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Patent foramen ovale with complex anatomy: Comparison of two different devices (Amplatzer Septal Occluder device and Amplatzer PFO Occluder device 30/35)☆

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ABSTRACT

Background: Patent foramen ovale (PFO) closure after a cryptogenic cerebral ischemic event is a routinely procedure. The most used device is Amplatzer™ PFO Occluder 25 mm, but PFOs with complex anatomy require larger device for closure. We compared Amplatzer™ Septal Occluder (ASO) device versus Amplatzer™ PFO Occluder 30 or 35 mm (A-PFO 30/35) about the safety of procedure and the presence of residual shunt during the follow-up.
Methods: From June 2002 to July 2016, 355 patients (pts) with PFO undergone closure at our institution. Among these ones, 70 pts (19.7%) had a PFO with complex anatomy and a single device with greater diameter was implanted. In these cases, the following devices were used: Gore® Septal Occluder (GSO) in 4 pts; ASO device in 33 pts (group I) and A-PFO 30/35 in 33 pts (group II). Patients treated with GSO device were excluded by our analysis.
Results: Comparing group I and group II, there weren't complications during the procedures. Two patients of group II were lost at follow-up. At last follow-up, 1 pt of group I (3%) and 10 pts of group II (32.3%) had a residual shunt ($p < 0.01$). 7 of 10 pts of group II and the only 1 of group I with residual shunt underwent a complete closure by Amplatzer™ Vascular Plug (AVP) devices.
Conclusions: ASO devices and A-PFO 30/35 devices are both safe to close complex PFO; but A-PFO 30/35 is associated with a more incidence of residual shunt.

1. Introduction

Percutaneous closure of patent foramen ovale (PFO) in patients with paradoxical embolism is a feasible choice, above all in recurrent cases [1]. A multicentre randomized trial (RESPECT trial) showed the benefits of percutaneous closure of PFO by Amplatzer Occluder devices than medical therapy [2]. The REDUCE Clinical Study demonstrated the effectiveness of Gore Helex devices in reducing cerebral ischemic events in patients with PFO and cryptogenetic stroke [3]. The Amplatzer™ PFO Occluder (St. Jude Medical-Abbott, Minneapolis, MN) is the most used device because of its safety and efficacy [4,5]. PFO balloon sizing is not recommended, but some authors are favourable, to better define the size and length of tunnel and to achieve more indications about PFO anatomy in patients with aneurysmatic septum, particularly [6,7]. Usually, when sizing is performed, a measure ≥13 mm is the cut-off to choose a bigger device. It is not clear what is the best device for treatment of PFO with complex anatomy and with balloon sizing ≥13 mm. In these cases, both Amplatzer™ Septal Occluder (St. Jude Medical-Abbott, Minneapolis, MN) and Amplatzer™ PFO Occluder 30 or 35 mm can be used. The purpose of this study is to compare safety and efficacy of these kinds of device.

2. Methods

2.1. Patients population

Between June 2002 and June 2016, 355 patients with PFO undergone closure at our institution. Among these ones, 88 pts (24.7%) had a PFO with complex anatomy (defined as PFO balloon sizing ≥13 mm associated to one or more of following features: misaligned septum, atrial septum aneurysm, multiple fenestrations). Patients required more than one prosthesis (18 pts) were excluded from analysis. All resting 70 patients (19.7%) required the implantation of a single device to close all sites of shunt. The following devices were used: Gore® cardioform Septal Occluder (GSO) in 4 pts; Amplatzer™ Septal Occluder (ASO) device in 33 pts (group I) and Amplatzer™ PFO Occluder 30 or 35 mm (A-PFO 30/35) in 33 pts (group II). Patients treated with GSO device were excluded by our analysis.

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Mean age and weight were 43.9 ± 11.9 years and 76.7 ± 14.6 kg, respectively; without significant statistically differences between the two groups (42.9 ± 13.8 years in group I vs 45 ± 9.6 years in group II, p-value = 0.5; 74.8 ± 16.6 kg in group I vs 78.7 ± 12.3 kg in group II, p-value = 0.3). The most of patients (60/66, 90.9%) needed to close PFO because of cerebral ischemic events. Less common reasons of closure were: disabling migraine (1 pt in group I), gas embolism during scuba diving (2 pts in group II), kidney ischemia due to paradoxical embolism (1 pt in group 1) and platipnea ortodeoxia (1 pt in group I and another one in group II). Only one patient had a positive thrombophilic pattern: homozygous mutation of the methylene tetrahydrofolate reductase gene (MTHFR), plus heterozygous mutation for angiotensinogen (AGT) and ataxia telangiectasia and Rad3-related protein (ATR-1), plus homozygous mutation of glycoprotein IIIa (GPIIIa). Interatrial septum (IAS) was: aneurysmatic (although with a single site of shunt) in 49 pts (23 cases in group I vs 26 cases in group II, p = 0.5), misaligned in 3 pts (2 cases in group I vs 1 case in group II, p = 0.06) and characterized by multiple fenestrations in 14 pts (8 cases in group I vs 6 cases in group II, p = 0.6), without statistically significant differences between the two groups. No patients had a tachyarrhythmia, while 3 pts had a bradyarrhythmia before the procedure: 1 sick sinus syndrome treated by pacemaker implantation (in group I), 1 complete atrioventricular block (AVB) with isorhythmic dissociation (in group I) and 1 atrioventricular block grade I (in group II). Patients characteristics are summarized in the Table 1. The study was approved by the institution's ethics board and informed consent was obtained from all participants.

2.2. Interventional procedure

PFO closure was guided by an antero-posterior or left anterior oblique angiographic view. Periprocedural transesophageal echocardiogram (TEE) was performed in all patients, except two patients underwent trans-thoracic echocardiogram (TTE) and one patient underwent intracardiac echocardiography (ICE) to avoid general anesthesia. All patients received an intravenous dose of heparin (5000 UI). The vascular access was achieved through the femoral vein (sheath introducer 10 F or 11 F). PFO was probed by a multipurpose catheter and then stretched through an Equalizer™ Occlusion Balloon Catheter (Boston scientific).

Table 1
Features of populations and procedural skills.

	Total (n = 66)	Group I (n = 33)	Group II (n = 33)	p-Value
General features				
Male	29 (43.9%)	12 (36.4%)	17 (51.5%)	0.8
Age (years)	43.9 ± 11.9	42.9 ± 13.8	45.0 ± 9.6	0.5
Weight (kilograms)	76.7 ± 14.6	74.8 ± 16.6	78.7 ± 12.3	0.3
Thrombophilia	1 (1.5%)	0	1 (1.5%)	
Reason of PFO closure:				
- Cerebral ischemic events	60 (91%)	30 (91%)	30 (91%)	
- Disabling migraine	1 (1.5%)	1 (3%)	0	
- Gas embolism (scuba diving)	2 (3%)	0	2 (6%)	
- Kidney ischemia (PE)	1 (1.5%)	1 (3%)	0	
- Platipnea ortodeoxia	2 (3%)	1 (3%)	1(3%)	
Echocardiographic features				
Aneurysm of IAS	49 (74.2%)	23 (69.7%)	26 (78.8%)	0.5
Misaligned septum	3 (4.6%)	2 (6.1%)	1 (3%)	0.06
Multiple fenestrations	14 (21.2%)	8 (24.2%)	6 (18.2%)	0.6
Sizing diameter	14.91 ± 1.41	14.88 ± 1.49	14.94 ± 1.34	0.7
PFO sizing diameter:				
- 13 mm	11 (16.7%)	6 (18.2%)	5 (15.2%)	0.7
- 14 mm	15 (22.7%)	7 (21.2%)	8 (24.2%)	0.8
- 15 mm	22 (33.3%)	12 (36.4%)	10 (30.3%)	0.8
- 16 mm	10 (15.2%)	5 (15.2%)	5 (15.2%)	1
- 17 mm	5 (7.6%)	1 (3%)	4 (12.1%)	<0.01
- 18 mm	1 (1.5%)	0	1 (3%)	
- 19 mm	2 (3%)	2 (6%)	0	
Device implanted:				
- ASO 12 mm		3 (9.1%)		
- ASO 13 mm		3 (9.1%)		
- ASO 14 mm		7 (21.3%)		
- ASO 15 mm		11 (33.3%)		
- ASO 16 mm		6 (18.2%)		
- ASO 17 mm		1 (3%)		
- ASO 18 mm		1 (3%)		
- ASO 19 mm		1 (3%)		
- A-PFO 30 mm			7 (21.2%)	
- A-PFO 35 mm			26 (78.8%)	

Categorical data are expressed like absolute number and percentage. Continuous data are expressed like mean value ± standard deviation.
IAS: interatrial septum; PFO: patent foramen ovale; PE: paradoxical embolism; ASO: Amplatzer Septal Occluder device; A-PFO: Amplatzer PFO occlude device.

Table 2
Preoperative and postoperative arrhythmias.

Arrhythmias	Preoperative	Postoperative
Sick sinus syndrome	1 (group I)	1 (group I)
Complete atrioventricular block	1 (group I)	1 (group I)
Atrioventricular block grade I	1 (group II)	1 (group II)
Atrial fibrillation	0	1 (group II)

The smallest balloon diameter needed to achieve a stop flow at echocardiographic evaluation, addressed the choice device size. The mean sizing diameter was 14.91 ± 1.41 mm, without significant statistically difference between the groups (14.88 ± 1.49 mm in group I vs 14.94 ± 1.34 mm in group II, p = 0.8). In the group I, the devices implanted were: 3 ASO 12 mm (9.1%), 3 ASO 13 mm (9.1%), 7 ASO 14 mm (21.3%), 11 ASO 15 mm (33.3%), 6 ASO 16 mm (18.2%), 1 ASO 17 mm (3%), 1 ASO 18 mm (3%), 1 ASO 19 mm (3%). In the group II, the devices used were: 7 A-PFO 30 mm (21.2%) and 26 A-PFO 35 mm (78.8%). Procedural and fluoroscopic time was 54 ± 15.06 and 6.8 ± 4.49 min, respectively. Dose adsorbed registered was 244 ± 198.06 mGy. In all patients, an intravenous load dose of acetylsalicylic acid (300–500 mg) was administered. Every patient assumed clopidogrel 75 mg at day for 3 months and acetylsalicylic acid 100 mg at day for 1 year after the procedure. Endocarditis prophylaxis was recommended for 1 year in all patients; and beyond for those ones with residual shunt. Echocardiographic and procedural features are summarized in the Table 1.

2.3. Follow-up evaluation

During follow-up, all patients were periodically checked through a cardiologic visit, an electrocardiogram and echocardiography. One year after the procedure, every patient underwent trans-cranic echography (TCE) for evaluation of an eventual residual shunt. Patients with a clear residual shunt at echocardiography or with a positive TCE underwent catheterization for percutaneous closure.

2.4. Statistical analysis

All statistical analyses were performed using Statistical Package for Social Sciences, for Windows, version 20 (SPSS, Chicago, Illinois). Continuous variables (weight or age) were presented as mean ± standard deviation or as median and interquartile range (IQR) when appropriate. Categorical data (as residual shunt at follow-up) were expressed as frequency (percentage). Continuous and categorical variables were analysed by *t*-Student test and chi-square test or Fisher exact test, respectively. Data analysis was considered statistically significant by a p-value <0.01.

3. Results

All patients underwent a successful closure of PFO. In both groups, there weren't hospital mortality or morbidity. Vascular complications weren't recorded. In one patient, the first device chosen (an ASO 15 mm) was retired because of its instability during the push-pull manoeuvre ("Minnesota wiggle") and substituted by an A-PFO 30 mm. In one case, because of anatomical features of PFO, interatrial septum was perforated by a Brockenbrough needle and then an A-PFO 35 mm device was implanted. The mean follow-up was 2.7 ± 1.3 years. During follow-up, 2 patients of group II were lost. There were neither deaths nor complications (cardiac erosion, embolization of device, fistulas or hematomas of vascular access site). Only 1 pt (group II) developed a

Table 3
Chi-square analysis about residual shunt.

	Residual shunt	No residual shunt	Total
One year after the procedure			
Group I (ASO)	1 (6.19) [4.35]	32 (26.81) [1.00]	33
Group II (A-PFO 30/35)	11 (5.81) [4.63]	20 (25.19) [1.07]	31
Total	12	52	64
Last follow-up			
Group I (ASO)	1 (5.67) [3.85]	32 (27.33) [0.80]	33
Group II (A-PFO 30/35)	10 (5.33) [4.10]	21 (25.67) [0.85]	31
Total	11	53	64

The contingency table below provides the following information: the observed cell totals, (the expected cell totals) and [the chi-square statistic for each cell]. One year after the procedure: the chi-square statistic is 11.05 and the p-value is 0.0009 (p < 0.01). At last follow-up, the chi-square statistic is 9.59 and the p-value is 0.002 (p < 0.01).
ASO: Amplatzer Septal Occluder device; A-PFO: Amplatzer PFO occlude device.

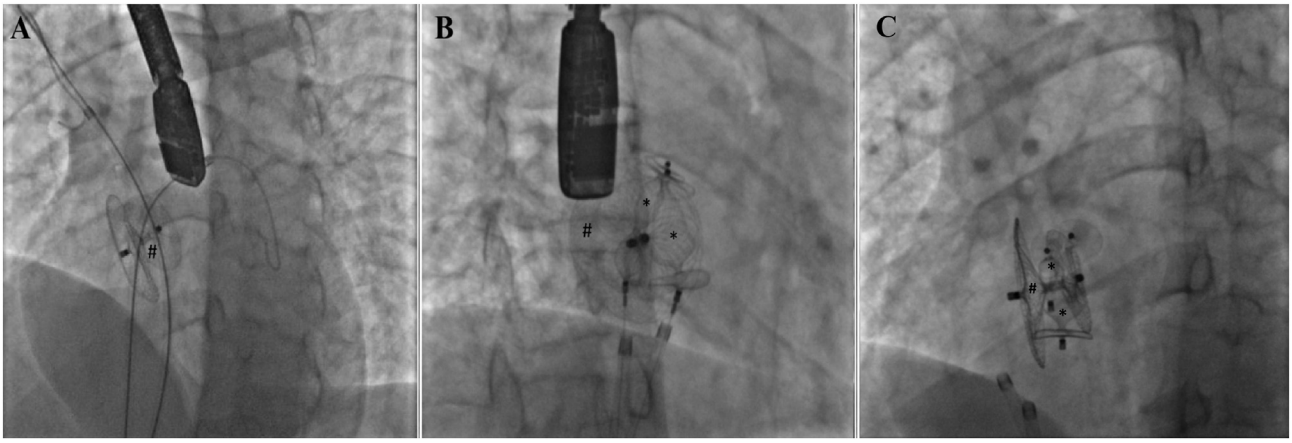

Fig. 1. Angiographic view of an Amplatzer PFO Occluder device 35 mm (#) with two sites of residual shunt. The inter-discal space was crossed by two wires and catheters (A) and then two Amplatzer Vascular Plugs (*) were released to allow better compaction of the disks and a complete closure of the residual shunts by filling the inter-discal space totally (B and C).

paroxysmal atrial fibrillation [Table 2]. New onset of arrhythmias was not noted in the other patients. One year after the procedure, only 1 patient (1/33, 3%) of group I had a residual shunt, versus the 11 patients (11/31, 35.5%) of group II ($p < 0.01$) [Table 3]. At last follow-up (2.7 $\pm$ 1.3 years), in 1 patient (1/33, 3%) of group I and in 10 patients (10/31, 32.3%) of group II there was a residual shunt ($p < 0.01$) [Table 3]. Among these 10 patients, 7 underwent percutaneous closure of residual shunt. Devices used were 9 Amplatzer™ Vascular Plug (AVP, St. Jude Medical-Abbott, Minneapolis, MN): two AVP type-I 8 mm, two AVP type-I 12 mm, one AVP type-II 8 mm, one AVP type-II 10 mm, two AVP type-II 12 mm and one AVP type-II 14 mm. Five patients required the implant of a single device to obtain a successful closure, while two patients needed the placement of two devices. During follow-up, only one of these seven patients showed a positive TCE, but a new catheterization didn't demonstrate the presence of a residual shunt. In the group I, the single patient with residual shunt was treated by AVP type II 12 mm.

4. Discussion

PFO closure in patients with paradoxical embolism is a routinely procedure, but sometimes the procedure becomes more complex because of foramen anatomy. In these cases, there is a high risk of incomplete procedure because of the presence of a residual shunt, by exposing the patient to one more catheterization for achieving a complete closure [8,9]. In these patients, device selection is a very important phase and it influences the complete successful of procedure. According to our experience, Equalizer™ Occlusion Balloon Catheter allows an adequate evaluation of PFO and it can address device choice. In these cases, Amplatzer™ Septal Occluder and Amplatzer™ PFO Occluder 30 or 35 mm are possible choices. Amplatzer™ Septal Occluder device has a wide waist that is useful to center the device [10], whereas Amplatzer™ PFO Occluder device has a flexible and narrow central pin that keeps each disc well attached to the other one [11].

Our analysis showed that PFO sizing is a valid system to address the interventional cardiologist to choose a device greater than Amplatzer™ PFO Occluder 25 mm. Safety is high for both major devices (ASO and A-PFO 30/35). Periprocedural mortality, morbidity and vascular complications weren't recorded. At follow-up, no patient developed main complications (as device embolization or cardiac erosion) and just 1 pt had the new onset of a tachyarrhythmia (atrial fibrillation). In patients treated with ASO device, effectiveness of closure is higher than those treated with A-PFO 30/35. At last follow-up, patients treated with ASO and those treated with A-PFO 30/35 had complete closure percentage of 97% and 72.7% ($p < 0.01$), respectively. The major effectiveness of ASO could be due to the wide waist of the device that allows itself a better placement and a high capability to occlude the inter-atrial tunnel of PFO. The waist gives high stability to the device by reducing the risk of residual shunt at follow-up, while the two disks of the A-PFO 30/35 are not able to "compact" the septum because not supported by a central waist. Therefore, the two disks remain separated not adhering to the septum, leaving an inter-discal residual shunt, that in our experience required the implantation of Vascular plug in-between the disks [Fig. 1].

The most part of patients of group II with residual shunt (77.8%) and the only one of group I underwent one more catheterization and they achieved a complete closure by using AVP device. No complications due to the new catheterization were recorded.

5. Study limitations

In this study, only two types of device were analysed. Other devices can be used for treatment of complex PFO, and these ones should be analysed to achieve a complete square about closure of these complex defects.

6. Conclusion

PFO size and anatomy can influence the choice of device. Sizing balloon of PFO is a feasible and adequate technique to evaluate the anatomy of foramen and to address the choice of device. Both Amplatzer Septal Occluder and Amplatzer PFO Occluder devices are safe for closure, although ASO is more effective and associated with a less risk of residual shunt at follow-up. Amplatzer Vascular Plug devices are safe and effective to achieve a complete closure of the residual shunts.

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