Balloon Angioplasty With Stent Implantation in Experimental Coarctation of the Aorta

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**Background** Balloon angioplasty of coarctation of the aorta is an effective method of treatment but is complicated by tearing of the aortic intima, formation of aneurysms, and restenosis. Stent placement at the time of balloon dilation could prevent restenosis and could also prevent progression of intimal tears to aneurysms. The purpose of this study was to evaluate the feasibility of balloon dilation and implantation of balloon-expandable stents in an experimental model of coarctation and to examine the effect of stent placement at the site of surgically created stenosis.

**Methods and Results** Coarctation of the aorta was surgically produced in 11 juvenile swine. Simultaneous coarctation angioplasty and stent implantation was performed in 10 animals 34±7.8 days after surgery. Repeat catheterization was performed 59±6 days after stent implantation. Five animals underwent reexpansion of stents with subsequent follow-up catheterization. Aortic specimens were examined by light microscopy and scanning electron microscopy. Coarctation angioplasty with stent implantation was successful in all, with an increase in coarctation diameter from 46±8.5% to 90±12.2% of proximal aortic diameter (P=.0001). Systolic pressure gradient decreased from 32±19.8 to 0.5±2.8 mm Hg (P<.001). All stents were patent at follow-up catheterization, with no evidence of intraluminal thrombosis. Reexpansion in five animals increased the stent diameter from a mean of 77.4±12.1% to 93±11.0% of proximal aortic diameter (P=.02). Gross examination of aortic specimens demonstrated formation of neointima over the stent wherever the stent struts were in contact with the aortic wall. The stent occupied a subintimal position and produced minimal compression of the underlying media. Medial compression was noted immediately beneath stent struts, but there was no evidence of intimal or medial dissection.

**Conclusions** Balloon angioplasty with simultaneous implantation of balloon-expandable stents is effective in relieving aortic obstruction in experimental coarctation. Reexpansion of the rigid stent can be performed in an area of surgical aortotomy and coarctation without significant intimal or medial injury. Stent implantation may be useful in preventing restenosis and aneurysm formation after angioplasty of coarctation. (Circulation. 1994;89:2677-2683.)

**Key Words** • coarctation • aorta • aneurysm • stents

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Balloon angioplasty of coarctation of the aorta is clearly an effective method of treatment, with relief of the coarctation gradient comparable to that achieved by surgical repair. Coarctation angioplasty produces a tear in the coarctation shelf that extends to a variable extent into the aortic intima and media. Not surprisingly, coarctation angioplasty has been complicated by the occurrence of aneurysms at the site of dilation in a significant number of patients. The formation of aneurysms at follow-up appears to be related to intimal tears that occur at the time of angioplasty. Although these aneurysms can be repaired safely, the occurrence of aneurysms and the uncertain natural history of the intimal and medial tears that accompany coarctation angioplasty have limited application of this technique in patients with unoperated coarctation.

In addition to the formation of aneurysms, in some patients balloon dilation produces only temporary or inadequate relief of obstruction. A balloon-expandable intravascular prosthesis, such as the Palmaz stent (Johnson and Johnson Interventional Systems), could be a useful adjunct to dilation procedures. Stent placement at the time of balloon dilation could prevent restenosis by resisting elastic recoil of the vessel wall. Moreover, intravascular stents might aid in the prevention of aneurysms by "reapplying" torn intima to the aortic media, providing structural support of the congenitally abnormal media, and establishing a surface for formation of neointima over intimal tears.

The purpose of this study was to evaluate the feasibility of balloon dilation and implantation of balloon-expandable stents in a surgical model of coarctation and to examine the effect of balloon angioplasty with stent placement on integrity of the aortic wall and on formation of neointima.

**Methods**

**Surgical Creation of Coarctation** Experimental procedures performed in animals conformed to the guidelines of the American Heart Association on research animal use and were approved by the institutional animal use and care committee. Surgical creation of coarctation was performed in 11 juvenile swine. We used a model of coarctation similar to that described by Lock et al. Animals were premedicated with ketamine hydrochloride (30 mg/kg IM) and underwent induction of anesthesia with sodium pentothal (10 mg/kg IV), and were maintained under general endotracheal anesthesia with a mixture of oxygen, nitrous oxide, and isoflurane (0.5% to 1.5%). The descending thoracic aorta was
exposed via a left thoracotomy. Vascular clamps were placed proximal and distal to the insertion of the ligamentum arteriosus, and an aortotomy was performed with excision of an ellipse of aortic wall equal in length to half the circumference of the aorta. The three edges of this ellipse were then closed with two running 5-0 prolene sutures. This produced a wedge-shaped defect in the contour of the aorta with an apparent aortic diameter at the site of coarctation of approximately 50% of the proximal aortic diameter. Three No. 1 presoaked chromic catgut sutures were then placed around the narrowest portion of this wedge without producing additional constriction. An 18F chest tube was placed in the left hemithorax through a separate stab incision, and the chest was closed. The animals were allowed to recover in a postoperative recovery unit and were given buprenorphine (0.01 mg/kg IM) every 10 to 12 hours for postoperative analgesia.

Coarctation Dilation and Stent Implantation

Simultaneous coarctation angioplasty and stent implantation was performed in 10 animals at an average of 34±7.8 days (mean±SD) after surgery. One animal did not undergo coarctation dilation or stent implantation. The animals that underwent implantation were anesthetized with general endotracheal anesthesia as described above. Both groins were steriley prepared and draped, and the femoral artery was entered by a percutaneous technique. An 11F or 12F Teflon sheath 30 cm long (Cook Inc) was inserted and advanced to the abdominal aorta, and heparin 100 U/kg was given through the long sheath. An end-hole catheter was advanced across the area of coarctation, and the coarctation gradient was recorded by use of a fluid-filled catheter system. Angiography of the thoracic aorta was performed in the lateral projection with a calibrated marker catheter (Bard/USCI). After correction for magnification, aortic diameter was measured in systole 1 cm proximal to the coarctation, at the narrowest portion of the coarctation, and 1 cm distal to the coarctation.

The proximal aortic diameter was used for selection of balloon catheters (Mansfield Scientific) as described for dilation of native coarctation in children.1 Balloon catheters were selected so that the expanded balloon would be equal to 1 to 3 mm greater than the proximal aortic diameter in systole. A 0.038-in guide wire was then advanced to the ascending aorta across the coarctation. A 30-mm-long, 3.4-mm-diameter stainless steel “iliac” stent (P-308, Johnson and Johnson Interventional Systems) was mounted coaxially over the unexpanded balloon and cramped manually. This stent-and-balloon assembly was advanced through the sheath over a guide wire and positioned in the descending thoracic aorta across the site of coarctation. The stent was expanded by rapid balloon inflation with the goal of relieving the waist produced by the coarctation. Because low-pressure balloon catheters were used, balloon inflation was performed without the use of a manometric syringe; therefore, maximum inflation pressure was not measured. The balloon was deflated and the balloon catheter was removed, leaving the guide wire in place across the site of coarctation. The coarctation was not predilated before stent implantation. An angiographic catheter was then advanced over the guide wire, and angiography of the descending aorta was repeated. Pressures were recorded proximal and distal to the site of coarctation.

Follow-up Catheterization and Reexpansion

Catheterization was repeated 59±6.0 days after initial stent implantation. Arterial pressure proximal and distal to the stent was recorded, and angiography was repeated. Reexpansion was performed in five animals, with balloon diameters selected to equal aortic diameter ±2 mm proximal to the stent. Angiographic and pressure recordings were repeated after reexpansion. One animal was killed immediately after reexpansion. The four remaining animals underwent a third catheterization for angiography and pressure measurements 64±36 days after reexpansion. All animals received acetylsalicylate 325 mg and dipyridamole 50 mg/d for 6 weeks after stent implantation and after reexpansion.

Gross and Histological Examination

All animals but one were killed 24 hours after follow-up catheterization. The aorta was excised and fixed under 100 mm Hg pressure with 10% buffered glutaraldehyde. After fixation, the aortic specimen was cut longitudinally into two halves. The luminal surface of the specimens was then photographed. One half was embedded in methyl methacrylate, and the methyl methacrylate block was cut with a diamond circular saw. The methyl methacrylate was then eluted with acetone. Fragments of the metallic stent struts produced by sectioning were gently removed, and the specimen was embedded in paraffin. Sections were then cut 5 to 6 μm in thickness with a standard microtome and were stained with hematoxylin and eosin, Masson's trichrome, and oil red O for light microscopic examination. The second half was postfixed in 2% osmium tetroxide, critical-point-dried, and sputter-coated with gold/palladium for scanning electron microscopic examination.

Statistical Analysis

Changes in stent diameter and pressure gradients before and after reexpansion were compared by a paired Student's t test. Statistical significance was set at P<.05.

Results

Coarctation Dilation and Stent Implantation

Coarctation of the aorta was successfully produced in each animal. To normalize for differences in the sizes of the animals, measurements of aortic and stent diameters are expressed as percent of aortic diameter proximal to the coarctation. Angioplasty with stent implantation was successfully performed in each animal (n=10), with a change in mean coarctation diameter from 46±8.5% to 90±12%. In one animal, two stents were placed in tandem because the first stent was not properly centered across the site of coarctation. The change in coarctation diameter was also associated with elimination of the coarctation gradient. Systolic gradient decreased from a mean of 32±19.8 mm Hg before dilation to 0.5±2.8 mm Hg after dilation (P<.001).

Fig 1 shows the typical appearance of the coarctation before and after dilation with stent implantation. The constriction of the aorta produced in this model was virtually completely relieved by dilation in each animal. In some animals, a mild degree of residual constriction remained. In addition to its effectively relieving the stenosis produced by the coarctation, there was no angiographic evidence of intimal or medial injury produced by dilation with concomitant stent implantation. Although initially straight, the rigid stent assumed a curved configuration with expansion and conformed well to the curved contour of the thoracic aorta.

All stents were patent at repeat catheterization an average of 2 months after initial implantation. There was no evidence of thrombosis and no absolute change in stent diameter with growth. However, there were various degrees of relative stenosis (Fig 1) as a result of growth of the aorta proximal and distal to the stent. Reexpansion in five animals increased the stent diameter from a mean of 77.4±12.1% to 93±11.0% of proximal aortic diameter (P=.02). In all but one case, reexpansion produced an increase in relative diameter that ranged from 20% to 30% of aortic diameter at the
**Fig 1.** A, Angiogram demonstrating the typical appearance of the surgically created coarctation before (left) and after (right) stent implantation. B, Angiogram demonstrating the appearance of the aorta before (left) and after (right) stent reexpansion. Reexpansion was performed for relative stenosis that occurred as a result of growth of the aorta proximal and distal to the rigid stent.
adherent to the surface neointima, but there was no intraluminal propagation of thrombus. In the remaining animals that were killed at a later date, there was no evidence of intraluminal or superficial thrombosis.

The thickness of the neointima, although generally thin, varied between animals and in different areas of the specimen with no predictable pattern. The development of the neointima was best appreciated by light microscopy (Fig 4). The stent struts occupied a subintimal position and produced minimal compression of the underlying media. In many areas, the neointima appeared to fill the defect between the struts, producing a smooth surface. Typically, there was formation of neovasculature and ingrowth of fibrous tissue immediately adjacent to the struts. In all specimens that had undergone angioplasty, there was atrophy of the media in the area of aortotomy and coarctation similar to that seen in the undilated specimen. There was no difference in the appearance of the aortic media or neointima between animals that did versus those that did not undergo reexpansion.

Scanning electron microscopy demonstrated a smooth covering of neointima over most of the stent struts (Fig 5). Stent struts were bare in areas in which they were not in contact with the aortic intima. Except in the one case noted above, there was no evidence of thrombosis, even in areas in which bare stent struts were exposed and neointima was incomplete.

Discussion

Balloon angioplasty is an effective method of treating coarctation of the aorta and other congenital and post-operative stenoses. Although successful in eliminating coarctation gradients in most patients, balloon dilation angioplasty has been associated with aneurysm formation and both early and late restenosis. Effective coarctation angioplasty produces tears in the aortic intima. These intimal tears may extend to the aortic media, which is known to be deficient in patients with coarctation. Although aneurysms are found at follow-up in a minority of patients, the long-term natural history of intimal and medial tears produced by coarctation angioplasty is unknown. Despite the apparent benefits of angioplasty, the occurrence of intimal tears and aneurysms after angioplasty has appropriately limited widespread application of this technique. Balloon dilation may also fail to eliminate the coarctation in a small number of patients. In some, immediate restenosis occurs as a result of elastic recoil of the aortic wall. Although surgical repair of coarctation is generally successful, balloon angioplasty can be accomplished with significantly less morbidity and cost.

Use of Intravascular Stents in Adults and Children

Angioplasty with concomitant implantation of the Palmaz balloon-expandable stent is clearly superior to angioplasty alone in adult patients with iliofemoral stenosis caused by atherosclerosis. Recently, angioplasty with implantation of balloon-expandable stents has been used successfully in children with pulmonary artery branch stenosis, stenosis of the great veins, postoperative stenosis of Fontan anastomoses, and in one patient with abdominal coarctation. In the patient with abdominal coarctation, stent implantation was used emergently to treat an aortic dissection. This

Fig 2. Low-power microscopy of an aortic specimen that did not undergo dilation. A fibrous ledge protrudes toward the luminal surface of the specimen. A transition can be seen from the normal aorta with well-organized media to the abnormal aorta at the site of coarctation with loss of medial elastic lamellae and replacement of smooth muscle by fibrous tissue.

area of greatest narrowing. In the one case in which reexpansion was unsuccessful, the stent diameter was 94% of proximal aortic diameter before reexpansion and did not increase substantially.

Gross and Histological Examination

Fig 2 shows the appearance of the surgically produced coarctation in the one animal that did not undergo angioplasty and stent implantation. In addition to a moderate degree of aortic narrowing where a fibrous ledge protruded into the lumen of the aorta, there was severe atrophy of the media with loss of elastic lamellae and replacement of smooth muscle by fibrous tissue. This atrophy was found at both the site of aortotomy and the area of the circumferential constricting catgut sutures. A granulomatous reaction with calcification could be seen in the area of the constricting catgut sutures.

Gross examination of aortic specimens with stents demonstrated formation of neointima over the stent where the stent struts were in contact with the aortic wall (Fig 3). In five specimens, the stent was not in complete contact with the aortic wall distal to the coarctation, and the stent struts were bare to various degrees. In one animal that was killed immediately after reexpansion, scattered superficial thrombi could be seen...
limited experience suggests a role for stent implantation as an adjunct to angioplasty of thoracic coarctation.

**Balloon Angioplasty and Stent Implantation**

We designed this study to test the use of balloon-expandable intravascular stents in a surgical model of coarctation. Angioplasty with implantation of intravascular stents was successful in all animals and produced nearly complete elimination of aortic constriction caused by the coarctation. In addition, reexpansion of implanted stents was successfully performed in four animals in which relative stenosis had developed with growth of the proximal aorta. Moreover, the implantation of stents was not associated with significant intimal or medial injury. In contrast, in a similar surgical model of coarctation, balloon dilation without stent implantation was associated with intimal and medial tears.

**Reexpansion of Intravascular Stents**

Although stent implantation was successful in this model of coarctation, there are a number of potential limitations to the use of rigid stents in children. Coarctation usually presents in young children and produces seriously abnormal hemodynamics. It is not possible or desirable to delay angioplasty and stent implantation until children have grown to near adult size. With growth of the child and lack of growth of the stented vessel, a relative stenosis develops. For rigid stents to be used in growing children, either gross overexpansion would be needed at initial implantation or reexpansion after growth would be required. We have previously shown that intravascular stents implanted in the normal thoracic aorta of swine can be reexpanded after growth with no significant injury to the neointima or media. In the present study, we observed the development of relative stenosis with growth in four of five animals that underwent reexpansion. Reexpansion was successful in each of these four animals. The ability to reexpand stents in this postoperative model suggests that stent reexpansion should be possible in children with coarctation.

**Stent Diameter and Expansion Ratio**

The Palmaz “iliac” stent is designed for use in the iliac arteries of adults. Although the balloon and stent assembly may be introduced through a 9F sheath, introduction of the unexpanded 3.4-mm-diameter stent over large angioplasty balloons in diameters of 12 to 18 mm requires the use of 11F or 12F sheaths. The large size of these sheaths is a limiting factor in children with small femoral arteries. Ideally, stent profile and expanded diameter (15 to 20 mm) could be designed with appropriately designed balloon catheters to allow the use of small delivery sheaths (6F to 8F), minimizing trauma to the femoral arteries.

**Intimal Dissections in Coarctation Angioplasty**

Experience in adults with atherosclerotic iliac stenosis has demonstrated the utility of placement of balloon-expandable stents when dissections occur at the time of balloon angioplasty. Although we did not examine the use of stents specifically for intimal dissection, analogies exist between the acute dissection of the iliac arteries, coronary arteries, and abdominal coarctation and intimal tears that occur at angioplasty of thoracic coarctation. Stent implantation may be useful in balloon angioplasty of coarctation because the stent will reapply the torn intima to the aortic media, allowing healing to occur without dissection and aneurysm formation.

**Conclusions**

Implantation of balloon-expandable stents is effective in relieving aortic obstruction in experimental coarcta-
Fig 4. Microscopic appearance of the aorta after stent implantation. A thin layer of neointima covered the stent struts (arrow) with minimal subendothelial stroma (A). Minimal compression of the medial elastic lamellae can be seen. There was formation of neovascularure and ingrowth of fibrous tissue immediately adjacent to stent struts (B).

tion, and repeat expansion of the rigid stent can be performed in an area of surgical aortotomy and coarctation without significant intimal or medial injury. Implantation of balloon-expandable stents may be a useful adjunct to balloon dilation of coarctation, would probably prevent restenosis, and may prevent aneurysm formation. The diameter and expansion ratio of the presently available "iliac" stent would allow implanta-
tion in children but would require large delivery sheaths. The results of this study support further development of the Palmaz stent specifically for use with aortic coarctation and initiation of trials studying the application of intravascular stents to the treatment of naturally occurring coarctation in selected patients.

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