An aortic aneurysm model for the evaluation of endovascular exclusion prostheses

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Purpose: **The purpose of this study was to develop an aortic aneurysm (AA) model with a predictable tendency for rupture for the evaluation of the efficacy of endovascular prostheses in preventing rupture and their long-term outcome after implantation.**
Methods: **An infrarenal AA measuring two to three times the diameter of the proximal aorta was created in 18 dogs with a full-thickness patch of jejunum. Seven dogs were allowed to survive without aneurysm exclusion. In 11 dogs the aneurysm was immediately excluded with a stented 8 mm Dacron graft mounted in a 14F delivery system introduced through the femoral artery with aortographic guidance. The pressure differential between the aorta and the excluded aneurysm was measured, and angiography, necropsy, and histologic examination were performed at 3- and 6-month survival.**
Results: **All animals survived aneurysm implantation. Without aneurysm exclusion, six dogs died of rupture within 1 to 6 days of surgery. In three dogs the exclusion failed because of graft-to-aorta size mismatch or misplacement demonstrated on angiography and by a low pressure differential between the aorta and the aneurysm (< 5 mm Hg); all three dogs died of rupture within 4 days. In eight dogs the aneurysm was successfully excluded on the basis of angiography results, with a mean aorta-to-aneurysm pressure differential of 51 mm Hg. Two dogs were killed at 1 and 6 days after surgery because of paraplegia produced by graft thrombosis because of kinking but without evidence of aneurysm rupture. Six dogs survived on a long-term basis, and angiography and necropsy performed at 3 and 6 months revealed patent grafts without migration, reduction in aneurysm size, no flow in the excluded lumbar arteries in five of six animals, and complete incorporation of Dacron graft and stents. No evidence of graft infection was found in any animal. The survival rate was significantly better ($p < 0.023$) in dogs with successfully excluded aneurysms ($n = 6$) compared with that in dogs without exclusion or with failed aneurysm exclusion ($n = 7$).**
Conclusion: **This aneurysm model demonstrates that without effective aneurysm exclusion all animals die of rupture and that successfully placed endovascular prostheses can prevent AA rupture with long-term graft patency and stability. Endovascular aortic Dacron grafts in dogs undergo complete incorporation at 3 months from implantation. This aneurysm model is useful for the evaluation of endovascular devices designed for the treatment of AAs. (J VASC SURG 1995;22:306-15.)**

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The technical feasibility of abdominal aortic aneurysm (AAA) exclusion with endovascular prostheses has been proven in studies on animals and human beings.[1-8] The first intraluminal aortic aneurysm exclusion in an animal model was reported by Balko et al.[1] in 1987. Since then, several investigators have reproduced successful experiences with a variety of endovascular grafts and stents for the exclusion of aneurysms in animals[2-6] and in human beings.[8,9] The effectiveness of endovascular stented grafts in preventing aneurysm rupture is intuitively appealing; however, it has not yet been demonstrated in experimental or long-term clinical studies. Further-

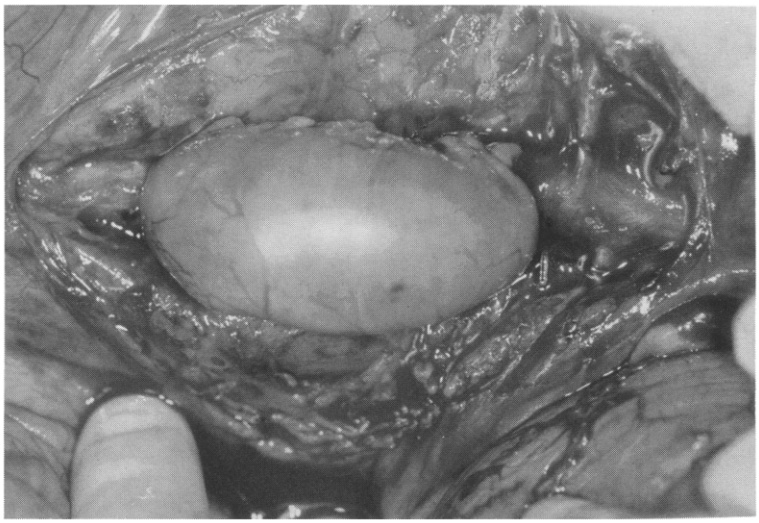

Fig. 1. Operative photo of infrarenal aortic aneurysm created by suturing patch of small intestine to anterior longitudinal aortotomy. Aneurysms created in this fashion typically measured two to three times diameter of adjacent proximal aorta. To right, inferior mesenteric and lumbar arteries are temporarily controlled with hemoclips that were removed at completion of procedure.

more, many questions regarding the short- and long-term effects of these new devices remain unanswered. The initial feasibility studies performed in animals used aneurysm models made of prosthetic material without any tendency for rupture. The purpose of this study was to develop an animal model of aortic aneurysm made of autogenous tissue with a predictable tendency for rupture to test the effectiveness of endovascular exclusion grafts in preventing rupture and to study the long-term behavior of endovascular prostheses in vivo.

MATERIAL AND METHODS

This animal study was approved by the Institutional Animal Care and Use Committee of the University of North Carolina, Chapel Hill. Before the long-term survival studies the surgical technique for creation of an infrarenal aortic aneurysm was tested in acute studies in six mongrel dogs. Intestinal patches were sutured to an anterior, longitudinal, infrarenal aortotomy, and the animals were observed under anesthesia for 4 to 6 hours and immediately killed. A number of intestinal patches were treated with two different concentrations of glutaraldehyde (1% and 4%) to assess their macroscopic characteristics and surgical handling, in the event that untreated fresh intestine would not be able to sustain aortic pressure without immediate rupture. This preliminary study demonstrated that hemostasis around the intestinal patch was complete and that immediate aneurysm rupture did not occur with untreated or treated intestine.

Eighteen male mongrel dogs weighing 22.7 to 38.6 kg were anesthetized with intravenous sodium pentobarbital and maintained with isoflurane under endotracheal intubation. The day before surgery the animals started receiving a clear liquid diet and were given 500 mg neomycin and 250 mg erythromycin by mouth. One gram of intravenous cefotetan was given before incision. With a sterile technique, a midline laparotomy was performed, a segment of proximal jejunum measuring 6 to 8 cm in length was resected, and the jejunum was reanastomosed end-to-end with 4-0 polyglyconate. The resected jejunum was opened along the mesenteric border and trimmed to form an elliptical patch of 4 to 5 cm in length and 3 to 4 cm in width and then placed in a solution of 100 ml normal saline solution with 80 mg gentamycin and 500 mg neomycin for approximately 45 minutes. Heparin was given intravenously (75 IU/kg), and the aorta was cross-clamped below the renal arteries and above the iliac bifurcation. The lumbar and inferior mesenteric arteries were temporarily controlled with hemoclips that were removed on completion of the aortic patch suture. A 4 cm longitudinal aortotomy was performed in the anterior aspect of the aorta just proximal to the inferior mesenteric artery. The jejunal patch was then anastomosed to the aortotomy with a running 4-0 polypropylene suture. This resulted in an aortic

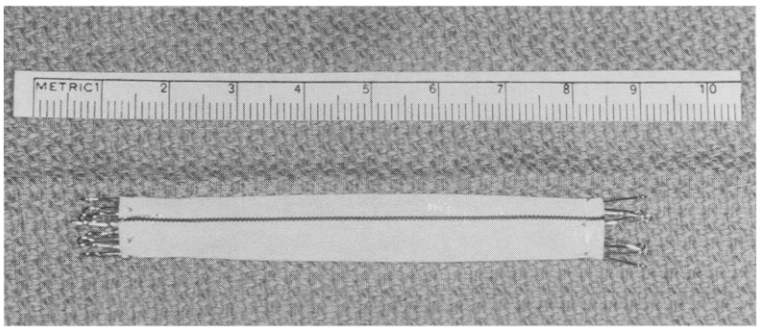

Fig. 2. Uncrimped Dacron grafts (Cooley Very Soft) sutured to Gianturco Z stents at both ends were used for endovascular exclusion of surgically created infrarenal aortic aneurysms in dogs.

aneurysm measuring two to three times the diameter of the normal adjacent aorta, with a 2 to 3 cm neck of normal aorta proximal and distal to the aneurysm (Fig. 1). The retroperitoneal layer was reapproximated over the aneurysm after hemostasis was complete. The abdominal fascia was closed with running 0 polyglyconate, and the skin was closed with absorbable suture. In seven dogs an aortic aneurysm was created without endovascular exclusion, and the dogs were kept alive long term. Four aneurysms were created with unaltered intestinal patch autografts, whereas three were constructed with glutaraldehyde-treated intestinal homografts. Two of the glutaraldehyde-treated intestinal patches were preserved in 4% glutaraldehyde for 48 hours, and one intestinal patch was preserved in 1% glutaraldehyde for 6 hours.

In 11 dogs the aneurysm creation was followed by immediate endovascular graft exclusion. In these animals, after creation of the aneurysm, the abdomen was temporarily closed with skin staples, and the right femoral artery was surgically exposed. The common, superficial, and deep femoral arteries were controlled with vessel loops, and an additional intravenous dose of heparin was given (150 units/kg). A transverse arteriotomy was performed in the common femoral artery and, under fluoroscopic guidance (OEC 9400 C arm; Diasonics, Milpitas, Calif.), a 0.018-inch diameter guide wire was advanced into the abdominal aorta. An angiogram catheter was introduced over the wire, and a subtraction angiogram was obtained by use of Renografin-60 contrast (5 ml per injection). The anatomy of the renal arteries, aneurysm, and aortic bifurcation was clearly defined to guide placement of the prosthesis. The angiogram catheter was removed, and the guide wire left in place across the aneurysm. Uncrimped Cooley very soft straight Dacron grafts (Meadox Medicals, Inc., Oakland, N.J.) measuring 70 to 75 mm in length and 8 mm in diameter (one graft measured 10 mm in diameter) were secured proximally and distally to Gianturco Z stents (Cook Inc. Bloomington, Ind.), with 6-0 polypropylene sutures. The proximal stent measured 17 mm in length and 20 mm in maximal expansion diameter and had three sharp prongs pointing distally and outward. Distally, 15 × 15 mm Gianturco stents without prongs were secured to the Dacron grafts in a similar fashion (Fig. 2). The stented graft was mounted on a coaxial carrier without preclotting and compressed into an introducer sheath with a previously described system.[5] The delivery system was advanced over the guide wire under fluoroscopic guidance. With the previously obtained angiographic road map, the proximal stent was advanced to the aortic segment between the renal arteries and the aneurysm. The sheath over the graft-stent system was then withdrawn, and the proximal stent deployed. Next, the distal stent was deployed by further withdrawing the sheath and allowing it to expand distal to the aneurysm sac, in accord with the technique previously described by Chuter et al.[5] A completion angiogram was obtained to document immediate aneurysm exclusion. The skin staples were removed from the abdomen, the aneurysm and aorta were examined, and the site of the prosthesis was determined by palpation. Blood pressures were measured immediately after exclusion without reversal of heparin in the aorta proximal and distal to the prosthesis via the angiographic catheter, and pressure within the aneurysm sac but outside the prosthesis was recorded with a 20-gauge needle connected to a pressure transducer. The femoral arteriotomy was closed with interrupted 6-0 polypropylene sutures. The retroperitoneal layer was reapproximated over the aorta and aneurysm, and the abdominal fascia was closed with a running suture of 0 polyglyconate. The skin was closed with absorbable suture.

Table I. Summary of 18 animal experiments creating an infrarenal aortic aneurysm by use of a patch of small intestine sutured to the aorta*

Dog no.	*Graft*	*Completion angiogram*	*Pressure Diff.*	*Outcome*
1	No	Intact aneurysm	N/A	Rupture within 18 hours
2	No	Intact aneurysm	N/A	Rupture within 18 hours
3	No	Intact aneurysm	N/A	Rupture within 30 hours
4	No	Intact aneurysm	N/A	Rupture within 42 hours
5	No	Intact aneurysm (4% GA)	N/A	Rupture within 5 days
6	No	Intact aneurysm (4% GA)	N/A	Rupture within 11 days
7	No	Intact aneurysm (1% GA)	N/A	Killed at 3 months, no rupture
8	Yes	Incomplete exclusion	5	Rupture within 3 days
9	Yes	Incomplete exclusion	5	Rupture within 4 days
10	Yes	Graft misplaced	N/A	Rupture within 4 days
11	Yes	Aneurysm excluded	35	Graft thrombosis at 6 days, no rupture
12	Yes	Aneurysm excluded	45	Graft thrombosis at 4 days, no rupture
13	Yes	Aneurysm excluded	15	Killed at 100 days
14	Yes	Aneurysm excluded	75	Killed at 94 days
15	Yes	Aneurysm excluded	60	Killed at 92 days
16	Yes	Aneurysm excluded	60	Killed at 207 days
17	Yes	Aneurysm excluded	52	Killed at 196 days
18	Yes	Aneurysm excluded	44	Killed at 189 days

Press. Diff, The difference in systolic pressure between the native aorta and the aneurysmal sac after exclusion; *GA*, glutaraldehyde.
*The first seven animals did not undergo aneurysm exclusion, whereas the last 11 did.

Postoperative management

All animals were given intravenous antibiotics for 24 hours after operation and oral antibiotics for 3 days thereafter. Postoperative analgesia was administered intravenously during the first 24 hours with butorphanol tartrate or morphine. An oral diet was resumed 24 hours after surgery. Seven to 10 days after aneurysm exclusion, anteroposterior and lateral aortograms were obtained with the dogs under anesthesia. All animals surviving aneurysm exclusion were kept alive on a long-term basis and were killed at 3 or 6 months. All animals underwent aortography at the time of euthanasia, and all animals underwent necropsy at the time of sacrifice or spontaneous death. The aortic segment containing the aneurysm and graft was harvested at the time of death in all long-term survivors and preserved in 1% formaldehyde for histologic examination.

Statistical comparison of survival data was performed by contingency table analysis.

Histologic methods

The abdominal aorta was perfusion fixed in situ with 4% buffered formalin. After excision, the aortic segment containing the stented graft was stored and fixed in 10% formalin. Histologic sections were taken from five different levels of each specimen, including sections where only aorta and stents were present proximally and distally, sections where the aorta encircled the Dacron and stents proximally and distally, and sections where the intestinal patch and aorta (aneurysm sac) encircled the Dacron graft without stents. The tissue was dehydrated with ethanol and infiltrated with glycol methacrylate compound. The tissue was mounted and cut on a Buehler Isomet low-speed saw with a diamond wafering blade (Buehler, Lake Bluff, Ill.). Sections were then mounted on petrograph slides and ground to 100 to 300 μm with a Buehler Minimet Polisher. A polishing cloth was mounted on the Minimet Polisher, and fine polishing was performed with Buehler's Metadi 9 μm aerosol spray diamond compound. The sections were then removed from the petrograph slides with acetone and remounted on standard slides for hematoxylin and eosin staining.

RESULTS

Four dogs with aneurysms created with untreated intestinal patches that did not undergo exclusion died within 18 to 42 hours after surgery (Table I). In all four animals massive retroperitoneal hemorrhage from jejunal patch rupture was documented at the time of necropsy. Among the three dogs with aneurysms made of glutaraldehyde-treated homologous intestine, two with intestinal patches preserved in 4%-glutaraldehyde for 48 hours died of aneurysm rupture at 5 and 11 days after surgery, respectively. One animal with an aneurysm made with intestinal patch preserved in 1% glutaraldehyde for 6 hours survived without rupture for 3 months until he was killed.

In two animals the aneurysm exclusion was followed by graft thrombosis caused by graft kinking at the time of deployment, which manifested as

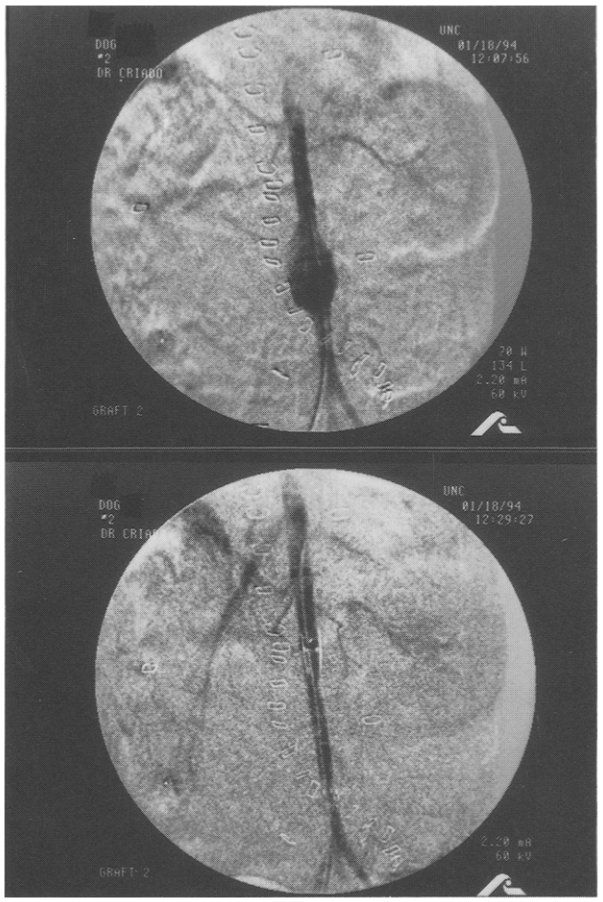

Fig. 3. Aortogram of infrarenal aortic aneurysm created in dog by suturing patch of small intestine to longitudinal aortotomy **(top)**. Completion aortogram after endovascular exclusion of aneurysm with stented Dacron graft **(bottom).**

paraplegia on the first and sixth postoperative day, respectively. In these two animals the completion angiogram revealed complete aneurysm exclusion, and the aorta-to-aneurysm pressure differential was 35 and 45 mm Hg, respectively. Both animals were killed because of their paraplegia, and at the time of necropsy both dogs had thrombosed aneurysms without any evidence of rupture. In three dogs, aneurysm exclusion was incomplete, as evidenced by opacification of the aneurysm sac and lumbar arteries directly from a focal leak coming from the proximal neck observed in real time angiography. The aorta-to-aneurysm pressure differential in these three animals was 0 to 5 mm Hg. These three dogs died at 3, 4, and 5 days after surgery of aneurysm rupture documented on necropsy.

Successful aneurysm exclusion was followed by uneventful long-term survival in six dogs. These six animals showed perfect exclusion of the aneurysm on completion angiography (Figs. 3 and 4), and their aorta to aneurysm sac pressure differential were 15, 44, 52, 60, 60, and 75 mm Hg, respectively, with a mean pressure differential of 51 mm Hg. Survival was significantly better ($p < 0.023$) in the animals with successful aneurysm exclusion without thrombosis ($n = 6$) compared with those animals with aneurysms made of unaltered intestine without exclusion or with failed exclusion ($n = 7$).

There was no evidence of infection in any of the animals in the study on the basis of clinical status, macroscopic findings at the time of autopsy, and histologic examination results. Aneurysm cultures, however, were not obtained.

Pathology results

The histologic changes associated with endovascular graft exclusion of experimental aortic aneurysms were examined at five different levels of the postmortem specimens of three dogs killed at 3 months and of three dogs killed at 6 months. All cases showed cross-sections of vessel wall with metal stents, Dacron mesh, or monofilament sutures. In the three 6-month specimens and in two of the 3-month specimens, the Dacron mesh was embedded in a fibrocellular proliferation present on both surfaces at all levels of cross-section (Fig. 5). Single fibroblasts were seen growing into, but not disrupting, the Dacron mesh. It was not possible to determine whether the fibroblasts were growing from the luminal or the abluminal surface of the Dacron or from both. The graft lumen in these five specimens was entirely patent. The thickness of the fibrointimal proliferation varied from 0.1 to 0.5 mm (mean thickness 0.25 mm). A similar but thinner fibrointimal proliferation (range 0.05 to 0.2 mm, mean thickness 0.1 mm), encased the metal stents. A cellular lining was seen on the lumenal surface overlying Dacron and stents, compatible with endothelial coverage. However, staining for factor VIII or other method to identify endothelial cells was not done. Foreign body giant cell reaction was not associated with either Dacron mesh or metal stents. In the region where the intestinal patch formed the aneurysm sac, two distinct smooth muscle cell layers of the intestinal muscularis propia were identifiable. The space between the Dacron and the intestine (aneurysm sac) was virtual and occupied by a thin layer of degenerating red blood cells and organizing scar, but no persistent thrombus was identified (Fig. 6).

The thickness and cellularity of the fibrointimal response encasing the Dacron was similar at all levels

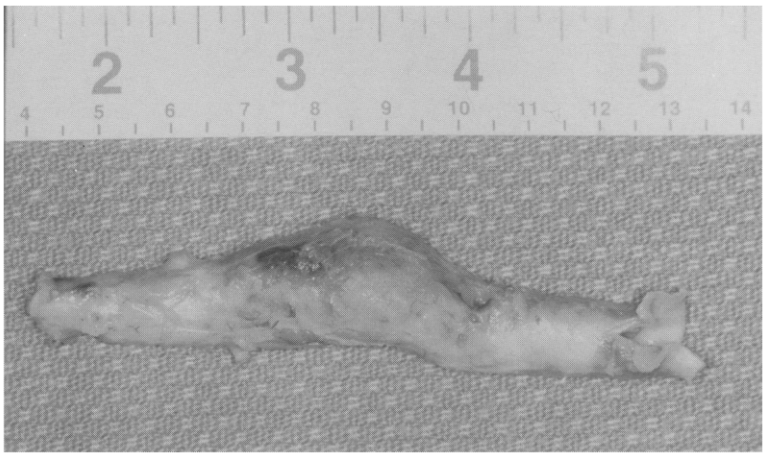

Fig. 4. Infrarenal aortic specimen, removed while patent 3 months after successful exclusion with stented Dacron endovascular graft. Note significant shrinkage of aneurysm sac relative to adjacent aorta, compared with size at implantation shown in Fig. 1.

of graft sections and not different between the 3- and 6-month specimens.

In one of the 3-month specimens, the proximal portion of the graft lumen revealed a tight stenosis (90%) occluded by a loose fibromyxoid proliferation consistent with organizing thrombus without fibromuscular hyperplasia. The remainder of the distal graft had a completely patent lumen. However, and in sharp contrast with the other five specimens, the lumenal surface contained no fibrointimal proliferation, and the cellular lining was discontinuous and sparse. In many areas Dacron mesh was covered by a thin layer of fibrin, platelets, and red blood cells. Fibrocellular proliferation was present encasing the external surface of the Dacron in this specimen.

DISCUSSION

Successful treatment of patients with AAA is measured by the complication-free long-term survival of these patients. In selected centers, the mortality rate for surgical repair of AAA is less than 5%, with a long-term complication rate less than 3%.[10] Although endovascular repair of AAA may reduce the perioperative morbidity and mortality rate for the procedure, mainly by minimizing the cardiovascular risks of the operation, the efficacy in preventing aneurysm rupture is yet to be proven, and a reduction in the long-term complications remains to be seen. This uncertainty is illustrated by a recent report by Lunsdem[11] describing the rupture of an aneurysm in a patient a few days after endovascular exclusion. Accordingly, the most important qualities of any endovascular device designed for the exclusion of AAA are effectiveness in preventing rupture and freedom from short- and long-term complications. These qualities depend on the performance of the endovascular graft-delivery system and maybe more importantly on the deployment technique. These factors need to be evaluated extensively before these devices are widely used in patients. If endovascular repair of aortic aneurysms is fraught with a significantly higher long-term complication rate and decreased graft patency rate, it would be difficult to justify its use in patients with acceptable risk for conventional operative repair. The early phase in the widespread clinical application of these devices, whenever it takes place, can produce disappointing results if the appropriate steps in their evaluation and in the acquisition of the deployment skills are not planned carefully. Animal testing of endovascular grafts and of their placement technique is an essential step for the successful clinical application of these devices.

Previous experimental studies of transfemoral aortic aneurysm exclusion with endovascular grafts focused on the technical feasibility of performing this procedure in large animals harboring surgically created aortic aneurysms in some instances,[1,3-5] or in normal animal aortas in others.[2,5] Some investigators used aneurysm models made of Dacron, sewing patches to the anterior wall of the aorta[1] or interposing fusiform Dacron cylinders in the infrarenal aorta.[4,6] Mirich et al.[3] created aortic aneurysms without using prosthetic material by balloon dilation of the aorta after surgical stripping of the tunica media. None of these aneurysm models, however, have been shown to have any tendency for rupture.

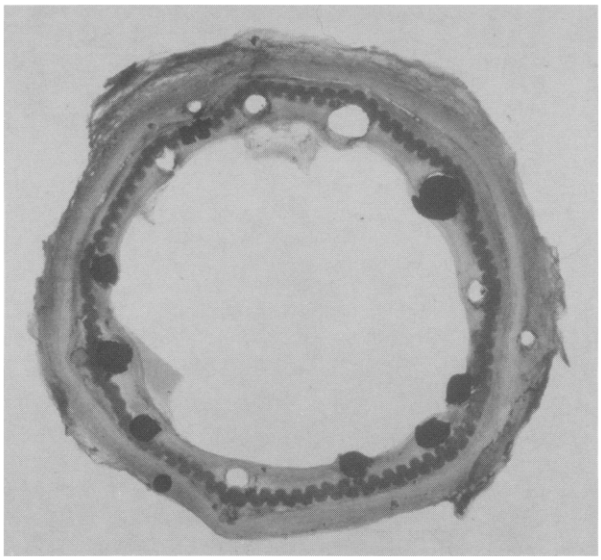

Fig. 5. Histologic section (low power) of proximal aspect of excluded experimental aortic aneurysm at 3 months after implantation. Dacron and stents are covered with fibrocellular layer on lumenal surface.

Furthermore, aortic aneurysm models without patent lumbar arteries[1,4,6] are unrealistic because the absence of branches facilitates thrombosis of the aneurysm sac even if a leak would exist at either end of the graft after endovascular exclusion. Therefore these models, although useful for the evaluation of the delivery system and graft deployment technique, cannot evaluate the efficacy of any particular device in preventing aneurysm rupture.

The various endovascular devices currently undergoing evaluation for exclusion of AAA in human beings are far from ideal and invariably will undergo modifications for improvement, whereas new devices will become available. Future new devices and modified versions of the available ones therefore will require animal testing before their use in human beings. Our aneurysm model may serve this purpose. It permits creating an aneurysm at any level of the aorta to test the deployment of any available or future endovascular graft and also can provide an immediate answer to the question of whether it can prevent aneurysm rupture. Preservation of the native aortic wall with patent lumbar arteries in the posterior aspect of the aneurysm sac and avoiding the use of prosthetic material provides a more realistic model to study the interaction between the endovascular stented graft and the host native tissues.

In accord with the recommendations of the Joint Council of the Society for Vascular Surgery/International Society for Cardiovascular Surgery Ad Hoc Committee on Reporting Standards in Vascular Surgery,[12] we used male dogs in our model. Our aneurysm model of untreated intestinal patch showed a constant tendency for rupture within a few days of its creation that occurred in all animals whose aneurysms were not excluded and in all those in whom the exclusion failed. The absence of aneurysm rupture in all the animals with successful exclusion demonstrates the effectiveness of the endovascular device used in our study.

Modification of the intestinal patch with glutaraldehyde may delay or prevent rupture of the experimental aneurysm. The mechanical characteristics of glutaraldehyde-treated tissue depend on the concentration and time of exposure.[13] Although our experience was very limited, however, we observed that intestine exposed to higher concentrations of glutaraldehyde (4%) for longer periods (over 48 hours) acquired rubberlike consistency and was stiff, difficult to suture, and likely to tear under tension. On the other hand, we observed that patches exposed to lower concentrations of glutaraldehyde (1%) for shorter periods (6 hours or less) had much better surgical handling. Such was the case in our third aneurysm created with glutaraldehyde-treated intestinal patch, which did not rupture, maintaining its aneurysmal shape for more than 3 months until the animal was killed. Further study is required to evaluate the use of glutaraldehyde-preserved intestine to create chronic aneurysms.

Graft migration after deployment is a concern with the use of endovascular devices. It did not occur, however, in any of our animals that survived long term, wherein the stent and graft remained anchored to their original aortic position bridging the aneurysm. This demonstrated the effectiveness of the stents used in our study in anchoring the graft to the aorta. In human beings, dilation of the aortic neck after aortic aneurysm repair is common, and its potential effect on dislodging the proximal stent with subsequent graft migration is a distinct possibility. In this regard, the effect of aortic enlargement on stent-graft stability requires further study in the laboratory.

Large-animal aneurysm models permit evaluation of the long-term patency of endovascular grafts and serve as a training ground before they are used in patients. In our experience, failed exclusions leading to aneurysm rupture occurred during the early part of the study. In a similar way, graft kinking, which led

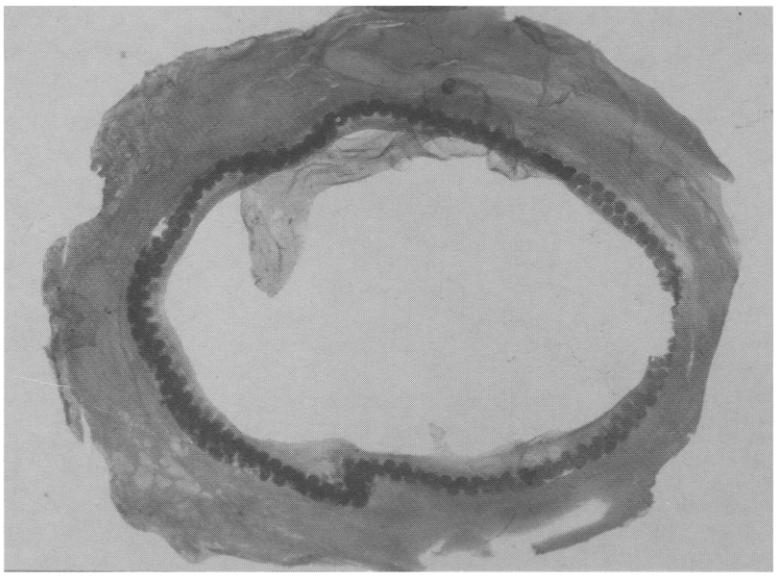

Fig. 6. Histologic section of mid portion (aneurysm sac) of excluded experimental aortic aneurysm at 3 months after implantation. Space between Dacron graft and intestine (aneurysm sac) is virtual and occupied by thin layer of degenerating red blood cells and organizing scar, but without persistent thrombus.

to graft thrombosis in two animals in spite of successful aneurysm exclusion, also occurred during the first part of our study. These technical problems during our early laboratory experience suggest that graft patency of endovascular devices may be curtailed by the technical skills in their deployment and illustrate that the learning curve involved in the proficient use of endovascular devices is likely to have an impact on their effectiveness and complication rate. It appears advisable therefore that a significant animal experience is acquired before engaging in the use of endovascular grafts for the exclusion of aneurysms in human beings. The technical demands involved in the use of bifurcated grafts for the exclusion of aortic aneurysms involving the iliac arteries are greater than those of straight grafts, therefore the learning curve required for their proficient use is likely to be longer. It is important to point out the little resemblance of this and other aortic aneurysm models with the features of AAA in human beings. The technical and physiologic problems encountered during endovascular repair of AAA in human beings may be quite different from those found in animals, and will vary depending on the anatomy of the patient and type of endovascular device used.

Histologic examination of our endovascular Dacron grafts revealed that incorporation of the graft to the luminal and abluminal surfaces was complete at 3 months after implantation, occurring in a similar fashion as that described in surgically anastomosed Dacron prostheses.[14,15] It also showed that the metallic stents were covered by the same cellular layer as the Dacron fabric. The absence of luminal coverage in one of our specimens with a tight stenosis in the proximal aspect of the graft suggests that cellular coverage of the lumenal surface may occur as a proliferative phenomenon initiated in the proximal native vessel that extends distally into the graft.

In summary, we have developed a simple aneurysm model with a predictable tendency for rupture and proved the efficacy of an endovascular stented Dacron graft in preventing aneurysm rupture. Endovascular Dacron prostheses anchored to the canine aorta with metallic stents maintain long-term patency without migration and experience rapid incorporation into the surrounding tissues, with complete fibrocellular coverage of the graft and stents. This aneurysm model is useful for the evaluation of the efficacy in preventing rupture of endovascular prostheses and of their long-term effects after implantation.

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DISCUSSION

Dr. Frank J. Veith (Bronx, N.Y.). This study addresses the crucial question: "Will endovascular stented grafts prevent aneurysm rupture?" Moreover, it does so in a cleverly designed animal model in which rupture occurs within a few days in the absence of some effective prophylactic treatment. This model also has the advantage of preserving patent branches like the inferior mesenteric arteries and the lumbar arteries that feed into the aneurysm. This kind of animal model validation is sorely needed in this field. However, Dr. Criado's model is still not perfect for proving that a stented graft will prevent aneurysm rupture in human beings for three reasons. First, if a stented graft in a patient with an aneurysm has a leak, the aneurysm may rupture late because the aortic pressure is transmitted to the aneurysm wall. Diseased human vessels may be more prone to such leaks than normal dog arteries. Indeed they are. Second, even if no leak is seen with angiography and the leak is sealed with a clot, the systolic arterial pressure may still be transmitted to the aneurysm wall, and it may rupture. This has occurred in several of Dr. Parodi's human cases. Third, if the stented graft is well seated into clot or diseased, normal-sized aorta, that aorta may enlarge, and the graft may develop a leak that may lead to rupture. This too has been observed clinically by Dr. Parodi and in one of our cases.

This leads to two conclusions. The first is that we need a model in which pressure within the aneurysm sac can be measured over the long term. The second and more disturbing conclusion is that there may be no totally valid animal model that will predict the ability of an endovascular stented graft to prevent aneurysm rupture. We will just have to find that out in patients with aneurysmal disease. Even in that perfect model it will take many years before we know because even moderate-size aneurysms, if untreated, may take many years to rupture.

Dr. Criado has performed one of the few available studies that show how endovascular grafts heal within an aneurysm. His observation that endothelium develops on these grafts is intriguing. We have also observed endothelialization of a few endovascular grafts placed within previously occluded human arteries (J VASC SURG 1995; 21:595-604).

What is the source of pressure within the excluded aneurysm? When all the branches are thrombosed, it is not clear how this pressure is generated.

Dr. Enrique Criado. I agree with the limitations of our model and with the differences between this animal model and what may happen in human beings. However, we submit this model for the evaluation of potential devices that will be appearing in the market in the future.

With regard to the potential enlargement of the arteries that may dislodge the stents and graft, we are now working in the laboratory to study further the effect of aneurysm neck enlargement on the stability of the graft. We are doing that in a pig growth model.

With regard to pressure data, our pressures were measured acutely while the aneurysm was still not thrombosed; therefore there was still a pressure transmission in the aneurysm sac at the end of the procedure. However, since the completion of this study, Dr. Marston and I have measured aneurysm pressures for several hours in acute experiments in a similar model but with large patent branches, and we found that the pressure dropped very quickly during the first few hours to equalize the pressure in the sac to that of the major branches, and there was no flow from the distal branches into the aneurysm.

Dr. Mitchell H. Goldman (Knoxville, Tenn.). How long were these intravascular grafts and are you sure the endothelialization is not just the pannus ingrowth from the end?

Dr. Criado. They were 7 cm, and they were completely incorporated from proximal to distal, and we cut these grafts at five different points with fibrointimal incorporation. Endothelialization was complete at all levels.

Dr. G. Patrick Clagett (Dallas, Texas). Where was the site of rupture in the patch?

Dr. Criado. Almost all of the animals had rupture in the middle aspect of the patch. A couple of the grafts ruptured at the anastomotic site by where the stitches were placed.