

Original Studies

Closure of Secundum Atrial Septal Defects by Using the Occlutech Occluder Devices in More Than 1300 Patients: The IRFACODE Project: A Retrospective Case Series

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Background: The Occlutech Figulla ASD device series (OFSO) shows an improved device design for interventional ASD closure, larger follow-up series are missing. **Methods:** We retrospectively reviewed the feasibility, safety, implantation properties, results, and follow-up of ASD closure using Occlutech devices over a 5 year period by establishing a multi-institutional collaborative result registry with 16 contributing

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Conflict of interest: NAH, AL, EO, and TD are proctors for ASD closure with the Occlutech devices. The other authors have no conflict of interest relevant for this article to declare.

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DBS and NAH share the authorship in this publication.

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centers from 11 countries (IRFACODE). **Results:** In 1315 patients of all age groups (female 66.9%), successful (98%) ASD closure was performed (mean age 28.9 years, weight 52 kg, height 148.6 cm). Of the defects, 47.9% showed no or only a deficient aortic rim; in 11.9%, there was more than one defect; a septum aneurysm was present in 21.5%; and the mean implanted device size was 20.5 mm. Immediate closure was achieved in 78.6%, at discharge in 83.1%, and 96.4% and 97.3% at 6 and 12 months follow-up, respectively. During a mean follow-up of 2.7 years (in total 3597 patient years), significant complications were minimal (total = 8, <1%) with secondary device embolizations in five and AV-blocks in three patients. No erosion or death was reported. **Conclusion:** ASD closure using OFSO is feasible in a large variety of patients, safe with only a minimal risk of severe side effects and especially without any aortic erosions despite a large percentage of large and complicated defects. © 2016 Wiley Periodicals, Inc.

Key words: ASD closure; IRFACODE project; Occlutech device; Flex; Flex II

INTRODUCTION

King and Mills performed the first transcatheter atrial septal defect (ASD) closure in the mid-1970s and since then, different device designs with advantages and disadvantages have been used [1,2]. Interventional ASD closure is considered the first choice whenever applicable, it is safe, superior to surgical ASD closure with regard to patient morbidity, shows fewer complications, shorter hospitalization, a reduced need of blood products, and in most countries considerably lower treatment costs [2–4,34].

While there is abundant information about the use of Amplatzer septal occluder (ASO) for now about 20 years and with good follow-up data [2,5,6], the use of the Occlutech Figulla[®] Septal Occluders (OSFO) has not been reported so frequently. These devices have important structural differences as compared to other devices, especially an absent left atrial hub and the last generations have a tiltable delivery system that seem to be advantageous with regard to feasibility of implantation in complex ASDs, device delivery as well as device alignment to the atrial septum and thereby echocardiographic assessment during implantation [7].

We collected and analyzed the procedural characteristics, the success, and the safety of device closure of ASDs with the OSFOs in a relatively large cohort of patients on an intention to treat basis. The data collection was possible by establishing a multi-institutional collaborative registration project and therefore named as the International Registry for ASD closure with the Occlutech Devices (IRFACODE).

METHODS

Data Acquisition

This was a retrospective study of patients treated with an Occlutech device for ASD closure. The primary goal of this study was to report the outcome of ASD closure with the Occlutech devices. The study population

included all patients who were considered for transcatheter ASD closure with an Occlutech ASD device at the participating institutions until December 2013 on an intention-to-treat basis. All relevant periprocedural data was documented as part of the local hospitals quality assurance programs. The retrospective analysis was reviewed and approved by the local ethical committee of the leading institution (Heart and Diabetes Center Bad Oeynhausen, Germany) (Ref No.: 64/2013) and the other centers wherever applicable. Based on the retrospective character of the study, an additional informed consent was waived by the institutional review board.

The data were collected and interpreted locally. A detailed questionnaire was sent to the participating centers and the following data was obtained: patient characteristics including gender, age, weight, height, diagnosis, reasons for closure of the ASD, the ECG, and ECHO parameters. Procedural characteristics included the mode of sedation/anesthesia, the procedural time (from time of catheter insertion to removal) and fluoroscopy time, the type of echocardiography used during the procedure, and the specific characteristics of the ASD. Patients with deficient posterior rims were usually not treated by interventional ASD closure; those with deficient or absent aortic rims were treated. A deficient aortic rim was defined as a distance ≤ 4 mm, while a “naked aorta” was defined when no aortic rim was present at all. An aneurysm was defined when the septum movement exceeded 10 mm during various cardiac cycles.

Device selection. In patients where a balloon sizing was performed, the actual device size was used according to the measured diameter or the next larger size suitable (i.e., 15 mm device for a 15 mm defect and 18 mm device for a 16, 17, and 18 mm defect). In patients without a balloon sizing, the defect was initially measured from 3 different views: four-chamber, short-axis, and bicaval view with the color Doppler. If the ASD was oval shaped (defined as the shortest diameter was <75% of the largest diameter), a device was selected that was 0–2 mm (in children) or 2–4 mm

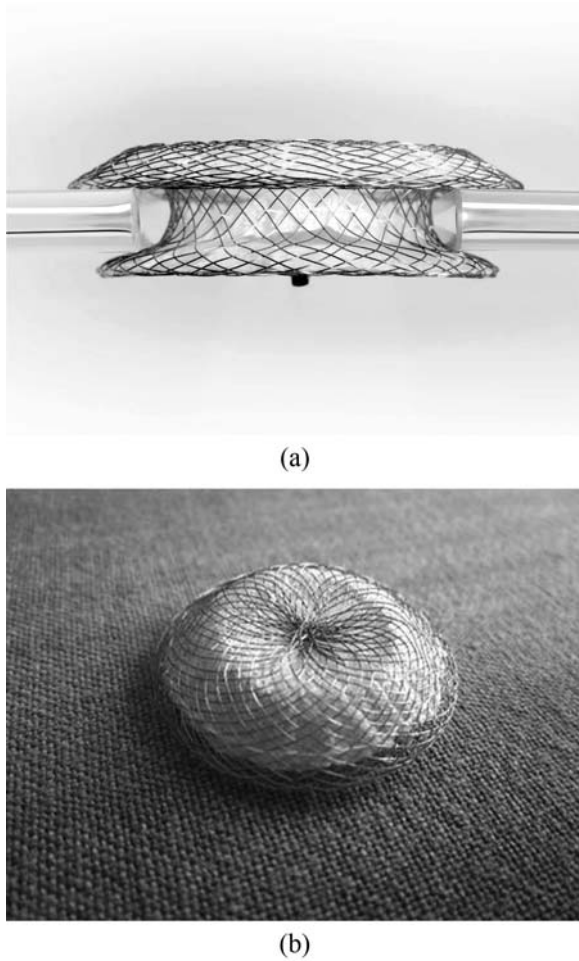


Fig. 1. The Occlutech Figulla Septum Occluder (OSO). Note the lack of the left-sided hub. (a) Lateral view; (b) en face view.

(in adults) larger than the maximum diameter. If the ASD was circular shaped (defined as the shortest diameter $\geq 75\%$ of the largest diameter), a device was selected with 2–4 (in children) and 4–6 mm (in adult) larger than the maximum diameter [23]. The overall device/defect ratio was about 1.2:1.

The Devices

The technical details are described elsewhere in detail [7,8]. One of the main devices differences of the OFSOs as compared to the ASOs is the lack of the left-sided hub that results in a softer left-sided disc despite comparable wire thickness. This creates a typical ball-shape appearance during deployment and results in less impingement on the surrounding structures (Figs. 2–4).

There have been three generations of OFSOs released so far, they are available in different sizes, ranging from

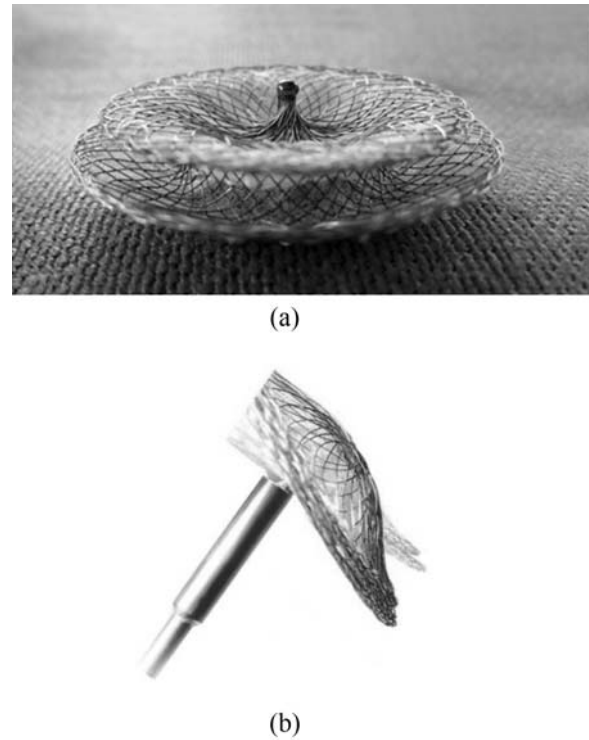


Fig. 2. The Figulla Flex Occluder (Flex). Note the ball-shaped connector design (2a) that allows a tilt angle of 45° during implantation (2b).

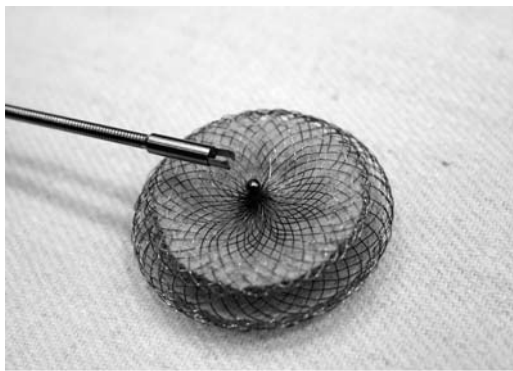
4 to 40 mm. All devices used were legally licensed and registered devices for ASD closure in the participating countries; especially, there is a CE mark for these devices to be used in the EU. The first generation (Occlutech Septal Occluder N, OSO) had no left atrial hub (Fig. 1), achieved CE mark in 2007, and were used with good results [9].

The second generation (Flex) had an improved delivery system that allowed a tilt angle of 45°, a new ball-shaped connector design, and reached CE mark in 2009 (Fig. 2). The system allows a septum alignment without any stress or tension on the septum, and thereby offers an improved flexibility during implantation [7].

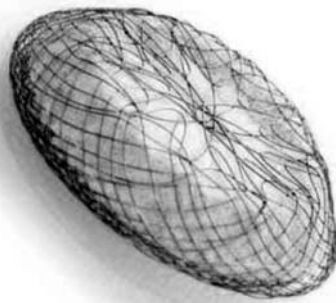
In the third-generation device (Flex II), the delivery system was changed to a biptome-like delivery system, allowing full circular movement, and less metal in the center provides better flexibility and a smaller delivery sheath (Fig. 3).

All devices have a lower profile on the left atrial side with less impingement of the aortic vessel walls if placed adjacent to it. During deployment, the left atrial part develops in a round, ball-like shape omitting the flat profile of other devices with a double sided hub (Fig. 4). This prevents a prolapse of the left-sided disc during the implantation process especially in large ASDs or those without or minimal aortic rim [7].

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(a)



(b)

Fig. 3. (a) Figulla Flex II Occluder (Flex II): The connecting mechanism is a specific biptome enabling optimal mobility. (b) A different design decreased the amount of material in the implant with less left-sided material.

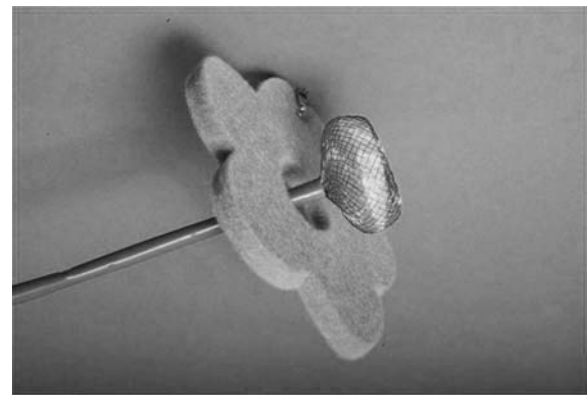
Patient Characteristics

The following data were obtained: patient gender, age, weight, height, diagnosis, reasons for closure of the ASD, the ECG, and ECHO parameters. Procedural data included the mode of sedation/anesthesia, the procedural and fluoroscopy time, the type of echocardiography used, and the specific characteristics of the ASD. A deficient aortic rim was defined as a distance ≤ 4 mm, while a “naked aorta” was defined when no aortic rim was present [10]. An aneurysm was defined when the septum movement exceeded 10 mm.

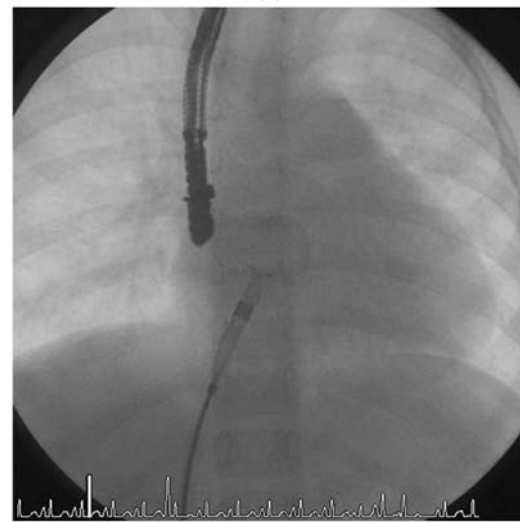
The data analysis included the size of the device and it was noted if more than one device was implanted. Additionally, it was recorded whether additional techniques were used or complications occurred. Finally, closure success (including ECHO) and complications were monitored during follow-up. Only those patients and data were included in the final analysis where the complete data set from the questionnaire was available.

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(a)



(b)

Fig. 4. (a) Development of the left-sided disc of the Figulla Flex[®] occluder at bench testing. Note the round, ball-like shape of the occluder. (b) Development of the left-sided disc of the Figulla Flex[®] occluder during implantation. Note the round, ball-like shape of the occluder (a.p. view).

Large defects. Defects with a stretched diameter >20 mm in diameter are usually regarded as large defects [11], those with a diameter >25 mm as very large defects [12] and may be linked with specific technical problems, especially those with deficient aortic rims.

Small children. Small children often present as a population with a challenging implantation procedure, a subgroup analysis for small children (body weight ≤ 15 kg) was performed regarding safety and feasibility of the ASD closure with the occluders [13].

Side effects during implantation and follow-up. The catheter protocols were reviewed to detect any periprocedural difficulties, i.e., any additional help to position the device at the left side, device embolization, transient or permanent AV block, or perforation. Echocardiographic examinations were analyzed for residual

TABLE I. Patient Characteristics

Patient number analyzed (treated)	<i>n</i> = 1315 (1478)
Female/male	880/435 (66.9%/33%)
Mean height (SD, median, range)	148.6 cm (26.1 cm, 158 cm, 43–195 cm)
Mean weight (SD, median, range)	52 kg (25 kg, 54 kg, 4–175 kg)
Mean age (SD, median, range)	28.9 y (21.4 y, 26 y, 0.3–83 y)
Age distribution	
0–5 years	<i>n</i> = 181 (13.8%)
Small children < 15 kg	<i>n</i> = 94 (7.1%)
6–10 years	<i>n</i> = 212 (16.1%)
11–15 years	<i>n</i> = 130 (9.9%)
>15 years	<i>n</i> = 792 (60.2%)
ECG	
Sinus rhythm	<i>n</i> = 1182 (89.9%)
Atrial fibrillation/flutter	<i>n</i> = 54 (4.1%)
Palpitations/arrhythmias	<i>n</i> = 119 (9%)
Reason for closure	
ASD hemodynamics	<i>n</i> = 1139 (86.6%)
Heart failure	<i>n</i> = 134 (10.2%)
Paradoxical embolism/stroke	<i>n</i> = 74 (5.6%)
Cyanosis	<i>n</i> = 7 (0.5%)

TABLE II. Device Characteristics

Devices implanted	<i>n</i> = 1315
Single device	<i>n</i> = 1261 (96%)
More than 1 device	<i>n</i> = 54 (4.1%)
Very large defects ≥24 mm	<i>n</i> = 511 (38.9%)
Sizes used	
Mean	20.5 mm
SD	7.5 mm
Median	18 mm
Range	6–40 mm
Device specifications	
OSOs	<i>n</i> = 553 (42.1%)
Flex	<i>n</i> = 543 (41.3%)
Flex II	<i>n</i> = 213 (16.2%)

defects. Follow-up data were scanned for arrhythmias requiring medical management such as atrial flutter or fibrillation.

Statistical analysis. Data were collected using Microsoft Excel software and are presented as mean, median, standard deviation, percentage, and ranges wherever appropriate and were analyzed descriptively. To compare the risk of balloon sizing to non-balloon sizing, logistic regression analysis was performed.

RESULTS

Patient Cohort

The patient and device characteristics are summarized in Tables I and II. Between May 2007 and December 2013, complete data sets were available in 1315 of 1478 patients and analyzed; patients in whom the complete

TABLE III. Indications for Closure

	Haemodynamics	Heart failure	Paradoxical embolism	Cyanosis
Total	1139	134	74	7
OSO	504 (44.2%)	32 (23.9%)	35 (47.3%)	–
Flex I	442 (38.8%)	76 (57.7%)	30 (40.5%)	6 (85.7%)
Flex II	191 (16.8%)	25 (18.7%)	7 (9.5%)	1 (14.3%)

data set was not available were not analyzed. In the remaining 163 patients, a successful ASD closure without complications was achieved and no complications on follow-up were detected. Incomplete data sets (i.e., fluoroscopy time, height of the patient, etc.), however, excluded these patients from complete analysis.

The mean age was 28.9 years (SD 21.4 years, median 26 years, range 0.3–83 years), the mean weight was 52 kg (SD 25 kg, median 54 kg, range 4–175 kg), and the height was 148.6 cm (SD 26.1 cm, median 158 kg, range 43–195 cm) in 880 female (66.9%) and 435 male (33%) patients.

One hundred and eighty-one patients were 5 or less years of age (13.8%), 212 between 6 and 10 years (16.1%), 130 (9.9%) between 11 and 15 years, and 792 patients were older than 15 years (60.2%). Ninety-four (7.1%) small children (≤15 kg) were included [13]. The ECG was normal sinus rhythm in 1182 patients (89.9%), atrial flutter or fibrillation was documented in 54 patients (4.1%), and 119 patients (9%) reported palpitations or possible arrhythmias.

Indications for Closure

Significant left-to-right shunting with right ventricular volume overload as assessed by ECHO existed in 1139 patients (86.6%); additional signs of right heart failure were present in 134 patients (10.2%), paradoxical embolism across an ASD was reported by the institutions or referring doctors as indication for ASD closure in 74 patients (5.6%) and cyanosis in 7 (0.5%) (Table III).

Devices Used

The mean device size used was 20.5 mm (SD 7.5 mm, median 18 mm, range 6–40 mm). The devices used were 6 mm in 8 patients, 9 in 45, 10.5 in 73, 12 in 127, 15 in 216, 18 in 187, 21 in 143, 24 in 168, 27 in 137, 30 in 88, 33 in 62, 36 in 38, and 40 in 18. As by definition, there were 511 very large ASDs ≥24 mm in diameter [12].

OSO was used in 553 (42.1%) patients: in 54 (4.1%) children between 0 and 5 years, in 96 (7.3%) children between 6 and 10 years, in 52 (4%) children between

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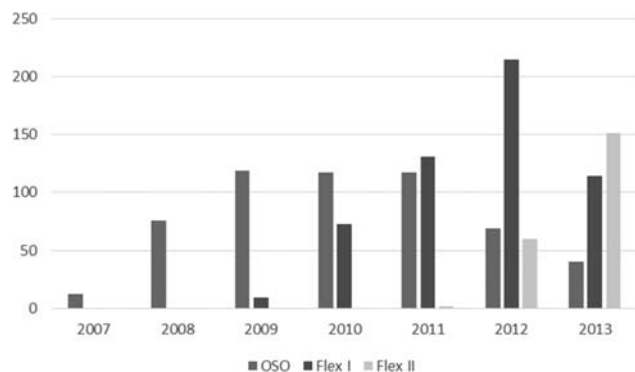


Fig. 5. Devices used: number of devices usage to close ASD from 2007 to October 2013, where dark grey represents OSO, black Flex and bright grey, the Flex II occluder.

11 and 15 years, and in 351 (26.7%) adults above 15 years of age (Tables II and III).

Flex was used in 543 (41.3%) patients: in 84 (6.4%) children between 0 and 5 years, in 78 (5.9%) children between 6 and 10 years, in 52 (4%) between 11 and 15 years, and in 329 (25%) adults above 15 years of age.

Flex II was used in 213 (16.2%) patients: it was used in 43 (3.3%) children between 0 and 5 years, in 36 (2.7%) children between 6 and 10 years, in 26 (2%) children between 11 and 15 years, and in 108 (8.2%) adults above 15 years of age.

The OSO was used from 2007 until 2013, the Flex from 2009 until 2013, and the Flex II from 2011 onward (Fig. 5).

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Procedural Data

The mean procedure time was 52.3 min (SD 34 min, median 45 min, range 7–262 min) and the mean fluoroscopy time was 8.7 min (SD 17.8 min, median 5.8 min, range 0–445 min). TTE only was used in 244 (18.6%) patients, TOE in 1073 (81.6%), and intracardiac ECHO (ICE) in 92 (7.0%). General anesthesia was used in 700 (53.2%), sedation in 677 (51.5%), and local anesthesia only in 96 (7.3%) patients.

Defect closure was obtained by straightforward device placement in 1221 cases (92.9%), additional techniques were used in 94 patients only (7.1%), balloon-assisted deployment in 26 cases (2%), a Hausdorf sheath in 2 (0.2%), a double wire technique in 4 (0.3%), device deployment in the left pulmonary vein in 37 (2.8%), and in the right pulmonary vein in 25 patients (1.9%) (Table IV). Balloon sizing was performed by stop flow technique.

ASD Characteristics

A typical ASD was present in 591 (44.9%) patients, 190 patients (14.4%) presented with a “naked aorta,”

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TABLE IV. Procedural Data and ASD Characteristics

	Mean	SD	Median	Range
Procedural time (min)	52.3	34	45	7–262
Fluoroscopy time (min)	8.7	17.8	5.8	0–445
TEE/ICE size (mm)	16.7	7.1	15.5	2–39
Balloon size (mm)	18.1	6.4	17.5	1–40
Procedure details				
TTE only	n = 244 (18.6%)			
TOE	n = 1073 (81.6%)			
ICE	n = 92 (7%)			
Balloon sizing	n = 919 (69.9%)			
General anesthesia	n = 700 (53.2%)			
Sedation	n = 677 (51.5%)			
Local anesthesia only	n = 96 (7.3%)			
Technical success:	1291/1315 (98.2%)			
Closure rate at discharge:	1093/1315 (83.1%)			
Closure rate at follow-up:	1271/1291 (98%)			
>1 Device used	n = 54 (4.1%)			
Additional techniques used				
Balloon assisted	n = 26 (2%)			
Hausdorf sheath	n = 2 (0.2%)			
Double wire technique	n = 4 (0.3%)			
Left pulmonary vein	n = 37 (2.8%)			
Right pulmonary vein	n = 25 (1.9%)			

TABLE V. Device Distribution

	OSO	Flex	Flex II	Total (%)
“Normal” ASD	251	232	105	588 (44.7%)
Difficult ASDs				
“Naked aorta”	94	76	18	190 (14.4%)
Deficient rim < 5 mm	191	186	60	440 (33.5%)
>1 defect	57	67	32	156 (11.9%)
Septum aneurysm	90	150	41	283 (21.5%)
Total	683	711	256	

Note: Combinations of difficult ASD anatomies is possible.

and a deficient rim (<5 mm) was present in 440 cases (33.5%). More than 1 defect could be detected in 156 patients (11.9%) and a septum aneurysm was present in 283 patients (21.5%). This implies that 630 of 1315 ASDs (47.9%) had no or 1 deficient rim and 818 of 1315 ASDs (62.2%) were deemed difficult to close by the underlying anatomy. The mean defect size was 16.7 mm (SD 7.1 mm, median 15.5 mm, range 2–39 mm) by ECHO and 18.1 mm (SD 6.4 mm, median 17.5 mm, range 1–40 mm) by balloon sizing if used. Balloon sizing was used in 919 (69.9%) patients. More than 1 device was used in 54 (4.1%) patients (Table IV). The distribution of the different defect types according to the devices used is shown in Table V (combinations of difficulties in ASD anatomy are possible).

T4

T5

Results

Successful implantation was achieved in n = 1291/1315 (98.2%) patients. Immediate closure was obtained

TABLE VI. Complications During Follow-Up (n = 1297)

	Device embolization	Perforation/erosion	AV-Block	Atrial flutter/fibrillation	Other arrhythmia requiring treatment	TIA	Stroke	Thrombus at device	Surgery with device removal	Arrosion of mitral valve	New onset migraine (headache)
Total (%)	5 (0.4%)	0 (0%)	3 (0.2%)	21 (1.6%)	25 (1.9%)	2 (0.2%)	2 (0.2%)	0 (0%)	5 (0.4%)	0 (0%)	19 (1.5%)
OSO	–	–	3	8	16	1	–	–	1	–	8
Flex I	4	–	–	9	6	1	2	–	3	–	9
Flex II	1	–	–	4	3	–	–	–	1	–	2

in 1034 (78.6%) and at discharge from the hospital in 1093 (83.1%). The closure rate increased to 96.4% (1247) at 6 months and 97.3% (1262) at 12 months and finally to 98% (1271) at 5-year follow-up. The residual shunts reported were trivial/trace in most cases and caused by additional small second defects in many patients that were not covered by the implanted device.

Complications at Implantation

Results. Device embolization occurred in 18/396 patients without balloon sizing (=4.54%), whereas this complication happened in only 2/919 patients (=0.22%) when balloon sizing was performed (OR = 21.8 (95% CI: 5.01–94.6); *P* < 0.001). In 4 patients, surgery was performed; one patient needed another device and in the remaining patients, the device could be retrieved by catheter techniques and the ASD was successfully closed interventionally. A transient AV block occurred during device delivery in 7 cases (0.5%). In two patients, the block disappeared spontaneously. The device was retrieved in 5 patients and replaced by a smaller device; in these patients, balloon sizing was not performed before implantation and an oversized device was initially used.

Significant arrhythmias that required treatment (medication, cardioversion) occurred in 16 (1.2%) patients but remained without clinical sequelae. There was no perforation or erosion during the implantation process.

Complications During Follow-Up

Follow-up was possible in 1297 of the initial 1315 patients summing up to a total of 3597 patient years of follow-up time. During a mean follow-up period of 2.7 years, there were 89 complications (6.8%); the majority was minor like arrhythmias commonly reported for this group of patients (Table VI). Significant complications occurred in 8 patients only (rate: 0.6%); these were device embolizations in 5 (4 without prior balloon sizing) and new onset AV blocks in 3 patients. In 1 patient, steroids were applied leading to a return to sinus rhythm with a persistent PQ prolongation (AVBlock I°) after about 1 week. In one elderly patient (74 years of age) with pre-existing intermittent atrial

flutter, a permanent VVI pacemaker was implanted. In the remaining teenager (14 years) who had a large and oversized device implanted without initial balloon sizing, the device was removed and the defect closed surgically by patch; the rhythm returned to sinus rhythm with a prolonged PQ conduction time (AVBlock I°). Atrial flutter or fibrillation occurred in 21 patients (1.6%), other arrhythmias requiring treatment in 25 (1.9%), 4 patients suffered from a TIA or minor, clinically not relevant stroke (0.3%), 19 patients reported transient episodes of new onset of headaches or migraine that were managed medically. In 5 patients, the device was removed, in 3 for reasons not primarily device related (1 due to embolization, and in another one impingement on the aortic root was noted and the device removed prophylactically). There was no erosion of the mitral valve or aorta and no thrombus formation at the device surface was detected.

Small Children

Ninety-four patients (7.1%) presented with a body weight ≤15 kg. Mean age was 3.7 years (SD 2.8 years, median 3.1 years, range 0.3–24), mean body weight was 13.3 kg (SD 2.1 kg, median 14 kg, range 4–15.8 kg), and mean body length was 95.3 cm (SD 11.9 cm, median 96.5 cm, range 54–15 cm). Mean procedural time was 66.5 min (SD 42.9, median 58 min, range 9–201 min) and mean fluoroscopy time was 11.1 min (SD 36.1 min, median 5.5 min, range 1.2–346 min). Thirty-nine children showed no or only a deficient aortic rim, 9 had multiple defects, and 12 had a septum aneurysm/floppy septum. Technical success was achieved in 94.7%, and overall closure rate was 95.7%. Complications occurred in 12 patients (12.8%).

Large Defects

Of 1315 patients, 511 were treated with a device ≥24 mm in diameter (38.8%). The mean age was 39.7 years (SD 18.4 years, median 41 years, range 3.9–83 years), the mean body weight was 63.4 kg (SD 19 kg, median 62.3 kg, range 12.5–157 kg), and their mean body length was 160.7 cm (SD 14.9 cm, median 162 cm, range 43–195 cm). Mean procedure time was

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49.8 min (SD 33.1 min, median 43 min, range 12–262 min) and mean fluoroscopy time was 9.9 min (SD 9 min, median 7.8 min, range 0–74.1 min). In 394 patients (77.1%), there was no or 1 deficient aortic rim, 54 (10.6%) had more than one defect and 135 (26.4%) had a septum aneurysm/floppy septum. Technical implantation was successful in 97.5%. Complications occurred in 36 patients (7%) and the overall closure rate was 92.4%.

DISCUSSION

After the first report by King et al. in 1974, interventional closure of ASDs is nowadays generally accepted and compared to surgery it has the advantage of fewer complications, shorter hospitalization, a reduced need of blood products and in most countries considerably lower treatment costs [1–5,35–37]. This was shown by many controlled investigations with high number of patients and different devices [2,14]. El-Said et al. recently reported the results of ASD closure within the C3PO project in 653 of 688 ASDs (94.9%), where 566 of 653 ASDs (87%) were closed with Amplatzer devices, 33 (5%) with the Helix devices, and 54 (8%) with Starflex or Cardioseal devices [15]. Ongoing assessment by registries is warranted to assess long-term device safety and facilitate adequate surveillance.

Occlutech Devices

The use of the three generations of OFSO have not been reported so frequently; to our best knowledge, <550 implantations using the OFSO are reported in the literature until now. First reports were published in 2008 followed by many other case reports [16,17]. Smaller case series used only the first generation; Pac et al. compared the results of ASO and OSO in 75 patients and found no differences [18]. Aytemir et al. presented early and mid-term follow-up results (mean 15 months) of 83 adult patients with ASD closure using OSO with an excellent closure rate and no complications [19]. Cansel et al. were able to successfully close 92% of ASDs in 74 adult patients [8], Ilkay reported successful closure in 28 adult patients [20], and Ammar in 17 symptomatic children younger than 2 years of age [21].

Until now, there are only very few reports regarding the use of the Occlutech Figulla Flex[®] device (Flex) for ASD closure. Mortezaiean et al. reported the successful use of the Flex in 45 children [22]. The unique characteristics of the Flex to align anatomically correct to the atrial septum was demonstrated in 122 consecutive patients [7]. Roymanee et al. recently published a

comparison between the OFSO and the ASO in 149 patients; there was a slightly higher success rate in the patients with an OFSO (97.4% vs 94.4%) and the median fluoroscopic time in the OFSO group was shorter (ASO 13.7 min vs OFSO 9.0 min) despite larger ASDs in this group [23]. Godart et al. compared the second and third generations of the Figulla ASD Occluder ($n = 31$), with the ASO ($n = 100$) in 131 patients [24]. No major differences between the groups were detected in complication and occlusion rate.

Implantation Technique

To date, there is no risk model for ASDs in terms of technical difficulty; an exact judgement and comparison of case series is therefore challenging. It is accepted that these ASDs are judged as difficult to close where additional maneuvers for device placement are necessary based on the underlying anatomy (i.e., large ASDs, those without rims), where implantation requires additional or longer imaging (multiple ASDs, those with floppy septum and septum aneurysms) or those when the device/heart ratio is a problem (i.e., large defects especially in small children). In many other devices, the left-sided disc immediately configures flat and may be diagonally pulled across the septum “slipping through the ASD” in a considerable number of cases. To overcome this problem, many different techniques have been described [25]. In our case series, this was necessary in only 94 implantations despite the fact that there was a considerable high amount of patients with large ASDs and deficient aortic rims; these findings may indicate the benefit in feasibility of ASD closure with the OFSO devices.

Fluoroscopy Time

Despite the fact that most of the procedures were performed in a high percentage of so-called complex or difficult ASDs, the overall procedure time (mean 52.3 min, SD 34 min, median 45 min) and fluoroscopy time (mean 8.7 min, SD 17.8 min, median 5.8 min) was considerably short. Fischer et al. reported a single-center series using the ASO in 200 patients with a median fluoroscopy time of 12 min [26]. In the MAGIC atrial septal defect, the mean overall fluoroscopy time was 18.46 min (SD 12.10); for simple ASDs, it was 17.66 min (SD 11.07) and for complex cases 20.85 min (SD 14.55) [14]. Similar fluoroscopy times exceeding a mean of 10 min are reported by many authors [27–29]. In direct comparison between OFSO and ASO, shorter fluoroscopy times were reported for the OFSO devices [23,24]. This may be an indication for the feasibility, simplicity, and thereby safety of device implantation using the OFSO in all

subgroups of patients or defects. A potential bias caused by a learning curve of the interventionalists may however not be completely excluded; in addition, the relative difficulty of cases might have differed.

Small Children

Our rate of 94/1315 (7.1%) of small children as well as the patient and ASD characteristics and rate of complications is comparable to the multicenter series presented by Cardenas et al. who reported 52 children out of 484 patients (15.4%) and complications in 8 (10.7%) [13]. A similar rate was reported by Diab et al. with 4/15 infants and Vogel et al. in 3/12 [30,31]. In addition, the procedure time (mean 66.5 min) as well as fluoroscopy time (mean 11.1 min) in our patient cohort was considerably less than that reported in the group from Belgium. Dalvi et al. reported of 32 children below 20 kg, where large ASO devices >20 mm were used. Balloon-assisted techniques were necessary in 20 patients [32]. Therefore, a technical advantage of the OFSOs with rapid and ideal septum alignment may play a role regarding implantation technique and the rate of side effects.

Large Defects

Many devices can be used for defects up to a diameter of 20 mm only [2]. Larger defects, i.e., those with a stretched diameter \gg 20 or 25 mm, require a stable device position and sometimes some “oversizing” for stable placement [29,32]. We used 511/1315 (38.9%) occluders measuring more than 24 mm; therefore, our series contains an adequate number of larger defects and with complex anatomy as compared to others [14,15,26]. However, there were only 7 patients with device embolization and 3 with AV-conduction problems. Four of those needed solvation by percutaneous retrieval or surgical removal. All other 497 ASD closures in this cohort were successful without the need for additional fluoroscopy or procedural time.

Side Effects

In one most recent report by El Said et al., procedural characteristics and adverse events (AE) at eight centers participating in the C3PO registry over a period of 40 months are reported with an 11% rate of any AE and a 4.7% rate of a higher severity AE (level 3 or 4) [15]. Our study has a very comparable setting with many participating centers over a comparable time-frame but shows a much lower overall rate of adverse events (6.8%) and rate of severe adverse events (<1%). A direct comparison of these two studies seems, how-

ever, difficult as different thresholds of adverse event report may be given.

Erosions

Many patients had no (14.4%) or only 1 deficient aortic rim (33.5%); however, we did not see any erosion during the first 48 h or the follow-up. In general, erosion rates are low, ranging from unique case reports up to 1% in some series, an incidence ratio of 0.1–0.3% seems realistic in ASO [38–40]; logically a number of 2–6 erosions would have been expected over the observed 3597 patient years [2,27,43]. There was one case with a 40 mm Occluder, where the device was noted to be impinging the aortic root during follow-up; the patient underwent prophylactic surgery for device removal. The design of the device increases the flexibility and reduces the shear forces as compared to the ASO; this may be beneficial as most of the ASO erosions reported are caused by oversized devices in patients with deficient aortic rims.

AV-Block

We did encounter seven AV-blocks during implantation; in four patients, the device was removed, and the defect was surgically closed. Three blocks occurred during follow-up encountering a rate of 3/1315 = 0.2%. Two of these patients were treated and sinus rhythm with PQ prolongation returned. This incidence is within the reported limits of other large series or registries [2,14,15,27,41,42].

Embolizations

Device embolization usually is another rare complication. Chessa et al. reported an embolization rate of 4/159 patients (2.5%), where a Cardioseal/Starflex device was used and 3/258 patients with the use of an ASO (1.1%) [33]. Butera reported of 7/824 patients with device embolization or malpositioning (0.8%), the MAGIC study reported 3/458 patients (0.7%). This is the first study that clearly demonstrates an increased risk of device embolization (OR = 21.8 (95% CI: 5.01–94.6); $P < 0.001$) when balloon sizing is not performed. We encountered 15/1315 (1.1%) embolizations during implantation and 5/1297 (0.4%) during follow-up. Except in four cases, all of them had no or 1 deficient aortic rim or a septum aneurysm and the majority of the embolized occluders were implanted without prior balloon sizing. These results clearly support the routine use of balloon sizing as standard of care for interventional ASD closure.

Study Limitations

The inclusion of the patients was not standardized prospectively; therefore, the study suffers the theoretical biases of such investigations. In addition, based on the retrospective character and the large number of patients, there was no assessment of the images by a central core lab nor was an auditing of the records performed. All the information presented was however continuously collected on an intention-to-treat basis according to the quality assurance program of the participating hospitals and comparable to a prospective investigation. In the same way, side effects, problems during implantation, and follow-up data were monitored; adverse events during follow-up were reported by the submitting centers based on the local follow-up program or the referring doctors only and only patients with a well-documented follow-up were included. All consecutive patients that were referred for device closure with Occlutech devices were recruited. Therefore, the possibility of inadequate data acquisition seems reasonably low. Having many different hospitals and investigators participating in this study may add difficulties in comparison of the skills and implantation methods used.

The sample size and the follow-up period may be judged only moderate. Many single-center reports of similar case series however present data of <100 patients over a comparable time period. The age range, the different sizes, and anatomies of the defects presented seem representative for a normal patient cohort for interventional ASD closure. The latest version of the OFSOs (Flex II) was only used in 16% of total cases. The results of this study, therefore, cannot represent the Flex II results. A follow-up study with 2000 Flex II devices is currently planned for detailed analysis (IRFACODE II study).

For a final judgement for rare complications such as erosions, more studies with a higher patient number are necessary. Based on the data published so far, we would have however expected a considerable number of cases of erosion reported in this study if relevant for the device.

Finally, we did not present any control group; it was not the aim of the study to create a comparison but to describe the specific properties of the OFSOs in detail. Therefore, it is not possible to postulate that specific aspects of the device design of the OFSOs led to improved outcomes without a head-to-head comparison of the devices in prospective trials.

CONCLUSION

The OFSOs have specific device properties different to the Amplatzer septal occluders and similar devices,

especially a lack of a left-sided hub generating a softer left-sided disc and different morphology during deployment and a tiltable connection to the delivery cable. Based on our data presented, ASD closure using the OFSOs was feasible in a large variety of patients and different ASD anatomy. Implantations were performed with a relatively short fluoroscopy time and there were only few severe side effects. We did not encounter any aortic erosion despite a large percentage of defects with no or only deficient aortic rim as shown in this large multinational outcome registration project (IRFACODE).

Based on the properties described, we believe that this occluder system is a significant improvement for the interventional ASD closure concerning feasibility as well as patients safety, and therefore a valuable addition to the armamentarium of ASD closure devices.

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