A New Animal Model for Abdominal Aortic Aneurysms: Initial Results Using a Multiple-wire Stent

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Objectives: The effect of a plain 48-wire self-expanding flexible stent (Wallstent-Schneider (Europe) AG) on abdominal aortic aneurysms has been studied in a new animal model.

Methods: Aneurysms were created by interposing fusiform segments of glutaraldehyde-tanned bovine internal jugular vein into the infrarenal aortas of 12 Large White pigs. The first six pigs were assessed after 6 weeks by ultrasonography and arteriography; they were then sacrificed for pathological examination. Endovascular placement of the stents, 2 weeks after aneurysm creation, was performed under arteriographic control in the next six pigs. These pigs were assessed by ultrasonography and arteriography 6 weeks after stenting; they were then sacrificed for pathological examination.

Results: At 6 weeks the aneurysms in the first group were pulsatile with partial endothelialisation and no mural thrombus. Placement of the stent in the second group was accomplished easily. Stenting resulted in an immediate reduction in wall pulsatility of all aneurysms and thrombosis of the excluded aneurysm sac occurred in three cases. In the other three cases the pulse pressure in the sac was reduced. In all cases there was a significant reduction in maximum aneurysm diameter when measured 6 weeks after stenting.

Conclusions: A pulsatile, non-thrombogenic aortic aneurysm model approaching human dimensions has been successfully developed for the study of endoprostheses prior to their clinical use. Endovascular placement of a plain, multiple-wire Wallstent was associated with reductions in aneurysm pulsatility, pulse pressure within the sac and maximum aneurysm diameter over the study period. Stenting was associated with thrombosis of the excluded aneurysm sac in 50% of cases.

Key Words: Aortic aneurysm; Animal model; Endovascular stent.

Introduction

There is currently widespread interest in the endoprosthetic management of abdominal aortic aneurysms. The use of endovascular grafts was first proposed by Dotter in 1969¹ but recently investigators have concentrated on the transfemoral intraluminal placement of graft/stent combinations using either self-expanding Gianturco or balloon-expandable Palmaz-type stents to anchor standard graft material within the lumen of the aneurysm.²-⁸ These graft/stent combinations are bulky and require large-calibre delivery systems that would make their use difficult in the presence of tortuous or severely diseased iliac arteries.

The development of newer multiple-wire, flexible, self-expanding stents for occlusive arterial disease raises the question of their applicability to the treatment of abdominal aortic aneurysms. In theory, a stent with a large enough number of wires would provide the barrier required to reduce or eliminate pulsatility and expansibility of an aneurysmal aorta without the addition of cumbersome graft material. The investigation of this thesis required the development of a new animal model since all existing models have used either an interposition graft of tailored Dacron, or a floppy Dacron patch aortoplasty neither of which exhibits inherent pulsatility. The new animal model and the initial results with the 48-wire Wallstent (Schneider (Europe) AG) are presented.

Materials and Methods

Animal model

Various biological materials were investigated in a pilot study in order to determine the most suitable for the formation of aneurysms in the infrarenal aortas of Large White pigs. The use of 60kg Large White pigs provides native infrarenal aortas of approximately 10mm diameter which allows the study of readily
available stents. The aortic diameter in these pigs increases to approximately 14mm over the period of study and the desired ratio of native aortic diameter to aneurysm diameter was at least 1:2. The most suitable material was found to be glutaraldehyde-tanned bovine internal jugular vein which has a natural diameter of 20mm. Initially this was used as a straightforward interposition graft but later larger aneurysms were produced by performing tailored segments of jugular using continuous 4/0 polypropylene suture material (Fig.1). These grafts were stored in 2% glutaraldehyde until 30 min before implantation at which time they were washed in 0.9% Sodium Chloride solution.

Sixty kilogram female Large White pigs were sedated with Azaperone 8mg/kg i.m. and anaesthesia induced by propofol 2.5 mg/kg i.v. The animals were then intubated and maintained on oxygen and Halothane 2-4% with clinical monitoring. Intravenous access was obtained and an infusion of Haemaccel started at a rate to allow the administration of 500ml over the period of the subsequent operation. This pigs were secured supine on the operating table and a laparotomy performed through a lower midline incision. Exposure of the infrarenal aorta was facilitated by the use of a table-mounted retractor system. The infrarenal aorta was dissected free of surrounding structures and it was normally necessary to ligate in continuity one of the lumbar arteries which arose singly from the dorsal aspect of the aorta in this region. After the administration of Heparin 5000 IU i.v., the infrarenal aorta was clamped and transected. The excision of a 2cm segment of aorta resulted in a defect of approximately 5cm owing to spontaneous retraction of the cut ends. The preformed, tanned and washed bovine jugular graft was then inserted as an interposition graft using 4/0 polypropylene suture material proximally and distally. The clamps were removed and, after haemostasis had been secured, the abdomen was closed using a loop 1 polydioxanone mass closure and subcuticular 2/0 polyglycolic acid suture material without reperitonealisation of the aorta/graft. The pigs were allowed to recover.

After a 2-week interval the pigs received a short general anaesthetic enabling them to be screened supine using Duplex and B-mode ultrasound to assess blood flow through the aneurysm and to measure the maximum diameter of the sac. Once more the pigs were allowed to recover. Six weeks later, the pigs received a similar general anaesthetic and were screened supine using Duplex, M-mode and B-mode ultrasound (Fig.2), and arteriography via a femoral artery cut-down (Fig.3). The animals were then sacrificed by administration of an overdose of intravenous pentobarbitone and subsequent exsanguination. At laparotomy, the aneurysm and attached lengths of native aorta were excised for histological examination.

Stenting

Aneurysms were created in a further six pigs using the method described above. After a 2-week recovery period each pig was reanaesthetised and screened using Duplex, M-mode and B-mode ultrasonography. The left common carotid artery was then exposed and aortography was performed by this route after direct arterial puncture. Using a roadmapping technique, a 14mm diameter 48-wire Wallstent (Fig.4) was then placed across the aneurysm sac aiming to deploy a 1cm length of stent in normal aorta both proximally and distally (Fig.5) After satisfactory positioning of the stent the delivery system was withdrawn and the common carotid artery ligated in continuity. The cervical wound was closed using subcuticular 2/0 polyglycolic acid suture material and the pig was recovered.

Six weeks after stenting, each pig was reanaesthetised and the aneurysm/stent complex examined using Duplex, M-mode and B-mode ultrasonography and aortography via the right common carotid artery. A laparotomy was then performed and the pressure within the aneurysm sac was compared with that within the stent lumen using a standard invasive blood pressure monitor via a 21G needle and extension tube. The pig was sacrificed by administration of an overdose of pentobarbitone followed by exsanguination and the aneurysm was removed along with the contained stent and attached normal vessels for histological examination. All animals had venous
Fig. 2. B-mode ultrasound appearance of the aneurysm at 6 weeks (sagittal plane).

Fig. 3. The appearance of the aneurysm at aortography.
blood taken for the estimation of urea and electrolytes at the time of stenting and again at sacrifice.

Results

Animal model

After removal of the clamps the aneurysms were immediately pulsatile and remained so on M-mode ultrasonography 6 weeks later. There was no significant change in maximum aneurysm diameter measured on B-mode ultrasonography at the beginning and end of the study period. Duplex imaging after 2 weeks and immediately prior to sacrifice demonstrated high-flow jets at the proximal and distal anastomoses with turbulent flow in the sac itself. No mural thrombus was identified on ultrasonography, arteriography or at histological examination (Fig.6). The high-flow jets recorded on Duplex imaging suggested that tight anastomoses had been created but histological examination of the anastomoses revealed the cause to be fibrointimal hyperplasia. Histological examination of the sac wall demonstrated a florid inflammatory reaction with foreign body giant cells. Scanning electron microscopy demonstrated endothelialisation at the anastomoses for a distance of approximately 10mm but no epithelium at the centre of the grafts. The median length of aneurysm was 30mm (range 27–34). The median diameter of aneurysm was 25mm (range 16–34) with an approximate aorta:aneurysm diameter ratio of 1:2.

During the development of the model, two pigs suffered caudal paraplegia within 24 h of aneurysm creation and another animal died from spontaneous rupture of the aneurysm 3 weeks after aneurysm creation. In both cases of paraplegia it was noted that more than one lumbar artery had been ligated at the time of aneurysm creation.

Fig. 4. The 48-wire Wallstent (Schneider U.K.).

Fig. 5. Aortography on completion of stent deployment. Note the low concentration of contrast within the excluded aneurysm sac (arrows). Same case as Fig.3.
Stenting

The first stent placed was overlong and deployed incorrectly such that it extended into the left common iliac artery and covered the origin of the right renal artery. All subsequent stents were reduced in length to approximately 7cm (deployed length). In one later case the stent was released slightly prematurely and fell short proximally; a second concentric stent was therefore placed more proximally to completely exclude the aneurysm sac. This second stent covered the origins of both renal arteries. In both cases, 6 weeks after stenting, there was no disturbance of renal artery blood flow at arteriography and renal function remained normal according to urea and electrolyte estimation. Similarly, in the first case, there was no diminution of blood flow in the covered right common iliac artery when compared with the stented contralateral vessel by arteriography either immediately or 6 weeks after stenting. Attempts at quantifying blood velocity in the vessels concerned using Duplex imaging were unsuccessful since it proved impossible to accurately insonate such small vessels in the retroperitoneum.

All other stents were placed correctly with ease and the anastomotic stenoses apparent on Duplex imaging and arteriography immediately prior to stenting became less obvious after deployment of the self-expanding stent. In all cases there was an immediately apparent subjective diminution of blood flow within the aneurysm sac at completion arteriography associated with a reduction in pulsatility of the aneurysm on M-mode ultrasound examination. At sacrifice, aneurysm pulsatility was abolished on M-mode ultrasound examination in all cases and in three cases there was thrombosis of the excluded aneurysm sac visible on B-mode ultrasound examination and confirmed on arteriography. Measurements of maximal aneurysm diameter made with B-mode ultrasound before and 6 weeks after stenting demonstrated a significant reduction in aneurysm size over the period of study irrespective of whether or not the aneurysm was thrombosed. These data are presented in Table 1. It proved impossible to satisfactorily image flow patterns in the stent lumen and sac using Duplex owing to interference caused by the stent. Direct pressure measurements at sacrifice demonstrated a reduction in systolic, diastolic and pulse pressures in the aneurysm sac when compared to those within the stent lumen (Table 2).

Histological examination of the specimens obtained at sacrifice confirmed thrombosis in those aneurysm sacs which had appeared excluded on ultrasonography and aortography. There was almost complete endothelialisation (approximately 90%) of the stent in all cases as demonstrated by scanning electron microscopy (Fig.7).

Table 1. Change in maximum aneurysm diameter measured by B-mode ultrasound before and 6 weeks after stenting.

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<th>Fig no</th>
<th>Aneurysm Diameter (mm)</th>
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Discussion

The animal model described provides a reliable, fusiform, non-thrombogenic aortic aneurysm which is immediately pulsatile and remains so at 6 weeks. This has been used to investigate the applicability of a new multiple-wire self-expanding vascular stent to the treatment of aortic aneurysms.

Several problems were encountered in the development of the animal model. The most important problem was the occurrence of caudal paraplegia if more than one lumbar artery was ligated at the time of aneurysm creation. Simple modifications of operative technique obviated this and other minor problems and resulted in the successful model presented.

The 48-wire Wallstent (Schneider (Europe) AG) using a one-stage 11.5F delivery system proved easy to use with the majority of stents being deployed correctly and without difficulty. The stent produced a
haemodynamic effect which reduced pulse pressure and peak pressure within the sac in all cases and resulted in thrombosis of the excluded sac in half of them. It must be presumed that the changes seen within the sac are the result of turbulent flow within a closed space. It is also possible that the haemodynamic effect of the stent within the aneurysm was increased shortly after deployment through thickening of its...
wire elements by endothelialisation, accounting for the successful exclusion of sacs which were not immediately excluded. Stenting also produced a significant reduction in maximum aneurysm diameter of all aneurysms whether thrombosed or not. Presumably this is a pressure-related effect rather than the fibrosis of chronic inflammation since no similar change in size was noted over the same period in the initial development of the animal model.

Interestingly, the inadvertent placement of a stent across the origin of a renal or iliac artery resulted in no obvious reduction of blood flow within that vessel according to the crude methods of assessment used. Similarly there was no alteration of renal function when the origins of one or both renal arteries were covered by the stent. It would appear that the haemodynamic changes induced within the aneurysm sac do not affect the flow in normal vessels whose origins are covered by the stent provided that those vessels have adequate run-off. Unfortunately it proved impossible to quantify the blood flow or velocity in renal or iliac arteries whose origins had been covered since we were unable to accurately insonate these vessels using Duplex and we had no access to flowmetry. A study is currently in progress which will provide data to substantiate our initial observations.

Increasing the number of wires in the stent would presumably lead to an increase in its haemodynamic effect. This would probably increase the proportion of aneurysm sacs which thrombose after stenting without the need for a bulky outer graft but would risk the occlusion of any vessel whose origin was covered inadvertently. This is particularly important in the region of the aneurysm neck and aortic bifurcation where it may be necessary to cover the origins of the renal and common iliac vessels in order to achieve adequate stent fixation. In addition, simply increasing the number of wires in the stent would also increase its bulk and the size of delivery system required, thereby limiting its clinical usefulness.

If an increased number of elements in the stent were provided by forming a co-woven metal/polyurethane or metal/PTFE stent then there would be an insignificant increase in bulk of the finished product which could be deployed using the same relatively small 11.5F delivery system employed with the Wallstent. This delivery system is narrow and flexible enough to be advanced through tortuous or severely diseased iliac arteries. While this would effectively solve the problems of stent delivery and sac exclusion the risk of inadvertent renal or iliac vessel occlusion would remain. It would appear that the ideal device would be a multiple-wire, self-expanding stent with a co-woven central portion intended to lie within the aneurysm but with a short length of plain stent remaining at each end for adequate purchase on normal vessel proximally and distally. As shown in this study, these plain stent portions could be placed over the renal artery origins or aortic bifurcation without risk of their occlusion.

In conclusion, we have presented a new animal model which provides a fusiform and non-thrombogenic aortic aneurysm which is immediately pulsatile and remains so at 6 weeks. It is apparent that a simple multiple-wire, self-expanding stent produces a haemodynamic effect on blood flow and pulse pressure within an aneurysm sac but does not affect such parameters in normal vessels whose origins it covers.

References


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