Outcomes After Stent Implantation for the Treatment of Congenital and Postoperative Pulmonary Vein Stenosis in Children

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Background—Pulmonary vein stenosis (PVS) is a rare condition that can lead to worsening pulmonary hypertension and cardiac failure in children, and it is frequently lethal. Surgical and transcatheter approaches are acutely successful but restenosis is common and rapid.

Methods and Results—We reviewed outcomes among patients who underwent transcatheter pulmonary vein stent implantation for congenital or postoperative PVS at <18 years of age. A total of 74 pulmonary veins were stented with bare metal, drug-eluting, or covered stents in 47 patients. Primary diagnoses included PVS associated with anomalous venous return in 51%, PVS associated with other congenital cardiovascular defects in 36%, and congenital (“de novo”) PVS in 13% of patients. Median age at the time of pulmonary vein stent implantation was 1.4 years. During a median cross-sectional follow-up of 3.1 years, 21 patients died. Estimated survival was 62±8% at 1 year and 50±8% at 5 years after pulmonary vein stent implantation. Stent placement acutely relieved focal obstruction in all veins. Of the 54 stents reexamined with catheterization, 32 underwent reintervention. Freedom from reintervention was 62±7% at 6 months and 42±7% at 1 year. Stent occlusion was documented in 9 cases and significant in-stent stenosis in 17 cases. Stent implantation diameter ≥7 mm was associated with longer freedom from reintervention (hazard ratio, 0.32; P=0.015) and from significant in-stent stenosis (hazard ratio, 0.14; P=0.002). Major acute complications occurred in 5 cases.

Conclusions—Transcatheter stent implantation can acutely relieve PVS in children, but reintervention is common. Larger stent lumen size at implantation is associated with longer stent patency and a lower risk of reintervention. (Circ Cardiovasc Interv. 2012;5:109-117.)

Key Words: pulmonary vein stenosis ■ endovascular stents ■ balloon dilation ■ drug-eluting stent ■ covered stent ■ stent fracture

Pulmonary vein stenosis (PVS) is a rare condition that can lead to worsening pulmonary hypertension and cardiac failure in the pediatric population. The condition is often progressive and is associated with poor survival.1–3 Intraluminal PVS has been described in association with other cardiovascular anomalies but also as an isolated condition in structurally normal hearts. The disease can manifest with focal, proximal vessel stenosis or extend into the distal vasculature, as is often seen with aggressive disease. Neither surgery nor transcatheter interventions have yielded satisfactory long-term results when this condition is recurrent.1,4–6

There are limited published data on transcatheter therapy for PVS. A recent study by Peng et al8 comparing conventional and cutting balloon angioplasty for relief of pulmonary venous obstruction showed acute angiographic and hemodynamic improvement with both therapies but no difference in freedom from reintervention and limited benefit in the longer term. Two early series suggested that although technically feasible, stent implantation was largely ineffective for treatment of PVS.7,8 However, given that these were relatively small studies and that newer stent technologies (eg, pre-mounted, covered, drug-eluting) have become available, re-examination of these issues is warranted. Gordon et al9 recently reported placement of polytetrafluoroethylene (ePTFE)-covered stents for the treatment of PVS in 3 patients with patency at least 3 months after implantation. Tomita et al10 demonstrated patency in 2 stents dilated to 8.4 mm and 5.6 mm, respectively.

Over the past 2 decades, we have explored multiple transcatheter interventional approaches to treat PVS, including conventional and cutting balloon angioplasty, directional atherectomy (direct tissue removal), and stent implantation...
with bare metal stents (BMS), covered stents (CS), and drug-eluting stents (DES), at our institution. When used, stent implantation has generally been performed for lesions that are recurrent after or resistant to balloon angioplasty. The acute outcome and safety of stent implantation, the patterns and frequency of in-stent restenosis, and the anatomic features conducive to stent patency have not been reported. Understanding the efficacy of stents for the treatment of PVS and documenting the longevity of therapy may aid in anticipatory management of this difficult disease.

WHAT IS KNOWN

- Intraluminal pulmonary vein stenosis is a progressive condition that is frequently lethal in children.
- Treatment approaches for relief of luminal stenosis are acutely successful, but with limited long-term benefit.

WHAT THE STUDY ADDS

- Although intravascular stents are acutely successful in the relief of luminal stenosis, the rates of restenosis are high.
- Stents implanted at a larger diameter appear to remain patent longer with lower risk of reintervention.

Methods

Patients

Consecutive patients <18 years of age who underwent transcatheter stent placement for congenital or postoperative PVS between January 1990 and January 2011 were identified retrospectively from the computerized database of the Cardiovascular Program at Children’s Hospital Boston. This study was approved by the Institutional Review Board of the Children’s Hospital of Boston.

Cardiac Catheterization, Hemodynamics, Angiography, and Intervention

Techniques for pulmonary vein dilation and stent implantation have been described previously. Approaches to balloon selection and methodology of balloon angioplasty for pulmonary veins have been previously published. In the absence of an atrial level communication, access to the left atrium was through transseptal puncture of the atrial septum. A long sheath was typically used for angiography, delivery of balloons, and stent deployment. Balloon size was determined by the operator, based on the angiographic appearance of the stenotic vessel. Hemodynamic data were extracted from the catheterization reports. The right ventricular pressure (RVP) and ratio of RVP to aortic pressure were recorded. Direct pulmonary vein gradients were not extracted.

Angiographic Analysis

Minimal lumen diameter of the vein was measured in the anteroposterior and lateral projections before and after balloon dilation and stent implantation. The location of the stent waist was used as the narrowest deployed diameter and the largest lumen diameter was recorded as the postimplant diameter. On follow-up catheterization, appearance of restenosis within the stent was classified on the basis of location (throughout stent, midstent, atrial end, or pulmonary vein end) and pattern of “in-stent narrowing” (concentric, eccentric—superior, inferior, anterior or posterior). Severity of “in-stent narrowing” was graded on the basis of the ratio of the diameter of vein lumen to the stent diameter: <0.5 = severe; 0.5–0.7 = moderate, 0.71–0.9 = mild, and >0.9 = no stenosis.

Data Analysis

Patient demographics, diagnosis, procedural complications, and death were reported with patient as the index unit. All other analyses were primarily by stented vein.

The primary outcome assessed was change in the minimum lumen diameter of the stented vein. Data are expressed as mean ± standard deviation, median (range), or number (% of patients or veins). Preintervention and postintervention minimum pulmonary vein diameter as well as RVP before and after intervention were compared using paired t tests. For BMS, CS, and DES, the relative changes in minimum lumen diameter were compared using the Kruskal-Wallis test. Analyses were repeated using generalized estimating equations methodology, which accounts for the correlation among multiple veins within the same patient, to ensure the results were consistent. Time-dependent outcomes such as freedom from reintervention and survival were assessed by the Kaplan-Meier method, and unadjusted Cox regression analysis was used for comparison between groups. Hazard ratios (HR) are reported with 95% confidence intervals (CI).

Patients who died without reintervention or who had not undergone reintervention at the time of most recent follow-up were censored event-free.

Results

Patients and Pulmonary Veins

A total of 74 pulmonary veins were stented in 47 patients who met inclusion criteria. This does not include 6 patients who underwent stent implantation of 8 veins for post–lung transplant PVS (n = 1), constrictive pericarditis with PVS (n = 1), fibrosing mediastinitis (n = 1), postablation PVS (n = 1), and PVS at age >18 years (n = 2). Patient demographics and diagnostic data are summarized in Table 1. Six (13%) of the patients had a diagnosis of isolated, congenital PVS, whereas 41 (87%) had some form of additional congenital heart defect as described in Table 1. Of these, 26 (55%) patients had functionally single-ventricle heart disease.

Most patients had undergone prior pulmonary vein interventions; prior pulmonary vein surgery had been performed in 29 patients (61%) and 39 (53%) of the stented veins. Similarly, previous transcatheter pulmonary vein interventions had been performed in 24 patients (51%) and 44 (59%) of the stented veins. In 23 patients and 30 (41%) veins, stent implantation was performed during the first interventional catheterization.

Stented Veins and Stent Types

Of the 47 patients, 25 had a single vein stented and 22 had multiple veins stented. Of the 74 stented veins, 46 (62%) were on the left side and 28 (38%) were on the right (Figure 1). In 4 veins, multiple stents were placed in overlapping fashion; 2 for long segment stenosis and 2 for malposition of the first stent.

All but 1 vein was predilated before stent implantation. BMS were used in 57 veins in 39 patients, DES in 7 veins in 5 patients, and CS in 11 veins in 9 patients. BMS types included Palmaz (Palmaz Scientific, Dallas, TX) renal or iliac stents in 25 veins, premounted Genesis or Blue (Cordis Corporation, Miami, FL) stents in 20, and nonpremounted Genesis stents in 2. DES were all premounted, small-diameter...
sirolimus (Cypher, Cordis Corporation, Miami, FL; n/H11005/6) or paclitaxel (Taxus, Boston Scientific, Natick, MA; n/H11005/1).

Eight of the CS were handmade, with a membrane of ePTFE fashioned into a tube and attached to the stents; 3 were commercially manufactured iCAST stents (Atrium Medical, Hudson, NH). Of the 11 CS used, 2 were deployed during reintervention on previously stented vessels. Median stent length was 12 mm (8–30 mm). Table 2 summarizes characteristics of the cohort grouped by stent type used.

Outcomes

**Hemodynamics**
At the first interventional catheterization in which a stent was implanted, among patients with a biventricular circulation, the median systolic RVp before stent implantation was 69 mm Hg (30–136 mm Hg) and the RVp to aortic pressure ratio was 0.9 (0.3–1.5). After stent implantation, there were significant decreases in the RVp, to a median of 58 mm Hg (22–135 mm Hg; P/H11005/0.03), and the RVp to aortic pressure ratio, to a median of 0.6 (0.3–1.4; P/H11005/0.01).

**Acute Changes in Vein Size**
Persistent/recurrent discrete stenosis or a thread-like pulmonary vein with severe intraluminal stenosis were the most common indications for pulmonary vein stent placement. In 1 patient, the indication for placement of a CS was treatment of a cardiac perforation incurred during intervention on severe stenosis. Figure 2 demonstrates vein diameter (grouped by stent type) before intervention, after balloon dilation, and after stent implantation. Figure 3 shows representative angiograms after balloon dilation and stent implantation, along with in-stent restenosis on follow-up catheterization. Overall, there was a statistically significant improvement in the lumen diameter after balloon dilation (P/H11005/0.001) and after stent implantation.

Table 1. Demographics and Diagnostic Data

<table>
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<th>Patients</th>
<th>47</th>
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<td>Female</td>
<td>22 (47%)</td>
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**Diagnosis**

| Congenital PVS | 6 (13%) |
| Totally anomalous pulmonary venous connection | 9 (19%) |
| Partially anomalous pulmonary venous connection | 2 (4%) |
| Hypoplastic left heart syndrome | 6 (13%) |
| Partially anomalous pulmonary venous connection | 1 |

**Cor triatriatum** | 2 |

**Pulmonary atresia/intact ventricular septum** | 3 (6%) |
| Heterotaxy | 10 (21%) |
| Other congenital heart disease* | 11 (23%) |
| Prior pulmonary vein surgery | 29 (62%) |
| Prior pulmonary vein catheterization | 24 (51%) |

**Median age at diagnosis of PVS, y**

| n/H11005/0.01–15.8 |
| 0.6 |

**Median age at first intervention for PVS, y**

| n/H11005/0.02–20.8 |
| 0.9 |

**Median age at first PV stent, y**

| n/H11005/0.02–20.8 |
| 1.4 |

**Pulmonary vein disease** | 47 |

**Common orifice of veins**

| One side | 14 (30%) |
| Both sides | 6 (13%) |

**At least 1 atretic branch at presentation** | 12 (26%) |

**Bilateral PVS** | 30 (64%) |

**Average No. of central pulmonary veins involved at first intervention**

| 3.3±1.4 |

**Pulmonary vein stented** | 74 |

**Right-sided veins** | 28 (37%) |
| Left-sided veins | 46 (63%) |

**Prior surgical intervention on stented vein** | 39 (53%) |
| Prior catheter intervention on stented vein | 44 (59%) |

Table 2. Stent Types and Characteristics in the Cohort

<table>
<thead>
<tr>
<th>Bare Metal Stents</th>
<th>Drug-Eluting Stents</th>
<th>Covered Stents</th>
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<tbody>
<tr>
<td>No. of stented veins</td>
<td>57</td>
<td>7</td>
</tr>
<tr>
<td>No. of patients</td>
<td>39</td>
<td>5</td>
</tr>
<tr>
<td>Stent length, mm*</td>
<td>12 (8–30)</td>
<td>10 (8–23)</td>
</tr>
<tr>
<td>Premounted stent</td>
<td>23</td>
<td>7</td>
</tr>
</tbody>
</table>

**Stented veins**

| Right | 23 | 2 | 3 |
| Left | 34 | 5 | 8 |

**Preintervention**

| Pre-BD MLD, mm* | 2.1 (0–14.7) | 2.1 (1.0–2.6) | 2.4 (1.5–2.7) |
| Pre-stent MLD, mm* | 2.7 (0.5–11.3) | 2.0 (1.0–3.2) | 2.4 (1.5–7) |

**Postintervention**

| Stent lumen diameter after implant, mm* | 5.9 (3.0–20) | 3.5 (2.6–4.5) | 6.0 (5.0–11) |

MLD indicates minimum luminal diameter.

*Data are presented as frequency or median (range).
implantation (P<0.001). Comparison by stent type showed a significant improvement after balloon dilation and stent placement for BMS (P=0.004, P<0.001 respectively). A smaller number of veins were treated with CS and DES and a statistically significant improvement in lumen diameter was seen only after stent implantation (P<0.001, P=0.01 respectively). Because some patients had more than 1 stented vein, analysis accounting for within patient correlation also showed a significant improvement in lumen diameter after balloon dilation (P<0.001) and after stent implantation (P<0.001). Stenotic pulmonary vein diameters before balloon dilation and before stent implantation did not differ significantly between stent types. Because available DES are designed for use in coronary vessels and are smaller in size, mean poststent luminal diameter among DES-treated veins was significantly smaller than veins treated with BMS (P=0.04).

Stent Embolization, Malposition, and Other Major Complications

Of the 6 embolized stents, 4 were immediate and 2 were noted to be embolized 1 day and 1 month later, respectively. No particular pulmonary vein deployment site was more prone to dislodgment (right lower pulmonary vein=2, right pulmonary vein confluence=1, left pulmonary vein confluence=1, left lower pulmonary vein=2). Embolization sites included the left atrium (n=1), ascending aorta (n=1), and descending aorta (n=4). All of the stents were retrieved in the catheterization laboratory and fixed in the infrarenal descending aorta (n=4), the iliac vein (n=1), or the aortic arch (n=1). In 4 of these cases, a stent was subsequently placed in the targeted vein without complications. A malpositioned but stable stent was removed from 1 vein and deployed in the inferior vena cava. Jailing or obstruction of other pulmonary veins as a result of stent placement seen by angiography was documented in 6 cases. Immediately after stent placement, 1 stent was found to have no flow of contrast. This stent was found to be occluded by a large thrombus on examination in the operating room, on the day of stent placement.

Figure 2. Mean change (±SD) in pulmonary vein diameter after balloon dilation (BD) and stent placement. Comparison of the entire cohort and selective comparison of bare metal stent (BMS) shows a significant improvement in luminal diameter after BD (P<0.001) and after stent implantation (P<0.001). In veins treated with covered stents (CS) and drug-eluting stents (DES), there was a statistically significant improvement in luminal diameter only after stent implantation (P<0.001, P=0.01 respectively).

Figure 3. Representative angiogram in a patient with postoperative discrete stenosis (arrow) in the right lower pulmonary vein (A). Discrete stenosis is relieved with successful deployment of a 12-mm premounted Palmaz Genesis stent (B). Concentric in-stent narrowing (arrow) along the length of the stent (C) and at the pulmonary vein end of the stent (D) are seen at follow-up catheterization at 1 and 1.5 months, respectively.
In addition to stent embolization, major acute complications during the catheterization occurred in 5 patients, including cardiac perforation in 1 and cardiac arrest in 4. The perforation was due to pulmonary vein atherectomy and was subsequently stabilized with placement of a CS. The 4 cases of cardiac arrest occurred (1) during pulmonary vein dilation, (2) after pulmonary vein stent embolization, (3) after Blalock-Taussig shunt dilation, and (4) during catheterization for unclear reasons. All cardiac arrests were successfully resuscitated without known sequelae.

Anticoagulation
Fourteen patients were maintained on aspirin before and continued after stent implantation, whereas an additional 16 were initiated on aspirin after stent implantation. Four patients were initiated on an additional antiplatelet agent after stent placement. Two patients were maintained on warfarin and continued after stent placement, whereas 7 were initiated on warfarin. A thromboembolic event was documented in 1 patient after stent implantation that was complicated by in-stent thrombosis requiring surgical removal and subsequent sutureless repair of the pulmonary veins. Multifocal cerebral infarction was documented on postoperative day 2 despite intravenous anticoagulation.

Follow-Up

Survival
Over a median follow-up of 3.1 years (1 week to 14 years), 21 of the 47 patients died. As depicted in Figure 4, estimated survival from the time of diagnosis of PVS by Kaplan-Meier analysis was 81±6% at 1 year, 66±8% at 2 years, and 60±8% at 5 years, and survival from the time of first stent placement was 62±8% at 1 year, 57±8% at 2 years, and 50±8% at 5 years (Figure 4). At the most recent follow-up catheterization (n=19 patients), the median systolic RV to aortic pressure ratio was 0.7 (0.3–1.5).

In-Stent Stenosis and Reintervention
Table 3 summarizes follow-up data for the entire cohort and grouped by stent type. Over the follow-up period, complete occlusion was documented in 9 stented veins, including 8 BMS and 1 DES. Stent occlusion was documented as the absence of contrast crossing the pulmonary vein stent into the atrium in levophase after wedge angiography in the corresponding pulmonary artery. The median duration from implantation to documentation of occlusion was 4.2 months (0 days to 1.4 years). Five of the 9 stents were occluded on the first follow-up catheterization, 3 were found to be occluded on a subsequent study, and 1 was noted to be thrombosed when it was surgically removed on the day of implantation.

Of the 54 stents that were studied with repeat catheterization a median of 3.9 months (0.1 month to 3.6 years) after implantation, complete occlusion was documented in 9 stented veins, including 8 BMS and 1 DES. Stent occlusion was documented as the absence of contrast crossing the pulmonary vein stent into the atrium in levophase after wedge angiography in the corresponding pulmonary artery. The median duration from implantation to documentation of occlusion was 4.2 months (0 days to 1.4 years). Five of the 9 stents were occluded on the first follow-up catheterization, 3 were found to be occluded on a subsequent study, and 1 was noted to be thrombosed when it was surgically removed on the day of implantation.
implant, in-stent narrowing was documented in 28 (52%) on the first postimplant catheterization (Table 3). There was severe in-stent narrowing in 8 of 44 stented veins in which appropriate measurements could be made, moderate narrowing in 9, and mild narrowing in 7. In-stent narrowing was usually present along the entire length of the stent rather than being confined to the venous or atrial end of the stent. Freedom from diagnosis of significant in-stent narrowing (occlusion, severe or moderate) was 54±9% at 6 months and 37±10% at 1 year (Figure 5).

Transcatheter reintervention was performed in 32 of the stents, with the first reintervention a median of 4.3 months after implant (1.1 month to 12 years); 24 of these interventions were at the time of first follow-up catheterization. All redilations were successful in enlarging the stent diameter and reducing the relative thickness of in-stent narrowing. Overall, freedom from reintervention on the stented vein was 62±7% at 6 months and 42±7% at 1 year (Figure 5). Six previously stented veins in 5 patients were restented. Of the 6, 5 were restented with the same type of stent, whereas 1 of the veins initially treated with a BMS was restented with a CS. Seventeen (38%) of the 44 stents had more than moderate narrowing (lumen:endiameter ratio <0.7) at repeat catheterization, 11 of which underwent reintervention. Of the occluded stents, 2 (both BMS) were successfully recanalized in the catheterization laboratory; there was minimal residual in-stent narrowing after recanalization. No subsequent catheterizations were performed on these patients to assess for patency of the recanalized stents.

Six of the 11 veins stented with CS were reexamined at a median duration of 4.3 months (1.1 month to 3.7 years); all reexamined CS underwent reintervention. Six of the 7 DES were reexamined at a median duration of 2 months (1.6–5.1 months); 4 of these were redilated.

Larger lumen diameter at the end of the implant procedure was associated with longer freedom from significant in-stent narrowing or stent occlusion (HR, 0.74 per mm [95% CI, 0.59–0.91], P<0.001) and longer freedom from reintervention on the stent (HR, 0.83 per mm [95% CI, 0.71–0.97], P=0.017). The optimal dichotomous threshold for association on the stent (HR, 0.83 per mm [95% CI, 0.71–0.97], P=0.001) and longer freedom from reintervention on the stent (HR, 0.83 per mm [95% CI, 0.71–0.97], P=0.017). The optimal dichotomous threshold for associating in-stent narrowing or stent occlusion (HR, 0.74 per mm [95% CI, 0.59–0.91], P=0.001) and longer freedom from reintervention on the stent (HR, 0.83 per mm [95% CI, 0.71–0.97], P=0.017). The optimal dichotomous threshold for associa-

Figure 5. Kaplan-Meier curves depicting freedom from reintervention on the stented pulmonary vein freedom from diagnosis of stent occlusion or severe in-stent stenosis, and combined freedom from death or reintervention.

Discussion

We describe our experience with the use of intravascular stents for the treatment of PVS occurring in isolation or in combination with other congenital heart disease. Our cohort of 47 patients had undergone a multitude of nonsurgical interventions including balloon angioplasty (standard, high pressure, and cutting balloons), prior atherectomy and/or brachytherapy, and prior or concomitant chemotherapy in addition to intravascular stents, which reflects the complexity of this disease process and the lack of a clearly superior therapeutic option. Consistent with previous reports,3 survival in this cohort was poor despite aggressive medical and surgical treatment. All stent implantations were acutely effective in the focal relief of stenosis, with few procedural complications. However, stent obstruction and reintervention were common. Thus, stent implantation appears to serve a primarily palliative purpose in most patients with PVS.

A large majority of the stents used in this series were BMS. As such, comparison by stent type was limited by the small numbers of alternative stent types. However, a few observations regarding CS and DES are worth highlighting. Most of the CS in this group were handmade with ePTFE. It was unclear how effectively the external surface

Figure 6. Kaplan-Meier curves depicting freedom from reintervention on the stented pulmonary vein stratified by stent diameter at implantation. Stents implanted with a narrowest diameter ≥7 mm had a significantly (P=0.02) longer freedom from reintervention than those with an implantation diameter <7 mm.
of the stent was covered in these cases. Commercially available CS (Atrium iCAST), used infrequently in this cohort, have a unique construction with stainless steel struts that are fully encapsulated by a thin layer of PTFE covering both internal and external surfaces of the stent. Conceivably, such a design may be an effective strategy to prevent encroachment of tissue between struts resulting in in-stent narrowing. Indeed, initial studies by Alexy et al\textsuperscript{15} showed better patency of the Atrium iCAST stents in the short term in comparison to BMS in a swine model. These explanted stents showed no evidence of in-stent growth at a follow-up of 3 weeks.\textsuperscript{9} Gordon and Moore\textsuperscript{9} subsequently showed the effective use of iCAST stents in 3 patients with refractory PVS with patency at 6 months after implantation. Though these studies and our observations of the iCAST stent show promise for application in PVS, further studies with larger numbers are required to fully evaluate its efficacy.

DES were not effective for the treatment of PVS. All of the DES used in our experience were small-diameter (eg, coronary artery) stents that could be expanded no larger than \(\approx 5\) mm, which was an intrinsic limitation. Thus, not surprisingly, stent lumen diameter at implantation of the DES was significantly smaller in this group. Though a threshold lumen diameter at implantation is not known, it is conceivable that the pharmacological benefit have been masked by smaller-size stents. Other plausible explanations for the ineffectiveness of DES in our patients include those cited in coronary applications (eg, suboptimal stent expansion) and diminution of the antiproliferative drug effect over time in the context of progressive PVS. Given our current understanding of the etiology of PVS in children, it seems likely that locally targeted therapy may be beneficial in arresting the disease process. Such a drug delivery platform warrants further exploration.

Among adults, PVS is seen after radiofrequency ablation for atrial fibrillation. In contrast to PVS seen in children, postablation PVS is due to periadventitial inflammation and/or collagen deposition secondary to thermal injury of the pulmonary vein musculature.\textsuperscript{16,17} In this growing population of acquired PVS, there is no consensus on the optimal treatment approach. However, stenting of pulmonary veins with stents \(\geq 10\) mm in diameter was reported to be effective and lasting for treatment of ablation related PVS.\textsuperscript{17–19}

The association between larger stent diameter at the time of implantation and shorter time to reintervention in our series is noteworthy. Consistent with a previous report showing longer patency when stent implantation diameter was at least 5.6 mm,\textsuperscript{10} our results suggest prolonged freedom from reintervention and less significant in-stent narrowing when the stent implantation diameter was \(\geq 7\) mm. Similar to data in adults,\textsuperscript{17} our findings suggest a threshold lumen size that may be conducive for stent implantation with a low risk of restenosis. The pathological basis for in-stent restenosis with smaller diameter stents is not clear. Of course, the same thickness of narrowing produces a smaller relative narrowing (lumen:stent diameter ratio) in larger veins. In addition to this obvious consideration, however, it is possible that aberrant flow patterns and differing shear stresses in smaller vessels stimulates a different and/or accelerated process of proliferation.\textsuperscript{20} In another study, patients with totally anomalous pulmonary venous connection with smaller pulmonary vein size had significantly higher mortality.\textsuperscript{21} Taken together, aberrancies in flow patterns promoting uninhibited intraluminal hyperplasia and/or an inherent aggressiveness to the disease characterized by smaller vessels could explain the increase in reintervention rates in this subpopulation. Placement of a stent with small lumen diameter may be a marker of significant distal disease. Thus, in hypoplastic, less compliant vessels, implantation of smaller stents may be the only viable option to prevent vessel atresia. As such, the discriminating value of 7 mm for lumen diameter could be used to categorize patients into a higher risk group in need of more frequent surveillance.

Stent malposition or embolization occurred in 8% of cases, but no single vein location or side (left versus right) was particularly prone to these complications. The severity of stenosis before or after predilation also did not preclude safe stent implantation. Sequential balloon dilation before stent implantation enlarged the lumen of the vein thereby increasing the stent lumen size at implantation. One plausible explanation for stent malposition or embolization is the involvement of the distal vasculature resulting in significantly small distal vessels. Consequently, with small, noncompliant distal vessels, dilating balloons frequently “milk” back into
the left atrium. This mechanism may also pose a risk of stent malposition and embolization in this setting. Because all but 1 of the stented veins were predilated, we cannot determine the relative safety and effectiveness of dilation and stent implantation. However, a sequential approach consisting of vein dilation followed by stent implantation appears to be technically safe.

The more recent practice pattern at our institution for management of PVS includes aggressive catheter-based reas- sessment and reintervention at approximately 4- to 8-week intervals in addition to pharmacological therapy. The benefit of this approach is difficult to evaluate at this stage. As we develop more experience with this disease process, our treatment practices continue to evolve. Our finding of shorter freedom from reintervention among patients with smaller stents identifies a vulnerable group that may benefit from more intensive surveillance after stent implantation. In our experience, the applicability of stents in this disease has been for proximal vessel disease. It is unknown whether more diffuse, distal vessel involvement that is often seen with aggressive disease is amenable to effective stent implantation. Stent therapy may be best suited for vessels with a geometric component to the obstruction (eg, kinking, angulation, compression), those with rapidly recurrent, severe, or long- segment obstruction, those with atriasia or near atriasia that are recanalized, or those that can be enlarged to at least 7 mm. Our current approach also offers the possibility of pulmonary vein rehabilitation facilitating implantation of a larger stent at a subsequent catheterization.

Limitations
Although this study on the experience of stents for PVS in children is the largest published to date, several limitations must be acknowledged. Children’s Hospital Boston is a referral center for PVS, and this series includes patients with varying disease severity who were often treated with multiple interventional, surgical, and pharmacological modalities in addition to stent implantation, with treatment approaches that changed over time. As such, comparison of treatment modalities was not feasible, nor was it possible to discern the isolated impact of stent implantation versus other preceding, concomitant, and subsequent therapies. Criteria for use of specific stent types were not standardized, and conclusions regarding their use with severe disease could not be made. Intervals between catheterization were determined by the primary practitioner, based largely on clinical status and noninvasive imaging findings, and consequently, no consistent interval follow-up was available. The efficacy of stent implantation in the acute setting was based on angiographic measurements only, which does not necessarily reflect the broader disease process in patients with PVS. Though our institutional practices are fairly standardized with respect to angiographic views, disease complexity and patient stability may have influenced consistency. Vein level analysis was done to compare the differences in vein diameter for the different stent types, which does not account within-patient correlation, particularly with the utilization of multiple stent types in the same patient. Further analysis was limited by the small number of patients in the subgroups. As outlined in the previous section, our approach to the treatment of PVS continues to evolve, and we have adopted a more aggressive strategy for treatment. Consequently, an era effect reflecting higher rates of reintervention cannot be excluded. All patients did not undergo follow-up catheterization, some because of interval death, so our outcome almost certainly is subject to survival bias and ascertainment bias.

Conclusions
In a high-risk population of children with congenital and postoperative PVS, transcatheter stent implantation with BMS, CS, and DES was effective in the acute relief of luminal stenosis, with an acceptable adverse event profile. Total stent occlusion in our cohort was relatively uncommon, but moderate to severe restenosis rates were high. Consequently, the need for pulmonary vein reintervention in this cohort remained high. Stents implanted at a larger diameter appear to remain patent longer than small stents, which is probably due to a combination of factors. Accordingly, stents implanted at smaller lumen diameters warrant closer vigilance for stent restenosis. Although no comparative analysis between stent types was possible in this cohort, CS and DES may be useful, particularly in severely hypoplastic veins. Stent implantation does not appear to offer a long-term survival benefit in patients with PVS but may provide lasting relief of PVS in older patients and temporizing relief while a more comprehensive management strategy is developed in patients with severe, aggressive disease.

Disclosures
None.

References


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