Original paper

Experience in patent foramen ovale closure with the CERA Lifetech occluder in patients with cryptogenic stroke

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Adv Interv Cardiol 2023; 19, 3 (73): 257–261
DOI: https://doi.org/10.5114/aic.2023.131479

Abstract

Introduction: Nowadays, percutaneous closure of patent foramen ovale (PFO) in patients after cryptogenic stroke is becoming a dominating strategy. The most commonly used and investigated device is the Amplatzer occluder. However, several other devices have been designed for transcatheter closure of PFO, which are not so well examined.

Aim: To assess the effectiveness and safety of PFO closure with the Lifetech CERA occluder.

Material and methods: A prospective, single-arm registry of patients with PFO treated with CERA occluder (Lifetech Scientific, Shenzhen, China) implantation was conducted. We assessed peri-procedural and 12-month follow-up. Patients were screened for the residual shunt in transcranial Doppler/transesophageal echocardiography.

Results: Ninety-six patients entered the registry. Most patients were women (76%) and the analyzed group was relatively young (mean age of 42.3 ±13.6 years). Before closure, most patients had a large shunt through the PFO. Procedures of PFO closure were performed under TEE guidance. All procedures were made under local anesthesia and all patients had the PFO successfully closed. No device-related complications were reported in the peri-procedural period or during follow-up. No recurrent neurological ischemic events were reported at 12 months. During follow-up we observed a 9% rate of residual shunts, which were mostly small.

Conclusions: The study confirmed excellent immediate and 12-month results of CERA occluder implantation in patients with PFO.

Key words: atrial septum, Amplatzer occluder device, prevention, follow-up study.

Summary

Percutaneous closure of patent foramen ovale (PFO) is becoming a dominating strategy of secondary prevention of cryptogenic stroke. Since the first use of the Amplatzer occluder in 1997 many other devices for PFO closure have been designed. One of them is the Lifetech CERA occluder. In a prospective, single-arm study of 96 patients with PFO treated with CERA occluder implantation, we assessed peri-procedural and 12-month follow-up. All patients had the PFO successfully closed. No device-related complications were reported in the peri-procedural period or during follow-up. No recurrent neurological ischemic events were reported at 12 months. During follow-up we observed a 9% rate of residual shunts, which were mostly small.

Introduction

Foramen ovale is a component of the fetal circulation that closes in ca. 70% of subjects during postnatal life, whereas in the remaining 30% it remains patent [1]. The management of patent foramen ovale (PFO) and its association with other medical conditions have been the subject of numerous publications [2–4]. Of these, the co-existence of PFO with stroke has been widely discussed.

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Received: 16.07.2023, **accepted:** 17.07.2023.

It is reported that up to 30–40% of strokes are cryptogenic, which means that despite neurological, vascular, and cardiac examination, as well as screening for coagulopathy, the etiology of stroke remains unknown [5, 6]. In the scenario of the coexistence of cryptogenic stroke and PFO, two strategies are considered: the conservative approach and percutaneous closure [7]. The latter is recently becoming a dominating strategy [8–10]. Percutaneous PFO closure is considered safe and effective if an experienced team performs it. The most commonly implanted and best-studied occluder is the Amplatzer PFO [11]. However, since the first use of the Amplatzer in 1997, other devices have been designed for percutaneous PFO closure [12]. The CERA PFO occluder (Lifetech Scientific, Shenzhen, China) is a transcatheter occlusion device for non-surgical PFO closure. Only small registries about CERA occluder implantation exist in patients with PFO [13, 14].

Aim

The purpose of this study was to collate real-world data on patients' outcomes and evaluate the procedural success, performance, and safety as well as a 12-month follow-up of the use of the Lifetech CERA Closure System in patients with PFO and a history of cryptogenic stroke.

Material and methods

Study design

It is a single-arm, prospective study focused on the analysis of the diagnostic and therapeutic process of PFO closure with the Lifetech CERA occluder. The analysis included patients treated in the years 2018–2020. The main objective was to assess procedural outcome, safety and performance of the device. The analysis included the peri-procedural period and 12-month follow-up. The study was approved by the local ethics committee. The inclusion criterion for entering the registry was confirmed PFO associated with cryptogenic stroke or transient ischemic attack (TIA). Main exclusion criteria were as follows: established cause of stroke other than PFO; intra-cardiac thrombi, especially in the left atrium or left atrial appendage; endocarditis and sepsis or other systemic infection occurring in 1 month before the procedure; bleeding disorder or any other contraindications to antiplatelet therapy; anatomy in which the device of the required size would interfere with intra-cardiac structures. The primary endpoint was procedural success, defined as the proper position of the occluder after implantation without peri-procedural complications including stroke//TIA, embolization, perforation of cardiac tissue, and mortality. Secondary endpoints were as follows: residual shunt; device or procedure-related adverse events (AEs) and serious adverse events (SAEs) at 12 months, device deficiencies, migration, embolization, and thrombosis of the device at 12 months.

Clinical follow-up was performed telephonically. Imaging assessment included transthoracic echocardiography (TTE) for assessment of occluder position and morphology as well as transcranial Doppler examination (TCD) and/or transesophageal echocardiography (TEE) for evaluation of residual shunt.

Investigated device

The CERA occluder is a self-expandable double-disc device made of a nitinol wire mesh shaped into two flat discs and a waist between them. Membranes made of PET are sewn into each disc and help to seal and provide a foundation for tissue growth over the occluder. The design of the CERA occluder is similar to the Amplatzer. Both devices have a double disc structure made of nitinol mesh with a polyester membrane. Disc sizes and waist lengths are comparable. The difference of the CERA occluder is that all metallic structures are plated with titanium nitride to improve biocompatibility. A significant feature of the CERA occluder is its delivery system, which should provide exceptional mobility and flexibility during the procedure. The CERA occluder is used in combination with the SteerEase introducer. The introducer contains a coil-reinforced sheath, dilator, loader, hemostatic valve, and delivery cable. It is used to advance the PFO occluder to the proper position. When the occluder is released from the sheath, the disc expands on each side of the PFO. Sizing of the device was made by measuring the distance from the target lesion to the aorta root and to the vena cava superior rim and selecting a device with the radius of the right disc not exceeding the lesser of these two distances.

Imaging assessment

Procedures of PFO closure were performed under TEE guidance. During the procedure there were two critical moments for imaging assessment. The first was to confirm the crossing of the guiding catheter through the PFO tunnel to the left atrium and left upper pulmonary vein. The second was to assess the proper positioning of the occluder on the target lesion before the final release of the device and monitoring of the release process itself.

Right to left shunt was assessed in TCD and/or TEE. For shunt detection and quantification the maximum number of either microbubbles in the left atrium or high intensity transient signals (HITS) in cerebral artery flow after the intravenous injection of contrast during the Valsalva maneuver was utilized. In TCD the shunt was assessed as small with less than 10 HITS, moderate with more than 10 HITS and large with many HITS, without the possibility of distinguishing and counting individual signals [15]. In TEE the shunt was graded small with less than 10 microbubbles, large with > 20 microbubbles and moderate in between those two values [16]. During the follow-up, position and morphology of the occluder were assessed in TTE.

Statistical analysis

Since the present analysis is a single-arm registry with no comparator or control group, only descriptive data are presented and no statistical hypothesis tests were performed. There was no sample size calculation for this study. The information from approximately 100 patients was subjectively considered to be sufficient to evaluate the safety and efficacy of the study device. Quantitative variables were described using means and standard deviation (for normal distribution) or median with the first and the third quartile (for non-normal distribution). Normality was assessed by the Shapiro-Wilk test. Categorical variables were presented as percentages. All analyses were performed using IBM SPSS Statistics software, version 28.01.0.

Results

Ninety-six patients entered the registry. Baseline clinical characteristics are presented in Table I. Most patients were women and the analyzed group was relatively young. All subjects were classified as New York Heart Association (NYHA) class I. Before closure, most patients had a large shunt through the PFO.

Procedural details are shown in Table II. PFO closure was successfully achieved in all patients. The vascular access site was the right femoral vein in all cases. Sizes of implanted occluders are presented in Table II. All procedures were performed under local anesthesia. No peri-procedural complications were observed. All patients were discharged home within 3 days of hospital stay. After PFO closure, all patients received dual antiplatelet therapy with 75 mg of acetylsalicylic acid daily and 75 mg of clopidogrel daily with a median duration of 6 months.

Table I. Baseline clinical characteristics (n = 96)

Parameter	Value
Female gender	76%
Age [years] mean (SD)	42.3 (13.6)
NYHA class I	100%
History of stroke	23%
History of TIA	91%
History of migraine	79%
History of deep vein thrombosis	7%
Shunt size	Small: 7% Medium: 0 Large: 93%

NYHA – New York Heart Association, TIA – transient ischemic attack.

At 12 months of follow-up, no neurological ischemic incidents and no AE/SAE or further complications were reported. There was a relatively low incidence of residual shunt of 9% in TCD/TEE assessment at approximately 8 months (Table III).

Discussion

The most important finding from our study is the good result of CERA occluder implantation in patients with PFO and a history of cryptogenic stroke. To the best of our knowledge it is the largest registry concerning the CERA PFO occluder, especially considering that complete 12-month follow-up focused on clinical events is provided. The presented data are consistent with the results of previous, smaller registries. In a study by Ulmi *et al.,* all patients had successful occluder implantation. The residual shunt rate after 6 months was 7% and it was not significantly higher compared to the Amplatzer PFO

Table II. Procedure and hospitalization details (n = 96)

Parameter	Value
Procedure time [min] median (Q1–Q3)	35 (30; 35)
Vascular access	Right femoral vein – 100%
Anesthesia	Local – 100%
Antithrombotic drug during procedure	Unfractionated heparin – 100%
Occluder successfully deployed on target lesion	100%
Occluder size [mm]	25 × 18 – 75% 30 × 25 – 15% 35 × 25 – 10%
Stroke/TIA	0%
Device embolization	0%
Cardiac perforation	0%
Death	0%
Hospitalization time [days]	1 – 35% 2 – 37% 3 – 28%

Table III. Clinical follow-up and imaging assessment (n = 96)

Parameter	Value
Clinical follow-up [months] mean (SD)	15 (4.5)
Neurological incidents	0%
AE/SAE	0%
Incidents of atrial fibrillation	0%
Imaging assessment [months] median (Q1–Q3)	8 (5; 12)
Residual shunt grade	None – 90.6% Small – 7.3% Medium – 1% Large – 1%
Residual shunt assessment method	TCD – 96% TCD + TEE – 3% TEE – 1%
Device deficiencies	0%
Occluder migration	0%
Device embolization	0%
Device related thrombus	0%

AE – adverse event, SAE – serious adverse event, TCD – transcranial Doppler, TEE – transesophageal echocardiography.

occluder (4%) [13]. Another low-volume registry showed promising results of CERA device implantation, with successful deployment in all cases and no complications observed during hospital stay and observation of up to 4 months [14].

The results of our study indicate that the efficacy of the CERA occluder is comparable to that of the Amplatzer PFO occluder, the most widely used occluder for PFO closure. In a study by Greutmann *et al.* [17], a residual shunt was observed in 19% of cases after 6 months from PFO closure with the Amplatzer. Similarly, in another study, the residual shunt rate was 21.6% after 3 months and 13.6% after 12 months following Amplatzer implantation [18]. In an analysis by Chatterjee *et al.*, residual shunt was observed in 4% of cases after 3–6 months from the procedure using the Amplatzer occluder [19]. Comparing acute results of individual devices for PFO closure is limited, as the procedure itself is relatively safe and is characterized by low risk of acute complications [20]. Thus the presence of shunt after PFO closure during follow-up is widely discussed. There is evidence of a higher recurrent stroke in patients with residual shunt, particularly moderate and large shunts [21]. In a comparative study of atrial occluders, the Gore Cardioform presented the lowest rate of residual shunt, yet it was associated with more frequent incidents of atrial fibrillation [22]. Possibly, the stronger force between the discs of this device provides more effective closure but may produce more irritation to the tissue of the atrial septum. Several studies have confirmed the safety and effectiveness of the Amplatzer occluder, highlighting the benefits of PFO closure in secondary prevention of stroke and showing superiority or non-inferiority of Amplatzer PFO for the risk of atrial fibrillation, residual shunt and device-related thrombus compared to other occluders [23]. In a meta-analysis including 703 patients with PFO and a history of cryptogenic stroke, PFO closure with the Amplatzer occluder was associated with a lower repeated stroke rate [24]. In our study, we did not observe recurrent stroke or any complications, including atrial fibrillation or device-related thrombus after CERA occluder implantation. Worth mentioning is the cost-effectiveness issue, as overall costs associated with the use of the CERA occluder are lower compared to those generated by implantation of the Amplatzer [19]. Another approach for PFO closure is a suture-mediated technique using the NobleStitch EL system [25]. The main advantage of this system is the lack of permanent closure with a device in the heart, which allows for percutaneous left heart access. To date, no comparative data between the NobleStitch EL system and CERA occluder exist.

In our study, during follow-up most patients underwent TCD for residual shunt assessment, mainly because of restrictions in TEE examinations due to the COVID-19 pandemic. There are two methods of assessment of residual shunt after PFO closure: TEE and TCD. Both examinations require intravenous administration of contrast agents and rely on visualization of the equivalent of right to left shunt after the Valsalva maneuver: microbubbles in TEE examination and HITS in TCD. The benefit of TEE manifests in the possibility of anatomic assessment including the size of the PFO tunnel, the presence of an aneurysm, or other septal defects. The advantages of TCD include less invasive examination with no sedation required and a potentially easier and more reliable Valsalva maneuver compared to TEE. Previous studies showed good accuracy of TCD compared to TEE for the diagnosis of PFO [26, 27]. TCD was reported as an adequate method for screening for PFO and for follow-up assessment of patients after PFO closure in terms of the presence of residual shunt [28, 29].

Our study has several limitations. First of all, it is a single arm registry with no control group and a relatively small sample size. Secondly, there was no randomization for use of the CERA occluder for PFO closure, which may provide some selection bias. Thirdly, anatomical details, including the size of the PFO or presence of atrial septal aneurysm, were not available, which hampers analysis of predictors of residual shunt in the present study. Finally, the sample size is relatively small; thus, conclusions from this registry should be confirmed on a larger group of patients.

Acknowledgments

Przemysław Węglarz and Michał Węgiel equally contributed to the study.

Conflict of interest

Przemysław Węglarz and Ewa Konarska-Kuszewska are members of the board and shareholders of Lifetech Scientific distributor and received remuneration for consultations, research and workshops.

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