Long-term follow-up of stents implanted to relieve peripheral pulmonary arterial stenosis: hemodynamic findings and results of lung perfusion scanning

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Abstract In recent years, percutaneous placement of stents has been used as an alternative to surgery or balloon angioplasty for the treatment of adults with peripheral pulmonary arterial stenosis. This therapy has also been proposed for children, but questions still remain about its indications in this group of patients. We describe here the results of intravascular placement of stents in a group of 29 patients, with a mean age of 12±7 (range 3-31) years and weighing 35±19 (range 11-74) kg. All were affected by postsurgical or congenital isolated pulmonary arterial stenosis, and have now been followed for 38±19 (range 6-65) months. The early hemodynamic results have been excellent, with a significant reduction of the pulmonary arterial systolic pressure, the systolic pressure gradient, and the ratio of systolic pressures in the pulmonary and systemic circuits, and with a significant increase of the diameter of the stented vessels in all the patients. Of the 29 patients, 24 have been recatheterized 18±10 months after the procedure, demonstrating the stability of the results, with a low incidence of late restenosis, this seen in only 1 patient (2%). Lung perfusion scanning, performed in 17 patients each year after the follow-up catheterization, has showed that the results are maintained at long-term follow-up (51±9 months).

Keywords: pulmonary arterial stenosis; stents, balloon dilation follow-up studies; blood vessels prosthesis

The results of surgical repair of peripheral pulmonary arterial stenosis are generally not satisfactory. Percutaneous balloon angioplasty also fails to resolve this problem in a large proportion of patients because of the elastic recoil of the pulmonary vessels.1,2 In order to overcome the recurrence of stenosis after angioplasty, balloon-expandable intravascular stents have been inserted which provide support for the dilated vessel.3-6 The feasibility, efficacy and safety of this procedure have been established in several studies, even in children.7,8 The criterions for selection of suitable children in whom stents can safely be implanted still need to be established, since there is variation in the incidence of late restenosis in the series of children thus far described,9-12 together with a paucity of long-term results.

Materials and method

Between August 1993 and September 1996, 29 patients, 18 males and 11 females, aged 12±7 (range 3-31) years, and weighing 35±19 (range 11-74 Kg) Kg, underwent implantation of endovascular stents because of stenosis of the pulmonary arterial branches. Of the patients, 27 had surgically induced stenosis subsequent to repair of tetralogy of Fallot with pulmonary stenosis in 21, tetralogy with pulmonary atresia in 5, and ventricular septal defect in the other patient. Of these patients, 22 had undergone construction of a systemic to pulmonary arterial shunt, and/or surgical angioplasty of pulmonary arteries. The patient with the ventricular septal defect had undergone banding of the pulmonary trunk. Two
patients had congenital isolated peripheral pulmonary arterial stenosis.

After clinical examination, chest X-ray, echocardiography and appropriate laboratory evaluation, and having obtained informed consent, all patients underwent lung perfusion scanning (99mTc-MAA), in order to assess the distribution of flow in the two lungs, evaluating the percentage of perfusion of each lung. On the basis of the results of scanning, patients were divided in 2 groups. The first group had scintigraphic signs of unilateral pulmonary arterial stenosis, with severe hypoperfusion of one lung with overperfusion and balancing of the base to apex flow of the other lung. The percentage of perfusion to the affected lung was less than 35% and to the unaffected lung was greater than 65% (Fig. 1).

In the second group, the presence of multiple perfusion defects in both lungs revealed bilateral stenosis. In these cases, the quantitative analysis was not considered a reliable index of the severity of the stenosis because of the redistribution of the flow in each lung in consequence of the bilateral stenosis (Fig. 2).

All patients underwent hemodynamic study under general anesthesia with inhalation of sevorane and mechanical ventilation. Right heart catheterization was performed from a percutaneous femoral approach in 27 patients, and from the right internal jugular vein in 2 because of femoral venous thrombosis. Systemic pressures were monitored from the femoral or radial artery. Selective pulmonary angiography was performed in axial projections to define the profile of the stenosis. Digital acquisition and display were obtained, measuring the diameter at the level of the stenosis and the adjacent normal vessel, calibrating by means of the size of the catheter. Balloon angioplasty using standard balloons was attempted in all patients.

Implantation of stents was based upon one or more of the following criterions:

- Pressure in the pulmonary trunk greater than half the systemic pressure
- Reduction of the diameter of the pulmonary arterial branch to less than half the adjacent normal vessel.
- Angiographically significant unilateral stenosis, with reduction in the diameter of the vessel by at least 50%, and scintigraphic evidence of severe hypoperfusion of the afflicted lung and overflow to the other lung, the proportion of perfusion to the affected lung being less than 35% together with normal or slightly elevated pressure in the pulmonary trunk.
- Dilatable stenosis, with complete disappearance of the waist at angioplasty, but failure of the area of stenosis to reach 75% of the diameter of the adjacent normal vessel due to immediate elastic recoil.

Placement was performed with the technique described extensively by other authors.3,7-10 We implanted 49 stents (Johnson and Johnson Interventional Systems) in 29 patients. All the stents were of the larger size (P 308 30x3.4 mm), and were expanded with balloons from 10 to 18 mm diameter.

Stents were implanted in the right pulmonary artery in 7 patients, in the left in 13 patients, while...
9 patients had bilateral implantation and 6 patients had multiple implantations, with a maximum of 6 stents placed in 1 patient.

All patients underwent intravenous administration of heparine sulfate 100 UI/kg at the beginning of catheterization, followed by 25 UI/kg/hr for 24 hrs, maintaining an activated clotting time of 200 seconds.

Lung perfusion scanning was performed the day after the procedure, and the patients were discharged receiving Aspirin (5 mg/kg/day) for 6 months.

Lung perfusion scanning was repeated after 6 months, and every year subsequent to the procedure. Hemodynamic and angiographic studies were performed 1 year after the placement of the stents.

**Statistical analysis**

Results are expressed as mean value ± 1 SD. Comparison between groups was performed using a two-tailed Student t-test. Significance was defined as a \( p \) value < 0.05.

**Results**

**Immediate results**

Adequate positioning of the stent was achieved in all patients. All the 49 stents were implanted correctly, straddling the stenotic lesion in the center of the implant, and avoiding the protrusion of the stent into the pulmonary trunk. There were no cases of reduced flow into the side-branches of the pulmonary arteries. Three stents slipped over the balloon catheter during manipulation. They were pushed distally in a more peripheral branch and expanded. A stent in proper position was then implanted.

Mean fluoroscopy time was 67 ± 35 (range 18-146) minutes for unilateral placement and 94 ± 32 (range 45-155) minutes for bilateral implantations.

The immediate results of implantation have been analyzed for the overall group of patients, and for the groups with unilateral or bilateral stenosis.

**Overall results (29 patients):** The mean systolic pressure in the pulmonary trunk fell from 54 ± 19 to 42 ± 13 mmHg \( (p<0.05) \). The mean ratio of the pulmonary trunk to systemic systolic pressure fell from 0.51 ± 0.17 to 0.36 ± 0.11 \( (p<0.001) \). The mean peak systolic gradient across the stenosis dropped from 36 ± 20 to 11 ± 12 mmHg \( (p<0.001) \). The mean diameter of the arteries at the level of the stenosis increased from 5.8 ± 1.9 to 10.9 ± 2.3 mm after the implantation \( (p<0.001) \).

**Unilateral stenosis:** on the basis of lung perfusion scanning, 14 patients were found to have unilateral stenosis: 3 with stenosis of the right branch and 11 of the left. The mean percentage of perfusion to the affected lung was 22 ± 10% (range 11-39%) and to the unaffected lung 78 ± 10% (range 61-89%). Hemodynamic and angiographic studies confirmed the scintigraphic diagnosis. In all the 14 patients, there was a significant reduction of the diameter of the pulmonary arteries at angiography, with a mean diameter at the level of the stenosis 46 ± 9% of the adjacent normal vessel. There was only a slight increase of the systolic pressure in the pulmonary trunk (39 ± 8 mmHg) because of the compensatory high vascular compliance of the unaffected lung. After implantation, the mean diameter of the vessel at the level of stenosis increased from 6.1 ± 2 to 10.7 ± 2.3 mm \( (p<0.001) \), and the mean systolic pressure in the pulmonary trunk was unchanged (38 ± 10 mmHg \( p=n.s. \)). At scanning 24 hrs after placement, the affected lung was seen to be reperfused, with reduction of the flow to the unaffected lung (Fig.3). The mean percentage of perfusion to the affected lung increased to 41 ± 12% (range 22-67%) \( (p<0.001) \), and decreased to 59 ± 12% (range 33-78%) in the unaffected lung \( (p<0.001) \). In one case with right pulmonary arterial stenosis, after successful implantation, the left lung became hypoperfused, with perfusion to the unaffected left lung falling from 76 to 33%, probably due to the increased vascular resistance produced by the long standing compensatory increased flow.

**Bilateral stenosis:** Scintigraphic signs of bilateral stenosis were present in 15 patients. The diagnosis of bilateral stenosis was confirmed in all by catheterization. The mean ratio of the diameter at the level of stenosis compared to the adjacent vessel was 42 ± 11%, and the mean systolic pressure in the pulmonary trunk was abnormally high (72 ± 14 mmHg). Of the 15 patients, bilateral implantation was achieved in 9, with a decrease of the pulmonary arterial systolic pressure from 71 ± 17 to 46 ± 14 mmHg \( (p<0.001) \), and scintigraphic evidence of reperfusion of most of the hypoperfused segments, with physiological redistribution between the lungs (Fig.4). Three patients with severe bilateral stenosis had a stent placed only in one branch because of technical problems. In these cases, the hemodynamic and scintigraphic results were not as good, with persistent high systolic pulmonary arterial pressure (54 ± 18 mmHg), and perfusion to the left lung of less than 35% after the procedure. Three patients presented angiographically severe stenosis of one branch, and mild stenosis of the contralateral branch. They underwent unilateral implantation,
with good hemodynamic and scintigraphic results in 2 patients, and with persistent hypoperfusion of the unstenited lung as revealed by scintigraphy in 1 patient. After placement of the stents, the mean diameter of the vessels changed from 5.5±1.6 to 10.1±3.1mm (p<0.001).

Complications
One patient with pulmonary hypertension suffered right lobar edema, which resolved completely after 48 hrs of pharmacological therapy with diuretics and mechanical ventilation.

In the three cases in whom the stents had slipped and subsequently expanded in peripheral vessels, no damage either to the vessel itself or to the adjacent branches was demonstrated at angiography. The scintiscan showed no related perfusion defect.

Follow-up results
The patients have been followed for 38±19 (range 6-65) months.
Three patients died during the period of follow-up from cardiac causes not related to implantation of the stents. All the 3 patients had undergone...
follow-up catheterization and the satisfactory result of the procedure itself had been demonstrated. Two of these patients, one with tetralogy of Fallot with pulmonary stenosis, and one with tetralogy and pulmonary atresia, died at home suddenly. Another patient with tetralogy and pulmonary atresia died from persistent pulmonary arterial hypertension and right ventricular failure. This patient had undergone closure of the ventricular septal defect after bilateral implantation of stents.

Three patients underwent reconstruction of the right ventricular outflow tract after placement of stents. Five patients were lost, after the evaluation at 6 months had shown no clinical and scintigraphic abnormalities. All the other patients are asymptomatic and doing well.

The scintigrams of 29 patients at 6 months follow-up were unchanged as compared to the immediate evaluation after implantation. The mean percentage of perfusion to the affected and unaffected lung in those with unilateral stenosis showed no change from the immediate study (41 ± 11% and 59 ± 11% respectively, p = n.s), as it did in 24 patients after 1 year of follow-up (mean percentage of perfusion to the affected lung in 11 patients with unilateral stenosis from 42 ± 13 to 42 ± 11% and to the unaffected lung from 58 ± 13 to 58 ± 11%, p = n.s). Only one patient, with bilateral implantation of stents, showed hypoperfusion of the left lung 1 year after implantation, with the percentage of perfusion to the affected lung falling from 50 to 39%.

Catheterization was undertaken in 24 patients aged 4-26 years and weighing 11-74 kg, 18 ± 10 (range 7-44) months after the procedure. In these patients, 43 stents had been placed.

At follow-up angiography, all the 43 stents were widely patent, even in the presence of a minimal neointimal proliferation that did not change the caliber of the stent. There were no cases of obstruction of secondary branches (Figs 5-7). One stent, with a residual waist at angiography, has been redilated, but with an unsatisfactory result because of the unavailability of high pressure balloons of adequate caliber.

The patient with modifications in perfusion to the left lung at the 1 year scintiscan showed severe stenosis at the origin of the left pulmonary artery, proximal to 4 stents placed in series. The lesion has now been treated with one additional stent, with an optimal angiographic result and with the reperfusion of the left lung at scintiscan (percentage of perfusion to the left lung increasing from 39 to 49%). The patient was re-evaluated 1 year after the last procedure and no restenosis had occurred.

Discussion

Peripheral pulmonary arterial stenosis can adversely affect the outcome of surgical repair of some congenital cardiac malformations because of the hemodynamic effect of right ventricular pressure overload, thus increasing the risk of sudden death and altering the distribution of flow to the lungs. The results of a recent study from the Boston group support the hypothesis that the abnormalities of some indexes of the exercise test, presented...
by the majority of patients with postoperative tetralogy of Fallot, are secondary to abnormal distribution of pulmonary flow. The abnormal flow, on one hand, impairs the capacity of the lungs to accommodate the stress-induced increment of pulmonary blood flow, producing pulmonary arterial hypertension and right ventricular overload and stress, and, on the other hand, causes mismatch in ventilation and perfusion, and alterations in the exchange of gases.

In our study, lung perfusion scanning has been used more extensively than in the others, in which this technique has had only a limited role.\textsuperscript{7-10,12} In patients with unilateral stenosis, the scintiscan demonstrated a severe impairment in the distribution of flow, both to the affected and the unaffected lung. In these cases, the pressure in the pulmonary trunk can be normal because of the compensatory high vascular compliance of the unaffected lung. After dilation, the increase in perfusion to the affected lung, together with the loss of overflow to the unaffected lung, have resulted in physiological redistribution of pulmonary flow. This is the reason why, although it has not yet been demonstrated that these results can produce an improvement in exercise performance, because the stress test has not yet been extensively used in such a population, we think that an aggressive approach is justified in patients with unilateral but severe scintigraphic abnormalities, even in the absence of right ventricular pressure overload. In the patients with bilateral stenoses, scintigraphic evaluation is more difficult because of the lack of quantitative indexes of perfusion for the different pulmonary segments. Right ventricular overload is the rule, however, when there are bilateral stenoses, and the significant change in pressure after dilation, together

**Figure 6.** Systolic pressure gradient across the stenosis in 23 patients before and after implantation of stents and at follow-up catheterization. The patient in whom the ventricular septal defect was left open has been excluded.

**Figure 7.** The diameter of the pulmonary arterial branches at the level of the stenosis in 24 patients before and after implantation of stents and at follow-up catheterization.
with the improvement in the distribution of flow at scanning, demonstrate the importance of dilation.

The treatment of peripheral pulmonary arterial stenosis by implantation of endovascular prosthesis has been introduced to overcome the failure of surgery and percutaneous balloon angioplasty. All the series reported have demonstrated a positive impact of the technique in the management of these patients.\textsuperscript{3,8,12}

The experience in our population confirms the optimal results, with 100% success, no major complications, and improvement of hemodynamic, angiographic and scintigraphic parameters in all patients. At follow-up catheterization, these results are maintained, all the stents are patent, even in the cases in which there is presence of a thin layer of neointimal proliferation as described by other authors.\textsuperscript{10,12}

The only patient in whom restenosis occurred during the follow-up, immediately after the initial stenting, presented a mild narrowing proximal to the origin of the first of 4 stents placed in series in the left pulmonary artery. This narrowing presumably produced turbulent flow, causing progressive intimal proliferation and the restenosis.

In the reports concerning the outcome of stents in the mid to long term follow-up,\textsuperscript{10-12} the incidence of restenosis has been very different. It can be argued that this variability is due to the different ages of the patients treated, thus reflecting the different size of the implanted stents. Our experience confirms this hypothesis, with low percentage (2%) of restenosis in a population of children with relatively high age in whom we were able to use larger sized stents. Hence, the policy to dilate the stents, at the initial placement, to the diameter of the adjacent vessel, also in cases of severe stenosis, has avoided cases of limited dilation (2% in our series). Moreover, this strategy, eliminating discrepancies of the luminal diameter of the vessels, has reduced the risk of intimal hyperplasia that occurs primarily in areas where there is an abrupt variation in diameter.\textsuperscript{10,12} For the same reason, it has avoided the overdistension of the stents as compared to the adjacent arterial segments.

Even with these optimal results, it must be stressed that sudden death, and severe hypoplasia of the pulmonary arteries in patients with tetralogy of Fallot and pulmonary atresia, can still adversely affect the outcome, with 10% mortality during the follow-up in our series.

We conclude that placement of stents is the treatment of choice for peripheral pulmonary arterial stenoses in young adults and children of suitable age to achieve definitive dilation.

References