Pulmonary Artery Growth After Palliation of Congenital Heart Disease With Duct-Dependent Pulmonary Circulation

Arterial Duct Stenting Versus Surgical Shunt

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Objectives
The aim of this study was to compare the pulmonary artery (PA) growth after arterial duct (AD) stenting versus modified Blalock-Taussig shunt (MBTS) in neonates with congenital heart disease with duct-dependent pulmonary circulation (CHD-DPC).

Background
Arterial duct stenting is increasingly deemed a reliable alternative to surgical shunt in CHD-DPC. A stented duct might better adapt to the PA anatomy than a surgical conduit, thereby promoting a more uniform PA development.

Methods
This study enrolled 27 patients with CHD-DPC submitted to AD stenting (n = 13, Group I) or MBTS (n = 14, Group II) at our institution. The PA growth was angiographically assessed with the Nakata and McGoon indexes as well as the individual PA z-scores. The right-to-left PA diameter ratio was considered as index of uniform growth.

Results
After 10 ± 5 months, both options had promoted a significant increase of the Nakata index (from 136 ± 72 mm²/m² to 294 ± 99 mm²/m², p < 0.0001, Group I; from 151 ± 74 mm²/m² to 295 ± 177 mm²/m², p < 0.003, Group II) and McGoon ratio (from 1.5 ± 0.3 to 2.1 ± 0.3, p < 0.0001, Group I; from 1.6 ± 0.3 to 2.0 ± 0.5, p < 0.01, Group II). However, the surgical shunt had caused a worsening of the left-to-right PA diameter ratio compared with AD stenting (0.9 ± 0.1 Group I vs. 1.6 ± 0.9 Group II, p < 0.01), due to preferential growth of the PA contralateral to the shunt.

Conclusions
Percutaneous AD stenting is as effective as MBTS in promoting a global PA growth in CHD-DPC. In addition, it ensures an even distribution of the pulmonary blood flow, thereby promoting a more balanced pulmonary vascular development than MBTS. (J Am Coll Cardiol 2009;54:2180–6) © 2009 by the American College of Cardiology Foundation

Arterial duct (AD) stenting is increasingly deemed an effective alternative to surgical systemic-to-pulmonary shunt in congenital heart disease with duct-dependent pulmonary circulation (CHD-DPC) (1–7). This option has been advocated either in high-risk patients unsuitable for primary repair or whenever a short-term pulmonary blood flow support is anticipated. Allowing the stent to conform to the pulmonary artery (PA) anatomy might have favorable effects on the development of the pulmonary vascular tree, due to even distribution of the pulmonary blood flow. However, no study so far has specifically addressed this hypothesis or compared the effects of ductal flow versus conventional modified Blalock-Taussig shunt (MBTS) in neonates with CHD-DPC.

The aims of this study was to evaluate the ability of AD stenting to promote the growth of the PAs in newborns with duct-dependent pulmonary circulation and to compare the mid-term results of this approach with respect to MBTS in a single tertiary referral center.

Methods

Patient population. Between April 2003 and January 2009, a total of 132 neonates and infants underwent either AD
stenting or MBTS at our institution, as palliation of CHD-DPC. The AD stenting was attempted in patients at high surgical risk or whenever a short-term support to the pulmonary circulation was anticipated. Stenting procedure was effectively completed in 45 of 49 patients (91.8%). Procedural morbidity and mortality were 6.1% and 0%, respectively. Overall, in-hospital mortality was 6.1% (n = 3), not related to the interventional procedure. The AD stenting patients had an age range of 1 to 84 days (mean 22 ± 39 days) and a weight range of 1.2 to 32.8 kg (mean 3.2 ± 0.9 kg). Surgical shunt was performed in cases of extreme AD tortuosity or when a longer-term support to the pulmonary circulation was anticipated because of planned surgical repair with prosthetic conduits. Eighty-seven patients underwent MBTS. Their age range was 7 to 76 days (mean 21 ± 30 days), and their weight range was 2.7 to 4.8 kg (mean 3.3 ± 1.2 kg). Surgical morbidity and mortality were 6.9% and 1.6%, respectively.

The criterion for inclusion in this study was the availability of the pulmonary angiography before either palliative procedures and over a mid-term follow-up.

Twenty-seven of the 45 patients submitted to AD stenting spontaneously improved over the follow-up and did not need any further therapeutic procedures. The remaining 18 underwent follow-up cardiac catheterization before surgical repair, due to progressive decrease of the systemic oxygen saturation. Five patients were excluded from the study, because the stented AD supplied an isolated PA (n = 3) or bilateral ADs supplied discontinuous PAs (n = 2). Thus, 13 patients were enrolled in the study as Group I. Five of them had complete duct-dependency of the pulmonary circulation due to trivial or absent antegrade pulmonary blood flow, whereas 8 patients showed a mild-to-moderate antegrade pulmonary flow in addition to the ducal flow.

Of 87 patients who received MBTS, only 14 underwent pre-procedural angiography due to suspected complex anatomy (n = 10) or a failed attempt of ductal stenting (n = 4), and these form Group II. Eight of these had the MBTS as the sole pulmonary blood flow source, and 6 showed additional pulmonary flow sources.

Demographic and clinical data of the patients enrolled in this study are summarized in Table 1. No difference was found in terms of additional pulmonary flow apart from either stented AD or surgical shunt between the groups.

**Interventional procedure.** The AD stenting was performed under general anesthesia following a previously described protocol (7). Prostaglandin infusion was stopped 6 h before the procedure to achieve a stable ductal constriction to grip the stent after its deployment. Arterial vascular access was used to image the AD and to perform the stenting procedure. The AD morphology, size, and length were assessed in multiple angiographic views, and the measurements were made with the catheter as reference. After AD visualization, a 0.014-inch coronary guidewire (Crosswire NT, Terumo Corporation, Tokyo, Japan; Balance Middleweight, Guidant Corporation, Santa Clara, California) was passed through the duct and anchored in a distal lower lobe PA branch. Positioning and deployment of the stent were angiographically guided by repeat injections through the introducer sheath or coronary guiding catheters. Open-cell, high-flexibility cobalt-chromium stents (Vision, Guidant Corporation; Driver, Medtronic, Inc., Minneapolis, Minnesota) were used. The length of the stent was chosen to cover the entire length of the AD, whereas the diameter of the stent was chosen individually, on the basis of the size of the patient and the expected time for which palliation was needed. The stent diameter was always approximately 75% of the proposed surgical shunt size in the belief that it acted more as a central shunt than a Blalock-Taussig shunt. After stent deployment, repeat angiographies were performed in multiple views to exclude any incomplete covering of the duct as well as to evaluate any potential stent-related PA stenosis.

Surgical shunt was made through left or right thoracotomy in the fourth intercostal space with poly-tetrafluoroethylene grafts (GORE-Tex, W.L. Gore and Associates, Ltd., Livingston, Scotland) interposed from the undivided innominate or subclavian arteries to the mid-segment of the PA contralateral to the aortic arch. The size of the graft was chosen by the operating surgeon on the basis of the size of the pulmonary and subclavian arteries. All anastomoses were performed with 6.0 or 7.0 synthetic suture material (Prolene, Ethicon, Somerville, New Jersey).

**Table 1. Demographic Data at Control Cardiac Catheterization of Infants Submitted to Percutaneous or Surgical Palliation of CHD With Duct-Dependent Pulmonary Blood Flow**

<table>
<thead>
<tr>
<th>Arterial Duct Stenting (n = 13, Group I)</th>
<th>Modified Blalock-Taussig Shunt (n = 14, Group II)</th>
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<tbody>
<tr>
<td><strong>Age (months)</strong></td>
<td><strong>8.1 ± 3.6 (range 3–15, median 7)</strong></td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td><strong>5.7 ± 1.8 (range 3.6–10.6, median 5)</strong></td>
</tr>
<tr>
<td><strong>Cardiac malformation</strong></td>
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<tr>
<td>Tetralogy of Fallot</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary atresia with intact ventricular septum*</td>
<td>5</td>
</tr>
</tbody>
</table>

*In 9 cases after pulmonary valve perforation and angioplasty; †after pulmonary valve perforation and angioplasty.

**Abbreviations and Acronyms**

- **AD**: arterial duct
- **Ao**: aorta
- **CHD-DPC**: congenital heart disease with duct-dependent pulmonary circulation
- **LPA**: left pulmonary artery
- **MBTS**: modified Blalock-Taussig shunt
- **PA**: pulmonary artery
- **RPA**: right pulmonary artery

**Abbreviations**

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**CHD**: congenital heart disease.
After either palliation, aspirin treatment was started at 3 to 5 mg/kg/day and continued until surgical repair.

**Angiographic measurements.** Pulmonary angiography was performed in posteroanterior, right anterior oblique, and 4-chamber views. The left (or contralateral to the shunt) and right (or ipsilateral to the shunt) PAs were measured just before their first branching point. The diameter of the descending aorta was measured at the diaphragm level. All values were obtained during ventricular systole and, if possible, from the same angiographic frame with the catheter size as reference. The indexed sum of the cross-sectional PA areas (Nakata index) (8) and the ratio of the sum of the diameters of both PAs to the diameter of the descending aorta (McGoon ratio) (9) were considered as being indicative of global growth of the pulmonary vascular tree. The diameter ratio of any main PA to the descending aorta as well as the right and left PA z-scores obtained from web nomograms were considered indexes of individual growth. Finally, the left-to-right PA diameter ratio was considered to indicate balanced vascular growth.

**Statistical analysis.** All analyses were performed with SPSS for Windows version 13.0 (SPSS, Inc., Chicago, Illinois). Results are expressed as mean ± SD. Comparisons within either group and between groups were performed with the paired and unpaired Student t test, respectively. Significance was defined as p < 0.05.

**Results**

The AD stenting was achieved with stents dilated to 3.3 ± 0.4 mm (range 2.5 to 4 mm). In all but 1 patient the surgical shunt was performed on the right side, with a prosthetic conduit of 4.4 ± 0.3 mm (p < 0.001 vs. AD stenting). Post-procedure oxygen saturation did not differ between the groups (87 ± 5% vs. 86 ± 3%, p = NS), as it was at follow-up cardiac catheterization (81 ± 7% vs. 82 ± 3%, p = NS). The latter was performed after 10 ± 5 months (range 3 to 22 months, median 8 months) and was significantly earlier in Group I (7 ± 3 months vs. 12 ± 6 months, p < 0.01), because in the majority of Group II patients the surgical repair was slightly postponed due to the expected use of a prosthetic conduit. At the time of control angiography, both approaches had promoted a significant growth of the pulmonary vascular tree (Figs. 1 and 2) in terms of Nakata index (from 136 ± 72 mm²/m² to 294 ± 99 mm²/m² in Group I, p < 0.0001; from 151 ± 74 mm²/m² to 295 ± 177 mm²/m² in Group II, p < 0.003) (Fig. 3A) and McGoon ratio (from 1.5 ± 0.3 to 2.1 ± 0.3 in Group I, p < 0.0001; from 1.6 ± 0.3 to 2.0 ± 0.5 in Group II, p < 0.01) (Fig. 3B), without any difference between the groups (Table 2). However, the AD stenting had promoted a more uniform development of the main PAs with respect to the MBTS (Table 2), as confirmed by a significant worsening of the left-to-right diameter ratio in Group II (from 1.1 ± 0.6 to 1.6 ± 0.9, p < 0.02) due to preferential growth of the PA opposite to the shunt (131 ± 75% vs. 70 ± 54% of the ipsilateral PA, p < 0.01) (Fig. 4). These changes resulted in a significant difference in the left-to-right PA diameter ratio between the groups at follow-up angiographic control (0.9 ± 0.1 in Group I vs. 1.6 ± 0.9 in Group II, p < 0.01) (Fig. 5).

**Discussion**

Despite current trends toward early primary repair, surgical systemic-to-pulmonary shunt is still an invaluable palliative option in some high-risk neonates with duct-dependent pulmonary circulation who are likely to achieve a biventricular repair and in all patients with single-ventricle physiology destined to the Fontan track. However, the effect of the shunt on the PAs remains controversial, especially with regard to distortion and stenosis (10–23). These known potential shunt-related complications have been reported in as high as 36% of neonates and small children (14) and might increase morbidity and mortality in subsequent corrective surgery (15–18). However, even perfect shunts might result in unbalanced development of the central pulmonary vessels, with preferential growth of the ipsilateral (19–21) or contralateral PA (16,22). Among the several factors that might influence vascular growth, conduit geometry and direction of flow from the shunt to the main PAs might play a major role (24). More centrally placed shunts result in better distribution of blood flow to the lungs, thereby enhancing symmetrical pulmonary vascular growth and minimizing any iatrogenic deformation of the pulmonary branches. To achieve this goal, several technical modifica-
Conforming the stent to the size and angulations of the main PAs might theoretically result in an even distribution of pulmonary blood flow and thereby promote uniform vascular development. This hypothesis is supported so far only by scanty data from large series reporting the global growth of the pulmonary vascular tree (6,7). However, no data exist on the growth of the individual PAs and the left-to-right balance resulting from stabilized ductal flow. In addition, no comparison between this approach and conventional surgical shunt has been reported in published data so far.

In our study, the stented duct resulted in similar systemic oxygen saturation over a mid-term follow-up, even though it was dilated to a smaller diameter than conventional MBTS. In addition, it promoted a global growth of the pulmonary vascular bed similar to the surgical shunt, even if it was left in place for a significantly shorter time. Furthermore, this approach promoted a more uniform development of the main PAs than surgical palliation, as confirmed by a significantly better left-to-right PA diameter ratio at control angiography. This was possibly due to an optimal angle between the AD, maintained with highly flexible coronary stents, and the main pulmonary branches that allowed significant and balanced pulmonary blood flow. Conversely, the capability of the stented duct to promote a significant and balanced PA growth in CHD-DPC has so far never been specifically addressed.
the surgical shunt produced both the overgrowth of the contralateral PA and a lesser development of the ipsilateral PA compared with the percutaneous approach, presumably due to unfavorable graft geometry and flow direction to the pulmonary vascular bed. Our findings confirm the data already reported in a different physiopathologic model (i.e., hypoplastic left heart syndrome) (33,34), after classic Norwood stage I or its Sano modification. In these studies, a significant left-to-right PA size discrepancy was found after classic Norwood palliation, despite a similar growth of the pulmonary vascular tree promoted by either MBTS or right ventricle-main PA conduit, presumably due to uneven distribution of the pulmonary blood flow.

**Study limitations.** The study aims to compare the midterm effect of AD stenting with conventional MBTS, because palliation of CHD-DPC might be hampered by some possible limitations. First, the patient population is quite small, thereby precluding any reliable multifactorial analysis of the impact of the patient’s demographic profile on the procedure or the accessory pulmonary blood flow on the pulmonary vascular bed. Our findings confirm the data already reported in a different physiopathologic model (i.e., hypoplastic left heart syndrome) (33,34), after classic Norwood stage I or its Sano modification. In these studies, a significant left-to-right PA size discrepancy was found after classic Norwood palliation, despite a similar growth of the pulmonary vascular tree promoted by either MBTS or right ventricle-main PA conduit, presumably due to uneven distribution of the pulmonary blood flow.

**Table 2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I (n = 13)</th>
<th>Group II (n = 14)</th>
<th>p Value (Between Groups)</th>
<th>p Value (Within Groups)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left PA z-score</td>
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<tr>
<td>Pre</td>
<td>0.6 ± 1.7</td>
<td>0.5 ± 2.1</td>
<td></td>
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<tr>
<td>Post</td>
<td>1.3 ± 1.2</td>
<td>2.1 ± 2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% increase</td>
<td>93 ± 43</td>
<td>131 ± 75</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>r Value (within groups)</td>
<td>0.0001</td>
<td>0.0001</td>
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<tr>
<td>RPA z-score</td>
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<tr>
<td>Pre</td>
<td>0.8 ± 1.4</td>
<td>1.0 ± 1.6</td>
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<tr>
<td>Post</td>
<td>1.2 ± 1.2</td>
<td>2.3 ± 2.3</td>
<td></td>
<td></td>
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<tr>
<td>% increase</td>
<td>95 ± 33</td>
<td>70 ± 54</td>
<td>NS</td>
<td></td>
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<tr>
<td>r Value (within groups)</td>
<td>0.0001</td>
<td>0.0001</td>
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<tr>
<td>LPA/Ao diameter ratio</td>
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<tr>
<td>Pre</td>
<td>0.8 ± 0.2</td>
<td>0.7 ± 0.4</td>
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<tr>
<td>Post</td>
<td>1.0 ± 0.2</td>
<td>1.2 ± 0.5</td>
<td></td>
<td></td>
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<tr>
<td>% increase</td>
<td>35 ± 26</td>
<td>79 ± 73</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>r Value (within groups)</td>
<td>0.0001</td>
<td>0.05</td>
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<tr>
<td>RPA/Ao diameter ratio</td>
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<tr>
<td>Pre</td>
<td>0.8 ± 0.2</td>
<td>0.7 ± 0.2</td>
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<tr>
<td>Post</td>
<td>1.1 ± 0.1</td>
<td>0.9 ± 0.3</td>
<td></td>
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<tr>
<td>% increase</td>
<td>35 ± 19</td>
<td>22 ± 48</td>
<td>NS</td>
<td></td>
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<tr>
<td>r Value (within groups)</td>
<td>0.0001</td>
<td>0.01</td>
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<tr>
<td>LPA/RPA diameter ratio</td>
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<tr>
<td>Pre</td>
<td>1.0 ± 0.1</td>
<td>1.1 ± 0.6</td>
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<td></td>
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<tr>
<td>Post</td>
<td>0.9 ± 0.1</td>
<td>1.6 ± 0.9</td>
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<td></td>
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<tr>
<td>% increase</td>
<td>35 ± 11</td>
<td>41 ± 36</td>
<td>0.01</td>
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<tr>
<td>r Value (within groups)</td>
<td>NS</td>
<td>0.02</td>
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<tr>
<td>Nakata index (mm²/m²)</td>
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<tr>
<td>Pre</td>
<td>136 ± 72</td>
<td>151 ± 74</td>
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<tr>
<td>Post</td>
<td>294 ± 99</td>
<td>295 ± 177</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% increase</td>
<td>156 ± 124</td>
<td>108 ± 104</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>r Value (within groups)</td>
<td>0.0001</td>
<td>0.005</td>
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<tr>
<td>McGoon ratio</td>
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<td></td>
</tr>
<tr>
<td>Pre</td>
<td>1.5 ± 0.3</td>
<td>1.6 ± 0.3</td>
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<td></td>
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<tr>
<td>Post</td>
<td>2.1 ± 0.3</td>
<td>2.0 ± 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% increase</td>
<td>41 ± 27</td>
<td>33 ± 36</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>r Value (within groups)</td>
<td>0.0001</td>
<td>0.01</td>
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</table>

Ao = aorta; LPA = left pulmonary artery; PA = pulmonary artery; RPA = right pulmonary artery.
Pulmonary vascular development. However, in this era of early surgical repair, either approach should be viewed as a short-term palliation, thus making less influential these variables on PA growth promotion. Second, the retrospective and nonrandomized nature of the enrollment might have introduced a potentially significant selection bias to evaluate the impact of either palliative options. However, there was no significant difference between the groups in terms of demographic data or pre-procedural PA size, and both options produced similar levels of percutaneous oxygen saturation over the study period. Third, the surgical shunt was left in-situ significantly longer than the stented duct, and this might have amplified any left-to-right growth imbalance. However, the growth of the pulmonary arterial tree poorly correlates with duration of follow-up, as previously reported (14). In addition, these results did not differ even when we compared the small subset of the surgical group (n = 9) matched against the percutaneous group in terms of duration of palliation. Finally, stent re-dilation might be successfully performed whenever the clinical conditions warrant, to prolong the lifespan of this therapeutic option, as consistently reported in published data (4,6,7).

Conclusions

Percutaneous AD stenting with high-flexibility coronary stents is as effective as MBTS in promoting a significant PA growth in CHD-DPC over a mid-term follow-up. In addition, this approach produces a more balanced growth of the PAs with respect to conventional systemic-to-pulmonary shunt, presumably due to a more uniform pulmonary blood flow. Thus, AD stabilization could be proposed as the first-choice approach in the short-term palliation of these malformations, in view of spontaneous improvement or early and safer corrective surgery. This option might be advisable even if a longer-term palliation was needed, because the stent re-dilation could be successfully performed to prolong the lifespan of the stented duct.

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REFERENCES


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