Prospective evaluation of the feasibility, safety, and efficacy of Cocoon Duct Occluder for transcatheter closure of large patent ductus arteriosus: A single-center study with short- and medium-term follow-up results

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Objective: To evaluate the feasibility, safety, and efficacy of a novel Cocoon Duct Occluder device for the transcatheter closure (TCC) of large patent ductus arteriosus (PDA).

Methods: In this prospective, non-randomized study, consecutive patients with large PDA (narrowest diameter: ≥3.5/4.0 mm in symptomatic/asymptomatic patients, respectively), who underwent TCC with Cocoon Duct Occluder at our institute between November, 2012 and June, 2016 were examined. TCC was performed using the standard technique, and devices were antegradely delivered via 6–10F delivery sheaths. Device embolization, residual shunt, hemolysis, left pulmonary artery (LPA) stenosis, procedural and fluoroscopy time, and mortality were assessed. Patients were followed-up by transthoracic echocardiography with color Doppler imaging at 24 h (D1), 1 month (D30), and 6 months (D180) after implantation.

Results: A total of 57 patients (age: 11.7±2.8 years; weight: 22.3±3.5 kg) were enrolled. The mean narrowest diameter was 7.4±0.7 mm. The PDA closure was successfully performed in each patient. Fluoroscopy and procedural time was 6.7±3.2 min and 23.9±2.7 min, respectively. Post-procedural angiography revealed that 49 (85.9%) patients had immediate and complete closure, whereas 8 (14.1%) had residual shunt. Color Doppler imaging at D1 revealed complete closure in 52 (91.3%) patients. At D30, complete closure was reported in all patients and was maintained at D180. Hemolysis, embolization, obstruction of LPA or descending aorta, and death were not reported till D180.

Conclusion: TCC using Cocoon Duct Occluder is feasible, safe, and effective in the management of patients with large PDA, with excellent results on short- and medium-term follow-up. (Anatol J Cardiol 2017; 18: 321-7)

Keywords: congenital heart disease, transcatheter closure, Cocoon Duct Occluder, large patent ductus arteriosus
which prevents nickel release and the corrosion of Nitinol wire coated over Nitinol wires by a process of plasma deposition, opacity, which enables easy positioning of the device. It is nano-
the size of pulmonary end i.e., 12/10). Platinum improves radio-
number, which is always 2 mm smaller than the first, denotes
first number denotes larger aortic end of device and the second
always 4 mm larger than the diameter of the quoted size (the
(Fig. 1b, c). The retention disk at the aortic end of the device is
of the device to induce thrombosis thereby closing the ductus
from 0.0004 to 0.0005 inch Nitinol wire mesh (Fig. 1a). It consists
expanding and self-centering, mushroom-shaped device, made
from Nitinol based, self-expanding occluder devices or coils are con-
sidered as the gold standard for TCC of PDAs and ADO is one of
the most widely used devices (4). In this regard, we conducted a prospective study to evaluate ana-
tomic heterogeneities among patients with large PDA, technical
considerations including challenges and complications, and short-
and medium-term follow-up results with the Cocoon Duct Occluder device (Vascular innovations, Nathambury, Thailand).

Methods

Study design and patient population
In this prospective, single-center study, 57 consecutive pa-
tients with large PDA who underwent TCC at L.P.S. Institute of
Cardiology, Kanpur, India between November, 2012 and June,
2016 were enrolled. Large PDA was characterized as the narrow-
est diameter of ≥3.5 mm in symptomatic or ≥4 mm in asymptom-
atic patients. The exclusion criteria were patients with weight <
5 kg, associated cardiac anomalies requiring corrective surgery, pulse-
monary vascular resistance > 8 Woods units/m², and bidental-
or right-to-left shunt. The protocol of the study was ap-
proved by institutional Ethics Committee. The study conformed
to the principles of good clinical practice and the Declaration of
Helsinki. Preprocedural written and informed consents were ob-
tained from all the patients or their legally authorized guardian.

Device description
The Cocoon Duct Occluder is a permanent implant with low-
profile intrinsic shape memory and is a platinum-coated, self-
expanding and self-centering, mushroom-shaped device, made
from 0.0004 to 0.0005 inch Nitinol wire mesh (Fig. 1a). It consists
of a retention disk, which assures secure positioning at the dis-
tal end of the ductus, and a cylindrical main body, into which
multiple poly propylene patches are securely sewn to the sides
of the device to induce thrombosis thereby closing the ductus
(Fig. 1b, c). The retention disk at the aortic end of the device is
always 4 mm larger than the diameter of the quoted size (the
first number denotes larger aortic end of device and the second
number, which is always 2 mm smaller than the first, denotes
the size of pulmonary end i.e., 12/10). Platinum improves radio-
opacity, which enables easy positioning of the device. It is nano-
coated over Nitinol wires by a process of plasma deposition,
which prevents nickel release and the corrosion of Nitinol wire
frame in the long-run and has superior biocompatible properties
compared with bare Nitinol after device implantation (Fig. 1a, d).
The delivery system consists of a delivery cable, loader, and
a pin vise which helps in unscrewing and releasing the device.
It requires sheath sizes varying 6–10F for delivery depending on
the device size. In majority of the patients with conical PDAs,
device size were 2 mm larger than the narrowest diameter of the
ductus, but in patients with larger ductus, even bigger sizes were
selected as the ratio of the retention disk diameter to the distal
device diameter becomes increasingly smaller with increasing
device size.

Procedural details
The procedures were performed under local anesthesia. The
femoral artery and vein were accessed with 5F sheath using modified Seldinger’s technique. Following sheath place-
ment, routine right and left heart catheterization tests were
performed in all patients to obtain the hemodynamics data. The
descending aortogram was performed in anteroposterior pro-
jection (AP), right anterior oblique (RAO) 40° with 30° cranial
angulation, and extreme lateral view to profile the ductus re-
garding its position, shape, and size and in both proximal and
distal end by positioning the distal end of the pigtail catheter
(Medtronic, USA) into the distal aortic arch (Fig. 2a, b). Each PDA
was classified according to Krichenko (11) on angiogram. The
contrast was injected using hand held syringe in pediatric pa-
tients and pressure injector in adult patients. With the help of
a straight tip Terumo wire (Terumo Inc., Japan), 5F multipurpose
catheter (MPA) was advanced from the venous side into PDA
in RAO cranial view and sometimes, in AP view. Once reached
into descending aorta, MPA was advanced till it reached the
descending aorta and then Terumo wire was exchanged with
a 0.035-inch J-tip super-stif Amplatz wire, thereby establishing
the femoral arteriovenous loop (Fig. 2c). MPA catheter was then

Figure 1. Cocoon Duct Occluder device morphology (B-1-distal diameter;
2-proximal diameter); C-red line indicates the retention disk diameter.
exchanged with a long delivery sheath (size depending on the device selected). The dilator was removed, leaving the long venous sheath (delivery sheath: 6–10F) in the descending aorta. In some cases where the delivery sheath could not be advanced in the usual fashion due to tortuous anatomy and poor support by the Amplatz wire, we held the distal end of Amplatz wire by gooseneck snare (Microvena, MN, USA) or customized snare to straighten it and then advanced the delivery sheath in the usual fashion (Fig. 2D). Then, the snare was removed and the pigtail catheter was re-introduced from the arterial side. A retrograde technique (i.e. from the descending aorta to the pulmonary artery) was used to establish a femoral arteriovenous loop when conventional antegrade technique failed in some patients with abnormal morphology, such as a smaller ostium of the side of the pulmonary artery compared with the side of the descending aorta, severe calcification, or tortuosity. Here, 5F MPA with long Terumo wire was advanced from the arterial side to the right atrium via PDA–MPA–right ventricle, where it was snared using the gooseneck snare and exteriorized from the venous end to establish the arteriovenous loop (Fig. 3a–c). Over this wire, the delivery sheath was advanced in the usual fashion (Fig. 3d, 4a). Subsequently, the delivery cable was passed through the loader and the appropriate device was screwed clockwise into its tip. The device and loader were immersed in a saline solution as the Cocoon Duct Occluder device was pulled into the loader to make it air-free. The loader was introduced into the delivery sheath, and the device was advanced into the descending aorta. The sheath was retracted enough to open the retention disk in the proximal descending aorta. The sheath, with the delivery cable in it, was pulled back as one unit until the retention disk was properly sitting against the aortic end of the ampulla. While maintaining the tension on the delivery cable, the sheath was further pulled into the pulmonary artery to deploy the tubular frame of the Cocoon Duct Occluder (Fig. 3e, 4b). With the device still attached to the cable, a descending aortogram was performed in the lateral and RAO cranial projections to confirm

Figure 2. Descending aortic angiogram in lateral projection. Large type-A PDA measuring 5.09 mm in its narrowest diameter in a symptomatic 9-month old baby (a, b), Antegrade wiring forming an arteriovenous loop (c); Amplatz wire being snared by gooseneck snare (d)
PDA - patent ductus arteriosus

Figure 3. The soft tip of Terumo wire being caught by a customized snare in the right atrium (a). A customized snare prepared using an exchange length BMW wire by passing it through the Judkins right diagnostic catheter and proximal end caught by arterial forceps (b), Establishment of the arteriovenous loop (c), Delivery sheath in the descending aorta (d); Successful deployment of Cocoon Duct Occluder device (e), Post-procedural angiogram confirming the device position and complete occlusion of PDA (f)

Figure 4. 11F Delivery sheath in the descending aorta (a), Fully opened PDA device attached with the delivery cable in lateral view (b) and in RAO cranial view (c), Well-deployed Cocoon Duct Occluder with no residual shunt in lateral view (d)
the device position (Fig. 3f, 4b–d). The device was recaptured and redeployed after upsizing if the device was not properly sitting across the defect prior to the release. Postimplantation angiogram was performed at 0 min and if device size was >10 mm, at 10 min. Once properly positioned, the device was released by turning the cable counter-clockwise using the pin vise. The arterial sheath was removed and local compression was applied with the help of a tight compression bandage and the venous sheath was removed and closed using the z-suture or figure of eight suture (Fig. 5).

Data collection and follow-up

At the time of enrolment, all patients were comprehensively assessed for clinical history, physical examination, routine hemogram, chest x-ray, and detailed transthoracic echocardiogram. Echocardiography was performed using Vivid 7TM (GE, USA) in parasternal long-axis and short-axis views for routine measurements and in high short-axis and suprasternal views for the sizing of PDA.

Postprocedural residual shunts on angiogram were labeled as: Grade 1- none; Grade 2- small (dye filling only proximal pulmonary artery branches); Grade 3- moderate (dye filling the main pulmonary artery and extending to the distal branches); and Grade 4- significant (dye filling the main pulmonary artery and branches extending to the peripheral vessels with contrast return to the left atrium) (4). Procedural complications such as device embolization, hemolysis, need for blood transfusion, arrhythmia requiring major treatment, pericardial effusion with tamponade, pulmonary edema, LPA stenosis and death were assessed as major events and local site complications, arrhythmia requiring minor treatment, and extremity tingling/numbness as minor events.

Follow-up 2D-transthoracic echocardiogram including color Doppler imaging was performed at 24 h (D1), one month (D30), and the end of sixth month (D180) to assess the device position and residual shunts, and Doppler flow velocities of LPA and the descending aorta for any stenosis. Residual shunts on echocardiogram were labeled as: Grade 1- none; Grade 2- trivial (a small color Doppler jet limited to the device); Grade 3-moderate (Doppler jet beyond the device but no audible murmur); and Grade 4- significant shunt (large Doppler jet with an audible murmur and continuous Doppler flow) (4).

Table 1. Baseline characteristics of patients including their demographic, hemodynamic, and angiographic variables (n=57)

| Age, years     | n (%) | Wt. kg±SD | PASP mm Hg±SD | Ao. Sys Pr mm Hg±SD | PVRI Woods U/m² | Duct size mm±SD |
|----------------|-------|-----------|---------------|---------------------|-----------------|-----------------|
| Group A: Infant (<1 year) | 9 (15.8%) | 6.2±0.4 | 51.4±2.6 | 71±5.2 | 4.6±2.1 | 7.8±1.3 |
| Group B: 1-5 years | 11 (19.3%) | 13.3±1.7 | 65.3±7.4 | 91.5±10.7 | 3.9±1.3 | 8.2±1.4 |
| Group C: 6-18 years | 19 (33.3%) | 21.7±5.1 | 71.1±8.3 | 94.5±9.1 | 4.4±1.2 | 10.3±2.3 |
| Group D: >18 years | 18 (31.6%) | 44.6±9.8 | 83.4±12.5 | 105.7±13.6 | 6.2±2.4 | 12.2±3.1 |

Ao Sys Pr- aortic systolic pressure; PASP- pulmonary artery systolic pressure; PVRI- pulmonary vascular resistance index; Wt-weight-woods U/m² = 79.92 dyn.s/cm⁵.
Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) program, version 15.

Categorical variables were expressed as frequency and percentages and continuous variables as mean ± standard deviation (SD).

Results

Baseline characteristics

A total of 57 patients (32 males, 25 females) were enrolled. The mean age was 11.7±2.8 years (range: 6 months–46 years), and the mean weight was 22.3±3.5 kg (range: 5.8–61.1 kg). All patients had continuous cardiac murmur on examination and 8 (14%) had a history of recurrent lower respiratory tract infection. Other baseline characteristics for overall patients and for patients stratified based on age (i.e. 1 year, 1–5 years, 6–18 years, >18 years) are described in Table 1. Clinical characteristics of patients, including presentation of other associated cardiac anomalies, and procedural details are given in Table 2. Of 57 the patients, 46 (80.7%) had type A, 6 (10.5%) had type B, 2 (3.5%) had type C, and 3 (5.2%) had type E PDAs. The mean PDA diameter on angiogram was 7.4 ± 2.9 mm.

Procedural outcomes

Successful PDA closure with the Cocoon Duct Occluder device was performed in all the patients without any major complications. Arrhythmias requiring minor treatment were noted in seven (12.3%) patients, of which, three had multiple atrial ectopics, one had atrial tachycardia, and three had ventricular ectopics. Vascular access complications in the form of local haematoma occurred in two (3.5%) patients, which were successfully and conservatively managed. Final postimplantation angiography showed complete closure in 49 (86%) patients, a small (Grade 2) shunt in seven (12.3%), and moderate (Grade 3) shunt in one (1.7%) (Table 3; Fig. 6).

Follow-up outcomes

All patients completed the echocardiographic follow-ups (i.e. at D1, D30, and D180). Color Doppler data at D1 showed that complete closure (no shunt, Grade 1) was achieved in 52 (91.3%) patients, trivial shunt (Grade 2) in three (5.2%), and moderate shunt in two (3.5%) with complete closure without any shunt at D30, which were consistent at D180 (Table 3). All the residual shunts required no specific treatment.

Discussion

In the present era, TCC has replaced surgical intervention as the first-choice management option. Despite its remarkable
safety, there is always a concern regarding complications, such as embolization and mild obstruction of LPA and descending aorta, particularly in infants with large PDA who require a relatively larger device (12, 13). Nevertheless, because of its design, the Cocoon Duct Occluder has made a cut through in the field of TCC and can be used for larger defects (up to 22 mm), with outcomes comparable to the ADO device (14). In addition, the retention disc on its distal aortic end which is 4 mm bigger than its size prevents its embolization to the pulmonary artery.

Our prospective, non-randomized study, showed 100% procedural success rate with the Cocoon Duct Occluder device in 57 patients with large PDAs. Further, the fluoroscopy and procedural times indicate that procedure with this novel device is feasible and simple with excellent safety profile without any incidence of embolization, haemolysis, or stenosis of adjacent structures, with excellent results on short- and medium-term follow-ups.

When larger devices were used (≥18/16) for larger PDAs (≥12 mm), they tended to have residual shunt at 10 min postimplantation and at 24 h on echocardiography. Although the incidence of residual shunt was slightly higher with the Cocoon Duct Occluder device (14% and 8.7% on angiogram and echocardiogram, respectively), all patients with a residual shunt achieved complete closure at 30 days without a need for special treatment, which indicates excellent efficacy of the device. Of note, ADO devices have certain limitations as they cannot be used to close a very large defect (≥11-mm minimum diameter) (15). Also, the height of the waist of ADO is small, which makes it unsuitable for certain PDA morphologies as it cannot completely expand, resulting in residual shunt and hemolysis.

TCC of certain PDAs may be challenging due to the anatomy of PDA or the kinking of the delivery sheath from the antegrade route for establishing an arteriovenous loop. In such patients, a retrograde technique may be helpful, as previously reported by Hijazi et al. (7) and Hsin et al. (16). In our study, retrograde wiring was used in 7.1% patients, which was similar to 6.25% reported by Yang et al. (15). As the antegrade deployment of the delivery sheath may not be straightforward sometimes, we used the retrograde snare to facilitate its delivery, the technique also reported by Yan et al. (17).

Earlier, Spies et al. (18) had reported a case of successful closure of a large 22-mm PDA using an Amplatzer atrial septal occluder. Yan et al. (17) had reported that Amplatzer muscular ventricular septal defect occluder can be used for a large PDA of up to ≤14 mm. Bilkis et al. (9) examined 209 patients with PDA (size: 1.8–12.5 mm) who underwent TCC with ADO and reported success in 98% patients, with complete occlusion in 44% patients after the procedure, 66% at 24 h, and 97% at 1 month. On the contrary, our study with the Cocoon Duct Occluder demonstrated better outcomes with successful procedure in 100% patients, and complete occlusion in 86% patients after the procedure, 91.3% at 24 h, and 100% at 1 month. Similarly, Yang et al. (15) had examined 112 patients with complex PDA and reported procedural success in 93.8% patients, postprocedural residual shunts in 8%, and residual shunts at 1-year follow-up in 1.8%, which was much higher than our study.

Device embolization was seen in 1.4% patients within 24 h of procedure, as reported by Bilkis et al. (9); however, it was not seen in our study. Furthermore, the incidence of hemolysis and vascular access complications was also significantly lower in our study, being 0% and 3.5% among patients respectively, as compared to 2.6% and 5.2% as reported by Yang et al. (15) Though rare, Simoes et al. (19) had reported a single procedure-related death with ADO due to mesenteric vascular complications and sepsis following embolization into the descending aorta in a study of 33 patients with PDA. In our series, the incidence of death was none. Therefore, an embolized device should always be retrieved from the aorta on emergency basis either by a transcatheter or surgical approach.

Study limitations

This was a small, non-randomized prospective study of patients with a great majority having type A morphology (80.7%). Therefore, a prospective study enrolling a higher number of patients with complex PDA morphology and longer follow-up may serve well to demonstrate the efficacy of Cocoon Duct Occluder devices.

Conflict of interest

None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – PK., M.JJ., S.K.S.; Design – S.K.S.; Supervision – S.K.S., R.N.P.; Fundings – C.M.V., U.P., V.K.; Materials–S.K.S., M.R., R.N.P.; Data collection &/or processing – All Authors; Analysis &/or interpretation – PK., PT., R.T.; Literature search – V.M., N.A.; Writing – M.R.,V.M., M.A.; Critical review – All Authors.

References

1. Mitchell SC, Korones SB, Berendes HW. Congenital heart disease in 56,109 births: incidence and natural history. Circulation 1971; 43: 323-32.
2. Campbell M. Natural history of persistent ductus arteriosus. Br Heart J 1968; 30: 4-13.
3. Gaia DF, Palma JH, Kim HC, de Souza JA, Alves CR, Buffolo E. Patent ductus arteriosus: endovascular treatment in adult patient. Arq Bras Cardiol 2008; 91: 25-7.
4. Abdelbasit MA, Alwi M, Kandavello G, Che Mood M, Samion H, Hijazi ZM. The new Occlutech® PDA occluder: Initial human experience. Catheter Cardiovasc Interv 2015; 86: 94-9.
5. Arora R, Kalra GS, Nigam M, Khalillulah M. Transcatheter occlusion of patent ductus arteriosus by Rashkind umbrella device: follow-up results. Am Heart J 1994; 128: 539-41.

6. Hijazi ZM, Geggel RL. Transcatheter closure of large patent ductus arteriosus (≥4 mm) with multiple Gianturco coils: immediate and midterm results. Heart 1996; 76: 536-40.

7. Hijazi ZM, Lloyd TR, Beekman RH 3rd, Geggel RL. Transcatheter closure with single or multiple Gianturco coils of patent ductus arteriosus in infants weighing < or =8 kg: retrograde versus antegrade approach. Am Heart J 1996; 132: 827-35.

8. Moore JW, George L, Kirkpatrick SE, Mathewson JW, Spicer RL, Uzark K, et al. Percutaneous closure of the small patent ductus arteriosus using occluding spring coils. J Am Coll Cardiol 1994; 23: 759-65.

9. Bilkis AA, Alwi M, Hasri S, Haifa AL, Geetha K, Rehman MA, et al. The Amplatzer duct occluder: experience in 209 patients. J Am Coll Cardiol 2001; 37: 258-61.

10. Thanopoulos BD, Tsaoouis GS, Djukic M, Al Hakim F, Eleftherakis NG, Simeunovic SD. Transcatheter closure of high pulmonary pressure persistent ductus arteriosus with Amplatzer muscular ventricular septal defect occluder. Heart 2002; 87: 260-3.

11. Krichenko A, Benson LN, Burrows F, Moes CA, McLaughlin P, Freedom RM. Angiographic classification of the isolated, persistently patent ductus arteriosus and implications for percutaneous catheter occlusion. Am J Cardiol 1989; 63: 877-80.

12. Schneider DJ, Moore JW. Patent ductus arteriosus. Circulation 2006; 114: 1873-82.

13. Atiq M, Aslam N, Kazmi KA. Transcatheter closure of small-to large patent ductus arteriosus with different devices: queries and challenges. J Invasive Cardiol 2007; 19: 295-8.

14. Thanopoulos BD, Hakim FA, Hiari A, Tsaoouis GS, Paphtits C, Hijazi ZM. Patent ductus arteriosus equipment and technique, Amplatzer duct occluder: intermediate-term follow-up and technical considerations. J Interv Cardiol 2001; 14: 247-54.

15. Yang SW, Zhou YJ, Hu DY, Liu YY, Shi DM, Guo YH, et al. Feasibility and safety of transcatheter intervention for complex patent ductus arteriosus. Angiology 2010; 61: 372-8.

16. Hsin HT, Lin LC, Hwang JJ, Ho SG, Tseng CD, Chiang FT. Retrograde wire-assisted percutaneous transcatheter closure of persistent ductus arteriosus with Amplatzer duct occluder in the elderly: a new application. Catheter Cardiovasc Interv 2004; 61: 264-7.

17. Yan C, Zhao S, Jiang S, Xu Z, Huang L, Zheng H, et al. Transcatheter closure of patent ductus arteriosus with severe pulmonary arterial hypertension in adults. Heart 2007; 93: 514-8.

18. Spies C, Ujivari F, Schrader R. Transcatheter closure of a 22 mm patent ductus arteriosus with an Amplatzer atrial septal occluder. Catheter Cardiovasc Interv 2005; 64: 352-5.

19. Simoes LC, Pedra CAC, Esteves CA, Camargo R, Braga SL, Loureiro P, et al. Percutaneous closure of ductus arteriosus with the Amplatzer prosthesis: The Brazilian experience. Arq Bras Cardiol 2001; 77: 520-31.