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Long-Term Outcomes After Percutaneous Closure of Ostium Secundum Atrial Septal Defect in the Young

A Nationwide Cohort Study

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ABSTRACT

OBJECTIVES This study sought to assess procedural characteristics, early clinical outcome, and long-term complications after transcatheter closure of atrial septal defect (ASD) in children.

BACKGROUND Transcatheter closure has become the preferred strategy in most cases of isolated secundum ASD. However, reported experience in the pediatric population is limited.

METHODS A 1998 to 2016 retrospective multicenter study was performed in 9 French tertiary institutions. All children who had an attempt of percutaneous ASD closure with an Amplatzer Septal Occluder were included.

RESULTS In 1,326 children (39% males; median age, 9 years [0.7 to 18]; weight, 29 kg [3.6 to 92]), transcatheter ASD closure was performed. Median ASD size was 15 mm (3 to 41); 254 (19.1%) patients had a large ASD (≥20 mm/m^2). Procedural success rate was 95.3% (95% confidence interval: 93.9% to 96.3%). No death was observed but periprocedural complications occurred in 24 patients (1.8%). After a median follow-up of 3.5 years (range 6 months to 18 years; 173 patients [13%] followed >10 years), delayed major complications were minimal (n = 12; 1.04%) including no death and/or cardiac erosion. Periprocedural and delayed complications rates were significantly higher in children ≤15 kg (5.2% vs. 1.5%; p = 0.007 and 3.1% vs. 0.7%; p < 0.007, respectively) and those with large ASD (3.5% vs. 1.4%; p = 0.008 and 1.7% vs. 0.7%; p = 0.052, respectively).

CONCLUSIONS Transcatheter ASD closure using Amplatzer Septal Occluder is safe in children with a minimal rate of periprocedural complications and a favorable long-term outcome, especially with no death or cardiac erosion despite a substantial proportion of large defects. Children ≤15 kg and those with large ASDs had a greater risk of complications. (J Am Coll Cardiol Intv 2018;11:795–804) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ASD = atrial septal defects

ASO = Amplatzer Septal Occluder

AVB = atrioventricular block

CI = confidence interval

LA = left atrium

TEE = transesophageal echocardiography

TTE = transthoracic echocardiography

Atrial septal defect (ASD) is a common congenital heart defect with a reported incidence of 1.0/1,000 live births (1). Untreated ASD can cause right ventricular overload with right heart failure, atrial arrhythmias, pulmonary hypertension, or systemic embolism and premature death (2,3). Over the last 15 years, transcatheter closure has become the gold standard treatment strategy for isolated, secundum ASD with suitable anatomy (4,5). A recent study comparing 4,606 percutaneous procedures and 3,159 surgical ASD closures at 35 children's hospitals showed that transcatheter closure was as safe as surgery and provided better short-term value when compared with surgical closure (6).

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The Amplatzer Septal Occluder (ASO, St. Jude Medical, Inc., St. Paul, Minnesota), a self-expandable double-disc consisting of a nitinol wire mesh, is the most widely used device for percutaneous ASD closure worldwide with more than 230,000 implantations reported so far (7). Feasibility and safety of ASO implantation has been demonstrated in adult and pediatric patients with a procedural success rate close to 95% (8,9). However, despite excellent early results, the expanding use of these devices brought to light some delayed but potentially lethal complications, such as aortic erosion, cardiac perforation, atrioventricular block (AVB), infective endocarditis, or cardiac arrhythmias (5,10–14). In the meantime, the growing experience with percutaneous ASD closure led to considering the treatment of younger and smaller patients (15–19). However, success and complication rates of transcatheter ASD closure in very small children are still poorly documented, mostly consisting in small series with a limited follow-up (20,21). Thus, in this specific pediatric population, there is a need to better assess early and long-term clinical outcomes, to provide an acute counseling to patients and comprehensive awareness of potential delayed complications to physicians (22–25).

We hypothesized that percutaneous closure of ASDs in children was feasible and safe. Here, we tested our hypothesis by evaluating early and long-term outcomes of children with ASD managed using the ASO in a large multicenter cohort.

METHODS

DATA COLLECTION. A retrospective multicenter study was conducted in 9 French tertiary institutions. All children who had an attempt of transcatheter closure of isolated ostium secundum ASD using the ASO between 1998 and 2016 were included in the database. Children were defined as patients <18 years. All patients had either a left-to-right shunt with evidence of right heart dilatation and/or paradoxical diastolic interventricular septal motion regardless of the presence of symptoms or a small ASD but a paradoxical embolism (2). Data were collected anonymously and retrospectively from medical records focusing on demographic characteristics, echocardiographic and procedural data, and both early and long-term follow-up data. All participating centers had exhaustive computerized databases for data collection of consecutive patients. The study was approved by the institutional review board of each participating center. Informed consent was obtained from each study participant's parents or legal guardian.

PRE-PROCEDURAL ASD ASSESSMENT. According to centers, transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) were performed routinely before ASD closure for each patient. Anatomic ASD features were recorded including ASD size (in mm, largest ASD diameter on any view), presence and location of deficient rims defined as <5 mm in length (20) (i.e., anteroinferior, posterosuperior, aortic, posterior, inferior, and superior rims), and left atrial (LA) maximal length (distance from the anterior mitral valve leaflet to the posterior LA wall). Anteroinferior and posterosuperior rims were analyzed on the 4-chambers view, aortic and posterior rims on the short-axis parasternal view, and inferior and superior rims on the subcostal view.

When not measured, LA length was calculated by the following formula: $0.597 + 0.404 \cdot \log$ body surface area (26). Special attention was given to pulmonary and systemic venous returns and pulmonary arterial pressure. Any potential associated cardiac

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abnormalities that would preclude percutaneous closure were ruled out.

PROCEDURAL DATA. Catheterization reports were used to collect the type of imaging guidance (TEE, TTE, or intracardiac echography), hemodynamic data (mean right atrial, mean LA, and mean pulmonary arterial pressures; pulmonary to systemic output ratio [Qp/Qs ratio]), stretched balloon/stop flow diameters, ASO device size, fluoroscopy time, and potential complications. Procedural success was defined as successful implantation of the device without embolization or malposition leading to pulmonary veins obstruction or atrioventricular valve damage.

FOLLOW-UP. Follow-up was obtained through both medical records review and telephone call of primary care physicians. Major complications were defined as device embolization, cardiac erosion, pericardial effusion, air embolus, ASO-related valvular regurgitation, thromboembolism, pulmonary hypertension (mean pulmonary artery pressures >25 mm Hg), stroke, AVB, sustained arrhythmias, and hemolysis. Delayed complications were defined as occurring beyond 1 month after closure. Pregnancy occurrence and outcome was also recorded.

STATISTICAL ANALYSIS. Continuous variables are expressed as median (range) and categorical variables as percentages and numbers of patients. Distribution normality for quantitative parameters was assessed with the Shapiro-Wilk test. Two-tailed Student's *t*-test or nonparametric Mann-Whitney U test was used for comparisons for quantitative data. Chi-square test or Fisher exact test was performed for qualitative variable comparison. Receiver operating characteristic curve analysis was performed to assess the effectiveness of ASD characteristics to predict the occurrence of complications. A logistic regression analysis was also performed to determine the strength of the association and the risk value of ASD characteristics with the occurrence of complications. The follow-up data on event-free were analyzed using standard Kaplan-Meier analysis. A p value of <0.005 was considered statistically significant. Data analysis was performed using the STATA software (StataCorpLP, College Station, Texas).

RESULTS

PATIENT POPULATIONS. Of the 1,395 children included in the study, 69 were subsequently excluded because of missing data, leaving 1,326 children (39% males; median age, 9 years [0.7 to 18.0]; median weight, 29 kg [3.6 to 92]; median height, 121 cm [51 to 189]) in the analysis (Figure 1). All but 3 patients had a significant left-to-right shunting as per our echographic definition, whereas closure of a small ASD was indicated in 3 children who had a cerebral stroke suspected to be related to paradoxical embolism. Patients baseline characteristics are summarized in Table 1. All patients but 2 (n = 1,324; 99.8%) were in sinus rhythm at the time of intervention, whereas 2 patients presented with complete AVB associated with Ebstein abnormality and had been previously implanted with a permanent pacemaker. Seven patients (0.5%) had a history of paroxystic supraventricular arrhythmia (excluding the patients with previous strokes).

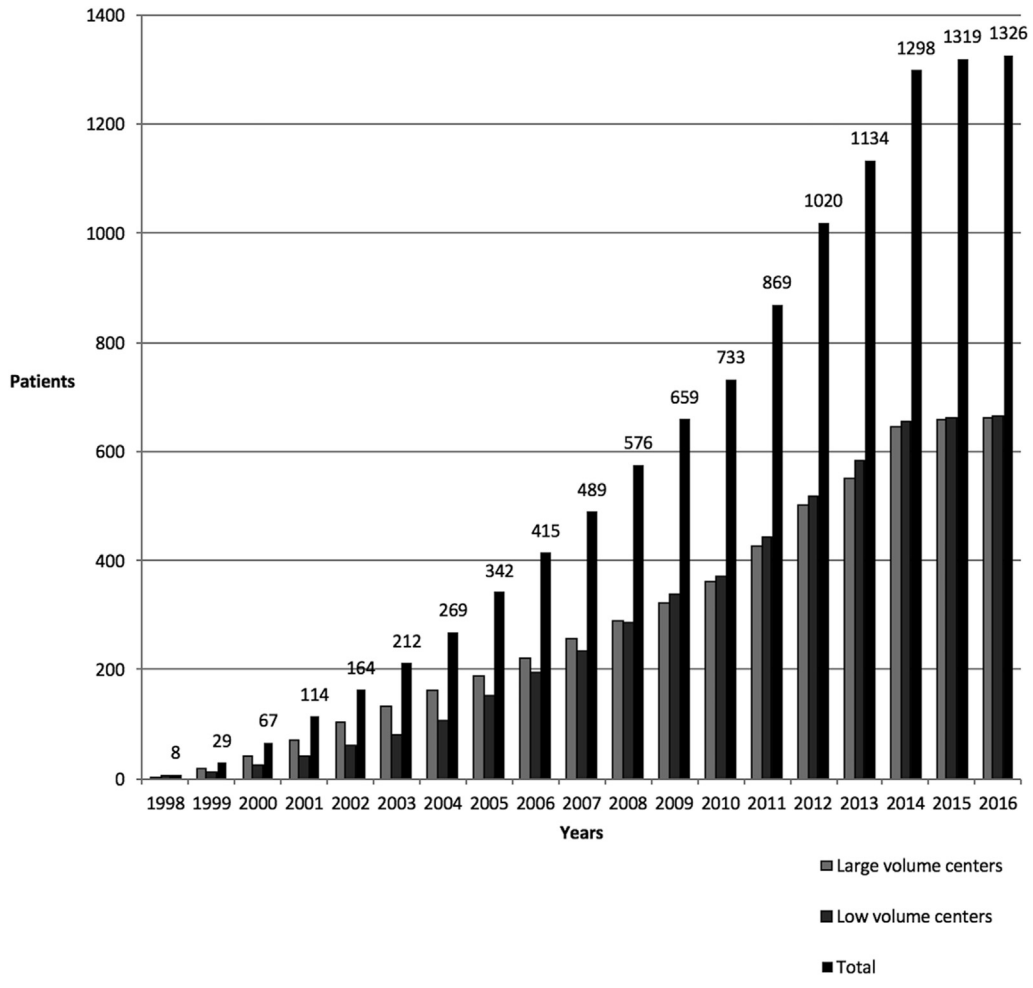
Pre-procedural TTE median ASD size was 15 mm (3 to 41) and median ASD/body surface area, ASD/weight, and ASD/height ratios were 14.8 mm/m^2 (3.5 to 48.6), 0.58 mm/kg (0.16 to 1.0) and 0.1 mm/cm (0.05 to 0.15), respectively; 254 (19.1%) patients had ASD ≥20 mm/m^2 (median, 23 mm/m^2; range 20 to 48.6) and 93 (7%) patients had ≥1 defect.

ASD CLOSURE. Femoral access was used in all but 1 patient who had an inferior vena cava interruption with azygos continuation and whose ASD was closed through a jugular route. In the 618 patients (46.6%) who had a suspicion of high pulmonary arterial pressure on echocardiography, based on the peak velocity of the tricuspid regurgitation jet, a pre-closure invasive hemodynamic assessment was performed. Among these patients, median Qp/Qs ratio was 2.3:1 (range 0.5:1 to 6.2:1) and median PA pressure was 16 mm Hg (5 to 40). Fluoroscopic guidance was used in all cases, with TEE imaging in 856 cases (6 centers; 64.5%) and TTE in 470 cases (3 centers; 35.5% patients); intracardiac echography was not used. ASD characteristics and patients' outcomes according to echographic guidance are detailed in Table 2. Although TTE-guided patients had larger and more complex defects, their procedural success was significantly higher compared with TEE-guided patients (98.1 vs. 93.5%, respectively; p < 0.001) and their median procedural time was significantly lower (4.5 vs. 6 min, respectively; p < 0.001) (Table 2).

Balloon sizing was used in 1,009 patients (76.1%). Overall, the median defect size was 15 mm (5 to 40) on periprocedural echocardiogram and 19 mm (6 to 42) by balloon sizing when performed.

Complete rims deficiency description was available in 1,133 (85.4%): aortic, posterior, anteroinferior, posterosuperior, inferior, and superior rims were deficient in 321 (28.3%), 161 (14.2%), 112 (9.8%), 25

FIGURE 1 Number of Patients Referred for Atrial Septal Defect Closure Across the Participating Centers Along the Study Period



Total number of patients included between 1998 and 2016 and distribution between large- and low-volume centers.

(2.2%), 155 (13.6%), and 49 (4.3%) patients, respectively. Procedural success rate was 95.3% (95% confidence interval [CI]: 93.9% to 96.3%). The median implanted ASO size was 18 mm (4 to 40). Two devices were implanted in 10 patients (0.7%) within the same procedure because of multiple defects. ASD characteristics and procedural data are displayed in Table 3.

Failing implantation occurred in 62 (4.7%) children. In 47 children (3.5%), the ASO was deployed but not released because the defect was considered too large to be closed with the device. Periprocedural device embolization occurred in 7 patients (0.5%). In 8 patients (0.6%), the device was deployed but not delivered because it was considered unstable (n = 5) or finally withdrawn to avoid device-related atrioventricular valvular damage (n = 2), reversible AVB (n = 1). Immediate trivial residual shunts were observed in 47 patients (3.7%).

ACUTE COMPLICATIONS. Major periprocedural complications occurred in 24 (1.8%; 95% CI: 1.1% to 2.5%) patients consisting in device migration (n = 10), pericardial effusion (n = 6), conduction abnormality (n = 5), mild mitral regurgitation (n = 1), transient hemolysis (n = 1), and air embolus without clinical sequelae (n = 1).

Of the 10 patients whose device embolized, 3 were diagnosed within 24 h after the case, whereas the 7 others were immediate ASO migration. Device

TABLE 1 Population Baseline Characteristics (n = 1,326)

Age, yrs	9 (0.7-18.0)
Age distribution, yrs	
0-5	229 (17.0)
6-10	650 (49.0)
11-18	447 (34.0)
Male	518 (39.0)
Weight, kg	28 (3.6-92)
≤15	96 (7.0)
>15	1,230 (93.0)
Body surface area, m^2	1 (0.2-2.1)
Other cardiac defects	137 (10.3)
Pulmonary valvular stenosis	44 (3.3)
Ebstein anomaly	12 (0.9)
Other	81 (6.1)
Extracardiac comorbidities	62 (4.6)
Genetic disorders	45 (3.3)
Prematurity	12 (0.9)
Bronchopulmonary dysplasia	5 (0.3)

Values are median (range) or n (%).

migrated into the right atrium (n = 2), LA (n = 2), right ventricle (n = 2), left ventricle (n = 2), and ascending aorta (n = 1); data were missing in 1 patient. Four of them underwent successful transcatheter ASO retrieval, whereas 6 were referred to surgery for device retrieval and surgical ASD closure.

TABLE 2 ASD Characteristics and Patient Outcomes According to Periprocedural Echographic Guidance Technique

	TEE Guidance (n = 856)	TTE Guidance (n = 470)	p Value
Age, yrs	9 (0.7-18)	8.7 (0.9-18)	0.63
Weight, kg	29 (3.6-92)	27 (6.4-88)	0.16
ASD diameter, mm	15 (3.0-41.0)	13 (5.4-33.9)	0.006
Deficient rims (n = 1,133)			
Aortic	182 (25.7)	139 (30.0)	0.008
Posterior	56 (7.8)	105 (22.0)	<0.001
Anteroinferior	32 (4.4)	80 (17.0)	<0.001
Posterosuperior	4 (0.5)	21 (4.5)	<0.001
Inferior	50 (7.0)	105 (22.0)	<0.001
Superior	26 (3.6)	23 (4.8)	0.11
ASO size, mm	18 (4-40)	18 (4-40)	0.9
Procedural success	801 (93.5)	461 (98.1)	<0.001
Fluoroscopy time, min (n = 1,214)	6 (0.5-120.0)	4.5 (0.6-34.0)	<0.001
Periprocedural complications	18 (2.1)	6 (1.2)	0.366
Device migration	7 (0.8)	3 (0.6)	0.66
Pericardial effusion	6 (0.7)	0 (0.0)	0.08
Conduction abnormality	3 (0.4)	2 (0.4)	0.87
Mitral regurgitation	1 (0.1)	0 (0.0)	0.47
Transient hemolysis	0 (0.0)	1 (0.2)	0.67
Air embolus	1 (0.1)	0 (0.0)	0.47

Values are median (range) or n (%).
ASD = atrial septal defect; ASO = Amplatzer Septal Occluder; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

TABLE 3 ASD Characteristics and Procedural Data

Preprocedural ASD assessment	
ASD echographic diameter, mm	15 (3-41)
Indexed diameter (ASD/body surface area, mm/m^2)	14.8 (3.5-48.6)
Large ASD (≥20 mm/m^2)	254 (19.1)
Deficient rims (n = 1,133)	
Aortic	321 (28.3)
Posterior	161 (14.2)
Anteroinferior	112 (9.8)
Posterosuperior	25 (2.2)
Inferior	155 (13.6)
Superior	49 (4.3)
Periprocedural ASD assessment	
Echographic diameter, mm	15 (5-40)
Balloon sizing, mm	19 (6-42)
Successful implantation	1,264 (95.1)
ASO device size, mm	18 (4-40; IQR: 15-24)
Reason for occlusion failure	62 (4.7)
Defect was considered too large to be closed with the ASO	47
ASO embolization	7
Unstable device	5
Atrioventricular valve damage	2
Atrioventricular block	1
Fluoroscopy time, min (n = 1,214)	5 (0.5-120.0)

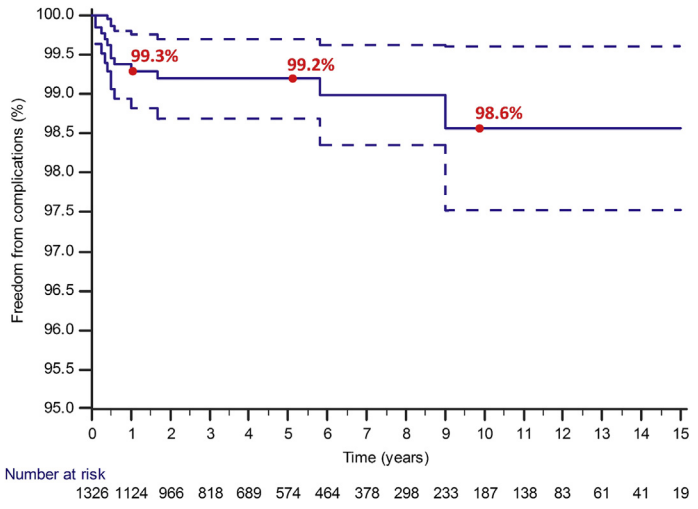
Values are median (range) or n (%).
IQR = interquartile range; other abbreviations as in Table 2.

Of the 6 patients who presented with a mild pericardial effusion, none had any hemodynamic instability and/or sign of cardiac perforation/erosion; their clinical course was spontaneously favorable under medical treatment without the need for pericardiocentesis; 2 of 6 had a deficient aortic rim.

A newly diagnosed cardiac conduction abnormality occurred in 5 patients including complete AVB in 2, second-degree AVB in 2, and first-degree AVB in 1. Conduction disorders resolved spontaneously or with systemic corticosteroid treatment in all patients, except for 1 complete AVB patient who needed surgical ASO removal at post-procedural day 2 and 1 patient with persistent but asymptomatic suprahisian second-degree AVB. None of these patients needed a permanent pacemaker implantation.

FOLLOW-UP. Of the 1,264 patients who had a successful ASD closure, follow-up was available in 1,158 (91.6%; 95% CI: 90.1% to 93.1%); 8.4% of patients were lost to follow-up, mainly because they were referred from overseas centers. After a median follow-up duration of 3.5 years (range 6 months to 18 years; interquartile range: 1 to 7 years) no death

FIGURE 2 Kaplan-Meier Curve Depicting Freedom From Complications Over Time



Kaplan-Meier curve of complication-free survival among the study period.

occurred; 173 patients (13%) were followed >10 years. At last visit, most patients were asymptomatic (n = 1,128; 96%). Delayed complications were observed in 12 (1.04%; 95% CI: 0.5% to 1.6%) patients. Cardiac arrhythmias were the main long-term complication, most occurring in 8 patients aged 3 to 13 years, after a median period of time of 6 months (range 1 to 108 months) from the procedure. All were in sinus rhythm before ASD closure and had an uneventful closure with a device size ranging from 12 to 30 mm. Two patients presented with device-unrelated arrhythmias, namely infundibular ventricular tachycardia (n = 1) and nodal re-entrant tachycardia (n = 1), both successfully managed by catheter ablation. One patient had atrial flutter treated with electrical cardioversion and the remaining 5 patients had atrial tachycardia/extrasystoles that were successfully managed by antiarrhythmic drugs. Among these 8 patients who developed post-procedural cardiac arrhythmias, the median follow-up duration was 3 years (range 1 to 10 years). At latest follow-up 3 patients were still receiving antiarrhythmic drugs. Those 3 patients had post-procedural atrial tachycardia/extrasystoles and only 1 of them was still symptomatic (palpitations) at latest follow-up.

Other delayed complications included pulmonary hypertension (n = 2) and transient ischemic stroke (n = 2), respectively, 1 and 3 months after the procedure while receiving antiplatelet therapy (no device thrombus was observed). The other symptomatic patients had migraine headache (n = 15) and atypical chest pain episodes without any evidence of pericardial effusion or erosion (n = 3).

Delayed cardiac erosion, infective endocarditis, or AVB were never observed. Overall, the 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 2).

A total of 69 women had 78 uneventful pregnancies after a median delay of 10 years (2 to 15); no thromboembolic complications were observed during the peripartum period.

SUBGROUPS ANALYSIS. Large defects. Using receiver operating characteristic analysis for predicting the occurrence complications according to the defect characteristics, ASD indexed diameter was the best parameter with an area under the curve of 0.638 (95% CI: 0.49 to 0.78; $p < 0.05$). The optimal cutoff value above which the occurrence of complications was significantly higher was 19 mm/m^2 (sensitivity, 62.5%; specificity, 74%; accuracy, 74%).

Therefore, to provide an easier take-home message, the subsequent analysis was performed with a cutoff of 20 mm/m^2 defining large ASDs, which were present in 254 patients (19.1%) (Table 4). Patients with large defects had significantly more complex ASDs regarding the presence of deficient rims and a lower procedural success rate (87.4% vs. 97.2%; $p < 0.001$). Finally, the rates of periprocedural and delayed complications were significantly higher in that subset of patients (3.5% vs. 1.4%; $p = 0.008$ and 1.7% vs. 0.7%; $p = 0.052$, respectively).

Small children. Children ≤15 kg (n = 86 patients; 7.2%) were also evaluated for procedural success and occurrence of complications. These patients had significantly larger defects (median indexed diameter of 25 vs. 14 mm/m^2; $p < 0.001$). Procedural success rate was not significantly different between patients ≤15 kg and >15 kg; however, periprocedural and delayed complications rates were significantly higher in patients ≤15 kg (5.2% vs. 1.5%; $p = 0.007$; 3.1% vs. 0.7%; $p < 0.007$, respectively).

DISCUSSION

Device closure of secundum ASD has become the preferred treatment strategy (2). Device-related mortality rates are low and long-term complications are well described (14). However, reported experience in the pediatric age group is scarce, mainly consisting of small series with a limited follow-up duration (20,21). Despite the encouraging experience and growing body of published data in adults achieving excellent

TABLE 4 Procedural Characteristics and Patient Outcomes According to Defects Size and Patients Body Weight

	Large Defects			Low Body Weight		
	ASD <20 mm/m² (n = 1,072)	ASD ≥20 mm/m² (n = 254)	p Value	≤15 kg (n = 96)	>15 kg (n = 1,230)	p Value
Age, yrs	10.1 (0.7–18)	6 (1–18)	<0.001	3.8 (0.7–6)	9.3 (6–18)	<0.001
Weight, kg	31 (3.6–92)	20 (3.7–78)	<0.001	13 (3.6–15)	30 (15–92)	<0.001
ASD indexed diameter, mm/m²	12 (3.5–20)	23 (20–48.6)	<0.001	25 (9.4–48.6)	14 (3.5–39)	<0.001
Deficient rims (n = 1,133)						
Aortic	246 (23.0)	75 (33.0)	0.52	19 (25.0)	378 (30.7)	0.32
Posterior	120 (11.4)	41 (18.5)	0.26	11 (14.0)	196 (15.9)	0.89
Anteroinferior	75 (7.1)	37 (16.5)	0.003	9 (12.5)	132 (10.7)	0.69
Posterosuperior	16 (1.5)	9 (4.0)	0.09	2 (2.6)	29 (2.3)	0.86
Inferior	112 (10.6)	43 (19.3)	0.06	12 (16.0)	180 (14.6)	0.72
Superior	29 (2.7)	20 (9.0)	0.001	8 (10.6)	52 (4.2)	0.01
ASO size, mm	18 (4–38)	20 (4–40)	0.007	16 (5–26)	18 (4–40)	0.001
Procedural success	1,042 (97.2)	222 (87.4)	<0.001	91 (94.7)	1,173 (95.4)	0.126
Fluoroscopy time, min (n = 1,214)	4.6 (0.5–54)	4.9 (0.5–120)	0.49	6 (2–38)	5.3 (0.5–120)	0.24
Periprocedural complications	16 (1.4)	9 (3.5)	0.008	5 (5.2)	19 (1.5)	0.007
Device migration	6 (0.5)	4 (1.5)	0.008	0 (0.0)	10 (0.8)	0.38
Pericardial effusion	3 (0.2)	3 (1.1)	<0.001	2 (2.0)	4 (0.3)	0.002
Conduction abnormality	3 (0.2)	2 (0.7)	0.008	2 (2.0)	3 (0.2)	0.001
Mitral regurgitation	1 (0.1)	0 (0.0)	0.59	1 (1.0)	0 (0.0)	0.02
Transient hemolysis	1 (0.1)	0 (0.0)	0.59	0 (0.0)	1 (0.1)	0.76
Air embolus	1 (0.1)	0 (0.0)	0.59	0 (0.0)	1 (0.1)	0.76
Follow-up, yrs (n = 1,158)	3 (0.5–18)	3 (0.5–17)	0.22	3 (0.5–17)	3 (0.5–18)	0.83
Delayed complications	8 (0.7)	4 (1.7)	0.052	3 (3.1)	9 (0.7)	0.007
Arrhythmias	6 (0.5)	2 (0.7)	0.27	1 (1.0)	7 (0.5)	0.44
Stroke	0 (0.0)	2 (0.7)	0.007	0 (0.0)	2 (0.1)	0.76
PAH	2 (0.1)	0 (0.0)	0.59	2 (2.0)	0 (0.0)	<0.001

Values are median (range) or n (%).
PAH = pulmonary arterial hypertension; other abbreviations as in Table 2.

results, lots of physicians remain concerned about implanting devices in young growing patients, who will theoretically carry them for the next 70 years. This paper reports, to the best of our knowledge, the largest series of children with percutaneous ASD closure with the ASO device. Although our data confirm safety and effectiveness of device ASD closure in pediatrics with favorable long-term outcomes, special consideration should be given to patients ≤15 kg and/or children with defects ≥20 mm/m², who both carry a greater risk of complications.

EARLY OUTCOMES. In our study, percutaneous ASD closure using the ASO was safe and effective in children with a 95.3% procedural success rate and even 97.2% when excluding large ASD patients. This high success rate compares with previous smaller reports (15–19,22) This also compares with success rates using other available devices, reported as 95.4% with the Gore Septal Occluder (W.L. Gore & Associates, Flagstaff, Arizona) in 173 children and 94.7% with the Occlutech Figulla Septal Occluders (Occlutech GmbH, Jena, Germany) in 94 patients (27,28).

Although surgical ASD closure also carries high success rates and low mortality rates in children, its major drawbacks are sternotomy and cardiopulmonary bypass-related morbidity. Ooi et al. (6) reported a significantly higher complication rate in 3,159 children who underwent surgical ASD closure compared with 4,606 children who had a percutaneous ASD closure (19.8% vs. 3.7%; odds ratio: 6.66; $p < 0.0001$). In our study, no death was observed. The acute complication rate of 1.8% was mainly caused by acute device embolization.

TEE-guidance is widely used worldwide for during ASO implantation in children (5,29). Recently, several reports demonstrating the feasibility and effectiveness of TTE-guided closure have been published in children, including challenging cases with large defects (20,21,30). Interestingly we found a higher success rate in TTE-guided cases, although patients

with transthoracic guidance had more complex shunts because of a high proportion of deficient rims. This later result should be considered cautiously, however, because it is highly likely that operators' experience plays a substantial role in these encouraging results (Online Table 1). In a previous randomized single-center trial performed in 40 children, TTE-guidance was shown to decrease fluoroscopic duration, which is also in line with our findings, confirming the cumulative benefits of this technique (30).

LONG-TERM OUTCOMES. Despite excellent short-term results, the expanding use of percutaneous ASD closure may carry some delayed, rare but potentially serious complications, including cardiac erosion, conduction abnormalities, cardiac arrhythmias, device thromboembolic events, or infective endocarditis (14). After a follow-up ranging from 6 months to 18 years, we observed a long-term complications rate of 1.04% (95% CI: 0.5% to 1.6%), which is slightly lower than previous reports on both adult and pediatric populations (4,31,32). A direct comparison of these studies and ours seems difficult, however, given the different thresholds and definitions of reported complications.

The most frequently observed delayed complication was cardiac arrhythmias in 8 patients without previous history of arrhythmias. Of them, 2 had device-unrelated events suitable for ablation. The remaining patients were successfully managed either by electrical cardioversion or antiarrhythmic drugs. This is consistent with the published data because atrial arrhythmias are known to be the most common complication after ASD closure in patients without pre-existent arrhythmias (3,14).

Although not the most frequent complication, cardiac erosion is probably the most worrying delayed complication, especially with the ASO device (14). Erosion incidence evaluation is based on estimates (and therefore probably underestimated) and ranges from 0.04% to 0.28%. (5,33). Forty percent of erosion cases are reported in children and this complication may occur up to 9 years after ASD closure (14). There is no sufficient evidence of specific mechanisms and root causes for device erosion to stratify patients individual risk. However, in a recent case-control study of 125 erosions, McElhinney et al. (34) showed that deficiency of any rim, device >5 mm larger than ASD diameter, and weight/device size ratio were strongly associated with cardiac erosion. In our series, no cardiac erosion was observed, despite a high proportion of patients with deficient rims, especially deficient aortic rims. We assume that the exact rate of erosion might have been underestimated in our series, because some cases of erosion may resolve spontaneously and we have a not negligible proportion of patients who were lost to follow-up. Indeed, we cannot state with certainty that none of the 6 patients who had periprocedural pericardial effusion did not have a minor erosion that might have resolved spontaneously. In addition, if an erosion occurred even in a few loss of follow-up patients, our conclusions would be different. Nevertheless, the absence of documented cardiac erosion in at least 1,158 children confirm the rarity of this complication.

There are few data available on the long-term tolerance of devices implanted in growing children. Recent echocardiographic and magnetic resonance imaging studies that focused on large implanted devices in children showed that the distance between the device and the surrounding structures increases with growth, although asymmetrically, likely decreasing the risk of long-term complications, such as cardiac erosion (35-37).

Another important element that needs to be considered in the long-term outcome of women is the occurrence of pregnancy. We showed in this study that 69 women (8.5% of females) had 78 uneventful pregnancies up to 15 years after ASD. These results provide a key reassuring element for patients and/or parents counseling before the procedure.

SUBGROUPS AT RISK OF COMPLICATIONS. Two specific patient subgroups were identified at risk of both periprocedural and long-term complications: namely children ≤15 kg and large defects ≥20 mm/m^2. With the expanding use of percutaneous ASD closure, there has been a trend for treating smaller patients and/or larger defects. In a retrospective series of 128 children ≤15 kg treated for ASD ranging from 4 to 20 mm using the ASO for a great majority, Bartakian et al. (22) showed a success rate of 98% but with a short-term rate of minor and major complications of 9.4% and 5.5%, respectively. No long-term complications were observed after a follow-up ranging from 8 months to 10 years. A recent study of 252 patients found that children of ≤15 kg were significantly more prone to have periprocedural major complications, compared with children of >15 kg (25).

Our study is the first reporting an increased risk of long-term complications in this subset of patients. Indeed, although when the periprocedural course of a child ≤15 kg is uneventful, the physician should adapt follow-up modalities with regards to this highest risk of elevated complications. Moreover, given the high

rate of spontaneous closure of 8-mm ASD in the first few years of life (38,39), associated with the absence of significant improvement in growth and moderate resolution of right heart enlargement reported by Bartakian et al. (22), one should be very cautious when referring those patients for percutaneous ASD closure and consider postponing the intervention in asymptomatic patients (22).

In patients with large ASD, we found a relatively low procedural success rate of 87.4% that might be explained by that most of them had complex defects with deficient rims. This subset of patients also had significantly higher rates of periprocedural and delayed complications and both operators and patients need to be aware of these issues.

STUDY LIMITATIONS. Although this study is the largest yet reported, our work has several limitations because of its retrospective nature, which inherently makes it susceptible to certain biases. The 18 years of data collected for this study represents a limitation, because experience has grown over time. As expected in a multicenter work with no standardized inclusion and follow-up of the patients, some data were lacking or incompletely collected. Similarly, the retrospective data collection at multiple medical centers may also have underestimated the incidence of adverse events during follow-up. In addition, based on the retrospective character and the large number of patients, there was no assessment of the ASD echographic features by a central core laboratory. Finally, we had a not negligible proportion of patients who were lost to follow-up. Therefore, we assume that if long-term complications occurred in even just a few of these patients the conclusions of our work would be different.

CONCLUSIONS

In the largest pediatric cohort reported so far, transcatheter closure of isolated secundum ASD was safe in children, with favorable early and long-term outcomes up to 18 years after the procedure. No cardiac erosion was observed on our large-scale sample of pediatric patients, confirming that this complication is exceptional. TTE-guidance was shown to be feasible and safe. Children ≤15 kg and ASDs ≥20 mm/m^2 were both at increased risk of periprocedural and delayed complications.

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PERSPECTIVES

WHAT IS KNOWN? Transcatheter closure has become the gold standard treatment strategy for secundum ASD but reported experience in the pediatric population is limited.

WHAT IS NEW? Our study showed transcatheter ASD closure had favorable early and long-term outcomes up to 18 years after the procedure. However, children ≤15 kg and ASDs ≥20 mm/m^2 were both at increased risk of complications.

WHAT IS NEXT? Prospective registries are needed in this area to better analyze the long-term impact of these risk factors.

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APPENDIX For a supplemental table, please see the online version of this paper.