Transcatheter closure of the patent ductus arteriosus with new-generation devices: comparative data and follow-up results

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Key words:
Interventional cardiology; Patent ductus arteriosus; Pediatric cardiology.

Background. **Many devices currently used for the closure of the patent ductus arteriosus are claimed to be safe and cost-effective, but only few data exist with respect to the gold standard of the Rashkind occluder. The aim of this study was to assess the efficacy and safety of three new different devices and to compare the results to those of a control group of patients carrying a Rashkind occluder. This should provide the basis for further cost-analysis studies.**

Methods. **The records of all patients who underwent closure of the patent ductus at our Institution from April 1989 to May 2001 were reviewed. Eighty patients (median age 10.3 years, median weight 27.6 kg) were treated (25 with a Rashkind device, 11 with Duct-Occlud coils, 35 with Cook detachable coils, 9 with the Amplatzer system).**

Results. **Kaplan-Meyer estimates of long-term complete occlusion of the ductus showed, compared to the Rashkind device, a significant improvement for the Cook and Amplatzer ($p = 0.025$ and $p = 0.003$, respectively) devices but not for the Duct-Occlud coils ($p = 0.165$). One patient of the Duct-Occlud group (9%) and 3 with the Rashkind device (12%) featured a significant residual shunt and needed a second intervention. The complication rate was 4% for the Rashkind occluder, 5% for the Cook coils, 9% for the Duct-Occlud system, and 11% for the Amplatzer device ($p > 0.05$).**

Conclusions. **The new devices are as safe as the Rashkind occluder and provide effective treatment. The Cook coils and the Amplatzer occluder offer better results compared to the Rashkind and Duct-Occlud devices.**

(Ital Heart J 2002; 3 (2): 122-127)

Received October 17, 2001; revision received December 7, 2001; accepted December 21, 2001.

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Transcatheter percutaneous closure of the patent ductus arteriosus (PDA) is widely accepted as an effective alternative to surgery for both children and adults[1]. Potential drawbacks of this technique include the risk of device embolization, stenosis of the pulmonary artery and/or descending aorta, hemolysis, residual shunt, late recanalization, and endocarditis[2,3].

The first device to offer a reliable and effective means for the percutaneous closure of the PDA was the Rashkind device, which is currently considered as outdated and not as reliable as the newer systems, such as coil occlusion or the Amplatzer system. However, the Rashkind device is supported by long-term follow-up data which are not yet available for all the other techniques. Thus, this older device is still considered as the optimal gold standard to which the newer devices should be matched in terms of safety, efficacy and costs. In this retrospective study we sought to compare the data we obtained for three of the newer PDA occlusion systems (the Duct-Occlud and Cook detachable coils and the Amplatzer device) to those of a control group of patients of similar age and weight and treated using the Rashkind device in order to provide a potential basis for future cost-efficacy analyses.

Methods

Study protocol. A retrospective study was performed on the clinical and catheterization laboratory records of all pediatric and adult patients submitted to percutaneous closure of a PDA from April 1989 to May 2001 at the Pediatric Cardiology Unit of the University of Bologna. The clinical and outpatient records were used to assess the long-term occlusion rate and incidence of complications. Patients with a silent ductus (i.e., detectable only at color Doppler

echocardiography) were excluded in accordance with the policy of our Institution to treat PDA patients only in the presence of a typical systolic or continuous murmur. Written informed consent was obtained from all patients or from their parents.

Definitions. Successful closure was defined as the complete occlusion of the PDA, without any sign of a residual shunt at color Doppler examination.

A residual shunt was classified as trivial, small, medium or large[4].

The diagnosis of stenosis of the left pulmonary artery or descending aorta was made in the presence of a systolic gradient > 10 mmHg at continuous wave Doppler examination[5].

While care was taken, early in our experience, to classify the ductal morphology according to the classification of Krichenko et al.[6], it is our current opinion that a simplified classification into "typical" or "window-type" PDA (the latter consisting of a short PDA without constriction at the pulmonary or aortic end, a morphology similar to the one defined by Krichenko et al. as type C) is a far more practical and technically meaningful approach. For the purpose of this study, we decided to maintain this classification since dealing with dichotomous variables allowed us simpler and more reliable statistics.

Patient selection. All patients who underwent PDA closure prior to 1995 were treated using the Rashkind occluder. Since March 1995, the Cook detachable coils are used for small to medium sized PDAs (≤ 3.5 mm) while the Amplatzer system replaced the Rashkind device in our inventory from January 1999. The Duct-Occlud system was tested on a consecutive series of patients between March 1995 and June 1996 without any specific selection policy but has since then been abandoned in our Institution.

Technique. The procedures were performed under general anesthesia in smaller infants and children whereas adolescents and adults were sedated. All patients received heparin (50-100 IU/kg) and antibiotic prophylaxis with cefuroxime (three doses daily each administered at 8-hour intervals). Four different types of device were used: the Rashkind double-umbrella (USCI Inc., Tewksbury, MA, USA), the Duct-Occlud coils (PFM, Cologne, Germany), the Cook detachable coils (Cook, Bloomington, IN, USA) and the Amplatzer Duct Occluder (Agamedical, Golden Valley, MN, USA). The technique for each device has been described previously[7-11]. Briefly, standard cardiac catheterization and angiography of the descending aorta were performed and the diameter of the narrowest point of the ductus was measured using magnification correction by comparison with known angiographic catheter diameters. The ductal morphology was classified into two main groups: with a well developed aortic infundibulum or with a window-type PDA.

For the Rashkind device, an 8F or 11F Mullins sheath was introduced through the femoral vein over a long super-stiff Amplatz guide-wire (Cook, Bloomington, IN, USA) positioned from the pulmonary artery through the PDA and then into the aorta (anterograde approach). The umbrella was inserted over the delivery system and gently pushed inside the sheath to the descending aorta. Careful withdrawal of the sheath and opening of the distal end of the occluder were followed by control aortography. If the position was considered satisfactory, the proximal part of the device was opened and released.

Duct-Occlud coils were chosen by matching the dimensions of the proximal and distal cones of the hourglass shaped coil with the ductus at its narrowest point. The occluder was delivered using an appropriate 4F system inserted through the femoral vein and crossing the ductus from the pulmonary arterial site. Following control angiography, the coil was released by unbuttoning it from the delivery wire.

The Cook detachable coils were positioned in the femoral vein using a 5F sheath or in the femoral artery using a 4F or 5F sheath. Coils 2 to 2.5 times wider than the narrowest ductal diameter and long enough to produce at least one loop at the pulmonary arterial end and three loops at the aortic end of the PDA were chosen. The technique was performed usually anterogradely (transvenous) from the pulmonary artery or retrogradely (transarterial) from the aorta in case of a very small ductus. The coils were then released by unscrewing the delivery wire.

The Amplatzer occluder was selected by matching the dimensions of the main cylinder of the device with the measured dimensions of the ductus. A 6F sheath was inserted through the femoral vein into the ductus and the device was gently pushed and opened into the aorta. Having excluded the presence of a significant residual shunt by means of control angiography, the device was unscrewed.

All patients underwent color Doppler echocardiography after 24 hours and 6 months and 1 year thereafter.

Prophylaxis of bacterial endocarditis was continued in all patients for 6 months after the procedure and, in cases with a residual shunt, indefinitely or until spontaneous complete occlusion occurred or a second device was placed.

Statistical analysis. Values are expressed as means ± SD unless otherwise stated. Statistical analysis was performed using the Fisher exact test and the log-rank test for the actuarial curves. A p value < 0.05 was considered statistically significant. The SPSS PC 8.0 (SPSS, Inc., Chicago, IL, USA) software package was used for the statistical calculations.

Results

Between April 1989 and January 2001, transcatheter closure of a PDA was accomplished in 80 patients (median age 10.3 years, range 3 months-59 years; median weight 27.6 kg, range 4-65 kg). Five patients (6.2%) had been previously submitted to surgical ligature.

In all patients, the presence of a PDA was confirmed at echocardiography. Three patients presented with signs of cardiac failure and 25 had echocardiographic evidence of left ventricular volume overload.

Associated anomalies were Down syndrome in 2 patients, Holt-Oram syndrome in 1, and Noonan syndrome in 1.

The Rashkind umbrella was used in 25 patients, the Duct-Occlud coils in 11, the Cook detachable coils in 35, and the Amplatzer Duct occluder in 9 patients.

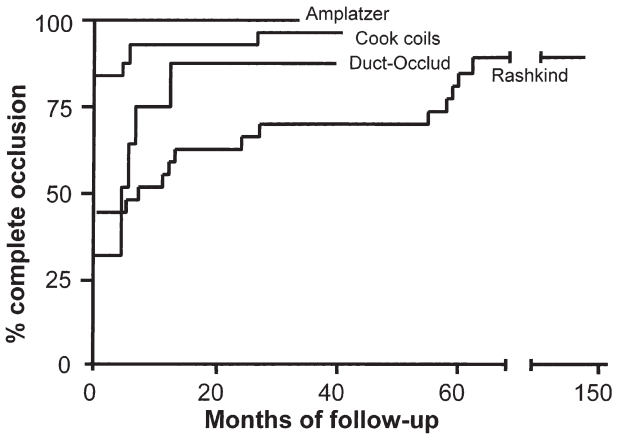

Figure 1. *Curves of actuarial freedom from residual shunt for the four different types of device used in the study.*

Efficacy. Figure 1 shows the actuarial freedom from residual shunt for each specific type of device.

The Amplatzer system and the Cook coils yielded better immediate results compared to both the Rashkind and the Duct-Occlud devices. The rates of complete occlusion were 100, 80, 48 and 35% respectively. During follow-up, a progressive increase in the rate of complete occlusion was observed for all the devices. Evaluation of the mid-term efficacy (30-month follow-up) revealed a 70% occlusion rate for the Rashkind device, an 85% occlusion rate for the Duct-Occlud coils, a 94% occlusion rate for the Cook coils, and a 100% occlusion rate for the Amplatzer device. The log-rank test showed that, overall, the performance of both the Cook and Amplatzer devices was significantly better than that of the Rashkind device ($p = 0.025$ and $p = 0.003$, respectively). This did not apply for the Duct-Occlud coils ($p = 0.165$). Table I shows the 30-month follow-up results of the different devices matched against the Rashkind device.

Table II shows the population data, the ductal morphology, and hemodynamic parameters. The mean age and weight at the time were similar for all our patient populations. While there was no statistically significant difference in the average size of the ductus between the Rashkind occluder and the two types of coils ($p > 0.05$), patients carrying an Amplatzer device had a significantly larger ductus compared to all the other groups ($p < 0.01$).

Window-type PDA was associated with a higher incidence of residual shunt in the Rashkind group ($p = 0.02$).

Table I. Univariate and actuarial analysis of mid and long-term complete occlusion of the patent ductus arteriosus.

	Univariate analysis for complete occlusion after 30 months	Log-rank test for long-term occlusion
Rashkind device	70%	–
Cook coils	94% (p = 0.04)	p = 0.025
Duct-Occlud coils	85% (p = 0.66)	p = 0.165
Amplatzer occluder	100% (p = 0.09)	p = 0.003

Table II. Demographic and procedural data of the different subgroups of patients.

	Rashkind device	Duct-Occlud coils	Cook coils	Amplatzer occluder
Age (years)	7.3 ± 6.1	6.8 ± 2.4	8.4 ± 7.7	6.9 ± 3.5
Weight (kg)	22 ± 8	27 ± 6	20 ± 10	21 ± 10
PDA window-type (%)	8	0	0	0
PDA diameter (mm)	2.8 ± 1.9	2.7 ± 1.7	2.3 ± 1.2	3.5 ± 0.6
Qp/Qs	1.5 ± 0.6	1.3 ± 0.4	1.2 ± 0.6	1.7 ± 0.8
sPAP (mmHg)	18 ± 10	16 ± 8	17 ± 5	20 ± 9

PDA = patent ductus arteriosus; sPAP = systolic pulmonary arterial pressure.

In only 1 patient was the positioning of multiple coils (two implanted during the same session) necessary.

The residual shunt was reported as trivial in all but one subject who had a moderately sized residual shunt after the positioning of a Duct-Occlud coil. This child underwent complete closure 2 years later when a Cook detachable coil was placed.

In 3 patients carrying a Rashkind device and featuring residual leaks, a coil was successfully implanted 2 years (1 case) and 4 years (2 cases) after the first procedure. Complete occlusion was achieved.

Regardless of the device implanted, in no case did delayed recanalization or redevelopment of the shunt through the ductus occur.

Complications. Device embolization into the pulmonary artery occurred in 3 patients (a Rashkind umbrella in 1 case and a Cook coil in the other 2), probably due to underestimation of the size of the ductus. In all cases the devices were successfully snared and retrieved.

In 1 patient in whom a Duct-Occlud coil was placed, a residual shunt was found to persist 2 days after the procedure. Severe hemolysis resulted and the patient underwent a second catheterization procedure with retrieval of the device and successful placement of a 17 mm Rashkind umbrella.

There were no vascular complications and in no case was blood transfusion necessary.

There was 1 case of aortic obstruction caused by an Amplatzer device implanted in a 5.5 kg infant (Fig. 2). As recorded in the catheterization laboratory shortly after deployment, a 35 mmHg peak systolic gradient across the isthmus resulted. The femoral pulses were not lost and it was decided to prescribe aspirin and to submit the child to routine Doppler evaluation. This regimen was chosen on the basis of the hypothesis that, due to the normal growth of the descending aorta, the gradient should progressively decrease over time. Two years after the procedure, the child is asymptomatic with normal femoral arterial pulses and a systolic Doppler gradient of 30 mmHg.

Overall, the incidence of complications was 4% for the Rashkind occluder, 5% for the Cook detachable coils, 9% for the Duct-Occlud system, and 11% for the Amplatzer. However, these differences did not reach statistical significance ($p > 0.05$).

Discussion

Transcatheter closure of the arterial ductus has been safely and effectively accomplished with different devices and is now the treatment of choice for PDA. While outdated and much more expensive than the newer devices, the Rashkind device is often considered as the standard device against which the newer systems should be compared in terms of efficacy and safety. However, in the literature such comparative studies are reported only for the Gianturco coils[12-15].

All types of devices had a comparable rate of complications, and may be therefore considered as safe.

Interestingly, a steady tendency over time towards spontaneous complete occlusion was observed for the Rashkind device. Indeed, our data were recently merged with those of other institutions showing that the long-term results for the Rashkind device were far better than previously reported in the literature[16]. Therefore, due to the limited follow-up (40 months) of their study, the 38% residual shunt rate formerly reported by Hosking et al.[17] may be considered as being rather overestimated. Our data from a 148-month follow-up show a final complete occlusion rate of 84%. In view of this, previous comparative studies may have overrated the benefits of the newer systems compared to the double-umbrella device.

If we look at the curves for actuarial freedom from residual shunt, there is a significant advantage after 2 years for both the Cook coils and the Amplatzer occluder. The incidence of residual PDA patency for the Duct-Occlud coils still reached 15% which is much higher than that recently reported in the phase I Food and Drug Administration clinical trial[18]. Owing to the relatively short experience we had with this device, we are not able to explain this finding. However, it should

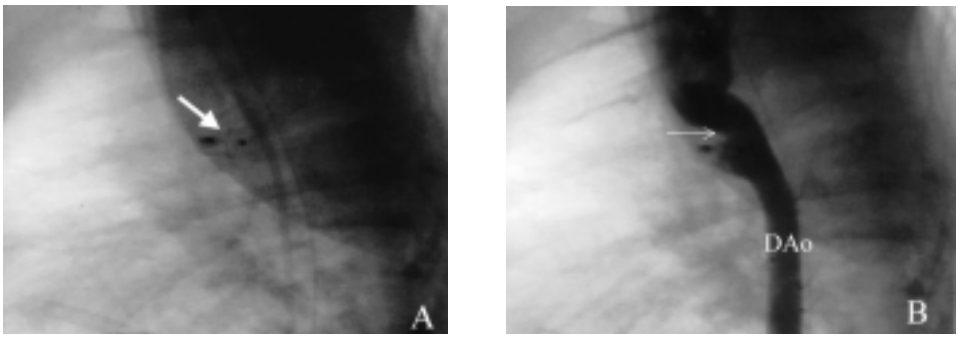

Figure 2. *An Amplatzer device* (arrow) *closing the patent ductus arteriosus of a 5.5 kg infant with congestive heart failure* (A). *The final aortogram* (B) *shows the upper edge of the device* (arrow) *causing mild obstruction of the descending aorta (DAo).*

be noted that other authors report even higher residual shunt rates with the Duct-Occlud coils[19]. Perhaps, due to the absence of an ongoing process of thrombotic ductal occlusion in the patients with residual shunt, the initial advantage observed for this device may progressively decrease and even disappear after a time as long as the one available for the Rashkind occluder. Indeed, if we look at the 30-month follow-up data reported by Cheung et al.[19] regarding the efficacy of the Duct-Occlud system, there is a very stable 19% incidence of residual shunt which persists well beyond the first 2 months without any sign of further occlusion.

A large ductus in the very small or preterm infant is still a matter of controversy. While the Amplatzer may be viewed as a possible solution, our patient with a residual gradient across the aortic isthmus prompts us to consider surgical treatment as still being the procedure of choice in such cases.

Study limitations. Results drawn from non-randomized retrospective studies including a comparative analysis of different therapeutic strategies may be jeopardized by the presence of several types of selection bias in the population, and this study is no exception. However, the univariate analysis performed on the demographic and procedural data of our patients show the absence of statistically significant differences between the subgroups. Only the Amplatzer device was shown to be associated with a larger PDA. However, this should not be a major limitation since a device associated with a 100% success rate in larger than average ducti should be equally effective in a medium-sized PDA.

Two of our study groups (the Duct-Occlud and the Amplatzer) consisted of a relatively small number of patients. Even if statistics were to take this factor into account in the form of degrees of freedom, we still need to be very cautious in drawing generalized conclusions on the basis of the experience of a single-center study. As an example, even if recent reports strengthen our opinion that a high rate of complete occlusion should be expected with the Amplatzer device[20,21], we are well aware that the small number of patients in our group may be the cause of an overestimation of the clinical impact of this device.

In conclusion, safe and effective transcatheter closure of the PDA can be achieved by careful selection of patients and by correct matching with the appropriate occlusion device.

Our experience shows that the results obtained with the currently used devices are at least as good as those observed for the Rashkind occluder. Significantly improved results have been achieved with the Cook detachable coils and the Amplatzer occluder. The incidence of complications is low. The Duct-Occlud device, even if less expensive, will probably not allow better long-term results if compared to the Rashkind device.

Acknowledgments

We thank Dr. Alessandro Giardini and Mrs. Giusi Dallolio for the data collection and Mr. Gabriele Cristiani for arranging the angiographic pictures.

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