ENDOVASCULAR AND SURGICAL TECHNIQUES

The Effect of Endovascular Aortic Stents Placed Across the Renal Arteries

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Objectives: To investigate renal artery patency and renal function after deployment of aortic stents covering the orifices of renal arteries.

Design: Prospective open animal study.

Setting: Department of Experimental Surgery at a university hospital.

Materials: Twenty-three pigs were used.

Methods: Ten pigs were observed for 1 h after graft-anchoring aortic stents, Gianturco (5) and Palmaz (5), were placed so that the stents covered the renal arterial orifices. In 13 pigs, Gianturco (6) and Palmaz (7) stents without grafts were placed over the renal arteries and left in situ for 7 days. Renal function and blood flow were measured by renograms, iohexol clearance and ultrasonic blood flow meter and patency was verified by angiograms. The kidneys were microscopically examined for signs of ischaemia and microemboli.

Results: One renal artery covered by a graft-anchoring Gianturco stent occluded. The remaining renal arteries remained patent without any significant decrease in renal blood flow after stent deployment. Normal renal function and histology was maintained.

Conclusions: Aortic stents placed at the level of the renal arteries do not affect renal blood flow within 1 week in this experimental model. This may prove valuable in endovascular treatment of aortic aneurysms and in other procedures involving stents.

Key Words: Aortic aneurysm; Endovascular treatment; Stent; Renal artery obstruction; Renal blood flow.

Introduction

The implantation of stents, both self expandable and balloon inflatable, has become a common tool in endovascular interventions.1-4 Intra-arterial stents are known to induce smooth muscle cell migration with the risk of restenosis. In animal experiments the stents will be covered by endothelial cells within months and may eventually be totally incorporated into the arterial wall.5-12

Exclusion of aortic aneurysms and bypassing of occlusive disease is feasible by endovascular techniques.13-17 Different stent devices are being utilised to anchor the graft to the aortic wall. However, the non-dilated proximal part of the infrarenal aorta — between the orifices of the renal arteries and the aneurysm — is often very short. It may then be impossible to safely anchor the stent to this "neck". If endovascular exclusion was attempted in these cases, the stent would have to be positioned more proximally, thus interfering with the origins of the renal arteries. Major arterial sidebranches often occur in the vicinity of the site of the proximal stent also when attempting endovascular grafting for occlusive disease.

There are reports that arterial side branches will stay patent for at least 36 months after their orifices have been covered by stents.10,19-20 These observations are based exclusively on angiographic findings concerning the internal iliac, inferior mesenteric and lumbar arteries. The renal arteries have only been scarcely investigated and functional evaluation such as actual flow measurements of the involved side-branches has not been reported upon. The objective of this experimental study was to investigate the effects of aortic
Table 1. Disposition of animals (n=23) involved in this study.

<table>
<thead>
<tr>
<th>Study</th>
<th>n  = 23</th>
<th>Stent</th>
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<tr>
<td>Graft anchoring stent covering renal arteries; feasibility study, 1 h follow-up</td>
<td>5</td>
<td>Gianturco</td>
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<tr>
<td>Blood flow in renal arteries, covered by stent; 7 days follow-up</td>
<td>6</td>
<td>Gianturco</td>
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<td>Palmaz</td>
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Inc., Ithaca, U.S.A.) placed in contact with both the renal arteries and the aorta separately. Basic flow values were obtained before stent deposition in the first series of animals where a laparotomy had to be carried out to enable deposition of the endovascular graft. In order to correct for variation in cardiac output, renal blood flow was expressed as a percentage of the infrarenal aortic blood flow.

Graft-stent placement

In 10 animals (Table 1) the aorta was clamped below the inferior mesenteric artery and a transverse aortotomy was performed. An 8 mm knitted Dacron graft (Haemashield®, Meadox Medicals Inc. U.S.A.), with a proximal and a distal stent sutured to the graft was introduced through a 16 F introducer sheath and deployed into the infrarenal aorta. Gianturco (Cook Inc., Bloomington, U.S.A.) or Palmaz (P-294, Johnsson & Johnson Interventional Systems Co, Warren, U.S.A.) stents were used in five animals each at random. The diameter of the expanded stents was 9 mm and the pore diameter was 5 and 3 mm respectively. The proximal, 30 mm long stent was attached to the graft in such a way that half of the stent was uncovered (Fig. 1). The uncovered part of the stent was placed over the orifices of the renal arteries and its position was controlled by angiography. After suturing the aortotomy, blood flow was measured repeatedly and after 1 h patency of the aorta and renal arteries was also verified by another angiogram. At the end of the experiment the aorta was clamped and the graft containing specimen excised. The patency of the renal arteries was examined as well as the exact location of the stent and graft margins and their relation to the renal arteries. Occurrence of thrombi was particularly noted. The kidneys were histologically examined by pathologists as described below. In the second series, with 1 week follow-up, stents without grafts were studied. The stents, Gianturco (6) and Palmaz (7), were introduced by a transfemoral approach into the aorta, and placed to cover the renal artery orifices. The position was verified by angiography.

Renal function

Renal function was monitored by renograms and creatinine registrations, preoperatively and postoperatively on day 2 and 7 in the Gianturco group. In the
Palmaz group the renograms were replaced by registrations of iohexol clearance due to technical failure of the gamma camera. Using computerised renograms, the time to maximal isotope uptake (T-MAX) as well as the initial inclination of the curve (INCL) were calculated. Plasma-clearance of iohexol was determined by the slope technique.\textsuperscript{22,23} Plasma concentration of iodine was obtained using the Renalyzer PRX90 (Provalid AB, Lund, Sweden) which is based on X-ray fluorescence technique. Plasma samples were taken 1, 2 and 3 h after the injection of 25 ml of iohexol 300 mg iodine/ml (Omnipaque, Nycomed, Oslo, Norway). On day 7 another angiogram was made. A laparotomy was then performed and renal blood flow was measured by the ultrasonic flowmeter. In the Palmaz-group, the blood pressure in the suprarenal aorta and the renal arteries were also compared.

Statistical tests were performed applying Winstat software by Kalmia Co Inc. The values were expressed as median and interquartile range (I.Q.R.). Wilcoxon signed rank test was used for paired data. U-test (Mann Whitney) was used for group comparisons. \( p < 0.05 \) was considered significant.

The study had been approved by the Animal Ethics Committee of Lund University and the animals were cared for according to the European Convention for Laboratory Animal Care.

Results

It was usually feasible to place the endovascular aortic graft immediately below the renal arteries with such a precision that the proximal graft-anchoring stent covered the renal arteries while the graft did not. However, in pigs, the right and left renal arteries often originate from different levels which explains why six of the total 46 renal arteries involved were either uncovered by the stent \((n = 4)\) or covered by both stent and graft \((n = 2)\) and therefore had to be excluded from further analysis. Investigation of the specimens showed that a stent wire actually crossed the renal artery orifice in all but one of the successfully stent covered renal arteries. The median introoperative blood flow in the renal arteries before stent deployment \((n = 10)\) was 148 ml/min which corresponded to 20 % \(\text{(I.Q.R.}\ 18 - 30 \%)\) of the infrarenal aortic blood flow.

Morphology

The aortic segment containing the stent was fixed together with the kidneys under physiological pressure by instillation of 2.5 % glutaraldehyde solution. The fixed specimen was excised. The renal arteries were cut off close to the aortic wall in order to expose the metallic stent wire and its relation to the arterial orifice (Fig. 2). The aorta was longitudinally cut open to observe the impressions the stents had left in the aortic wall. Again, the relation to the renal arteries was noted (Fig. 3). The stent area was carefully searched for thrombus formation. The kidneys were examined by two pathologists. Each kidney was cut into thin slices to identify macroscopic signs of local infarction. Multiple sections from different parts of each kidney then underwent light microscopic examination in search of local ischaemia and thrombosis or platelet deposition, particularly in the glomerular capillaries.\textsuperscript{24,25}

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Fig. 1. Specimen of pig aorta. A longitudinal aortotomy exposes the gianturco stent protruding above the dacron graft. The free part of the stent has been anchored at the level of the renal arteries \((R)\). In this case the left renal artery has been accidentally covered by both stent and graft. Minor thrombotic depositions are seen on the stent wires.
Fig. 2. The aortic specimen has been cut to make the stent ends visible (S). The renal artery has been resected close to the aortic wall exposing not only the stent wire crossing its orifice (O) but also any potential thrombus that may have been located in this region.

Graft-stent study with 1 h follow-up

One Gianturco stent covered renal artery occluded. The remaining arteries that had been successfully covered by stents all stayed patent (Fig. 4) and the median flow after 1 h was 14 % of aortic flow (I.Q.R. 7 – 22 %), which was not significantly different compared to before stent deployment \( p = 0.3 \). On angiography, in one animal, both renal arteries covered by a Palmaz stent had a lumen reduction with a mean blood pressure gradient between the suprarenal aorta and the involved renal artery of 6 and 12 mmHg respectively. All other renal arteries were morphologically normal.

Median T-MAX of 692 s (I.Q.R. 405 – 795 s) before stent placement and 675 s (535 – 785 s) on day 7. The median INCL was 6.6 counts/s (I.Q.R. 5.3 – 7.7 counts/s) before intervention, and 9.0 counts/s (6.1 – 9.5 counts/s) on day 7. None of these differences were statistically significant. The iohexol-clearance replacing the renograms in the Palmaz group was 67 ml/min (I.Q.R. 60 – 74 ml/min) before stent deposition and 70 ml/min (I.Q.R. 66 – 75 ml/min) after 1 week (N.S.). The median blood pressure gradient between the suprarenal aorta and the Palmaz stent covered renal arteries was 5.4 mmHg (I.Q.R. –0.9 – 6.8 mmHg).

Morphology

Stent study with 1 week follow-up

Renal blood flow at one week was 23 % of the infrarenal aortic blood flow (I.Q.R. 21 – 28 %), 23 % in the Palmaz and 24 % in the Gianturco groups. This was not significantly different from the flow of 20 % in the aforementioned un-stented arteries \( p = 0.32 \). The final angiograms revealed no lumen discrepancies. The median creatinine level before stent deposition was 80.4 \( \mu \text{mol/l} \) (I.Q.R. 80 – 88 \( \mu \text{mol/l} \)) and it remained at 76 \( \mu \text{mol/l} \) (72 – 89 \( \mu \text{mol/l} \)) 7 days after the stents had been placed (N.S.). There was no difference between the Gianturco and Palmaz stents. The renograms in the Gianturco group showed a median T-MAX of 692 s (I.Q.R. 405 – 795 s) before stent placement and 675 s (535 – 785 s) on day 7. The median INCL was 6.6 counts/s (I.Q.R. 5.3 – 7.7 counts/s) before intervention, and 9.0 counts/s (6.1 – 9.5 counts/s) on day 7. None of these differences were statistically significant. The iohexol-clearance replacing the renograms in the Palmaz group was 67 ml/min (I.Q.R. 60 – 74 ml/min) before stent deposition and 70 ml/min (I.Q.R. 66 – 75 ml/min) after 1 week (N.S.). The median blood pressure gradient between the suprarenal aorta and the Palmaz stent covered renal arteries was 5.4 mmHg (I.Q.R. –0.9 – 6.8 mmHg).

Discussion

In the 1 week follow-up series, no macroscopic thrombotic depositions could be noted on the stent or adjacent vessel wall. In the graft-stent series, minor thrombotic depositions on both graft and stent were seen in all cases after 1 h. No signs of focal infarctions were noted on macroscopic examination of the kidneys. Light microscopy revealed no signs of local ischaemia or capillary obstruction by thrombus or platelet depositions.

Endovascular exclusion of abdominal aortic aneu-
A number of different endovascular graft deployment systems are under development and evaluation. Although these new techniques are less extensive procedures than a conventional operation, complications have been reported. For example, in the series by Parodi et al., a number of cases had leakage around the graft and in two cases microembolisation occurred. Fear of occluding a renal artery may lead to a suboptimal placement of the proximal stent resulting in proximal leakage or stent displacement. A major limitation for endovascular grafting is that for proper anchoring of the graft a 15–20 mm long infrarenal neck is required. Because of this, some 30–40% of aneurysms are unsuitable for endovascular repair by the present technique. If the anchoring stents could be placed above the orifices of the renal arteries, a larger proportion of patients with abdominal aortic aneurysms could be treated by the endovascular technique. Also, it would enable usage of longer stents optimising the attachment to the aortic wall.

In this experimental model it was technically feasible in most cases to attach the aortic graft immediately below the renal arteries with such an accuracy that the renal arteries were covered by the graft-anchoring stent only. The two cases where a renal artery was accidentally covered by stent and graft and consequently occluded, illustrate the hazards of intentionally placing stentgrafts in the vicinity of the renal arteries. Since the Gianturco stents consisted of 12 longitudinally arranged wires and the circumference of vessels with the diameter of 12 mm was 38 mm, there was a longitudinally running wire...
every 3 mm. Under those circumstances, the probability that a renal artery may have stayed uncovered by a stent wire was small which also applied to the Palmaz stent where the pore diameter was smaller. The present study confirmed that all but one renal artery orifices were indeed crossed by a stent wire. The one occlusion seen in this series occurred in an artery covered by a Gianturco stent anchoring a graft that was of a slightly too wide diameter. Consequently, this graft was not ideally expanded and we assume that the renal artery occlusion was caused by the thrombogenicity of the graft rather than by the stent itself. For this purpose, the second part of the experiment was designed involving stents only. The diameter of the human aorta is wider with higher flow rates, why it may be expected that graft thrombogenicity will not cause renal artery occlusion in humans.

The stent material has a fairly high thrombogenicity, but Palmaz et al. reported that a combination of dextran and heparin reduced the clot formation, and that addition of aspirin and dipyridamole had the best antithrombotic effect. In our study we used heparin and dextran but some thrombotic depositions were noted after 1 h on the stents in the graft-stent study (Fig. 1). However, no macroscopic thrombotic material was seen on the stent wires after 1 week (Fig. 2). Any such deposition would have been revealed by the approach including vital fixation and careful observation of the aortic lumen through the renal ostium. Vital fixation preserves thrombus while removing blood, thus facilitating the distinction between thrombus and postmortal clot. There was a possibility that minor thrombi could have been formed and embolised peripherally but this seems less probable as renal function, measured as creatinine level, radioactive uptake and iohexol clearance, was not affected within 1 week. Furthermore, on historical examination there were no signs of microemboli in the kidneys which is usually readily seen on light microscopy both as depositions in the capillaries and as focal areas of ischaemia. Thus, this study could not reveal any differences in thrombogenicity between the stent types although their mechanical properties were different and although the metallic surface exposed to the blood stream was substantially larger in the Palmaz stents.

In our study, during the 1 week follow-up part, renal blood flow, renograms and creatinine values were unchanged. An unchanged GFR after 1 week has been reported. The angiograms at 1 week did not show any lumen reduction in the renal arteries. However, at the initial placement, slight lumen reductions were noted in one case. This could be due to spasm, a phenomenon that is seen after manipulation of vessels, as exemplified by angioplasty of the suprarenal aorta in rabbits which may lead to spasm of the renal arteries. The fact that no lumen reductions were seen after 1 week, supports this hypothesis.

The results of animal experiments can never be directly applied to humans. Before adopting a new technique for humans additional basic testing in animals must be done. Further studies on the patency of accidentally stent covered collaterals in humans are also needed. It is highly desirable to investigate whether intimal hyperplasia will influence stent covered sidebranches. The present short term study demonstrates that thrombogenicity by itself does not influence their patency in this animal model. If it proves possible to place aortic stents over the orifices of renal arteries safely, it would be possible to treat a larger proportion of patients with abdominal aortic aneurysms by the endovascular technique.

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