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Transcatheter Closure of Patent Ductus Arteriosus with a Self-Expanding Platinum-Coated Nitinol Device

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ABSTRACT: Background. An occluding device for closure of patent ductus arteriosus (PDA) was developed from meshed nitinol wires coated with platinum for prevention of nickel release after implantation. **Objectives.** Our purpose was to assess the immediate and short-term results of transcatheter PDA closure with this device. **Methods.** Sixty patients (13 males and 47 females) underwent catheter-based PDA closure. The age ranged from 9 months to 65 years, with a median age of 4 years. The weight ranged from 4.2– 65 kg, with a median of 15.2 kg. The mean PDA diameter at the narrowest segment was 4.7 ± 2.2 mm, with a range of 2.0–15.1 mm. Eighteen cases had serial blood samples for serum nickel analysis taken before and at 1, 3 and 30 days after device implantation. **Results.** The devices were successfully deployed in all 60 patients. There were no serious procedural complications. Color Doppler demonstrated complete occlusion rate of 78.3%, 90.0% and 100% at 1 day, 1 month and 1 year after implantation, respectively. There was no statistical difference in serum nickel concentrations between pre- and post-implantation. **Conclusion.** Transcatheter PDA closure using a platinum-coated nitinol device can be performed safely and successfully. There was no evidence of nickel release or nickel reaction after device implantation. This device model may be an alternative for PDA closure, especially in patients with potential nickel allergy.

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Key words: patent ductus arteriosus; transcatheter closure; platinum-coated nitinol device; nickel release

Nitinol, an alloy composed of 55% nickel and 45% titanium, has been widely applied in many medical implant products. During the past decade, a variety of nitinol-containing devices were designed and studied for catheter-based closure of atrial septal defect (ASD), patent foramen ovale (PFO) and patent ductus arteriosus (PDA). At present, Amplatzer occluders (nitinol-containing devices) have been used worldwide for transcatheter closure of ASD, PFO and PDA. A large amount of literature exists indicating excellent outcomes, even in very large defects.[1-8] For the nickel component in nitinol alloy, transient release of nickel into the circulation was demonstrated after ASD and PFO closure with the Amplatzer occluder *(AGA Medical Corp., Plymouth, Minnesota)*.[9,10] There were a number of reported cases about systemic allergic reaction after closure of ASD, PFO[11–13] and PDA[14] with a nitinol-containing device. Thus, nickel release after nitinol device implantation is a concern, especially in patients with a history of nickel allergy. With nanotechnology, ultrathin layers of platinum coated on the surface of nitinol can avoid exposure of the nickel-containing alloy to the bloodstream and also prevent nickel release after device implantation. This concept presents an innovative model of a nitinol-based PDA occlusion device that is platinum-coated for prevention of nickel reaction after implantation. This device may be an alternative for PDA closure, especially in patients who have clinical evidence of nickel allergy, or in those who would like to avoid the possible adverse effects from nickel reaction.

The purpose of this study was to evaluate the immediate and short-term outcomes of transcatheter PDA closure with a platinum-coated nitinol device and to study the serial serum nickel concentrations before and after device implantation.

Methods

Patient population. The study protocol and informed consent form were approved by the ethics committee of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. The consent forms were signed by the patients or their parents for participation in the study. Patients beyond the neonate age who were diagnosed by clinical and echocardiographic findings with a PDA requiring closure were invited to participate in the study. Between August 2005 and April 2008, 60 patients (13 males and 47 females; 49 pediatric and 11 adult cases) were enrolled in the study. The median age was 4 years (range: 9 months to 65 years). The median weight was 15.2 kg (range: 4.2–65 kg).

Device design. The system consists of an occlusion device, a delivery cable and a loader. The device is braided with nitinol wires, nanocoated with platinum and filled with 5 polypropylene sheaths to enhance thrombogenicity (Figure 1). A delivery cable can be connected to the proximal end of the device with a screw connection for controlled release. The device is tubular in shape, with a diameter 2 mm larger at the distal end than at the proximal end. A thin disc is located on the distal end, which has a diameter 4 mm larger than that of the distal end. The size of the device is indicated by the diameter of its smaller proximal end. We demonstrated the safety and successful occlusion results with this device in our previous animal experiment.[15] Although this device appears similar to the Amplatzer Ductal Occluder,

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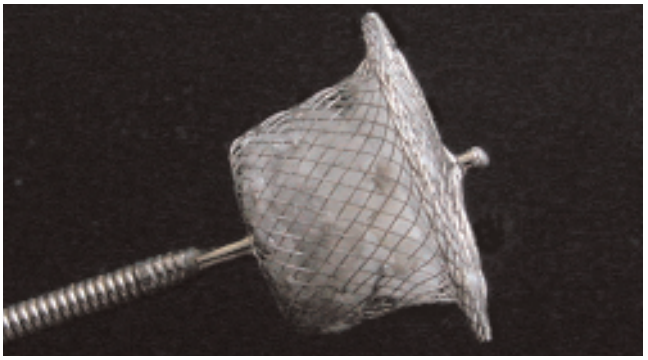

Figure 1. *The platinum-coated nitinol patent ductus arteriosus device is attached with the delivery cable by screw connection.*

the size of the precoated nitinol wires, the platinum coating on the surface of the meshed nitinol wires and the fabric used inside differentiate it from the Amplatzer device.

Closure protocol. Under intravenous midazolam and fentanyl sedation, conventional right- and left-heart catheterization was performed for hemodynamic assessment. Right anterior oblique and lateral aortograms were obtained to evaluate PDA size and morphology. The closure device size was selected by using 2–3 mm larger than the narrowest PDA diameter measured in the lateral aortogram. The device was loaded into a long vascular sheath that was previously introduced via a femoral vein to the right heart, pulmonary artery and through the ductus into the descending aorta. It was then deployed with the distal thin disc at the aortic end, the body stenting at the narrowest part of the ductus, and the proximal end minimally protruding into the pulmonary artery. Aortography was performed after device deployment to assess its position and alignment. After the finding was satisfactory, the delivery cable was unscrewed to detach from the device. Another aortogram was performed to assess the occlusion (Figure 2).

Serum nickel analysis. Serial blood samples for serum nickel concentrations were collected from 18 patients preprocedure and 1 day, 3 days and 1 month after implantation. Samples from 100 normal subjects were also collected as a control. The blood was centrifuged immediately and the serum collection was frozen at -20°C until analysis was performed. Serum nickel analysis was conducted by electrothermal atomic absorption spectrophotometry (ETAAS), the same technique as previously reported.[16]

Statistical analysis. Data were expressed as mean ± standard deviation. The serum nickel levels after implantation were compared to the preimplantation baseline by using the paired t-test. The difference in nickel concentrations in the patients and normal subjects was analyzed by the independent samples t-test. A p-value < 0.05 was considered statistically significant.

Results

The devices were successfully deployed in all 60 patients. The narrowest PDA diameter by lateral aortography ranged from 2–15.1 mm, with a mean of 4.6 ± 2.2 mm. Device size ranged from 4–18 mm, with a mean of 7.0 ± 2.3 mm. The associated lesions were mild aortic stenosis in 3 cases, mild pulmonic stenosis in 1 case, a small atrial septal defect (ASD) in 1 case, and post pacemaker implantation for congenital heart block in 1 case. One patient, who had a residual PDA of 3.4 mm after surgical ligation, was also included in the study. No serious procedure-related complications occurred.

During the mean follow-up period of 13.2 ± 11.3 months (range: 1–37 months), all the patients were doing well. One patient had minimal protrusion of the device into the aorta. No other device-related complications were noted. Two-dimensional and color Doppler echocardiographic studies revealed complete occlusion rates of 78.3% (47 patients) at 1 day, 90.0% (54 patients) at 1 month, 93.3% (56 patients) at 6 months, and 100% (60 patients) at 12 months post implantation. The patient who had minimal protrusion of the device into the aorta was a 4.2 kg, 10-month-old girl who had a 3.6 mm PDA closed using a 6 mm device. At 1-year follow up, color Doppler demonstrated flow velocity of 1.22 m/second (pressure gradient of 6.0 mmHg) across the descending aorta, but there was no difference in noninvasive blood pressure measurement obtained from both upper and lower extremities. The largest PDA case (15.1 mm) was a 13-year-old girl who weighed 37 kg. She had severe pulmonary hypertension, with a mean pulmonary pressure of 85 mmHg prior to PDA occlusion. An 18 mm device was successfully deployed, and her mean pulmonary pressure declined to 52 mmHg immediately after occlusion. Color Doppler echocardiography

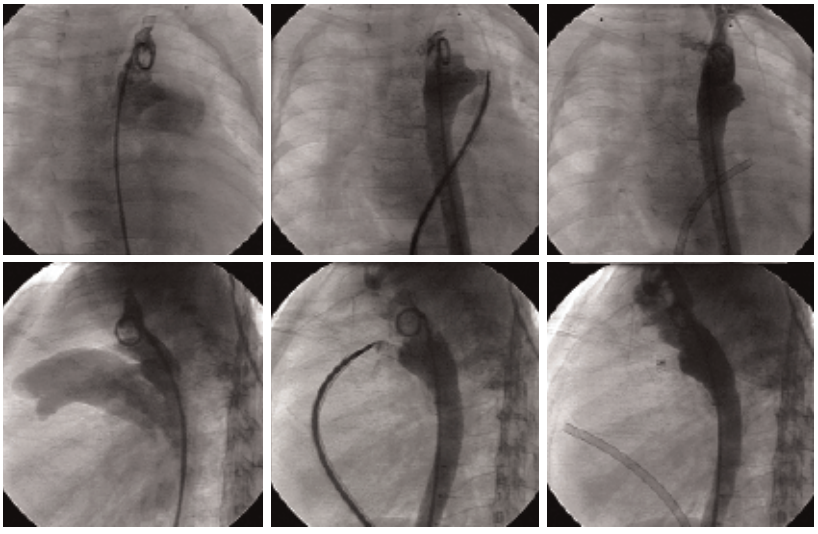

Figure 2. *Aortograms in the right anterior oblique (upper panels) and lateral (lower panels) views of a 9-month-old girl. The left panels were the pre-implantation aortogram to evaluate patent ductus arteriosus (PDA) morphology and measure PDA narrowest diameter (4.2 mm in lateral view). The middle panels show proper position and alignment of a 6-mm device that was still attached to the delivery cable. The right panels reveal complete occlusion after the device was released from the delivery cable.*

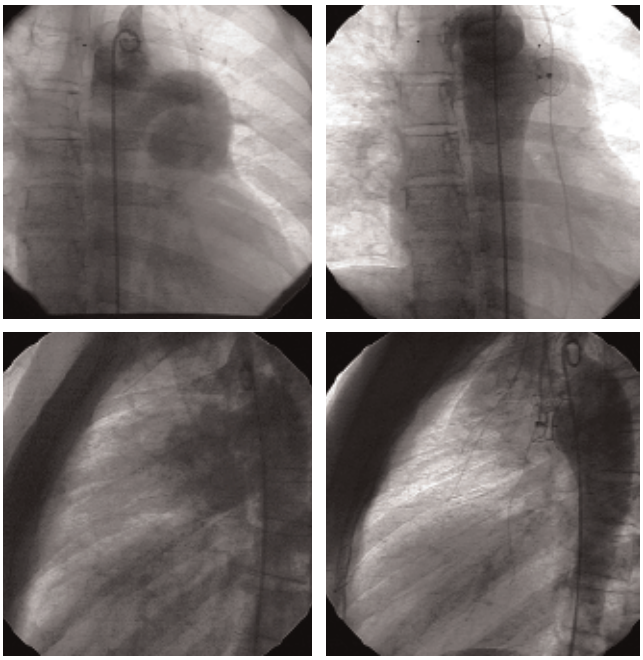

Figure 3. *Aortograms in right anterior oblique (upper panels) and lateral (lower panels) views of a 13-year-old girl with 15.1 mm patent ductus arteriosus that was closed with an 18-mm device. The left panels were before implantation. The right panels were at 7 months after implantation.*

demonstrated complete PDA closure 1 day after implantation. Seven months after device occlusion, a second cardiac catheterization was performed to evaluate the patient's pulmonary pressure. The patient still had residual pulmonary hypertension, with a mean pulmonary pressure of 44 mmHg. Repeat aortography demonstrated proper position and alignment of the device and complete PDA occlusion (Figure 3).

Eighteen patients who underwent serial blood sample collection for serum nickel analysis had a mean PDA size of 5.3 ± 3.0 mm and a mean device size of 7.9 ± 3.0 mm. The mean serum nickel levels at baseline (n = 18), day-1 (n = 14), day-3 (n = 13), and day-30 (n = 13) were 0.59 ± 0.19, 0.57 ± 0.18, 0.57 ± 0.15, and 0.68 ± 0.27 ng/ml, respectively. There was no statistical difference in serum nickel concentrations between the pre- and post-implantation measurements (Figure 4). *P*-values comparing mean pre-implantation with mean post-implantation levels at day-1, day-3, and day-30 were 1.0, 0.51 and 0.55, respectively. The mean serum nickel levels in the study patients (pre- and post-implantation serum levels of 58 samples) were not statistically different from those of the 100 control subjects (0.57 ± 0.21 vs. 0.60 ± 0.30 ng/ml), with a *p*-value of 0.53.

Discussion

Amplatzer devices have been widely used for ASD, PFO and PDA closure during the past decade with excellent outcomes.[1-8] Reports by Ries et al[9] and Burian et al[10] described the significant increase in serum nickel levels after transcatheter closure of ASDs and PFOs with Amplatzer ASD and PFO occluders. The nickel release occurred transiently for a period of 3–6 months after device implantation. Calcium-phosphate layer formation on the passive oxide film of the nitinol wires or neoendothelialization on the surface of the implanted device may explain the drop to normal levels.[9,10] There are also reported cases on systemic allergic reaction after nitinol-containing device implantation for ASD and PFO closure.[11–13] Recently, Kim et al[14] reported a case of a 31-year-old female who developed generalized pruritic erythematous maculopapular skin eruption on the day following PDA closure with an Amplatzer Ductal Occluder. The patient was treated with prednisone 40 mg daily and the skin lesion disappeared after several days. An allergic skin patch test revealed a strong positive reaction to nickel. Overall, a small number of cases have been reported in which patients developed a systemic allergic reaction after nitinol-based device implantation compared to the very large number of implant cases, but practitioners should be aware of the potential for this type of allergic reaction, especially in patients with nickel allergy. Rigatelli et al[17] reported on 8 out of 9 patients with proven nickel allergy who developed a sort of "device syndrome" 1–2 days after ASD or PFO closure with full-nitinol devices such as the Amplatzer ASD and PFO occluders or a low-dose-nitinol device such as the Premere™ PFO Closure System *(St. Jude Medical, Inc., St. Paul, Minnesota)*. The syndrome included concurrent chest discomfort, exertional dyspnea, asthenia and mild leukocytosis in the absence of arrhythmia, instrumental pericardial inflammation or effusion, device thrombosis or femoral vascular complication. Interestingly, none of the other 37 patients without nickel allergy developed the post-closure symptoms similar to those of the nickel allergy patients. It would appear that nickel was released from the surface of the nitinol wires into the circulation after implantation. The phenomenon ceased once the device was endothelialized or after a calcium-phosphate layer had formed on the passive oxide film of the nitinol wires.[9,10] This is where platinum activation of the nitinol surface by nanotechnology becomes relevant. Nanotechnology makes it possible to deposit layers of platinum atoms over the surface of meshed nitinol wires by a process called plasma deposition. The platinum-coating layer creates a biocompatible and noncorrosive zone, which can prevent the adverse effects from nickel release. In addition, it also preserves the superelastic and shape-memory properties of nitinol. Even though the platinum-coated nitinol PDA device in this study appears similar to that of the Amplatzer Ductal Occluder, several changes are apparent from an engineering standpoint. For example, the wires are of a different thickness than those of the Amplatzer Ductal Occluder and are platinum-coated after the device is formed. Furthermore, the fabric used inside the device is spunbound polypropylene. The platinum-coated nitinol PDA device is an innovative model designed to solve the nickel-reaction problem. We presented our previous study on transcatheter ASD closure using a nanoplatinum-coated nitinol ASD device.[16]

The platinum-coated nitinol device avoids nickel exposure including nickel adverse effects; it also yields results equal to those of a bare-nitinol device. In this study, successful implantations occurred in all attempted cases, with a complete closure rate of 90% within 1 month, and 100% within 1 year after the

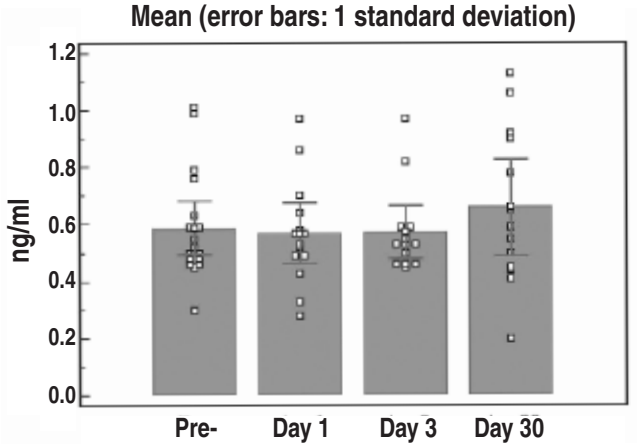

Figure 4. *Serum nickel levels pre- and post- implantation.*

procedure. In our smallest patient (a 4.2 kg girl with a 3.6 mm PDA), there was even minimal protrusion of the device into the descending aorta. She was doing well and weighed 8.3 kg at 1-year follow up. Our largest PDA case (15.1 mm) had a preclosure mean pulmonary pressure of 85 mmHg; despite a large PDA and elevated pulmonary pressure, an 18 mm device was successfully deployed. Although the device has a single disc placed on the aortic end and no disc on the pulmonary end, it can tolerate high pulmonary pressure in the event of pulmonary hypertension. This finding supports the feasibility of this device model for safe implantation in large PDAs with pulmonary hypertension. The procedure was performed by upsizing the device so that the body stented tightly within the PDA and the device's proximal end (which protruded into the pulmonary artery) was large enough to tolerate the elevated pulmonary pressure.

We did not study the serum nickel levels in patients after implantation of the Amplatzer Ductal Occluder as a relative comparator. This is our early experience in catheter-based PDA closure with an occlusion device. However, our study has demonstrated no difference in nickel levels between pre- and post-implantation, even in the case where an 18-mm device was deployed. There was no report of nickel release after implantation of the Amplatzer Ductal Occluder. In addition, the size, as well as the amount of nitinol in the Amplatzer Ductal Occluder, are much smaller than those of the Amplatzer ASD and PFO occluders. However, there was at least one reported case of allergic dermatitis after Amplatzer Ductal Occluder implantation in a female patient whose allergic skin patch test was strongly positive for nickel.[14] Furthermore, it has been demonstrated that an allergic reaction could occur after implantation of Amplatzer devices that are entirely composed of nitinol as well as other devices that are partially comprised of nitinol.[17] This should mean that the allergic reaction does not depend on the amount of nitinol in the device. During follow up, we had no clinical information that suggested any other device-related complications, including potential nickel-related reactions. These findings support the notion that nickel release can be prevented by platinum coating on the nitinol surface. However, further studies are needed to test for possible device-related adverse effects.

Conclusion

Transcatheter PDA closure using a platinum-coated nitinol PDA device can be performed safely and successfully with good results. Serum nickel analysis suggested no evidence of nickel release after implantation. Our patients developed no symptoms or signs suggesting a nickel reaction during follow up. This device may be an alternative for catheter-based PDA closure, especially in patients with a potential allergy to nickel.

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References

1. Masura J, Gavora P, Formanek A, Hijazi ZM. Transcatheter closure of secundum atrial septal defects using the new self-centering Amplatzer septal occluder: Initial human experience. *Cathet Cardiovasc Diagn* 1997;42:388–393.
2. Chan KC, Godman MJ, Walsh K, et al. Transcatheter closure of atrial septal defect and interatrial communications with a new self expanding nitinol double disc device (Amplatzer septal occluder): Multicentre U.K. experience. *Heart* 1999;82:300–306.
3. Masura J, Gavora P, Podnar T. Long-term outcome of transcatheter secundum type atrial septal defect closure using Amplatzer septal occluders. *J Am Coll Cardiol* 2005;45:505–507.
4. Wang JK, Tsai SK, Wu MH, et al. Short- and intermediate-term results of transcatheter closure of atrial septal defect with the Amplatzer septal occluder. *Am Heart J* 2004;148:511–517.
5. Rao PS. Techniques for closure of large atrial septal defects. *Catheter Cardiovasc Interv* 2007;70:329–330.
6. Masura J, Walsh K, Thanopoulous B, et al. Catheter closure of moderate to large-sized patent ductus arteriosus using the new Amplatzer duct occluder: Immediate and short-term results. *J Am Coll Cardiol* 1998;31:878–882.
7. Bilkis AA, Alwi M, Hasri S, et al. The Amplatzer duct occluder: Experience in 209 patients. *J Am Coll Cardiol*. 2001;37:258–261.
8. Pass RH, Hijazi Z, Hsu DT, et al. Multicenter USA Amplatzer patent ductus arteriosus occlusion device trial: Initial and one-year results. *J Am Coll Cardiol* 2004;44:513–519.
9. Ries MW, Kampmann C, Rupprecht HJ, et al. Nickel release after implantation of the Amplatzer occluder. *Am Heart J* 2003;145:737–741.
10. Burian M, Neumann T, Weber M, et al. Nickel release, a possible indicator for the duration of antiplatelet treatment, from a nickel cardiac device in vivo: A study in patients with atrial septal defects implanted with an Amplatzer occluder. *Int J Clin Pharmacol Ther* 2006;44:107–112.
11. Fukahara K, Kazutomo M, Riess N, et al. Systemic allergic reaction to the percutaneous patent foramen ovale occluder. *J Thorac Cardiovasc Surg* 2003;125:213–214.
12. Singh HR, Turner DR, Forbes TJ. Nickel allergy and the Amplatzer septal occluder. *J Invasive Cardiol* 2004;16:681–682.
13. Lai DW, Saver JL, Araujo JA, et al. Pericarditis associated with nickel hypersensitivity to the Amplatzer occluder device: A case report. *Catheter Cardiovasc Interv* 2005;66:424–426.
14. Kim KH, Park JC, Yoon NS, et al. A case of allergic contact dermatitis following transcatheter closure of patent ductus arteriosus using Amplatzer ductal occluder. *Int J Cardiol* 2008;127:e98–e99.
15. Lertsapcharoen P, Khongphatthanayothin A, La-orkhun V, et al. Self-expanding nanoplatinum-coated nitinol devices for atrial septal defect and patent ductus arteriosus closure: A swine model. *Indian Heart* J 2006;58:315–320.
16. Lertsapcharoen P, Khongphatthanayothin A, Srimahachota S, Leelanukrom R. Self-expanding platinum-coated nitinol devices for transcatheter closure of atrial septal defect: Prevention of nickel release. *J Invasive Cardiol* 2008;20:279–283.
17. Rigatelli G, Cardaioli P, Giordan M, et al. Nickel allergy in interatrial shunt device-based closure patients. *Congenit Heart Dis* 2007;2:416–420.