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Ceraflex versus Amplatzer occluder for secundum atrial septal defect closure

Multicenter clinical experience

Abbreviations

ASD	Atrial septal defect
ASO	Amplatzer septal occluder
CSO	Ceraflex septal occluder
PET	Polyethylene terephthalate
TEE	Transesophageal echocardiography
TTE	Transthoracic echocardiography

Since the first transcatheter closure of atrial septal defect (ASD) performed by King and Mills in 1974 [1], multiple devices have been designed and tested in clinical studies [2, 3, 4]. Today, device closure of secundum ASD has proved to be a safe technique and the Amplatzer septal occluder (ASO) is the most frequently used implant because of its simple deployment technique, applicable defect size range, and occlusion rate compared with other devices [5, 6, 7]. The Ceraflex ASD occluder (Lifetech Scientific, Shenzhen, China) is a novel septal occluder designed to treat secundum ASDs. Construction and deployment procedures are similar to ASO. The device consists of a nitinol wire frame without a left atrial hub covered by a polyethylene terephthalate (PET) membrane that minimizes the chance of clot formation and increases flexibility. Furthermore, animal experiments and clinical trial have shown that ceramic membrane occluders can decrease the dissolution of nickel ion efficiently and promote the growth of endothelial tissue [8].

In this study, we evaluated the efficiency and safety of the Ceraflex septal occluder (CSO) device in patients with a secundum ASD and compared the outcomes of this novel device with the ASO outcomes in a series of patients.

Patients and methods

The study included 125 patients (90 women; mean age 40±16 years) who underwent percutaneous transcatheter closure for secundum ASD between 2010 and 2014 from four study centers in Turkey. All clinical, procedural, echocardiographic, and outcome variables were prospectively collected.

We included all consecutive patients referred to our hospital for secundum ASD closure and right ventricle volume overload. Exclusion criteria were similar for both devices. Patients with complex congenital cardiac malformations, insufficient septal rims, left ventricular dysfunction, severe pulmonary artery hypertension, or small ASD with a pulmonary/systemic flow ratio (Qp/Qs) of <1.5:1 and no signs of right ventricular dilatation were excluded from the study. Informed written consent was obtained from all patients before the procedure.

The CSO device

The CSO device consists of self-expandable double disc devices, which are made of a nitinol wire mesh shaped into two flat discs and a 4-mm waist between the two discs. PET membranes are sewn into each disc to seal the hole and provide a foundation for growth of tissue over the occluder after placement. A special feature of this device is the ceramic coating (titanium nitride) on the wire mesh that reduces the ability of the device to produce a thrombus, providing faster endothelialization and improved biocompatibility. The CSO differs from the ASO device in the mesh design; it comprises only one stainless steel hub at the right atrial disc for cable connection and a connection system to the delivery cable (**Fig. 1**).

The size of the device is determined by the diameter of the waist, available ranging from 6 to 42 mm with 2-mm increments. The left atrial discs are 12–16 mm and the right atrial discs are 8–12 mm larger than the waist, respectively. Devices ranging in size from 6 to 10 mm require 8-Fr; 12-mm devices require 9-Fr, devices ranging in size from 14 to 18 mm require 10-Fr, devices ranging in size from 20 to

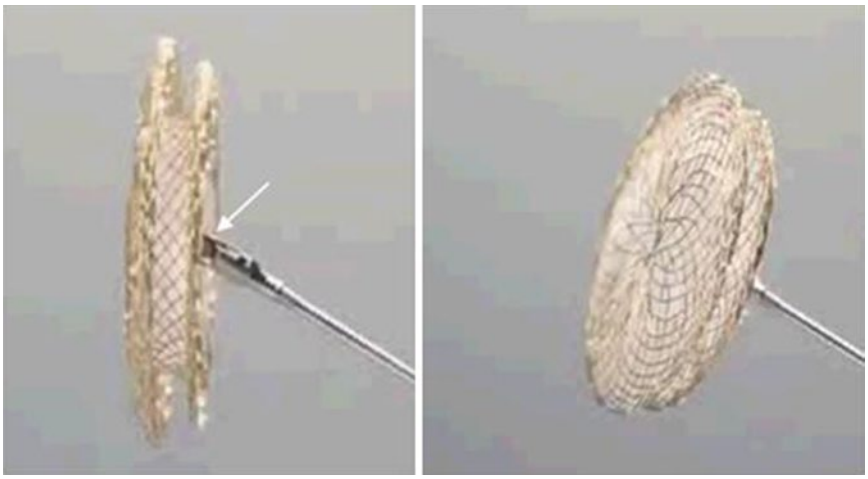

Fig. 1 ▲ **a** The CSO consist of two flat discs with a 4-mm connecting waist attached by a cable mechanism onto a delivery system (*arrow*). **b** The left atrial disc without a hub

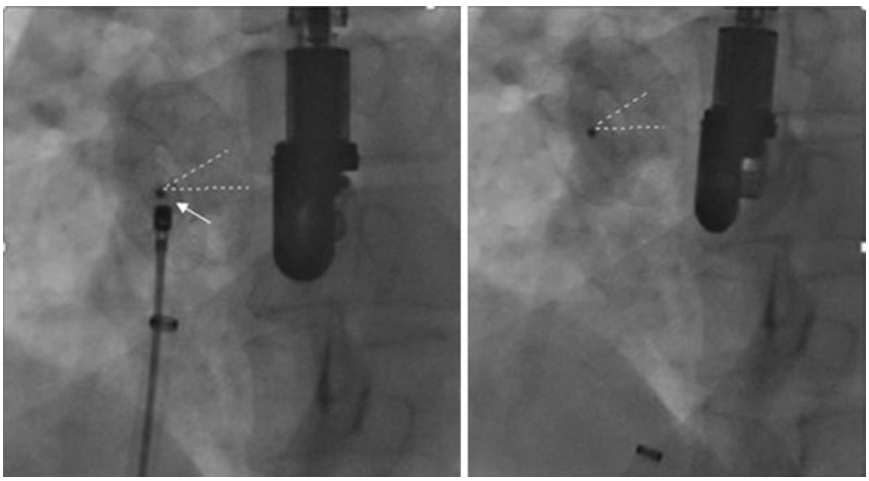

Fig. 2 ▲ **a** The Ceraflex septal occluder has a unique delivery system with 360° rotation (*arrow*), to allow accurate positioning during the procedure. **b** The operator can observe the final position of the device on the atrial septal wall before release

28 mm require 12-Fr, and devices ranging in size from 30 to 42 mm require 14-Fr delivery sheaths.

The ASO device consists of two self-expandable round disks made of a 0.004- to 0.0075-in nitinol wire mesh that are linked together by a 4-mm connecting waist, corresponding to the thickness of the atrial septum. The prosthesis is filled with Dacron fabric to facilitate thrombosis. The device is attached by a microscrew mechanism onto a 0.038-in delivery cable made of stainless steel. The size of the device is determined by the diameter of the waist, available in the range from 4 to 40 mm with 1-mm increment for sizes 4–20 mm and 2-mm increments for sizes 20–40 mm. The device is delivered through a 6-Fr to 12-Fr sheath.

The device size was selected using the stretched diameter of the defect assessed by angiographic measurement plus 1–2 mm for both procedures.

Technique

The CSO implantation procedure is similar to the technique used for ASO implantation. All procedures were performed with patients under general anesthesia using fluoroscopic and transesophageal echocardiography (TEE) imaging. All patients received 300 mg aspirin before the procedure and intravenous heparin (100 IU/kg) during the procedure. After placement of the right femoral vein sheath, a guide wire was positioned into the upper left pulmonary vein through the septal defect and the stretched diameter of the defect was measured as previously described [9, 10]. The device was placed using the standard technique. The position and stability of the device were checked by the Minnesota maneuver. Once the device was implanted well in position, it was released from the loader system.

Follow-up

All patients underwent clinical examination, electrocardiography, chest radiography, and transthoracic echocardiography (TTE) before discharge, at 1, 6, and 12 months after the procedure, and yearly thereafter; 300 mg aspirin daily was prescribed for 6 months. Prophylaxis for infective endocarditis was recommended during the first 6 months.

Statistical analysis

Data are presented as mean ± SD for continuous variables and as proportions for categorical variables. Differences between proportions were assessed by the chi-square test and replaced by the Fisher exact test when the expected cell count was <5. Differences between outcomes with different devices were analyzed with unpaired Student's *t* test or the Mann–Whitney test. Statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, Ill.). A two-tailed *p* value of <0.05 was considered significant for all analyses.

Results

In all, 125 patients were screened for inclusion in the study between 2010 and 2014. Enrolments were distributed among the four study centers in Turkey. Patient demographics, procedural data, and follow-up outcomes are presented in **Tab. 1**.

The CSO device was used in 58 patients, while the ASO was used in 67. All procedures were carried out with a combination of TEE and fluoroscopic guidance. The stretched size of the defect, device size, and fluoroscopy time were not significantly different between the groups. The delivery sheath size was different in both groups; however, there were no cas-

es of a significant vascular access-related complication in either group.

All devices were successfully delivered and deployed (100%) with only procedural complications related to the device. After release of the ASO device, a thrombus attached to the center of the left atrial disk was seen on TEE. Treatment with continuous infusion of heparin was started. On repeat TEE the following day, there was full resolution of the thrombus with no clinical consequences. Immediate (within 24 h) and follow-up (12 months) complete occlusion rates for both groups were 100%. Eleven patients in the CSO group and seven patients in the ASO group required either no treatment or medical treatment for transient atrial arrhythmias after implantation. These patients tended to be older, with an average age of 50 years, a factor known to predispose patients toward arrhythmia. The hospital stay was similar in both groups, all patients being discharged the following day.

All patients were evaluated by TTE during the follow-up. In all these patients the device was in the appropriate position and no interference with the surrounding cardiac structures was observed. None of the patients presented with new pericardial effusion, residual shunt, procedure-related stroke, cardiac perforation, device erosion, or embolization during the follow-up.

Discussion

This study is, to our knowledge, the first to assess the CSO device for closure of ASDs and to compare it with the ASO device. This clinical experience with the CSO has demonstrated its feasibility, safety, and efficacy as a novel implant for the treatment of ASD. There were no short- or mid-term complications; however, long-term data and higher patient numbers are needed to see whether these results have a long-term benefit.

The CSO device has a simple design that permits precise positioning with a single handle control. In addition, the system is held by the cable and the operator can evaluate the final position and orientation of the device without tension from the delivery catheter. This system provides accurate positioning during the procedure

Abstract · Zusammenfassung

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Ceraflex versus Amplatzer occluder for secundum atrial septal defect closure. Multicenter clinical experience

Abstract

Aim. The Ceraflex atrial septal defect occluder is an alternative device to the Amplatzer septal occluder with some structural innovations including flexible connection, increased flexibility, and minimized amount of implant material. We evaluated the efficiency and safety of the Ceraflex septal occluder device in percutaneous closure of secundum atrial septal defects.

Patients and methods. This was a prospective, nonrandomized, multicenter study of patients undergoing transcatheter closure for an atrial septal defect with the Ceraflex and the Amplatzer septal occluder devices. A clinical evaluation and follow-up transthoracic echocardiography were performed at 1, 6, and 12 months.

Results. Between 2010 and 2014, 125 patients underwent atrial septal defect closure with the Ceraflex septal occluder (*n*=58) and the Amplatzer septal occluder (*n*=67) under transesophageal echocardiography guidance. Patient characteristics, the stretched size of the defect, device size, and fluoroscopy time were similar between the groups. The immediate and follow-up complete occlusion rates for both groups were 100%. There was no device embolization, procedure-related stroke, or pericardial effusion.

Conclusions. The Ceraflex septal occluder is a safe and efficient device for closure of secundum atrial septal defects with no procedural complications. The Ceraflex has similar outcomes when compared with the Amplatzer septal occluder device. The advantage of the Ceraflex septal occluder device is that it can be deployed without the tension of the delivery catheter.

Keywords

Atrial septal defect · Interventional cardiology · Occlusion device · Amplatzer · Ceraflex

Ceraflex™- vs. Amplatzer™-Occluder zum Verschluss eines Vorhofseptumdefekts vom Sekundumtyp. Klinische Multizenterstudie

Zusammenfassung

Ziel. Der Ceraflex™-Occluder zum Verschluss eines Vorhofseptumdefekts stellt ein alternatives System zum Amplatzer™-Occluder dar, das mit einigen strukturellen Innovationen einschließlich einer flexiblen Verbindung, erhöhten Flexibilität und Minimierung der Menge implantierten Materials einhergeht. Untersucht wurde die Wirksamkeit und Sicherheit des Ceraflex™-Occluders bei perkutanem Verschluss von Vorhofseptumdefekten vom Sekundumtyp.

Methoden. Es handelte sich um eine prospektive, nichtrandomisierte Multizenterstudie an Patienten mit Verschluss eines Vorhofseptumdefekts mittels eines Katheters, und zwar dem Ceraflex™- oder dem Amplatzer™-Occluder. Nach 1, 6 und 12 Monaten erfolgten bei den Patienten mit Vorhofseptumdefekt eine klinische Untersuchung und eine transthorakale Nachsorgeechokardiographie.

Ergebnisse. Zwischen 2010 und 2014 wurde bei 125 Patienten der Verschluss eines Vorhofseptumdefekts mit dem Ceraflex™-Occluder (n=58) bzw. dem Amplatzer™-Occluder (n=67) unter transösophagealer Steuerung durchgeführt. Patientenmerkmale, Defektgröße unter Dehnung, Größe des Occluders und Durchleuchtungsdauer waren in beiden Gruppen ähnlich. Die vollständige Verschlussrate lag unmittelbar nach dem Eingriff und im Verlauf für beide Gruppen bei 100%. Es gab keine Occluderembolie, interventionsbedingten Schlaganfälle oder Perikardergüsse.

Schlussfolgerungen. Der Ceraflex™-Occluder ist ein sicheres und wirksames System zum Verschluss eines Vorhofseptumdefekts vom Sekundumtyp ohne interventionsbedingte Komplikationen. Für den Ceraflex™-Occluder liegen ähnliche Ergebnisse vor wie für den Amplatzer™-Occluder. Der Vorteil des Ceraflec™-Occluders liegt darin, dass er eingesetzt wird, ohne dass der Platzierungskatheter Zug daran ausübt.

Schlüsselwörter

Vorhofseptumdefekt · Interventionelle Kardiologie · Okklusionssystem · Amplatzer™ · Ceraflex™

Tab. 1 Comparison of baseline characteristics, procedure variables, and complications among groups[a]

Characteristic	CSO (*n*=58)	ASO (*n*=67)	*p*
Demographics			
Sex, female/male	42/16	48/19	0.92
Age, years	39.8±14.4	41.2±15.8	0.51
Qp/Qs	2.24±0.78	2.61±1.56	0.49
Aortic rim <5 mm	29	31	0.85
ASD diameter			
TEE (mm)	16.2±6.3	15.2±6.2	0.37
Stretched (mm)	17.8±4.2	17.0±5.4	0.36
Occluder size (mm)	20.2±7.8	20.3±8.5	0.94
Procedure			
Delivery sheath size (French)	11.5±1.1	10.2±0.9	<0.001
Fluoroscopy time (min)	7.6±2.7	8.2±2.1	0.16
Residual shunt at procedure	7	11	0.036
Residual shunt at discharge	2	4	0.55
Residual shunt at 1 month	0	1	–
Residual shunt at 6 months	0	0	–
Residual shunt at 1 year	0	0	–
Major complications			
CA requiring major treatment	0	0	–
Death	0	0	–
Device embolization	0	0	–
PE with tamponade	0	0	–
Device dislocation	0	0	–
Minor complications			
CA requiring no/minor treatment	11	7	0.27
Thrombus formation	0	1	–
Puncture site hematoma	0	0	–
Venous thrombosis	0	0	–

ASO Amplatzer septal occluder, *ASD* atrial septal defect, *CSO* Ceraflex septal occluder, *PE* pericardial effusion, *Qp/Qs* pulmonary/systemic flow ratio *TEE* transesophageal echocardiography [a]Data are presented as mean ± SD

and minimizes any unwanted drag or pull on the implant (**Fig. 2**). This point constitutes one of the main advantages of the CSO system compared to ASO device.

The ASO is the most widely used septal occluder for closing ASDs and has been demonstrated to be highly effective and safe in pediatric and adult patients [11, 12, 13, 14]. There will be no learning curve with the CSO and its delivery system since the implantation procedure is similar to that of the ASO. Although it looks similar to the ASO, there are significant differences between the two devices. The ASO consists of a nitinol wire tube that is clamped in two stainless steel hubs on each side of the discs, whereas the CSO device is braided, avoiding a distal clamp, thereby offering potential benefits to decrease the chance of clot formation on the left atrial disc and to increase flexibility of the disc for better adaptation in the interatrial septum.

Thromboembolic events are a recognized complication of all currently used devices and often seen on the left atrial side. The type of device and amount of material in the left atrium are the most common risk factors for thrombus formation. We experienced only a complication related to clot formation in the ASO group. However, randomized studies comparing the two devices with respect to thrombus formation or other complications are still needed.

Atrial arrhythmia is a frequent complication following placement of all transseptal devices [15]. Symptoms usually develop within the first 2 weeks after implantation and generally resolve within 1–2 months. In the present study, atrial arrhythmias occurred in 18 patients, and during the follow-up period all symptoms had resolved in these patients.

Procedure-related complications including transient ischemic attacks, atrioventricular block, arrhythmias, thrombosis, cardiac perforation, and pulmonary thromboembolism are usually related to oversized ASDs and choosing larger devices [16, 17, 18]. In our study, only atrial tachyarrhythmias and thrombosis were observed.

Interestingly, 48% of patients had an aortic rim of <5 mm. All the patients with deficient aortic rim had successful closure at follow-up.

The present study has several limitations. We only evaluated the clinical use and safety of the CSO device in the short and midterm. Studies to assess long-term results (>3 years) evaluating late complications (device erosion) will be necessary to confirm these outcomes.

Another limitation is that we evaluated all patients by TTE before discharge and at 1, 6, and 12 months. TTE does not suffice to exclude trivial shunt or thrombi on the devices.

Conclusion

This study demonstrates that the CSO device implantation is a feasible, safe, and effective in the closure of secundum ASDs, with less material on the left atrial side, rendering it more flexible for adaptation in the interatrial septum. The other advantage of the CSO device is that it can be deployed without tension of the delivery catheter. Further studies with a larger number of patients and longer fol-

low-up are needed to evaluate these two advantages of the device.

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Compliance with ethical guidelines

Conflict of interest. M.A. Astarcioglu, M. Kalcik, T. Sen, A.C. Aykan, T. Gokdeniz, O.M. Gursoy, S. Karakoyun, S. Kulahcioglu, S. Gunduz, C. Kilit, M. Oylumlu, and B. Amasyali state that there are no conflicts of interest. The accompanying manuscript does not include studies on humans or animals.

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