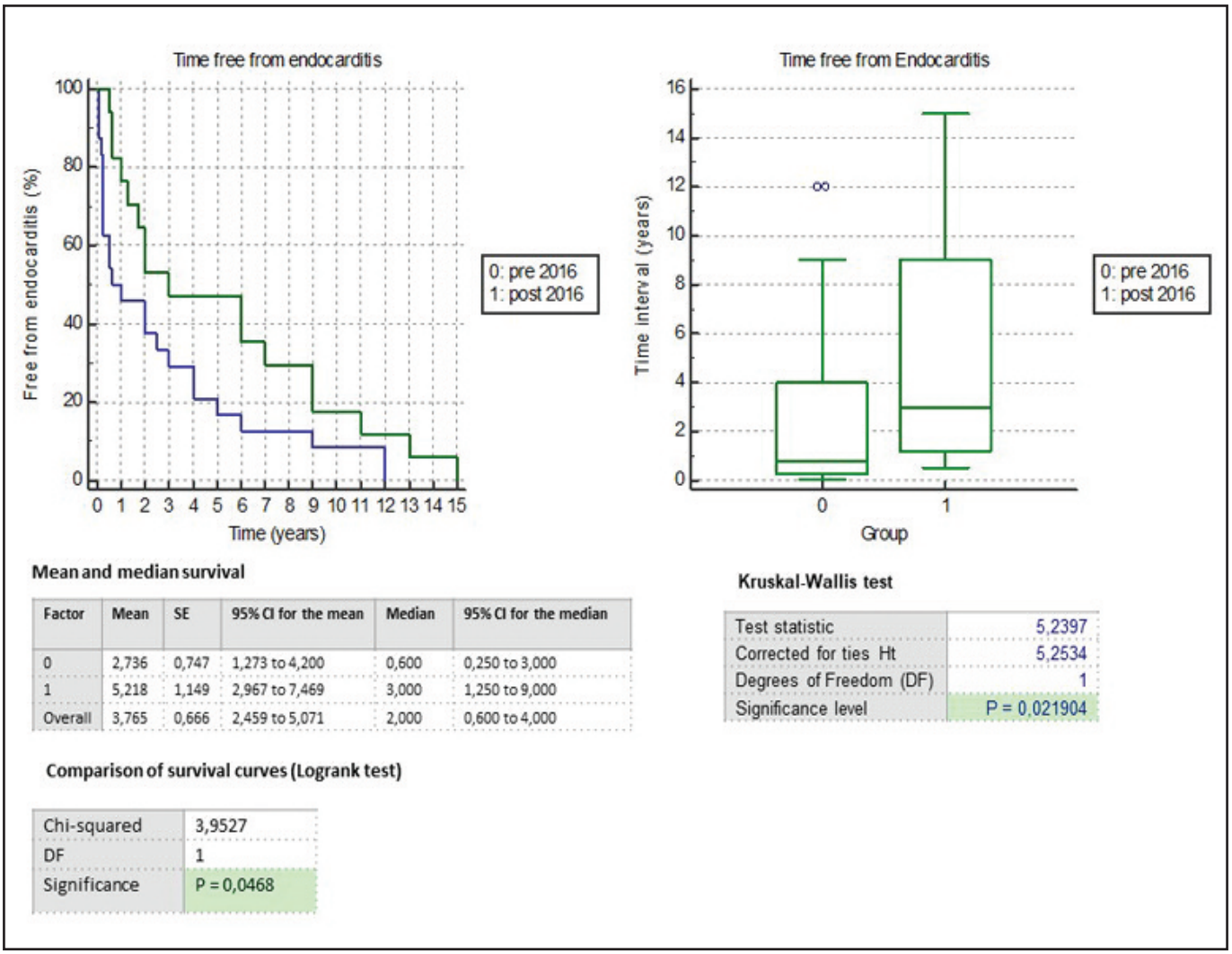
Clinical data		n
Microorganism (sometimes in combination)	Staphylococcus aureus	28
	MRSA	5
	MSSA	8
	β-Hemolytic Streptococcus	3
	lactam antibiotic Coagulase-negative	1
	Staphylococcus	1
	Bacillus pumilus	1
	Candida albicans	1
	Klebsiella pneumoniae	1
	Acinetobacter	1
	P. aeruginosa	1
	Staphylococcus lugdunensis	1
	Streptococcus pyogenes	1
	Escherichia coli	1
	Streptococcus pneumoniae	1
	Corynebacterium diphtheriae	1
	Streptococcus oralis	1
	Haemophilus parainfuenzae	
Antibiotic therapy (often in combination)	β-lactam antibiotic	16
	Glycopeptide	15
	Vancomycin	14
	Aminoglycoside	11
	Gentamycin	10
	Cephalosporin	9
	Antitubercular	5
	Cyclic lipopeptides	5
	Antifungals	2
	Carbapenem	2
	Quinolone	2
	Oxazolidinones	1
	Nitroimidazoles	1
	Lincosamide	1
	Acyclovir	1

Symptoms and Diagnosis

Most of the patients presented with intermittent or high fever, Janeway lesions, body aches and myalgias, fatigue, weight loss and chills. Other common presentations were sepsis and septic shock, thromboembolism and, more rarely, Osler nodes. Frequently, the patients reported neurological symptoms, such as lethargy, altered sensorium, unconsciousness, photophobia, or headache, or presented with meningitis on admission. Other peculiar presentations were spondylodiscitis and palpitations. Diagnosis was achieved through blood cultures associated with transthoracic and/or transesophageal echocardiographic assessments. In some cases, additional cultures were obtained, such as of thoracic drainage liquid, urine, liquor, wound, joint aspirate and surgical sample cultures. If needed, imaging assessment was performed with coronary angiography evaluation and CT scan.

Microbiological results and treatment approach

Three case reports describe the presence of signs of infection before device implantation. While Bullock et al.[17] reported recurrent lower respiratory tract infection, Goldstein et al.[50] and Calachanis et al.[18] mentioned sore throat and low-grade fever. In those papers, the time interval between device implantation and evidence of endocarditis was short: 2 days to 10 weeks. While the most frequently encountered pathogen was Staphylococcus aureus (27/50, 54%), either MRSA or MSSA, another recurrent pathogen was β-hemolytic Streptococcus. The most commonly used antibiotics were vancomycin, gentamicin, and β-lactam antibiotics. The complete list of pathogens and associated antibiotic therapies is reported in Table III.



Factor	Mean	SE	95% CI for the mean	Median	95% CI for the median
0	2,736	0,747	1,273 to 4,200	0,600	0,250 to 3,000
1	5,218	1,149	2,967 to 7,469	3,000	1,250 to 9,000
Overall	3,765	0,666	2,459 to 5,071	2,000	0,600 to 4,000

Test statistic	5,2397
Corrected for ties Ht	5,2534
Degrees of Freedom (DF)	1
Significance level	P = 0,021904

Chi-squared	3,9527
DF	1
Significance	P = 0,0468

Figure 4. Increased time from procedure to endocarditis. The Kruskal-Wallis test demonstrated that, among cases described after the paper by Amedro et al.,(8) the mean time between the interventional procedure and the manifestation of endocarditis increased.

Statistical analysis

For the statistical analysis, we divided the patients into two groups. The first group included cases up to 2016, which were reported in the last review of the literature on device endocarditis by Amedro et al.[8] The second group included cases from 2016 to April 2023, which our team found in the literature. The first distribution plot shows 16/50 (32%) cases following PFO closure and 34/50 (68%) cases following OS closure (Fig. 3A). The second plot shows 17/50 (34%) early cases and 33/50 (65%) late cases (Fig. 3B). A Kruskal-Wallis test demonstrated (p=0.021) that, in cases described after the article by Amedro et al., the mean time between the interventional procedure and the manifestation of endocarditis increased. The mean time from the procedure increased from 2.7 to 5.2 years (Fig. 4).

DISCUSSION

This is the first report to collect information on the diagnosis, natural history and management of IE on closure devices for ASD since Amedro et al.[8] In this review, we included papers over the last five years and analyzed differences in characteristics and trends with respect to those in the previous period.

Considering the large number of patients included in the present review, we can confirm that infective endocarditis following percutaneous ASD device closure is an exceptional event, as previously reported. In fact, we found only 50 cases of infective endocarditis from among 42,365 patients treated with such procedures.

Unlike the findings reported by Amedro et al.,[8] nearly 66% of the cases of IE in this setting occurred late, after at least 6 months from the procedure (33/50 patients). The statistical analysis clearly showed that the mean time from the procedure to IE increased over the last five years.

Before considering the possible causes of this increase, it is important to highlight how to best prepare for the procedure. To minimize the risk of IE in a non-febrile patient, percutaneous ASD device closure must be performed. Additionally, blood analyses such as white blood cell counts, c-reactive protein, procalcitonin, blood and urine cultures should be obtained to exclude the possibility of bacteremia. From cases in which infective signs were present before implantation, it is evident how the procedure can be easily complicated with IE in a brief time (from 2 days to 10 weeks).

While the real cause of late IE is still unclear, we can speculate that this is probably due to several reasons: a) antibiotic prophylaxis is recommended for the

first 6 months after implantation in the absence of residual shunts,[4] and b) a delay in the device endothelization process increases the possibility of bacterial adhesion.[21]

While it would be unnecessary to extend antibiotic prophylaxis beyond 6 months in all patients, it could be indicated in those with severe comorbidities and/or a history of injectable drug abuse.

In addition, the current guidelines suggest that antiplatelet therapy (APT) should be used to aid complete device endothelization, but this may be a very long process that may take up to 5 years.[56-59]. In case of OS closure, dual APT (DAPT) is recommended for 3 months, followed by single APT (SAPT) for another 3 months. In case of PFO closure, DAPT is recommended for 1 to 6 months followed by SAPT up to 12 months (5 years according to the latest consensus),[56,60] which is different from previous guidelines which suggested SAPT for 6 months.[61] If we consider all of the patients in our review, it is clear that the antiplatelet regimen was applied according to the old guidelines and this could probably have justified a delay in endothelialization in some cases.

Management of IE on an ASD occluder should always be discussed in the setting of a multidisciplinary heart team that includes a cardiologist, cardiac surgeon, and anesthetist. While surgical strategies gave excellent results, conservative management might be considered in cases of small-size IE vegetations and when the patient is in good general condition. However, in these cases, the patient must be closely observed with repeated blood and instrumental tests.

CONCLUSION

While infective endocarditis is relatively rare after percutaneous ASD closure, it can lead to several complications. Considering the unresolved controversies, a better pre-procedural evaluation of the infectious disease state and improved infection prevention following the procedure in these patients are mandatory.

We must educate patients about the risk of infection in everyday life and ways to limit it. While it would be unproductive to modify the current guidelines by extending the period of antibiotic prophylaxis in all patients, this may be necessary for some in high-risk categories.

For patients with a history of intravenous drug abuse, we may also consider intensifying inpatient drug rehabilitation, performing a closer and lifelong follow-up, and customizing treatment for other infective diseases. STI

AUTHORS' DISCLOSURES

The authors declare that there are no conflicts of interest.

REFERENCES

1. Holland TL, Baddour LM, Bayer AS, Hoen B, Miro JM, Fowler VG. Infective endocarditis. Nat Rev Dis Prim 2016;2. doi: 10.1038/nrdp.2016.59
2. Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380(9859): 2197-223. doi: 10.1016/S0140-6736(12)61689-4
3. Murdoch DR, Corey RG, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century The international collaboration on Endocarditis-prospective cohort study. Arch Intern Med 2009;169(5):463-73. doi: 10.1001/archinternmed.2008.603
4. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis. Eur Heart J 2015;36(44):3075-123. doi: 10.1093/eurheartj/ehv319
5. Cahill TJ, Prendergast BD. Infective endocarditis. Lancet 2016;387(10021):882-93. doi: 10.1016/S0140-6736(15)00067-7
6. Delahaye F, M'Hammedi A, Guerpillon B, et al. Systematic Search for Present and Potential Portals of Entry for Infective Endocarditis. J Am Coll Cardiol 2016;67(2):151-8. doi: 10.1016/j.jacc.2015.10.065
7. Jain V, Yang MH, Kovacicova-Lezcano G, Juhle LS, Bolger AF, Winston LG. Infective endocarditis in an urban medical center: Association of individual drugs with valvular involvement. J Infect 2008;57(2):132-8. doi: 10.1016/j.jinf.2008.05.008
8. Amedro P, Soulatges C, Fraisse A. Infective endocarditis after device closure of atrial septal defects: Case report and review of the literature. Catheter Cardiovasc Interv. 2017;89(2):324-34. doi: 10.1002/ccd.26784
9. Butera G, Biondi-Zoccai G, Sangiorgi G, et al. Percutaneous versus surgical closure of secundum atrial septal defects: A systematic review and meta-analysis of currently available clinical evidence. EuroIntervention 2011;7(3):377-85. doi: 10.4244/EIJV7I3A63
10. Zotov AS, Borisov DV, Klypa TV, Vachev SA. Surgical removal of atrial septal defect occlusion device and mitral valve replacement in a 39-year-old female patient with infective endocarditis. Kazan Med J 2018;99(1):140-3. doi: 10.17816/kmj2018-140
11. Abaci A, Unlu S, Alsancak Y, Kaya U, Sezenoz B. Short and long term complications of device closure of atrial septal defect and patent foramen ovale: Meta-analysis of 28,142 patients from 203 studies. Catheter Cardiovasc Interv 2013;82(7):1123-38. doi: 10.1002/ccd.24875
12. Sievert H, Babic UU, Hausdorf G, et al. Transcatheter closure of atrial septal defect and patent foramen ovale with the ASDOS device (A multi-institutional European trial). Am J Cardiol 1998;82(11):1405-13. doi: 10.1016/S0002-9149(98)00650-X
13. Sadiq M, Kazmi T, Rehman AU, Latif F, Hyder N, Qureshi SA. Device closure of atrial septal defect: Medium-term outcome with special reference to complications. Cardiol Young 2012;22(1):71-8. doi: 10.1017/S104795111100093X
14. Verma SK, Tobis JM. Explantation of patent foramen ovale closure devices: A multicenter survey. JACC Cardiovasc Interv 2011;4(5):579-85. doi: 10.1016/j.jcin.2011.01.009
15. Saguner AM, Wahl A, Praz F, et al. Figulla PFO occluder versus Amplatzer PFO occluder for percutaneous closure of patent foramen ovale. Catheter Cardiovasc Interv 2011;77(5):709-14. doi: 10.1002/ccd.22737
16. Wilkinson JL, Goh TH. Early clinical experience with use of the 'Amplatzer Septal Occluder' device for atrial septal defect. Cardiol Young 1998;8(3):295-302. doi: 10.1017/S104795110000679X
17. Bullock AM, Menahem S, Wilkinson JL. Infective endocarditis on an occluder closing an atrial septal defect. Cardiol Young 1999;9(1):65-7. doi: 10.1017/s1047951100007411
18. Calachanis M, Carrier L, Grimaldi R, Veglio F, Orzan F. Infective endocarditis after transcatheter closure of a patent foramen ovale. Catheter Cardiovasc Interv 2004;63(3):351-4. doi: 10.1002/ccd.20185
19. Balasundaram RP, Anandaraja S, Juneja R, Choudhary SK. Infective endocarditis following implantation of amplatzer atrial septal occluder. Indian Heart J 2005;57(2):167-9.https://pubmed.ncbi. nlm.nih.gov/16013359/. Accessed December 14, 2020.
20. Divchev D, Podewski EK, Mengel M, Meyer GP, Drexler H, Schaefer A. Inflammatory, abscess-forming foreign body reaction mimics a thrombus formation on an atrial septal defect closure device: A commented case report. Eur J Echocardiogr 2007;8(4):298-302. doi: 10.1016/j.euje.2006.03.015
21. Slesnick TC, Nugent AW, Fraser CD, Cannon BC. Incomplete endothelialization and late development of acute bacterial endocarditis after implantation of an Amplatzer septal occluder device. Circulation 2008;117(18). doi: 10.1161/CIRCULATIONAHA.107.754069
22. Zahr F, Katz WE, Toyoda Y, Anderson WD. Late Bacterial Endocarditis of an Amplatzer Atrial Septal Defect Occluder Device. Am J Cardiol 2010;105(2):279-80. doi: 10.1016/j.amjcard.2009.09.011
23. Stöllberger C, Bastovansky A, Finsterer J. Fatal septicemia in a patient with cerebral lymphoma and an Amplatzer septal occluder: A case report. J Med Case Rep 2011;5:2-4. doi: 10.1186/1752-1947-5-554
24. Doguet F, Leguillou V, Godin M. Infected amplatzer device. J Card Surg 2011;26(1):75. doi: 10.1111/j.1540-8191.2010.01139.x
25. Walpot J, Amsel B, Rodrigus I, Pasteuning WH, Koeman J, Hokken R. Late infective endocarditis of an atrial septal occluder device presenting as a cystic mass. Echocardiography 2011;28(6):E131-E133. doi: 10.1111/j.1540-8175.2011.01387.x
26. Aruni B, Sharifian A, Eryazici P, Herrera CJ. Late bacterial endocarditis of an Amplatzer atrial septal device. Indian Heart J 2013;65(4):450-1. doi: 10.1016/j.ihj.2013.06.002
27. Krantz SB, Lawton JS. Subacute endocarditis of an atrial septal closure device in a patient with a patent foramen ovale. Ann Thorac Surg 2014;98(5):1821-3. doi: 10.1016/j.athoracsur.2013.12.079
28. Iezzi F, Cini R, Sordini P, Pristipino C. CASE REPORT Bacterial endocarditis on transcatheter Amplatzer device. J Case Reports Pract 2014;2(1):4-5.
29. Białkowski J, Pawlak S, Banaszak P. Incomplete endothelialisation of an Amplatzer Septal Occluder device followed by meningitis and late acute bacterial endocarditis. Cardiol Young 2016;26(4):808-10. doi: 10.1017/S1047951115002383
30. Jha NK. Late endocarditis of amplatzer atrial septal occluder device in a child. World J Cardiol 2015;7(10):703. doi: 10.4330/wjc.v7.i10.703
31. Thibodeau-Jarry N, Ibrahim R, Ducharme A, Sia YT. Late Infection of an Atrial Septal Defect Closure Device: A Possible Complication. Can J Cardiol 2015;31(9): 1204.e9-1204.e11. doi: 10.1016/j.cjca.2015.01.043
32. Nguyen AK, Palafox BA, Starr JP, Gates RN, Berdjis F. Endocarditis and Incomplete Endothelialization 12 Years after Amplatzer Septal Occluder Deployment. Tex Heart Inst J 2016 Jun 1;43(3):227-31. doi: 10.14503/THIJ-14-4949.
33. Toporcer T, Kolesár A, Ledecký M, Sabol F. Late infective endocarditis of an Amplatzer atrial septal device twelve years after implantation. Cor Vasa 2018;60(2):e174-e178. doi: 10.1016/j.crvasa.2017.01.006
34. Sinning C, Schrage B, Müller GC, Zengin E. Endocarditis of an ASD Occluder Mimicking Adult-onset Still Disease in a Grown-up with Congenital Heart Disease. J Adv Ther Med Innov Sci 2016;1:54-5. doi: 10.17987/jatamis.v1i0.290
35. Kumar S, Mani R, Kumar S, Krishnan R, Murugan B. Late endocarditis of Amplatzer septal occluder device in a child. Indian J Thorac Cardiovasc Surg.

2017;33(2):159-161. doi: 10.1007/s12055-016-0480-z
36. Matamala Morillo MA, Belmonte Pintre Z, Rodríguez González M, Segado Arenas A. Endocarditis tardía en un portador de un Amplatzer. Manejo conservador en un paciente pediátrico [Late onset endocarditis in Amplatzer carrier. Conservative management in a pediatric patient]. Arch Argent Pediat 2019 Oct 1;117(5):e489-e492. doi: 10.5546/aap.2019.e489. (in Spanish)
37. Ng J, Downton T, Davidson N, Marangou J. Corynebacterium diphtheriae- infective endocarditis in a patient with an atrial septal defect closure device. BMJ Case Rep 2019;12(5):1-4. doi: 10.1136/bcr-2019-229478
38. Alvi N, Qadir S, Liu S, et al. A Surprising Case of Late-Onset Bacterial Endocarditis Associated With Gore Helex Septal Occluder Device Seven Years Since Implantation. J Am Coll Cardiol 2020;75(11):2854. doi: 10.1016/s0735-1097(20)33481-1
39. La Sala MS, Zohourian H, McKeown J, Snyder S. Late Bacterial Endocarditis in an Intravenous Drug User With an Amplatzer Septal Occluder. Tex Heart Inst J 2020 Aug 1;47(4):311-4. doi: 10.14503/THIJ-18-6903.
40. Tamura Y, Yonehara Y, Horibata Y, Uesugi H, Sawamura T, Sakamoto T. The first described case of late infective endocarditis after implantation of Figulla Flex II ASD occluder. J Cardiol Cases 2021;23(5):214-7. doi: 10.1016/j.jccase.2020.11.013
41. Le Gloan L, Guérin P, Gallet J, Baruteau A. Infective endocarditis late after device closure of an atrial septal defect. Int J Cardiol Congenit Heart Dis. 2021;3(March):100124. doi: 10.1016/j.ijcchd.2021.100124
42. Naimi I, Egan M, Kveselis D, Smith F, Atallah-Yunes N. Late Endocarditis of Atrial Septal Occluder. J Am Coll Cardiol 2021;77(18):2733. doi: 10.1016/s0735-1097(21)04088-2
43. Alvarez-Navarro P, Pradas Irun C, Romero Ferrer B, et al. Late Bacterial Endocarditis Due to Haemophilus After Implantation of an Amplatzer Septal Occluder. J Clin Med Images. 2021;5(9):1-3. https://www.clinandmedimages.com/wp-content/uploads/ 2021/05/ JCMI-v5-1433.pdf.
44. Kitamura H, Yamamoto M, Kagase A. Mobile vegetations on a poorly endothelialized atrial septal defect closure device. JTCVS Tech 2021;7:240-1. doi: 10.1016/j.xjtc.2021.01.010
45. Sharma N, Weena U, Medamana J, et al. Atrial Septal Defect Closure Device–Related Infective Endocarditis in a 20-Week Pregnant Woman. JACC Case Reports 2021;3(2):300-3. doi: 10.1016/j.jaccas.2020.09.057
46. Sharma GK, Samoon QA, Abbasi T, et al. Infective endocarditis of a completely endothelialized cardioSEAL patent foramen ovale closure device — extremely rare entity —. Circ J 2017;81(9):1246-53. doi: 10.1253/circj.CJ-17-0114
47. Yamaoka H, Takaya Y, Watanabe N, et al. Infective Endocarditis of Patent Foramen Ovale Closure Device Presenting as an Amoeboid-Like Mass. JACC Cardiovasc Interv 2018;11(22):2337-8. doi: 10.1016/j.jcin.2018.06.055
48. Thiagaraj AK, Bloomingdale R, Telila T, Afonso LC. A remarkable case of late-onset biatrial bacterial endocarditis of the Gore HELEX septal occluder. J Cardiol Cases 2017;16(6):202-4. doi: 10.1016/j.jccase.2017.08.009
49. Chien YH, Lin MT, Wang JK. Infective endocarditis involving atrial septal occluder. Arch Dis Child 2018;103(12):1149. doi: 10.1136/archdischild-2017-314245
50. Goldstein JA, Beardslee MA, Xu H, Sundt TM, Lasala JM. Infective endocarditis resulting from CardioSEAL closure of a patent foramen ovale. Catheter Cardiovasc Interv 2002;55(2):217-20. doi: 10.1002/ccd.2999
51. Kim DJ, Shim CY, You SC, Lee SH, Hong GR. Late bacterial endocarditis and abscess formation after implantation of an amplatzer septal occluder device. Circulation 2015;131(25):e536-e538. doi: 10.1161/CIRCULATIONAHA.115.016339
52. Mejía Sanjuanelo AM, Manzur Barbur MC, Martínez-Ávila MC, García Domínguez JC. Late Infective Endocarditis Associated with an Atrial Septal Defect Occluder Device. Eur J Case Rep Intern Med 2022 Mar 15;9(3):003238. doi: 10.12890/2022_003238.
53. Parekh P, Narasimhan S, Karim F, Ambrose M, Hiremath G. Early Infective Endocarditis Associated with an Amplatzer Atrial Septal Occluder Device in a 14-Year-Old Male. Pediatr Cardiol. 2023 Jun;44(5):1187-9. doi: 10.1007/s00246-023-03172-3.
54. Gaibazzi N, El Qarra S, Niccoli G, Suma S, Guerra E. Late-onset Amplatzer-related endocarditis. Eur Heart J Cardiovasc Imaging 2022 Apr 18;23(5):e238. doi: 10.1093/ehjci/jeab265
55. Toyoshima Y, Tanaka T, Matsuhisa H. A case of infective endocarditis in an 8-year-old boy 3 months after transcatheter atrial septal defect closure using Figulla Flex II occluder. Cardiol Young November 2022:1-3. doi: 10.1017/S104795112200347X
56. Pristipino C, Sievert H, D'Ascenzo F, et al. European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism. EuroIntervention 2019;14(13):1389-402. doi: 10.4244/EIJ-D-18-00622
57. Marchese N, Pacilli MA, Inchingolo V, Fanelli R, Loperfido F, Vigna C. Residual shunt after percutaneous closure of patent foramen ovale with amplatzer occluder devices - influence of anatomic features: a transcranial doppler and intracardiac echocardiography study. EuroIntervention 2013;9(3):382-8. doi: 10.4244/EIJV9I3A61
58. Cheli M, Canepa M, Brunelli C, et al. Recurrent and residual shunts after patent foramen ovale closure: Results from a long-term transcranial doppler study. J Interv Cardiol 2015;28(6):600-8. doi: 10.1111/joic.12255
59. Davies A, Ekmejian A, Collins N, Bhagwandeen R. Multidisciplinary Assessment in Optimising Results of Percutaneous Patent Foramen Ovale Closure. Heart Lung Circ 2017;26(3):246250. doi: 10.1016/j.hlc.2016.06.1211
60. Olasinska-Wisniewska A, Grygier M. Antithrombotic/Antiplatelet Treatment in Transcatheter Structural Cardiac Interventions—PFO/ASD/LAA Occluder and Interatrial Shunt Devices. Front Cardiovasc Med 2019;6(June):1-7. doi: 10.3389/fcvm.2019.00075
61. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: Guidelines from the American Heart Association. Circulation 2007;116(15):1736-54. doi: 10.1161/CIRCULATIONAHA.106.183095

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