Early and Intermediate-Term Complications of Self-Expanding Stents Limit Its Potential Application in Children With Congenital Heart Disease

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OBJECTIVES We report on the early and intermediate-term follow-up results of self-expanding Wallstent (Schneider, Switzerland) implanted in children with congenital heart disease.

BACKGROUND The inherent shortcomings of balloon-expandable stents prompted the trial of an alternative stent.

METHODS Twenty patients underwent 22 implantations of 25 self-expanding Wallstents between December 1993 and June 1997 in two institutions. The mean age and weight were 10.8 ± 4.5 years and 30.5 ± 14.2 kg, respectively. The patients were divided into two groups: 1) Group I comprised 17 patients with pulmonary arterial stenoses, 2) Group II comprised four patients with venous stenoses (one belonged to both groups). Sixteen patients underwent recatheterization at a median of 5.8 months (range 0.5 to 31, mean 8.1 months) after stenting. Hemodynamic and angiographic changes after the interventional procedures and complications were documented.

RESULTS All the stents were successfully deployed in the intended position. In Group I, the narrowest diameter of the stented vessel increased from 4.1 ± 1.5 to 8 ± 2 mm (95% increase, \( p < 0.0001 \)) while the systolic pressure gradient across decreased from 24.6 ± 15.8 to 12.1 ± 11.4 mm Hg (51% decrease, \( p = 0.001 \)). In Group II, the dimensional changes of the narrowest segment increased from 4.3 ± 0.5 to 7.5 ± 0.4 mm (75% increase, \( p = 0.003 \)), and the pressure gradient reduced from 5.0 ± 2.9 to 0.9 ± 1.0 mm Hg (82% decrease, \( p = 0.04 \)) across the stented venous channel. Distal migration of two optimally positioned stents occurred within 24 h of implantation. At recatheterization, significant neointimal ingrowth (>30% of the expanded diameter) was noted in 7 (28%) of the 25 implanted stents. This responded poorly to balloon dilation. Predisposing factors for the neointimal ingrowth included stents of smaller diameter (<9 mm) and longer period after implantation.

CONCLUSIONS Self-expanding Wallstent could be deployed easily and safely to relieve vascular stenoses in children. The complications of distal migration, significant neointimal ingrowth and its unyielding design to overdistension limit its application to this patient group. (J Am Coll Cardiol 2000;35:1007–15) © 2000 by the American College of Cardiology
Table 1. Indications for Implantation of Self-Expanding Wallstents

<table>
<thead>
<tr>
<th>Cardiac Diagnosis</th>
<th>No. of Patients</th>
<th>No. of Stents</th>
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<tbody>
<tr>
<td><strong>Group I: Pulmonary Arterial Stenoses (n = 17)</strong></td>
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<tr>
<td>Post-RVOTR</td>
<td>7</td>
<td>16</td>
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<tr>
<td>PAVSD</td>
<td>5</td>
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<tr>
<td>TOF</td>
<td>1</td>
<td></td>
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<tr>
<td>PAIVS</td>
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<td></td>
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<tr>
<td>Post-Fontan operation</td>
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<td></td>
</tr>
<tr>
<td>DORV, TGA, unbalanced AVSD</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PAVSD, TGA, hypoplastic RV</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>DILV, TGA, subaortic stenosis and CoA</td>
<td>1*</td>
<td></td>
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<tr>
<td>Palliative Shunting</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PAVSD, disconnected pulmonary arteries, bilateral modified Blalock-Taussig shunts</td>
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<tr>
<td><strong>Group II: Venous Stenoses (n = 4)</strong></td>
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<tr>
<td>TGA, post-Mustard operation SCV-baffle stenosis</td>
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<td>2</td>
</tr>
<tr>
<td>Right SCV stenosis postcardiac transplant</td>
<td>1*</td>
<td>1</td>
</tr>
<tr>
<td>Left SCV stenosis postrepair of CoA and arch reconstruction</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

*This patient developed severe protein losing enteropathy after Fontan operation and underwent cardiac transplantation.

METHODS

Patients. Between December 1993 and June 1997, 25 self-expanding Wallstents (Schneider, Switzerland) were placed in 20 patients. Ten were treated at Grantham Hospital, University of Hong Kong, while the remainder were treated at British Columbia’s Children’s Hospital, Vancouver, Canada. Their mean age and weight were 10.8 ± 4.5 years and 30.5 ± 14.2 kg, respectively. The patients were divided into two groups (Table 1). Group I comprised 17 patients with pulmonary arterial stenoses. One had concomitant narrowing extending up the Goretex tube (WL Gore & Associates, Flagstaff, Arizona) of the modified left Blalock-Taussig shunt. Group II comprised four patients with obstruction of the systemic venous drainage. One patient belonged to both groups.

Indications. Branch pulmonary arterial stenoses were considered significant in the presence of exercise intolerance, clinical evidence of right heart failure or echocardiographic features of right ventricular dysfunction. Transcatheter intervention was the initial management of choice. Endovascular stenting was attempted when the expandable arterial and venous stenoses recoiled after balloon angioplasty. Self-expanding Wallstents were chosen in the following situations: a tortuous course to the site of stenosis where passage of the long delivery sheath for balloon dilatable Palmaz (Johnson & Johnson, Cordis USA) stents were judged to be difficult, long-segment hypoplasia and stenosis and unsuccessful attempts of Palmaz stent placements. Significant systemic desaturation (<60%) was the major indicator for stenting in a patient with pulmonary atresia, ventricular septal defect and disconnected pulmonary arteries. Previous multiple surgical revisions of the modified Blalock-Taussig shunts on both sides failed to improve the size of the pulmonary arteries, and the parents were reluctant to agree to the relative high risk total correction. Balloon dilatation of the stenosed shunt and the pulmonary artery at the anastomosis had an initial successful result, but the narrowing recurred.

Methods. Balloon dilatations were performed in all patients with the accepted standard protocol. This served to ascertain that the stenoses were dilatable and to break the fibrotic tissue prior to stent implantation. The self-expanding Wallstent was then placed according to the method described previously (5). The size of the stent was chosen such that close approximation to the vessel proximal and distal to the stenosis was achieved. The ratio of the size of stent to the diameter of stenoses was 2.9 ± 1.1. The length of the stent was between 20 to 56 mm (mean = 36 mm). Mild hourglass appearance was common after complete deployment, and this was accepted. In two patients, moderate hourglass deformity (a reduction of more than 15% of the diameter) of the expanded stent was present. This was abolished by dilation using a balloon of size equal to the diameter of the fully expanded stent.

Of the 22 implantation procedures performed, 20 were under general anesthesia and 2 under local anesthesia. The mean procedural and fluoroscopic times were 181 ± 66 and 52 ± 26 min, respectively (this excluded one patient who had a 5-h procedure due to the embolization of the initially deployed Palmaz stent and requiring subsequent implantation of a Wallstent). Systemic heparinization was given in all but three procedures. Oral aspirin or warfarin was given for three months after the stent implantation. For patients after Fontan operation, oral warfarin was continued beyond three months.

The hemodynamic and angiographic changes were documented before and immediately after stenting and on follow-up catheterization. The diameter of the stenotic segment was measured using the catheter size as the magnification factor (Grantham Hospital) or isocentric magnification correction at standard image intensifier height (British Columbia’s Children’s Hospital). The systolic and mean pressure gradients across the arterial and venous stenoses were assessed, respectively. The systolic right ventricular pressure and the simultaneous systemic systolic blood pressure for those who had right ventricular outflow tract reconstruction and pulmonary arterial stenoses were documented. Significant neointimal ingrowth was
arbitrarily defined as reduction of more than 30% of the luminal diameter, which corresponded to a decrease of more than 50% of the cross-sectional area (cross-sectional area = \(\pi \times \text{diameter}^2/4\)). Early and late complications were noted. Sixteen (80%) patients were recatheterized at a median duration of 5.8 months (range 0.5 to 31, mean = 8.1 months) after the initial stent placement. Fourteen patients belonged to Group I, and three to Group II (including one who belonged to both groups).

Statistics. The changes in diameter of the stenosis, pressure gradient across the stenotic segment, systolic right ventricular pressure and ratio of systolic right ventricular to systemic systolic pressure before and after stent implantation and at the time of restudy were compared using paired, two-tailed Student \(t\) test. Univariate analysis of possible risk factors contributing to significant neointimal growth was performed using the paired Student \(t\) test and chi-square test where appropriate. The results were expressed as mean ± standard deviation, unless otherwise stated. Statistical significance was set at 5%.

RESULTS

Early results. Group I (pulmonary arterial stenoses). All the premounted catheters could be negotiated across the stenoses with successful deployment of the 20 stents. The diameter of the stenosed vessel increased from 4.1 ± 1.5 to 8 ± 2 mm after stent implantation (95% increase, \(p < 0.0001\)) (Fig. 1A). The pressure gradient across the stenotic segment was reduced from 24.6 ± 15.8 to 12.1 ± 11.4 mm Hg (51% decrease, \(p = 0.001\)) (Fig. 1B). For patients whose right ventricle supported the pulmonary circulation, there was no significant change in the absolute right ventricular pressure or its ratio to the systemic pressure (Fig. 1C). This was attributed to the relative small number of patients and the concomitant stenotic lesions often present in other parts of the pulmonary arterial tree. The patient with the concomitant stenosed modified left Blalock-Taussig shunt had immediate improvement of her systemic oxygen saturation from 58% to 73%.

Group II (venous stenosis). Five Wallstents were placed optimally across all the venous stenoses. The diameter of the stenosed venous pathways increased from 4.3 ± 0.5 to 7.5 ± 0.4 mm (75% increase, \(p = 0.003\)) after stent implantation. The mean pressure gradient across the stenoses was reduced from 5 ± 2.9 to 0.9 ± 1 mm Hg (82% decrease, \(p = 0.04\)).

Complications. Distal migration of the stents occurred in two patients. One had a long segment stenosis of the left pulmonary artery after total correction of tetralogy of Fallot. A Wallstent of 8 mm in diameter was placed across the 3.3 mm stenotic segment, and mild hourglass appearance of the expanded stent was noted. Despite optimal positioning, routine chest roentgenogram at 24 h after the implantation revealed distal migration of the stent (Fig. 2, A and B). The systolic pressure gradient before and after stent implantation in this patient appeared higher than those of nonmigrated stents placed in pulmonary arteries after previous right ventricular outflow tract reconstruction (preimplantation: 50 vs. 27.1 ± 13.7 mm Hg, postimplantation: 30 vs. 10.5 ± 8.5 mm Hg, \(p < 0.001\) in both situations). At the second stenting procedure, the migrated stent was pushed further distally during manipulation of the catheter and guidewire. Instead of the intended overlapping of the two stents, a small gap between the facing ends of the two stents was inadvertently introduced.

The second patient had a previous Mustard operation with superior caval venous baffle stenosis. Its caliber tapered from 8 mm to 5 mm. Despite initial optimal positioning, a 12-mm stent migrated into the left atrium and encroached upon the mitral valve on the day after stent implantation (Fig. 2, C and D). This required urgent operative removal. In both cases, the diameter of the stent was 2.4 times that of the narrowest segment. This ratio did not differ from those of the patients whose stent did not experience distal migration (2.8 ± 1.2, \(p = 0.63\)).

Bilateral brachial plexus palsy occurred in a patient with left pulmonary arterial stenosis after surgical correction of tetralogy of Fallot. The initial attempt to deploy a Palmaz stent was complicated by migration of the stent to the distal left pulmonary artery before full expansion was achieved. Further manipulation of the sheath across the stenosis proved unsuccessful. Delivery and deployment of a Wallstent over the guidewire was accomplished with ease. The whole procedure lasted 5 h and 15 min. The patient recovered completely after three months of physiotherapy.

Follow-up. The patients were followed up for a median of 14.8 months (range 0.3 to 42 months). The results of the cardiac catheterization restudies are shown in Table 2. Comparing with the immediate poststenting status, the stented pulmonary arteries and venous pathways showed insignificant decrease in the luminal diameter (\(p = 0.075\) and 0.15, respectively). The increase in pressure gradient across the arterial stenoses was significant (\(p = 0.02\)) in contrast to the insignificant increase across the venous stenoses (\(p = 0.33\)). For patients with right ventricular outflow tract reconstruction and stenting of the stenosed pulmonary arteries, there was no significant drop of the right ventricular pressure noted on follow-up.

Significant intimal proliferation, defined as >30% reduction of the expanded luminal diameter, occurred in seven stents: five implanted in pulmonary arteries (Fig. 3), one each in the left superior caval vein and the modified left Blalock-Taussig shunt. One stent implanted in the upper lobe branch of the right pulmonary artery was completely occluded. As for the other stents, neointimal proliferation occurred in the midportion or proximal end of the stents. The patient who required a second Wallstent implantation, after distal migration of the first deployed self-expandable stent, had the most severe neointimal ingrowth. Its thickness amounted to 40% of the stented luminal diameter. The
Figure 1. Line plots showing: (A) the increase in diameters of the pulmonary arterial stenosis and (B) decrease in systolic pressure gradients before and immediately after implantation of self-expanding Wallstents. For patients with a functional right ventricle, no significant change of the right ventricular to the systemic systolic pressure ratio could be documented (C). Figure 1, part C on facing page.
proliferation was maximal at the gap in between the facing ends of the two stents, extending proximally to involve the midportion of the newly placed stent. The stented modified Blalock-Taussig shunt had irregular heaping of the intima at the proximal and distal ends of the stent. The risk factors associated with significant neointimal proliferation were a smaller diameter of the stents \( p = 0.01 \) and longer period after implantation \( p = 0.04 \) (Table 3). Angiographically, there was no evidence of any disturbance of blood flow to the side branches that the stents crossed. The migrated stent in the distal left pulmonary artery was free of excessive intimal coverage, and blood flow to the distal branches was not jeopardized.

Balloon dilation was attempted in six stented vessels with significant neointimal proliferation. In five, the diameter increased from \( 4.4 \pm 1.6 \) to \( 5.9 \pm 1.4 \) mm \( p = 0.0004 \). This amounted to 83% of the initial stented luminal size. Unsatisfactory balloon angioplasty for the restenosis of a stented left superior caval vein prompted the placement of a balloon expandable Palmaz stent and a second Wallstent at either end of the caval vein, with considerable overlapping of the stents. The completely occluded stent was treated conservatively.

**DISCUSSION**

**Immediate results.** Self-expanding Wallstent has been extensively used in Europe for adult patients with iliac and femoral arterial stenoses (8,9) and malignant caval venous obstruction (10). Reports on the use of self-expandable stents in children with congenital heart disease are limited, and intermediate term follow-up results are lacking (5,6). Most other publications on stenting of stenosed vessels in children were relating to the experience on balloon-expandable Palmaz stents (1–4).

The immediate results after Wallstent implantation were impressive. Implantation of these self-expandable stents in an optimal position was feasible in all the patients. The ability to pull the partially deployed Wallstent proximally allows for exact placement across the narrowest segment. Optimal positioning of Palmaz stents was reported to be possible in 95% to 96% of the patients (1–3), but it was unclear how many procedures were abandoned as a result of failure to pass the large-bore sheath through a tortuous stenotic passage. The ease of delivery and position of the Wallstent over the guidewire is an obvious advantage over the Palmaz stent. The significant increase in the diameter of stenoses and the decrease in pressure gradient parallel that of the experience of the Palmaz stent (1,2,7). Once fully expanded, however, both types of stents could not be retrieved by transcatheter techniques. Our results attest to the efficacy of Wallstents in relieving stenotic lesions in congenital heart disease.

**Early complications.** This gratifying result was, however, undermined by the occurrence of delayed migration of two optimally positioned stents (one from each center). A
similar event had been described after Wallstent implan-
tation for the treatment of malignant superior caval
venous stenosis (11) but has not been reported with the
use of Palmaz stent. The cause of the delayed migration
could only be speculative at this stage. In contrast with
the more flexible Wallstent, the rigidity of Palmaz stent
after balloon expansion could resist the compressive
forces of the expanded stenotic lesion, and this probably
prevents any delayed migration. Furthermore, the radial
force of expansion exerting on different portions of the
stented vessel may differ when self-expansion of the stent
is incomplete (12). With gradual increase in the diame-
ter, the radial force decreases and development of eccen-
tric radial force due to unequal rate of expansion may
propel the stent to migrate in either direction. “Fixing”
the Wallstent by balloon dilatation after deployment may
perhaps reduce the risk of migration. Since delayed
migration could result in restenosis or the stent encroach-
ing onto valvar apparatus of the heart, consideration especially of the latter occurrence must be given in selecting patients for self-expandable stent implantation.

**Late complications.** Significant neointimal ingrowth occurred at an alarmingly high incidence of 28% (7/25) at a mean follow-up duration of 8.1 months in this study. This is in sharp contrast with the experience of Palmaz stents where the incidence of significant restenosis was only 1.5 to 3% (2,4,13). Previous experimental studies in animals, however, failed to show differences in neointimal thickness in the stented arteries for the two types of stents (14,15). Similar patency rate of the two stents in the iliac system was demonstrated in another multicenter adult clinical trial (16). What has been shown to be different, however, was the delay in maturation of the neointimal growth of the Wallstent when compared with the Palmaz stent in canine iliac and femoral arteries (14). A recent report further suggested that the Wallstents placed in transjugular intrahepatic portosystemic shunts were more thrombogenic than Palmaz stents (17). Differences in maturation and thrombogenicity may be related to the design of the stent, woven mesh with expanding radial force (Wallstent) versus that of rigid slotted tubes with smooth and even surface (Palmaz). Alternatively, regions of the self-expanding stent might not be adhering close enough to the luminal wall of the vessel, predisposing to friction, abrasion, inflammation and ultimately neointimal proliferation. The possibility of chronic friction would persist despite the use of antiplatelet therapy. Perhaps active “fixing” of the Wallstent onto the vessel by balloon dilation might reduce this friction and abrasion. Additionally, we observed that a smaller Wallstent and a longer period of implantation before restudy were risk factors relating to the development of significant neointimal proliferation. A further problem in the use of the self-expandable stent is that one could not use an oversized balloon to dilate the stent or the stented lesion which restenosed. The maximum diameter of the balloon chosen could only be that of the size of the original stent placed (5). This has resulted in suboptimal expansion of the restenosis related to neointimal proliferation in our patients. This could be a major drawback when compared with the Palmaz stent, which allows the use of an oversized balloon to dilate its restenotic region (4), with further advantage of the latter to accommodate the growth of the child.

The unyielding design of the Wallstents for overdilation when used in children who are actively growing has always been a concern. Implantation of an over-sized

<table>
<thead>
<tr>
<th>Table 2. Angiographic and Hemodynamic Data Immediately After Stent Implantation and at Follow-up Catheterization Restudy</th>
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<tbody>
<tr>
<td>Diameter (mm)</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Arterial stenoses (n = 16)</td>
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<tr>
<td>Venous stenoses (n = 3)</td>
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<tr>
<td>Gradient (mm Hg)</td>
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<tr>
<td>Systolic gradient across arterial stenoses (n = 13)</td>
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<tr>
<td>Mean gradient across venous stenoses (n = 3)</td>
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<tr>
<td>Systolic right ventricular pressure after pulmonary arterial stenting (n = 11)</td>
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<tr>
<td>Right ventricular to systemic systolic pressure ratio after pulmonary arterial stenting (n = 11)</td>
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Difference in the total number (n) is related to (1) placement of more than one stent in two patients, (2) complete occlusion of the vessel lumen in one patient, and (3) assessment of the right ventricular pressure only in those after right ventricular outflow tract reconstruction.
A self-expanding stent would pose the risks of stimulating neointimal growth, vessel erosion and aneurysm formation (3,18). As Wallstents could not be overdilated beyond the preset limits, balloon dilatation in our patients was limited to those with suboptimal self-expansion after initial deployment or those complicated by significant intraluminal ingrowth. The results for the latter circumstance were not so rewarding.

Study limitations. A major limitation of this study was the relatively small number of patients involved. Without prior knowledge on the long-term effect of this self-expandable stent, we have limited its application to patients who would obviously benefit from the simple and easy deployment. The pooling of the results from two centers helped to expand the experience and add weight to the conclusion. Indeed, the similar occurrence of neointimal proliferation and delayed migration of stents in the two centers eliminated significant technical errors introduced from one specific center. Accepting that our duration of follow-up was relatively short (longest was 42 months), we felt that the incidence of neointimal proliferation was alarmingly high for this intermediate-term result and were compelled to report this without further delay. If, indeed, increased thrombogenicity and delayed maturation of the neointima were intrinsic properties related to the self-expanding Wallstent, longer term follow-up could see a higher incidence of neointimal proliferation. While the definition of significant neointimal proliferation was arbitrarily set at \(\geq30\%\) reduction of the original expanded luminal diameter, this reduction could result in significant impairment of perfusion or hemodynamic disturbance (1). We felt that this arbitrary cutoff was justified.

Conclusions. On the whole, three major issues of the self-expanding Wallstent appear formidable at present. First, the significant degree of neointimal ingrowth with unsatisfactory response to balloon dilatation negates the initial increase in vascular diameter. Second, the failure to keep pace with growth limits its use in a young child. Third, the possibility of distal migration demands careful selection of suitable candidates. As a word of caution for those centers planning to initiate stent placement, although it would be tempting to use self-expandable Wallstents for their ease of deployment, one should be fully aware of these important limitations. The use of the self-expanding Wallstents should be reserved for adolescents and adults in whom Palmaz stent implantation would not be feasible and larger caliber Wallstents could be implanted.

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REFERENCES