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# Stenting the Neonatal Arterial Duct in Duct-Dependent Pulmonary Circulation: New Techniques, Better Results

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**OBJECTIVES** The goal of this study was to assess a new approach to stent the arterial duct in neonates with a duct-dependent pulmonary circulation.

**BACKGROUND** Previous attempts to stent the neonatal arterial duct were unsatisfactory. Learning from these failures, we speculated that covering the complete length of the duct with current low-profile stents might avoid previous problems.

**METHODS** Ten neonates with duct-dependent pulmonary circulations through a short straight duct were treated with stent implantation. The duct was crossed with an atraumatic 0.014-inch wire. A low-profile premounted coronary stent (outer diameter <4F, length 13 to 24 mm, diameter 3.0 to 4.0 mm) was positioned within the duct, not protected by a sheath; care was taken to cover the complete length of the duct from the aortaductal junction until well within the pulmonary trunk.

**RESULTS** All stents could safely be deployed with adequate pulmonary flow at early- and medium-term follow-up. There were no procedure-related complications; one patient died early from sepsis. All patients had adequate relief of cyanosis for at least three to four months. During follow-up, the pulmonary vasculature bed had grown without distortion. Acute occlusion of a stented duct was not observed. Ductal flow progressively decreased slowly over several months by luminal narrowing, until the stented duct had either become redundant or was dilated/restented or until elective staged surgery was performed.

**CONCLUSIONS** With current technology, complete stenting of a short straight duct is a safe and effective palliation, allowing adequate growth of the pulmonary arteries. (J Am Coll Cardiol 2004; 43:107–12) © 2004 by the American College of Cardiology Foundation

It has long been realized that patients with a duct-dependent pulmonary circulation would benefit if duct patency could be maintained reliably for several months (1,2). Conventional palliative treatment in neonates with such a duct-dependent circulation currently consists of treatment with prostaglandin E1 for some days, followed by the surgical creation of an aortopulmonary shunt if early repair is not feasible. Shunt-related complications such as chylothorax, phrenic and vagal nerve palsy, early or late shunt occlusion or stenosis, distortion, and differential growth of the pulmonary arteries (PAs) as well as surgical adhesions are well-recognized and may add to the complexity of subsequent surgeries (3–5).

Today, many vascular lesions are treated percutaneously, and endovascular techniques can be extended to this clinical setting. However, because of technical difficulties and unpredictable outcomes, several previous investigators have cautioned against routine placement of such stents in neonates with duct-dependent pulmonary blood flow (PBF) (6,7). Previous attempts to stent the neonatal duct with early generation, rigid, bare stents using relatively bulky, stiff wires, balloons, and sheaths frequently resulted in complications such as worsening cyanosis, bleeding, vessel rupture, duct spasm, tissue prolapse, or acute thrombosis. Additionally, incomplete covering of the duct frequently resulted in duct constriction, with inadequate pulmonary flow within hours or days after implantation. Learning from these failures, we speculated that covering the complete length of the duct with current low-profile, flexible, premounted stents with good scaffolding might avoid such problems. This report describes the experience from two university pediatric cardiac centers over a two-year period with stenting of the arterial duct in duct-dependent PBF.

## METHODS

**Patients.** Between March 2001 and November 2002, stent implantation of the arterial duct was attempted in 10 neonates and infants with duct-dependent pulmonary circulation in two centers (University Hospital Leuven, Belgium, and the Hospital for Sick Children, University of Toronto, Canada). The procedure was offered as an alternative to surgical palliation after parental informed consent was obtained. Only patients with a short and straight duct were considered for this study; patients with a long and tortuous duct, as typically seen with pulmonary atresia and ventricular septal defect, were excluded. Early in the experience, the procedure was offered only to patients who carried a high surgical risk (premature infant, single lung) or whose pulmonary circulation was not completely duct-

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**Abbreviations and Acronyms**
PA = pulmonary artery
PBF = pulmonary blood flow

dependent. As experience grew, the procedure was offered to all patients fulfilling the morphologic criteria for stent implantation. All procedures were performed in agreement with the ethical guidelines of each participating center.

The age of the patients ranged between one and 42 days, median 6 days (Table 1). The body weight ranged from 2.5 to 3.7 kg, median 3.3 kg. The underlying pathology in the 10 patients was as follows: 3 had pulmonary valve atresia and intact ventricular septum, 5 had critical pulmonary valve stenosis with a hypoplastic right ventricle (1 in association with double inlet left ventricle and subvalvular pulmonary stenosis), and 2 patients had isolated PAs (1 in association with tetralogy of Fallot, right aortic arch, and left arterial duct to the left PA, and one patient with normal intracardiac anatomy, left aortic arch, and bilateral arterial ducts, with isolation of the right PA).

**Cardiac catheterization and stent implantation.** The initial interventional therapy in 7 of 10 patients consisted of: radiofrequency perforation and balloon dilation of pulmonary atresia in three patients and balloon dilation only of critical pulmonary valve stenosis in 4 patients. This was done on the same day in three patients, and 2, 5, 11, and 33 days before stent implantation in four patients (allowing assessment of the possibility of the pulmonary circulation not being duct-dependent). In two patients with excluded single PA and in the patient with complex univentricular heart, there was no additional procedure but implantation of the stent. The procedure was performed under general anesthesia in all patients. Angiography (typically in profile or perpendicular to the arch of the duct) was performed to demonstrate the anatomy of the arterial duct, of which the median length was 17 mm (range, 12 to 20 mm) (Fig. 1).

Stent implantation was performed from the femoral vein in eight patients (in most patients through a 5F right coronary guiding sheath) and from the femoral artery in two patients (4F sheaths). After crossing the duct with a 0.014-inch guidewire, the infusion of prostaglandin was discontinued to promote duct constriction; in patients without previous ductal constriction, prostaglandin infusion was stopped 6 h before the procedure. The duct was not crossed with a sheath; a transvenous right coronary guiding catheter ensured stability and allowed contrast flushes for accurate positioning.

Coronary stents with good scaffolding properties, premounted on low-profile balloon dilation catheters were used: Multi-link Tetra/Penta stents (Guidant, Santa Clara, California) in six patients, Express Monorail (Boston Scientific, Maple Grove, Minnesota) in two patients, and a Coroflex (B Braun Medical, Emmenbruche, Switzerland) and a Tristar stent (Guidant, Santa Clara, California) each in one patient. The mean stent diameter was 3.8 mm (range, 3.0 to 4.0 mm). We aimed to stent the complete length of the duct with a single stent. Stent length was chosen slightly longer than the duct length. When positioning the stent, care was taken to align the superior aortic end of the stent with the cranial aortoductal junction, avoiding any protrusion into the aorta; the stent therefore would protrude slightly into the pulmonary trunk (Fig. 2). We aimed not to reach the zenith of the main PA, because this may cause erosion or perforation.

After stent implantation, repeat angiography was performed to confirm the stent position and to exclude incomplete stenting of the duct (Fig. 3). In case of incomplete stenting, an additional stent was implanted to cover the whole duct.

Prophylactic antibiotic treatment (cefazolin in most patients) was given for 24 h.

During follow-up, nine patients were on antiplatelet agents (1 to 3 mg/kg acetylsalicylic acid alone in eight patients, and in combination with low-molecular-weight heparin and clopidogrel in one patient). One patient received low-molecular-weight heparin alone for two weeks.

## RESULTS

In the 10 patients, a total of 13 stents were successfully implanted; a single stent was required in seven patients, and two stents were implanted in two patients at the initial procedure. In Patient 3, two procedures were required on consecutive days: the first stent covered the duct except 3 mm at the aortic end, which was widely open at that time; within 20 h the aortic end showed significant duct constriction, which was relieved by a second stent. The results are summarized in Table 1. The median fluoroscopy time was 28 min (range, 9 to 58 min) including the primary procedure when done in a single session.

The mean length of the final stent (either single stent or combination of two stents) for this group was 19 mm (range, 13 to 24 mm). There were no deaths directly related to the procedure. One patient died four days after implantation due to E. coli septicemia, where, in retrospect, the septic episode may have begun before the procedure. At autopsy, the stent was widely patent. Three patients (all with stent diameter of 4.0 mm) initially required antifailure treatment due to increased PBF. Repeat cardiac catheterization was performed in seven patients 4.7 months after implantation (range, 1.4 to 9.1 months). In all of these patients, adequate growth of the PAs was observed without distortion. Luminal narrowing within the duct had resulted in a significant reduction of the inner diameter in most patients. The aortic lumen was not affected by any implant. In Patient 1, the duct was restented 4.7 months after implantation with a 4-mm stent with a good clinical result. A bidirectional cavopulmonary shunt was subsequently performed in two patients, and is scheduled in another patient. Patients 5 and 8 underwent elective unifocalization of the PAs at 3.9 and 2.3 months; both stents were widely

**Table 1.** Patient Characteristics, Stent Data, and Clinical Outcome

| Patient | Diagnosis | Age, days | Weight, kg | Duct Length, mm | Lungs | Stent Length, mm | Stent Diameter, mm | Immediate Result | FU Months | Reintervention/ Last Echocardiography at FU |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | PA-IVS, TS | 35 | 3.3 | 18 | 2 | 20 (18 & 9) | 4.0 | Generous flow, mild decompensation | 7.5 | Restent 4 mm/18 mm after 4.7 months; then CPS at 7.5 months |
| 2 | Critical PS | 1 | 2.8 | 12 | 2 | 13 | 3.5 | Adequate flow, no decompensation | 7.7 | Spontaneous occlusion stent, no residual PS, PFO bidirectional shunt |
| 3 | PA-IVS, TS | 4 | 3.2 | 18 | 2 | 22 (18 & 13) | 4.0 | Adequate flow, mild decompensation | 6.2 | CPS shunt, RV overhaul at 6.2 months |
| 4 | Critical PS | 6 | 3.7 | 17 | 2 | 18 | 3.5 | Adequate flow, no decompensation | 14.7 | Small residual ductal shunt, clinically no cyanosis |
| 5 | TOF, excluded left PA | 42 | 3.6 | 15 | 1 | 18 | 4.0 | Adequate flow, no decompensation | 3.9 | Repair TOF with unifocalization at 3.9 months |
| 6 | UVH, DILV, sub PS & PS | 7 | 3.4 | 14 | 2 | 18 | 4.0 | Adequate flow, slight protrusion of stent in Ao | 0.1 | Patient died 4 days after stenting (E coli sepsis) |
| 7 | PA-IVS, TS | 2 | 3.5 | 20 | 2 | 24 | 4.0 | Adequate flow, moderate decompensation | 9.1 | Adequate ductal flow, scheduled for RV overhaul |
| 8 | Excluded right PA | 3 | 2.6 | 14 | 1 | 15 | 3.0 | Generous flow, transient reperfusion edema | 2.3 | Implantation RAP into pulmonary trunk at 2.3 months |
| 9 | Critical PS | 6 | 2.5 | 18 | 2 | 22 (18 & 13) | 3.0 | Adequate flow, no decompensation | 4.6 | Adequate growth RV, duct spontaneously closed |
| 10 | Critical PS, TS | 12 | 2.5 | 16 | 2 | 20 | 3.0 | Adequate flow, no decompensation | 5.2 | Adequate growth RV, duct redundant >3 months |
| Median | | 6.0 | 3.3 | 17 | | | | | 5.7 | |

Ao = aorta; CPS = cavo pulmonary shunt; DILV = double inlet left ventricle; FU = follow-up; IVS = interventricular septum; PA = pulmonary artery; PA-IVS = pulmonary atresia-intact ventricular septum; PFO = patent foramen ovale; PS = pulmonary valve stenosis; RAP = right pulmonary artery; RV = right ventricle; TOF = tetralogy of Fallot; TS = tricuspid stenosis; UVH = univentricular heart.

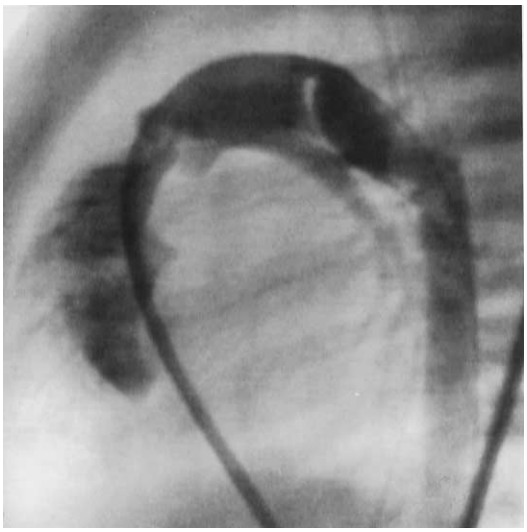

**Figure 1.** Angiogram (profile) in pulmonary artery through the 5F right coronary guiding sheath. Duct constriction at the pulmonary end is clearly seen; the aortic end of the duct is wide open.

patent at the time of surgery. There were no technical problems caused by the stents during the subsequent surgeries, and the stents could easily be occluded completely by simple external compression (no recoil).

Adequate right ventricular growth had occurred in four patients, making the stented ducts redundant; medication was stopped, leaving the stents to occlude spontaneously. Spontaneous ductal occlusion was documented echocardiographically in two patients 4.6 and 7.7 months after stent implantation; minimal duct flow persisted in the two remaining patients 5.2 and 14.7 months after stenting.

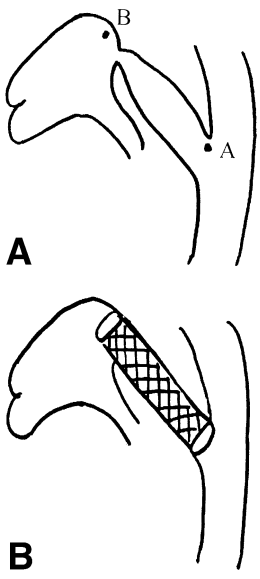


**Figure 2.** Schematic representation of stent sizing and positioning. **(A)** The stent should stretch from the cranial aortoductal junction **(point A)**, until halfway to the ductal constriction and the zenith of the ductal arch **(point B)**. **(B)** When positioning and deploying the stent, the distal end of the stent should be aligned with **point A** without protrusion in the aorta; the proximal end of the stent will then protrude into the pulmonary trunk.

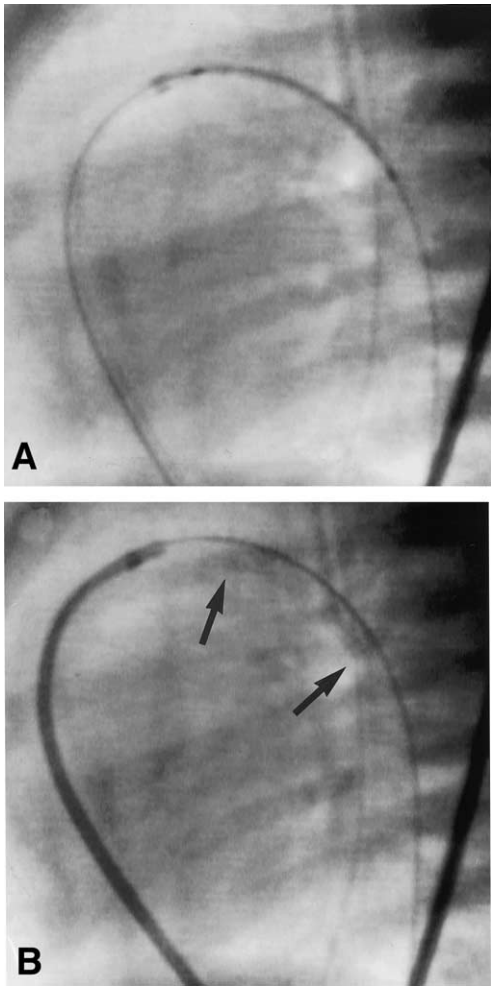


**Figure 3.** Cine-frames showing positioning of the stent **(A)** and final stent position after deployment **(B)**. The radio-opaque gastric tube is very useful as reference.

## DISCUSSION

Several authors have highlighted technical difficulties encountered when stenting the arterial duct in duct-dependent cyanotic congenital heart disease (8–10). However, improved materials resulted in broadened indications for percutaneous intraluminal techniques, whereby many of the technical difficulties encountered in the past now can be avoided.

**Current technique.** Long, flexible stents, premounted on low-profile balloons are used. When choosing a stent, important features are stent length, diameter, and design.

STENT LENGTH. The most distal parts of the duct appear to have a remarkable power to constrict even when only a few millimeters are left unsupported (9). Previous animal studies revealed that placement just proximal to the duct orifice resulted in an intimal process that eventually led to complete closure within days of implantation (11). Therefore, great care must be taken to cover the duct completely from the aortic end until well within the pulmonary trunk. The stent

length is, thus, chosen slightly longer than the length of the duct.

**STENT DIAMETER.** Surgeons use a 4- or 5-mm interposition tube when creating a modified Blalock-Taussig shunt in neonates; however, the restriction of these shunts early after creation lies within the orifice of the subclavian artery. A stented duct is more comparable with a central shunt, which has no restriction at the aortic end; surgeons prefer in neonates for such shunts conduits from 3 up to 4 mm. The final lumen within the stent, however, will depend on the stent diameter at implantation, which will decrease within hours-days by contraction of the vessel wall leading to tissue prolapse through the stent struts, and later on will further decrease by endothelial hyperplasia. Table 1 shows the immediate result in function of stent diameter, patient weight, and single or double lung perfusion. All neonates with stent diameters of 4.0 mm initially had excessive pulmonary flow.

**STENT CHARACTERISTICS.** The stent design and material determine cross-sectional area, strut thickness, and radial force. Larger metallic cross-sectional areas, thicker struts, and smaller cell-areas result in good scaffolding with limited tissue prolapse, which is important when used in the arterial duct. However, these properties reduce the flexibility and conformability of the stent, and are known to enhance in-stent restenosis rate in coronary arteries. Radial force and side-branch accessibility are no issue for a stent deployed in the arterial duct.

Schneider et al. (11) observed, within days after implantation, significant stenosis within a gap articulation in the Palmaz-Schatz coronary stent; this was treated with an additional stent across the articulation. In patients with a tortuous duct, we attempted to stent with flexible stents with more conformability to follow the curves; however, stents with a larger cell area allow significant tissue prolapse, with a restrictive cobblestone appearance within hours in some cases. For the short straight duct in the patient group reported in this study, we chose stents with small cell area and good scaffolding; the somewhat reduced flexibility caused no problem when positioning these stents, and conformability is not required for this type of duct.

**DUCT AND PROSTAGLANDIN.** In order to grip the stent at deployment, some ductal constriction is required. If the duct has not constricted since birth, as typical in patients with fetal or very early neonatal presentations, where prostaglandins are started very early, this medication should be stopped several hours (e.g., 6 h) before the procedure. In patients presenting after duct constriction with cyanosis, prostaglandins can be stopped at the beginning of the procedure, or after the duct has been crossed with the guiding wire. Enhanced constriction during the procedure can be obtained by administering intravenous indomethacin or ibuprofen.

**ANTICOAGULATION AND ANTIAGGREGATION.** It is difficult to determine the role of anticoagulant and antiplatelet drugs. During the procedure, standard heparin should be given. We currently do not neutralize the heparin at the end of the procedure, but acetylsalicylic acid 1 to 3 mg/kg/day is started for as long as stent patency is required. The value of clopidogrel needs to be determined.

With growing confidence in the technique, patients are now considered for hospital discharge within 48 h after implant, provided there is no other indication for a prolonged stay.

**Neointimal proliferation.** Duct patency after stenting is limited by in-stent restenosis, which occurs due to neointimal proliferation and/or peal formation (8,11). The ideal stent for this procedure still needs to be defined. Stent design determines (non-)metal surface area, radial force, flexibility, conformability, scaffolding, and prevention of tissue prolapse. Drug-eluting stents or covered stents have been proposed as a means of preventing in-stent restenosis in adults (12,13). Covered stents are slightly more bulky and require larger introducer sheaths (currently +1 to 2F sizes). The drug-eluting coatings contain agents that inhibit thrombus formation (e.g., heparin), inflammation (e.g., dexamethasone), and cellular proliferation (e.g., sirolimus or paclitaxel) (14). Stents eluting antimitotic agents such as sirolimus and paclitaxel show the most promising results in coronary artery disease, with significant inhibitory effects on neointimal hyperplasia. Studies to evaluate the efficacy and safety of duct stenting with such coated stents in newborn animals will be initiated in the near future. This promising development in stent technology may prolong the duration of duct patency, rendering it an even more attractive alternative to a surgical shunt. On the other hand, in-stent stenosis can be managed by redilating or restenting the implant as a function of patient growth and/or intimal proliferation.

**Comparison with the gold-standard: the surgical shunt.** This enhanced technology obviously needs to be compared with the standard surgical shunt. While the stented arterial duct obviously will provide only temporary augmented pulmonary flow, as with any aortopulmonary shunt, we have been impressed by the fast recovery of the patients after stent implantation, much faster than with any surgery. The procedure is well-tolerated, even in the premature and small infants, who constitute a subgroup with higher operative risks. Without stent implantation, such premature infants would require prolonged prostinoid infusions, allowing the surgeon to operate on a larger child with more limited morbidity. In this small series, the stent strategy appears to be more cost-effective.

The lumen of a stented duct appears to narrow faster than a surgical shunt; however, all stented ducts gave adequate pulmonary flow for several months. There were no acute stent occlusions. If required, the stented duct can be redilated, which allows titration of pulmonary flow to patient size. Such redilation-restenting must be considered

when assessing cost-effectiveness of each strategy (15). Nevertheless, based on this early experience and these considerations, stent implantation has now become our treatment of choice for the short, straight duct.

**Conclusions.** With the current technology, stenting the arterial duct in selected patients with duct-dependent pulmonary circulation is a safe and efficient alternative to a surgical shunt.

Compared with primary surgery, this approach is less invasive and offers the possibility of adapting to clinical needs in the individual patient. Compared with long-term prostaglandin infusions, early duct stenting significantly shortens hospitalization and reduces treatment costs. In our series, no acute thrombosis of the stented duct occurred, only slow progressive luminal narrowing. The ability to influence and optimize the stent size by repeat balloon dilation or restenting during follow-up is an additional advantage of this approach, allowing for patient growth. The stented arterial duct fulfills its function as a surrogate for an aortopulmonary shunt, augmenting the PBF until a definitive surgical procedure can be performed or until the duct flow becomes redundant. Future research should be directed towards improved stent design for more complex tortuous ducts.

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## REFERENCES

1. Blalock A, Taussig H. The surgical treatment of malformations of the heart in which there is pulmonary stenosis or pulmonary atresia. JAMA 1945;128:189–202.
2. Gibbs JL. Stenting the arterial duct. Arch Dis Child 1995;72:196–7.
3. Fermanis GG, Ekangaki AK, Salmon AP, et al. Twelve year experience with the modified Blalock-Taussig shunt in neonates. Eur J Cardiothorac Surg 1992;6:586–9.
4. Tamisier D, Voühe PR, Vermant F, Leca F, Massot C, Nerveux J. Modified Blalock-Taussig shunts: results in infants less than 3 months of age. Ann Thorac Surg 1990;49:797–801.
5. Poirier RA, McGoon DC. An alternative approach to the closure of the Blalock-Taussig anastomosis at open heart surgery. J Thorac Cardiovasc Surg 1976;72:792–5.
6. Ruiz CE, Bailey LL. Stenting the ductus arteriosus: a "wanna-be" Blalock-Taussig. Circulation 1999;99:2608–9.
7. Gibbs JL, Uzun O, Blackburn MEC, Wren C, Hamilton JRL, Watterston KG. Fate of the stented arterial duct. Circulation 1999; 99:2621–5.
8. Gibbs L, Martin TR, Rees MR, Parsons JM, Blackburn ME, Ruiz CE. Stenting of the arterial duct: a new approach to palliation for pulmonary atresia. Br Heart J 1992;67:240–5.
9. Rosenthal E, Qureshi SA. Editorial: stent implantation in congenital heart disease. Br Heart J 1992;67:211–2.
10. Abrahms SE, Walsch KP. Arterial duct morphology with reference to angioplasty and stenting. Int J Cardiol 1993;40:27–33.
11. Schneider M, Zartner P, Sidiropoulos A, Konertz W, Hausdorf G. Stent implantation of the arterial duct in newborns with duct-dependent circulation. Eur Heart J 1998;19:1401–9.
12. Topol EJ, Serruys PW. Frontiers in interventional cardiology. Circulation 1998;98:1802–20.
13. Bertrand OF, Sipehia R, Mongrain R, et al. Biocompatibility aspects of new stent technology. J Am Coll Cardiol 1998;32:562–71.
14. Babapulle MN, Eisenberg MJ. Coated stents for the prevention of restenosis: part 1. Circulation 2002;106:2734–40.
15. Bökenkamp R, Kaulitz R, Paul T, Hausdorf G. Stepwise interventional approach in a neonate with pulmonary valve atresia and intact ventricular septum. Eur J Pediatr 1998;157:885–9.