Kardiologia Polska 2012; 70, 11: 1142–1146 ISSN 0022–9032

ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Medium-term results of transcatheter closure of patent foramen ovale (PFO) with Amplatzer PFO and Cribriform occluders

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Abstract

Background: The use of an Amplatzer Cribriform Septal Occluder (ACSO) for percutaneous patent foramen ovale (PFO) closure (especially in cases with atrial septal aneurysm) has been recently described as superior compared to that of an Amplatzer PFO Occluder (APFO).

Aim: To assess immediate and medium-term clinical outcomes of patients with PFO with paradoxical embolism event (EE) who underwent transcatheter PFO closure with an APFO or an ACSO.

Methods: Overall, 56 consecutive patients underwent percutaneous closure of PFO with an APFO device; the results were compared to those in seven patients treated with ACSO. Deaths due to embolism, stroke or transient ischaemic attack (TIA) were considered recurrent EE. Pre- and 6 month post-intervention right to left shunting (RLS) were evaluated with intravenous contrast injection by transcranial Doppler examination of the middle cerebral artery during Valsalva manoeuvre.

Results: The procedure was successfully completed in all patients in both groups. No procedure-related complications were observed during hospitalisation. Residual RLS was noted at six months in 14/56 (25%) patients in the APFO group and 4/7 (57%) patients in the ACSO group ($p < 0.05$). Recurrent TIA was observed in three patients in the APFO group (one of them had small residual shunt immediately after procedure and at six-month follow-up). Another patient from that group experienced stroke one month after the procedure. No recurrence of EE was recorded in the ACSO group.

Conclusions: Transcatheter PFO closure with both Amplatzer devices is a minimally invasive procedure with high success and low complication rates. Taking in consideration residual RLS in the medium-term period, the application of a Cribriform device is not superior to that of an Amplatzer PFO device. Results of randomised trials are necessary to confirm the effectiveness of transcatheter therapy in patients with PFO and a paradoxical thromboembolic event.

Key words: patent foramen ovale, transcatheter closure

Kardiol Pol 2012; 70, 11: 1142–1146

INTRODUCTION

Patent foramen ovale (PFO) is an anatomical variant of the interatrial septum with an overall prevalence of 27% in autopsy studies [1]. A high prevalence of PFO has been reported in approximately 50% of patients with cryptogenic transient ischaemic attack (TIA) or ischaemic stroke, suggesting an association between the presence of PFO, with or without aneurysm of interatrium septum, and a paradoxical thromboembolic event (EE) [2, 3]. The optimal management to prevent an EE in these patients remains controversial. Transcatheter PFO closure is a potential option for patients with PFO and thromboembolic phenomena, in that it avoids the morbidity associated with surgical closure or life-long anticoagulation therapy.

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Received: 11.03.2012 **Accepted:** 13.06.2012

We reviewed data relating to 63 patients with PFO and a history of EE who received treatment either with an Ampaltzer PFO Occluder (APFO) or an Amplatzer Cribriform Septal Occluder (ACSO), taking in consideration the medium-term effect of such therapy.

METHODS

Patients

Between August 2003 and March 2010, a total of 90 consecutive patients with PFO and at least one documented cryptogenic stroke or other EE, underwent transcatheter PFO closure with Ampaltzer devices: 80 with an APFO and ten with an ACSO. The choice depended on the availability of the devices. PFO was defined as a flap-like opening in the atrial septal secundum with the septum primum serving as a one-way valve allowing permanent or transient right-to-left shunt (RLS). Atrial septal aneurysm was defined as the presence of a localised protrusion of the fossa ovalis, with a base width > 15 mm and mobile septum excursion > 10 mm into the left or right atrium.

An EE was considered to be due to a paradoxical embolism when the following criteria were met: presence of PFO with spontaneous or provocable (Valsalva manoeuvre) RLS during transoesophageal echocardiography (TEE). All echocardiographic evaluations prior to transcatheter PFO closure were made with a multiplane TEE probe. Quantification of PFO shunt volume was determined in TEE by contrast injection at rest and during the Valsalva manoeuvre. A 'small' shunt volume was defined as 5–20 bubbles and a 'large' shunt volume as more than 20 bubbles in left atrium after injection of agitated saline contrast. Transcranial Doppler with contrast (c-TCD) was performed using 10 mL of air-mixed saline, injected into the right antecubital vein. Microembolic signals (MES) were recorded bilaterally from the middle cerebral artery, during normal breathing and Valsalva manoeuvre, and each procedure was repeated two times. Recording of MES was started 5 s after the beginning of the contrast injection and continued for 60 s. Categorisation of RLS was based on MES count — grade 0: 0 MES, grade 1: 1–10 MES, grade 2: > 10 MES and no curtain, grade 3: uncountable — 'curtain' according to previously established protocols [4, 5]. All TCD examinations were performed by one experienced neurologist (MW) and TEE study by experienced cardiologists. Moreover, magnetic resonance imaging (MRI) or computed tomography (CT) confirmed ischaemic stroke or TIA symptoms: neuro-radiologically (MRI or CT) or symptoms unequivocally due to TIA. Only patients with positive TEE contrast injection study who had more than 1st grade MES count were qualified for transcatheter closure. Any identifiable causes of thromboembolic event other than PFO were excluded.

All patients had scheduled follow ups: clinical examination and transthoracic echocardiography (TTE) at one, six and 12 months after the procedure and annually thereafter. Six months after the procedure, an additional TCD examination was performed. Only 56 patients from the APFO group fulfilled this protocol and seven from the ACSO group. Data of these 63 patients was analysed in this study.

Table 1. Amplatzer Patent Foramen Ovale (APFO) and Amplatzer Septal Cribriform Occluder (ACSO) groups of patients — baseline characteristics

	APFO	ACSO
Number	56	7
Sex: male/female	35/21	5/2
Mean age [years]	43.4 (from 13 to 67)	37.7 (from 16 to 56)
Indication for PFO closure:		
One stroke	18	3
2–4 strokes	5	0
Stroke + TIA	3	0
One TIA	11	2
Two TIA	7	0
TIA + migraine	11	2
Decompression sickness	1	0
Atrial septal anatomy:		
Length of PFO canal [mm]	9.0	7.9
PFO alone	52	5
PFO + atrial septal aneurysm	4	2
Applied device:		
APFO 25/18 mm	36	0
APFO 35/25 mm	18	0
APFO 18/18 mm	2	0
ACSO 25 mm	0	6
ACSO 35 mm	0	1

PFO — patent foramen ovale; TIA — transient ischaemic attack

Demographic characteristics, and data of atrial septal anatomy and that relating to transcatheter closure are set out in Table 1.

Device characteristics and implantation procedure

APFO and ACSO (AGA Medical Corp, Plymouth, USA) are double disk self-expandable devices made from a nitinol wire mesh with polyester fabric sewn inside each disk. The round disks are linked by short connecting waist and the two disks have different diameters in an APFO. They are available as 25 or 35 mm for the right disk with corresponding left atrial disk diameter of 18 and 25 mm, respectively.

ACSOs feature both disks with similar diameters (namely 25 or 35 mm).

The implantation technique of PFO closure has been described in detail elsewhere [6]. The procedure was carried out under TEE and fluoroscopy monitoring. Following sheath placement in the right femoral vein, 100 U/kg of bodyweight heparin was administered intravenously (i.v.). Heparinisation was continued through two days following the procedure. For prophylaxis of EE after device implantation, patients were treated with acetylsalicylic acid (300 mg) for six months. Prophylaxis of bacterial endocarditis was recommended for six months. Before the procedure, cefazolin 1.0 g was administered i.v. and thereafter the same two doses after each 8 hours (prophylaxis of infective endocarditis).

Statistical analysis

Frequency of incidence of residual shunt in both groups was compared using exact Fisher test.

RESULTS

The devices were implanted successfully in all patients with PFO. APFO was used in 56 patients and ACSO in seven. The sizes of the applied Amplatzer devices are shown in Table 1. Mean fluoroscopy time was 2.6 min in the APFO group and 2.2 min in the ACSO group. Mean follow-up was 3.45 years in the APFO group and 1.89 years in the ACSO group. TCD six months after the procedure detected a positive result (MES degree 1–3) in 14/56 (25%) patients in the APFO group and 4/7 (57%) patients in the ACSO group (exact Fisher test $p = 0.022$) (Table 2).

In the APFO group, 4/56 (7%) patients had post-procedural new neurological events. In three of them, TIA were observed (6–8 months after the procedure) and in one a new stroke — one month after the procedure. In these three patients, TCD and TEE examinations were negative, in one both TCD and TEE were positive, but new atherosclerotic changes in vertebral arteries were also noted. This patient — a 56 year-old woman — is now four years after PFO closure; consecutive catheterisation to close residual PFO shunt two years after the first procedure was ineffective. In the ACSO group, there were no EE in post-procedural follow-up.

Table 2. Right to left shunt during Valsalva manoeuvre during transcranial Doppler at least six months post patent foramen ovale (PFO) closure in the Amplatzer PFO group (APFO) and the Amplatzer Septal Cribriform Occluder (ACSO) group of patients

Microembolic signals degree	APFO	ACSO
0	42	3
1	3	1
2	9	2
3	2	1

No device-related thrombosis or aortic erosions were observed on follow-up in echocardiography. Minor adverse events, including chest discomfort, palpitations and dyspnoea were reported within one month of the procedure in both groups but had disappeared in most patients at six-month follow-up.

DISCUSSION

The association between PFO and cryptogenic stroke has been described in different studies, but the most appropriate therapy for such patients is still undetermined. Various devices have been used for transcatheter PFO closure. The use of an ACSO designed for multiperforated atrial septum defects has been described as superior compared to that of a Cardioseal device [7]. Similar observations were made related to an APFO designed especially for PFO closure. It has been suggested that an ACSO might offer advantages in terms of EE rate or residual shunt compared to an APFO device, especially in PFO patients with associated atrial septal aneurysm [8]. Moreover, the recent publication of Rigatelli et al. [9] featured encouraging long term results after the application of an ACSO in patients with PFO and atrial septal aneurysm. Unfortunately, in both these recent papers [8, 9], RLS validation was made at six post-procedural months only by TEE or TTE but not by TCD. TCD examination is very sensitive for such purposes, being less invasive and more comfortable than TEE [10]. Our experience in the application of APFOs and other devices confirms the observations of others regarding the effectiveness in short-term follow-up. But its medium-term effectiveness remains controversial. We documented that after application of a Cribriform device to close PFO, the presence of RLS, detected by the very sensitive transcranial Doppler technique, is higher than after APFO. The cause of this result, which contrasts with the study of Musto et al. [8], could lie in the methodological details. In the study of Musto et al. [8], RLS shunt was evaluated by TEE study, which is less sensitive that TCD. Moreover, in their material only patients with atrial septal aneurysm and PFO were treated percutaneously. In our study, the number of patients with such morphology of interatrial septum was limited. Residual shunt detected in TEE in the Musto et al. [8] study six months after the procedure was present in 5.5% of patients treated with an APFO and none treated with a Cribriform device. In our study, performed after six months with TCD, the figures were respectively 25% and 57%. The significance of this data is difficult to evaluate, as in the bibliography the percentage of residual shunt after percutaneous closure in the medium-term period varies and depends on the device used for closure, the period of follow up etc. Herrmann at al. [6] documented a combination of moderate and severe positive contrast studies of RLS (not specified by which method) six months after procedure in 52% of patients treated with a Cardioseal device and 29%

treated with an Amplatzer PFO device. Recently, the results of the randomised 'Closure I' trial have been published and this study was negative (closure of PFO with a CardioSeal/ /Starflex device did not offer a greater benefit than medical therapy alone in preventing recurrent stroke or TIA) [11]. Perhaps the type of applied device may have influenced these results. On the other hand, the study of Walsh et al. [12] confirmed the efficacy of percutaneous PFO closure compared to medical therapy. According to the guidelines of the European Stroke Organisation (2008), endovascular closure of PFO may lower the risk of recurrent stroke compared to medical treatment.

Another problem is the recurrence of paradoxical embolism after percutaneous closure of PFO. In our material, this occurred in 7% of patients from the APFO group and none in Cribriform patients. But the follow-up was longer in the APFO group. In other studies, data is also varied. In the study of Musto et al. [8], it was 8% in patients treated with APFO vs. none in Cribriform; in the study of Herrmann et al. [6] it was 1.4%; in the study of Giardini et al. [13] it was 5.3%, and in the study of Rigatelli et al. [9] it was zero. Interestingly, in most of these papers, as in our study, there were no strict correlations between the presence of residual RLS and the appearance of recurrent EE. Nevertheless, the goal of transcatheter closure of PFO is total occlusion of this communication to prevent subsequent neurological events.

Limitations of the study

The results of the present study show several limitations. For example, the study is not randomised. It is possible that one described recurrent EE observed after one month of follow-up could have occurred before complete endothelisation, and could therefore have been secondary to embolism from device despite antiplatelet therapy. It is possible that the rate of residual RLS is overestimated, since some patients in both groups were not controlled by TEE. The small sample size of our study population and relatively short follow-up did not allow us to identify predictors of recurrent events following device implantation. The number of subjects in each group is massively disproportionate.

CONCLUSIONS

Transcather PFO closure is a minimally invasive procedure with a high success rate and a low complication rate. Taking in consideration residual RLS in the medium-term, the application of a Cribriform device is not superior to that of an Amplatzer PFO device. Results of randomised trials are necessary to confirm the effectiveness of transcatheter therapy in patients with PFO and paradoxical thromboembolic event.

Conflict of interest: *none declared*

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Wyniki średnioterminowe przezcewnikowego zamykania przetrwałego otworu owalnego za pomocą implantów Amplatzer: PFO i Cribriform

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Streszczenie

Wstęp: Ostatnio opisano wyższość zastosowania Amplatzer Cribriform Septal Occluder (ACSO) w porównaniu z Amplatzer PFO Occluder (APFO) w przezskórnym zamykaniu przetrwałego otworu owalnego (PFO) (zwłaszcza w przypadkach z obecnym tętniakiem przegrody międzyprzedsionkowej).

Cel: Celem niniejszej pracy było określenie bezpośrednich i średnioterminowych wyników przezcewnikowego zamknięcia PFO za pomocą APFO lub ACSO u pacjentów z kryptogennymi udarami ośrodkowego układu nerwowego w wywiadzie (EE).

Metody: Porównano wyniki uzyskane u 56 pacjentów, u których PFO zamykano za pomocą APFO, z rezultatami uzyskanymi u 7 pacjentów, u których zastosowano ACSO. Nawrotem EE określono śmierć spowodowaną zatorem, wystąpienie udaru ośrodkowego układu nerwowego czy też przemijający atak niedokrwienny (TIA). Przed zabiegiem i 6 miesięcy po nim za pomocą kontrastowego przezczaszkowego badania doplerowskiego tętnicy środkowej mózgu określono brak bądź obecność prawo-lewego przecieku (RLS) podczas próby Valsalvy.

Wyniki: Zabieg przezskórnego zamknięcia PFO ukończono z sukcesem u wszystkich pacjentów z obu grup. Nie zaobserwowano żadnych powikłań u pacjentów podczas ich pobytu w szpitalu po zabiegu. Resztkowy RLS stwierdzono po 6 miesiącach po zabiegu u 14/56 (25%) osób w grupie APFO i 4/7 (57%) osób w grupie ACSO ($p < 0,05$). W grupie APFO nawrót TIA wystąpił u 3 pacjentów (u 1 miesiąc po zabiegu udar ośrodkowego układu nerwowego). U 1 z nich zaobserwowano po interwencji obecność RLS. Nie stwierdzono nawrotów EE w grupie ASCO.

Wnioski: Przezcewnikowe zamknięcie PFO za pomocą implantów Amplatzer jest bezpiecznym i skutecznym zabiegiem. Nie wykazano wyższości w zastosowaniu implantu Cribriform nad Amplatzer PFO Occluder w odniesieniu do częstości występowania resztkowego RLS w średnioterminowym okresie obserwacji. Nadal brakuje randomizowanych badań potwierdzających wartość przecewnikowego zamknięcia PFO w zapobieganiu kryptogennych udarów ośrodkowego układu nerwowego.

Słowa kluczowe: drożny otwór owalny, przezcewnikowe zamknięcie

Kardiol Pol 2012; 70, 11: 1142–1146

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Praca wpłynęła: 11.03.2012 r. **Zaakceptowana do druku:** 13.06.2012 r.