Comparative Study of Two Surgically Created Swine Models of Abdominal Aortic Aneurysm

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Citation

Abstract
Our aim was to compare two surgically created AAA models, to determine which one of them could be more useful in the development and training in endovascular techniques. Ten pigs underwent the creation of infrarrenal AAAs with autologous peritoneal (Group A (n=5)) or gastric serosa (Group B (n=5)) patches. Serial angiograms and ultrasonograms were obtained to measure aneurismal diameters over time. On day 90, animals were euthanized for pathological evaluation. The surgical procedure took significantly (p=0.022) longer to complete in group B. Survival times were longer in group A. Both models exhibited an increase in diameter during the first third of the follow-up period (up to a 243% of the original diameter in group A and a 216% in group B) that subsequently stabilized. The peritoneum model is technically easier to create, and it exhibits higher postoperative dilatation, so it could be more useful in the short term development, training and evaluation of new endoprostheses.

INTRODUCTION
Abdominal Aortic Aneurysms (AAA) represent a major cause of death in modern society. In 2003, AAA rupture was recognized as the 12th leading cause of death in people aged 65 or over in the U.S. As the population ages, so does the incidence and prevalence of AAA.

Since the first endovascular AAA exclusion was reported in 1991, the technique has been increasingly used and accepted by the medical community, especially in high risk patients, and in spite of several drawbacks and limitations of this therapeutic approach having been described. Varied designs of endografts have been developed with modifications to suit various anatomic locations and morphologic variations. All new devices need to be evaluated, as preclinical testing may be useful to screen out poor designs prior to clinical use, and after the first clinical trials animal testing could help in analysing clinically observed failures and in evaluating device modifications.

Minimally Invasive procedures for AAA therapy, including laparoscopy, are relatively new, and are therefore still under development. An animal model of AAA that could be used both in research and training in these procedures would be helpful in defining the role of each technique, as well as in exploring future possibilities, such as combined therapies, both in terms of combining endovascular with laparoscopic approaches and in regards to the use of drug-eluting stent grafts.

It has been recommended that animal studies of endovascular grafts focus on the assessment of the delivery systems and biological responses to the device. Different animal models of AAA have been described in the literature. However, many of them are not adequate for assessing tissue incorporation or inflammatory responses to deployed grafts, having been created with either synthetic or treated tissues. Other models do not exhibit aneurysmal growth and subsequent tendency to rupture, and therefore the protection from rupture conferred by an endograft cannot be evaluated in these models.

For a AAA model to be useful, it should maintain patency of collateral vessels and exhibit a predictable growth capacity and tendency to rupture. Moreover, its induction should be technically reproducible and, if possible, take into account animal welfare considerations. Our group has previously...
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worked with two different surgical models of AAA. In order to determine which one of these models better meets the requirements listed above, they should be compared under similar environments and with an exhaustive follow up regimen. To our knowledge, no in deep comparison has been made to date between any two models. Thus the aim of this study was to compare two surgically created models of AAA, in order to determine which one of them would be more useful for AAA therapy investigation and training.

MATERIAL AND METHODS

Ten Large White swine, with a mean weight of 40.45±9.18 kg were used for this study. The protocol was approved by the Institutional Ethical Committee for Animal Research, and it complied fully with the Guide for the Care and Use of Laboratory Animals.

Animals were randomly allocated to two groups of five pigs each. An infrarrenal Abdominal Aortic Aneurysm was created in all animals by suturing a patch of autologous tissue to an incision made in the anterior aortic wall. In Group A, the patch was composed of peritoneum, and in Group B gastric serosa was used.

Preprocedural dorsoventral and lateral aortograms were obtained in all cases. While under general inhalant anesthesia, the pigs were fixed at the operating table in supine decubitus with caudal extension of the hind limbs. Under sterile conditions, a right femoral arterial access was established using the Seldinger technique and a 6 Fr introducer sheath was placed percutaneously into the femoral artery. Under fluoroscopic guidance (Philips Mobile Digital Angiographic System-BV300, Philips, Inc. Netherlands), a 5 Fr marked pigtail catheter (Royal Flush II; Cook Inc. William Cook Europe A/S, Denmark) was introduced over a 0.035” hydrophilic guide wire and positioned into the abdominal aorta approximately two centimeters cranially to the origin of the renal arteries. Dorsoventral digital subtraction abdominal aortography was performed using 30 ml of 76% Urografin (Schering Inc., Germany) at an injection rate of 15 ml/sec. The diameter and length of the infrarrenal aorta were measured and calibrated by measuring the distance between two of the radiopaque markers on the catheter to adjust for magnification. Once angiography was completed, surgery began. The techniques used to create both models have been previously described. Both surgical techniques differ mainly in the material used for the aortic patch. In summary, a midline laparotomy was performed in both groups and the patches were harvested. In group A, the peritoneum was harvested using blunt dissection to obtain a 6cm width piece of peritoneum that was carefully separated from the abdominal fascia and cleaned of all fatty tissue. The patch was folded on itself by its main axis with the visceral surfaces facing outwards and interrupted 3/0 polypropylene sutures were used to fix both layers. This patch was tailored into an oval shape and submerged in saline while the aorta was being dissected (Figure 1).

Figure 1

Figure 1: Peritoneum patch preparation. A section of peritoneum was harvested from the ventral abdominal wall. The patch was folded in itself by its main axis, both layers were sutured together with interrupted suture and the peritoneum was then tailored into an oval shape.

In group B, the stomach was exteriorized through a long midline laparotomy, and a 12x3 cm rectangle was delineated on the gastric surface using diathermia. Blunt dissection was then used to separate the serosa patch from the gastric wall. After obtaining the patch, the greater omentum was used to cover the denudated gastric surface. Patch tailoring was performed in a manner similar to that used in group A, but this patch was folded by its lesser axis with the visceral surface on the outside. After cutting the double layered serosa patch into an oval shape, it was submerged in saline to avoid its dessecation while the aorta was being dissected (Figure 2).
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Figure 2

Figure 2: Serosa patch preparation. After exposure of the stomach, a 12x3cm rectangle was delineated on the gastric wall to guide dissection of the patch. Once obtained, the patch was folded on itself by its lesser axis and both layers sutured together using interrupted polypropylene suture. The patch was cut into an oval shape and submerged in saline until its use.

Once the infrarrenal aorta had been dissected, from the level of the renal arteries to the bifurcation, 150 UI/kg of heparin were administered to all the animals. 5 minutes after systemic heparinization, all lumbar arteries in the infrarrenal aortic segment were temporary occluded using small Diffenbach clamps, and the aorta was crossclamped immediately below the origin of the caudal renal artery. A silicon loop was placed immediately cranial to the inferior mesenteric artery to avoid backbleeding. The peritoneum and serosa patches were sutured to a 5-6 cm long incision performed in the anterior aortic wall using 5/0 polypropylene running suture. Special care was exerted at this step to include both layers of the patch in the suture. Once the suture was completed, the lumbar clamps and the distal silicon loop were removed and the junction between the patch and the aorta carefully observed for bleeding before removing the Satinsky clamp. Whenever it was considered necessary, hemostatic sutures were applied to reinforce the original suture line.

Completion angiography was performed using the above described technique immediately before closing the laparotomy and recovering the animal. Lateral and dorsoventral aortic diameters were measured in all angiographies. A successful aneurysm model was defined by at least a 1.5-fold increase in diameter compared to the diameter of the native aorta, as demonstrated by angiography.

During anesthetic recovery, animals were observed for any signs of excessive postoperative pain, in which case 10 µg/kg of buprenorphine were administered IM.

Follow up ultrasonographic and angiographic examinations were carried out on days 7, 14, 30, 45, 60 and 90 after model creation in all surviving animals. In each case, longitudinal B Mode and Doppler (Power and spectral analyses) ultrasonographic examination of the aneurysmal vessel was performed (The Panther Ultrasound Scanner type 2002, B&K Medical A/S, Gentofte, Denmark) using a curved array 5MHZ probe (Type 8534, B&K Medical A/S, Gentofte, Denmark) placed on the animals’ left flank. Aortography was then performed in both dorsoventral and lateral views. Aneurysmal diameters were measured by both imaging techniques in all examinations.

Three months after model creation animals were euthanized with a lethal dose of intravenous KCl while under general anesthesia, target arteries harvested and pathological examination performed. Specimens were stained using Hematoxilin-Eosin, and were then observed under light and fluorescence microscope, in order to better image elastic tissue.

Quantitative variables studied in this protocol were: total surgical time (measured from the moment the arterial access was established to the removal of the sheath after finishing the whole protocol), aortic cross-clamping time, survival times and aortic diameters thorough the study, as obtained with dorsoventral and lateral angiography and longitudinal ultrasonography. These data are expressed as mean ± standard deviation (S.D.) for each experimental group at each interval. Differences in these variables obtained at each interval, both intra and intergroups, were studied using non-parametric Wilcoxon test, at a significance level of p<0.05. Qualitative data, such as the quality of recovery from anesthesia in each group, thrombus formation inside the aneurysmal sacs and pathological examination of the patches after follow-up were also studied.

RESULTS

All the animals survived the surgical procedure, that took significantly longer to complete in Group B (194±23.82 minutes in group A versus 233±23.61 minutes in group B. p=0.022). Cross-clamping time was similar in both groups (Group A: 70.40±10.71 minutes and Group B 71.80±12.13 minutes). Completion angiograms demonstrated saccular aneurysms in all animals (Figure 3 A and B).
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Figure 3
Figure 3: Post procedural angiography demonstrated saccular aneurysms in all cases. 3A: Lateral angiogram obtained immediately after AAA model creation using a peritoneum patch. 3B: Dorsoventral angiography obtained immediately after AAA model creation in group B.

Mean aortic diameters obtained using angiography are shown in Table 1. In all cases, the angiographic criterion for successful aneurysm creation was met. Group A evidenced a 69.7% increase over the original diameter (from 9.72±1.56 mm to 16.5±4.24 mm) in the DV angiogram that reached up to a 73.3% increase over the original diameter (from 9.74±1.63 mm to 16.88±2.67 mm) in the lateral projection. Group B aneurysms were smaller, reaching up to a 63.1% increase (from 8.14±2.14 mm to 13.28±1.18 mm) in the dorsoventral view and a 61.1% increase (from 8.44±2.34 mm to 13.6±1.69 mm) on the lateral angiogram. This difference in aneurysmal diameters between groups only reached statistical significance in the lateral projection (p=0.029).

Figure 4
Table 1: Angiographic measurements in millimeters of aneurysmal diameters obtained during follow-up. Mean Â± Standard Deviation. DV: dorsoventral projection. Lat: lateral projection. *: Intragroup comparisons: Significant differences between means were observed at these intervals (p<0.05). †: Intergroup comparisons: Significant differences between means were observed on the postoperative study and on day 14 (p<0.05).

Anesthetic recovery was uneventful in all animals. Group A pigs needed only one dose of postoperative analgesia in all cases but one, where a second dose was deemed necessary. Group B animals, however needed two analgesic doses in all cases. Feeding was resumed in the peritoneum group 24 hours (n=2) or 48 hours (n=5) after the surgical procedure, whereas in the serosa groups animals did not accept the offered food until 72 hours (n=3) or 96 hours (n=2) after AAA model creation.

There were two cases of postoperative paraplegia in this study, one from each experimental group. Aortic cross-clamping times in the affected animals were 61 minutes in the peritoneum model and 52 minutes in the serosa model. The paraplegic animal from group A died on the 19\textsuperscript{th} postoperative day of aneurysmal rupture. The pig from group B presenting with paraplegia was euthanized 30 days after model creation, because it presented with evident muscular atrophy of the hind quarters and a worsening general condition.

Survival times were longer in Group A, where only the above mentioned animal died of aneurysmal rupture on postoperative day 19, whereas two animals died of this cause in Group B, on days 6 and 10. This represents a 20% rupture rate on the peritoneum group Vs a 40% rupture rate on the serosa group. The postmortem examinations evidenced hemoperitoneum in all three animals, and a rupture site
could be identified in the patches away from the suture line.

In all cases, angiographies performed during follow-up demonstrated continued patency of collateral vessels, without any image suggesting the existence of thrombus inside the aneurysmal sacs in any animal (Figure 4 A and B).

**Figure 5**

Figure 4: All collateral vessels remained patent during follow-up. No angiographic evidence of thrombus could be seen in any animal thorough the three months study period. 4A: Peritoneum. 4B: Serosa.

Both models exhibited similar postoperative behaviour, evidencing an increase in diameter during the first third of the follow-up period. This trend was more evident in the peritoneum group, which reached up to a 243% of the original diameter on day 14. Group B aneurysms were smaller, with the maximum dilatation reaching up to 216% of the original diameter. Figure 5 illustrates the evolution of mean aneurysmal diameters measured by lateral angiography. As can be observed in this figure, after day 30 no further aneurismal growth was observed. Despite Group A aneurysms being consistently larger, intergroup differences in aneurysmal dimensions obtained during follow up only reached statistical significance on day 14 (p=0.017).

**Figure 6**

Figure 5: Aneurysmal diameters obtained during follow-up using lateral angiography. Group A is represented by a broken line, and Group B by a solid line. * Significant differences in diameters were observed on day 14 (p<0.05).

Ultrasonographic follow-up allowed visualization of the operated vessels and surrounding tissues in all cases. B Mode scans did not show any image suggesting the existence of thrombus inside the aneurysmal sacs in any animal. Aneurysmal diameters were measured in longitudinal power Doppler images (Table 2), and the results confirmed the tendency observed using angiography, with Group A diameters consistently, but in this case not significantly, larger than Group B diameters. No statistically significant differences were observed either in ultrasonographic measurements obtained thorough follow-up as regards to measurement times. The maximum diameters observed were 19.60±2.84 mm on day 14 (Group A) and 17.17±2.93 mm, on day 30 (Group B). These diameters then decreased, stabilizing by the second half of the follow-up period (from day 45 onwards).
Figure 7
Table 2: Ultrasonographic measurements of aneurysmal diameters obtained during follow-up (longitudinal scan). Data expressed in millimeters. Mean ± Standard Deviation.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 7</td>
<td>18.04±3.52</td>
<td>15.25±2.02</td>
</tr>
<tr>
<td>Day 14</td>
<td>19.60±2.84</td>
<td>16.33±6.62</td>
</tr>
<tr>
<td>Day 30</td>
<td>18.75±3.30</td>
<td>17.17±2.93</td>
</tr>
<tr>
<td>Day 45</td>
<td>16.12±1.89</td>
<td>15.00±0.71</td>
</tr>
<tr>
<td>Day 60</td>
<td>15.87±2.06</td>
<td>15.50±2.12</td>
</tr>
<tr>
<td>Day 90</td>
<td>16.37±4.95</td>
<td>15.50±1.41</td>
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</table>

Pathological results were very similar in the two studied groups. Typically, the animals that completed the study (2 from the serosa group and 4 from the peritoneum group) evidenced the same histological appearance. Three clearly defined areas could be identified in these specimens. The dorsal part, corresponding to the native aortic wall, showed the typical three layered arterial structure, with a slight irregular thickening of the intimal layer in an otherwise normal appearing healthy aorta. Intimal thickness increased towards the junction between the aorta and the serosa and peritoneum patches. In this area the internal elastic membrane was interrupted, and an inflammatory infiltrate with foreign body reactions related to the suture material could be identified in all specimens. Calcified and necrotic foci were also present in some cases. The typical lamellar structure of the media was also interrupted in this area. The ventral area of the specimens, where the patches were located, showed considerable thickening, primarily due to collagen fibers and fibroblastic-myofibroblastic cells. No clear organization in layers could be identified in this area, and there was no evidence of internal elastic membrane. The luminal surface was smooth and covered by an endothelium that did not appear to be differentiated from the one lining the native aortic wall. No sign of thrombus formation was seen inside the sacs in any animal.

Histological findings in the animals that did not complete the three months follow up vary in relation to the survival times. The paraplegic animal from group B, that was sacrificed on day 30, presented microscopical appearance very similar to the above described findings, but the changes are less evident, with less intimal thickening at the native aortic wall and also less thickening in the serosa patch. The inflammatory infiltrate was, however, more abundant in this animal.

The three pigs dying prematurely from aneurysmal rupture presented a different histological appearance when compared to the other samples. No evidence of endothelial lining could be seen in any of these specimens, and extravasated red blood cells were abundant in all three. In the animals that died on days 6 and 10 (Group B), the two layers of the serosa patch could be identified, with some proliferation of immature fibroblastic cells. In the animal that died on day 19 (Group A) these two layers could not be identified. However, no other clear difference could be seen between the patches. In all cases, the rupture sites were identified away from the suture line, and focal thinning of the patches with progressive disappearance of the collagen fibers could be seen at these areas.

DISCUSSION
Abdominal Aortic Aneurysms are gaining importance as causes of death in developed countries. There is a considerable percentage of affected patients presenting with significant comorbidities, which in many cases place them at high risk for surgery, even disqualifying them for conventional surgical operation. Minimally Invasive therapies offer an accepted alternative for these patients. However, these therapies are still evolving. An aneurysmal model representative of the human condition would be needed for preclinical screening of endograft designs, and in the development of new or modified prostheses or therapeutical strategies.

Although it has been recognized that preclinical testing of endovascular grafts is not always 100% predictive of clinical performance, it is the only way to assess, albeit imperfectly, biological responses to different therapies, providing at the same time a useful tool for training in their application.

Among the models previously described, we have focused on comparing two surgically created experimental AAAs, in order to determine which one of them could be more useful in the development and training in endovascular techniques for aortic aneurysm exclusion.

The main difference between the two studied models lies in the material chosen to create the patches. The choice of
either peritoneum or gastric serosa for the models creation was based on these tissues’ embryologic origin. In the early embryologic stages, the mesoderm differentiates into two kinds of epithelial cells: on the one hand, the mesothelial tissues, covering the body's internal cavities (such as the peritoneum, gastric serosa, etc.), and on the other hand the endothelium, lining the internal surface of heart and vessels. In the early nineties, it was reported that mesothelial cells cultured from human peritoneum can secrete prostacyclin, just as vascular endothelial cells do (9). There are some previous reports of the use of peritoneum for vascular reconstruction in both the venous and the arterial systems. Despite no similar studies having being found in the literature using gastric serosa in the vascular system, the common embryologic origin and function to avoid friction between visceral surfaces within the abdominal cavity suggest that, as with peritoneum, serosa should not cause excessive thromobogenic reactions when used as a patch in the arterial system. 

The surgical procedure was technically more demanding in the serosa group, which resulted in significantly longer surgical times in these animals. This was mainly attributable to the time needed for harvesting the patch. The peritoneum was easy to harvest in all cases, whereas the serosa, a fine and delicate membrane, required extremely careful dissection to avoid its rupturing. Previous reports do not normally focus on surgical times when creating an experimental AAA model. In our opinion, however, this information is important, and should be included when reporting experimental works performed with animals, as it may have direct impact on the animals' welfare and postoperative course.

Aortic crossclamping times were similar for both experimental groups, with 70.4±10.71 minutes in Group A and 71.80±12.13 minutes in Group B. These times are amongst the highest found in the literature. Only in the previous work conducted with peritoneum in AAA modeling are longer crossclamping times reported.

Aortic occlusion times may be related to the risk of postoperative paraplegia. Transient of permanent neurological deficits secondary to aortic cross-clamping are a recognized risk in aortic surgery. In human, the risk of medullar lesions is related, amongst other reasons, to the level of occlusion, so its occurrence is relatively rare in abdominal aortic surgery. In animals, however, medullar irrigation is mostly carried by the lumbar arteries, thus increasing the risk of paraplegia during aortic interventions. Based in previously reported data, where only one pig out of 27 developed paraplegia (3.7%) when aortic crossclamping was performed at the same level as in the present study and for even longer times (78±16 minutes), we did not consider necessary to perform any medullar protection manoeuvres when undertaking the present study. Postoperative paraplegia was observed, however, in two animals of this series, reaching a 20% rate (one from each group). As stated above, these animals were not those subjected to longer aortic occlusion times. In view of these results, we think that the risk of paraplegia secondary to aortic crossclamping in the pig is probably related to individual characteristics, such as sensitivity to ischemic-reperfusion metabolites, variations in vascular anatomy, etc. These points were not, however, addressed in the present study, so no conclusions can be drawn from it regarding this subject.

The two AAA models under study were created by suturing autologous tissue patches to the anterior aspect of the abdominal aorta. Several previously reported models use similar patch techniques with varying results. The highest postoperative dilatation obtained with this surgical technique was reported by Wu et al., who created aneurysms that reached up to 168.7% over the original diameter. In our case, aortic diameter after surgery increased to a mean 73.3% over the original measurement on the lateral view in Group A, and to 61.1% in Group B. Despite having used the same dimensions when tailoring the patches, Group B aneurysms were smaller. This may be attributed to the difficulty encountered when manipulating the serosa patches, that may have forced the surgeon to inadvertently include more patch material in the suture to avoid its rupturing or bleeding through the suture line. On the other hand, when declamping, dilation of the sac was found to be subjectively greater in the peritoneum model.

Postoperative recovery was subjectively assessed, and it was found to be clearly superior in the peritoneum models. Group A animals accepted the offered food earlier, and needed less postoperative analgesia. When using experimental animals, utmost care must be taken to assure animal welfare and humane conditions for the animals. Therefore, if two models exhibit similar characteristics, the model that causes less pain and distress to the experimental subjects should be preferred. It is important to note that the two animals that developed paraplegia did not otherwise exhibit any sign of discomfort or pain. The decision to
ethanize the surviving one on day 30 and not earlier was taken because on daily veterinary surveillance the animal did not show any distress.

Many models described to date lack a clear tendency to rupture, which is one of the key characteristics if a AAA model is going to be used to evaluate the protection from aneurysm rupture that a given therapy may confer. Experimental AAAs created using synthetic tissues, tanned biological tissues or intravascular stent overdilatation do not have a tendency to rupture. Most authors consider that a tendency to rupture is instrumental in defining model usefulness for endovascular therapy investigation. When choosing an experimental model for research in AAA, it would be desirable that it exhibited the highest possible rupture rate. Despite no significant difference being shown between the two groups as regards to survival times, aneurysmal rupture occurred more frequently in the serosa group. This apparent greater resistance of the peritoneum model, however, is dependant on aneurysmal length. In the previous study conducted with peritoneum patches for AAA model creation, aneurysms longer than 6cm in length evidenced higher tendency to rupture than those under 6cm (70% versus 20% rupture rate). All the models created in the present study would have fallen in the later group, and therefore their expected rupture rate was not higher than 20%, which was the actual rate encountered.

Another important characteristic in an experimental AAA model is that it should exhibit postoperative dilatation. When an endograft fails to properly exclude an aneurysm, it is frequently seen clinically as increased aneurysmal diameter. In most instances, this phenomenon is associated with demonstrable endoleaks, but it is not always so. Therefore, to be useful for endograft testing a model should allow for aneurysmal growth in cases of failed exclusion. Both models studied in this experience evidenced growth during the first postoperative month, as demonstrated by both imaging techniques used. Therefore, within this time limit, both may be useful for endograft testing.

In cases of incomplete exclusion, aneurysmal rupture is a recognized risk. The fact that the latest rupture in this study occurred at day 19 limits the above suggested time frame, and it may be stated that the usefulness of the two models could be restricted to the first two weeks after creation, therefore limiting their use to acute studies.

The rate of postoperative dilatation was higher in the peritoneum model. The highest dilatation obtained in an aneurysmal model to date was reported by Anijdar et al. using elastase infusion in rats' aortas. Their results, albeit excellent in rodents, have not been consistently reproduced in bigger species, and are therefore of limited usefulness in endovascular devices research or for training in their use.

Persistent or recurrent blood flow into the excluded aneurysmal sac, known as endoleak, is one of the main concerns regarding the effectiveness and durability of endovascular AAA repair. As demonstrated by the exhaustive imaging studies performed in both models, all collateral vessels maintained patency during follow-up. In case of an endograft being deployed, this continued patency could result in a type II (branch to branch) endoleak development. Despite the fact that they rarely cause adverse clinical consequences, rupture has been reported to occur in the presence of type II endoleaks, and it is generally recognized that the existence of a type II endoleak, when associated with sac enlargement, requires therapy. A type II endoleak model has been recently described in swine, using a technique for AAA creation similar to the two described here, but with a synthetic material, to explore the possibilities of combined endovascular and laparoscopic treatment for AAA. Both models studied in the present report could be of use for these investigations, with the added advantage of the aneurysm presenting a tendency to enlarge and rupture.

The pathological results were very similar to those previously reported when using autologous materials, such as muscular fascia, peritoneum or serosa. The inner surface of the patches appeared completely endothelialized in the animals than completed the follow-up. An important aspect of evaluating an endovascular prostheses is the study of its effects in the device-vessel interface. A fully endothelialized internal surface in the aneurysms could provide a more favourable environment for the study of the device effects at this level than non endothelialized models, such as those constructed using synthetic or tanned biological tissues.

Considerable tissue thickening was seen at the level of both peritoneum and serosa patches. This was mainly due to collagen fibres and fibroblast/miofibroblasts, with very little or no elastin present. This finding is consistent with both patches experiencing a retraction similar to that happening in scar tissues, whose main components are also collagen fibers and fibroblastic cells. Further studies are needed to clarify this issue. Moreover, if this was the case, it would be...
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theoretically possible to pharmacologically act on this tissue to prevent contraction, therefore avoiding tissue retraction and extending usefulness of the model farther than the first month.

The limitations of this comparative study are related to the limitations of both models in themselves. The pigs were clinically healthy and normotensive, and therefore had healthy, straight arteries. To partly offset this limitation, animals may be fed a hypercholesterolemic diet. A further limitation of the studied models, which has been mentioned above, is the time frame during which the models may be useful for therapeutic research, limited by the fact that ruptures only occur at the early stages and that diameters tend to decrease with time, after an initial period of increase.

CONCLUSION

Despite the fact that no single ideal AAA model exists because no model completely mimics the human response to disease, the peritoneum and serosa models compared in this study could both be useful tools in the development and acute evaluation of new endoprostheses or therapeutic strategies, and to train specialists in their use. Among the two, the peritoneum model is technically easier to create, causing the animal considerable less postoperative discomfort. Moreover, this model exhibits a higher rate of postoperative dilatation, and therefore it could prove to be more useful than the serosa model.

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