A Clampless and Sutureless Aorto-Prosthetic End-to-Side Anastomotic Device: An Experimental Study

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Abstract

Objectives: A feasibility study.

Methods: Eight pigs (all females; mean weight: 29 kg) underwent a conventional transperitoneal aortic approach with implantation of an aorto-prosthetic end-to-side anastomosis using a Clampless device and deployment of a 5-mm polytetrafluoroethylene (PTFE) graft. After proximal ligature, a conventional end-to-end anastomosis was then performed between the graft and the left iliac artery.

Results: The first pig died during the procedure due to graft misplacement. The seven other procedures were successful with a mean operative and anastomosis time of 101 min (range: 81–115 min) and 3.35 min (range: 2.25–4.25 min), respectively; mean blood loss was 152 ml (range: 30–235 ml). Another pig with a patent graft died at day 4 as a result of a severe unrelated pneumonopathy. The angiogram performed during the procedure and before sacrifice, at 2 (n = 2), 4 (n = 2) and 6 weeks (n = 2), showed no graft stenosis or thrombosis. Microscopic examination revealed a tissue covering the intraluminal stent, which evolved over time, with no visible endothelial proliferation or inflammation.

Conclusion: An aorto-prosthetic anastomosis can be performed safely and efficiently with our new clampless and sutureless device. The next step will be a laparoscopic Clampless implantation.

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In 2007, the TransAtlantic Society Consensus recommended surgically performing a conventional aorto-bifemoral bypass as the first choice for type D aorto-iliac occlusive disease (AIOD) (a diffuse disease with severe stenoses or
occlusion involving the aorta and both iliac arteries), and as the preferred treatment for good-risk patients with type C lesions (bilateral common iliac occlusion or severe and long bilateral external iliac artery stenoses). However, these bypasses are associated with a mortality rate of 0–3.3% and a morbidity rate of 8.3–13%, mainly because of cardio-respiratory complications. The two main explanations for these severe complications are the long midline or flank incisions needed, and which contribute to major fluid shifts, as well as the aortic cross-clamping time, which induces tissue ischaemia and cardiac stress.

Since 1996, along with other authors, we have developed minimally invasive laparoscopic or laparoscopy-assisted techniques to decrease surgical aggression trauma as evidenced by shorter intensive care and hospital stays, associated with a more rapid recovery. On the other hand, despite the technical improvements made by the surgical teams, the operative and aortic cross-clamping times necessary for performing the laparoscopic aorto-prosthetic anastomoses remain long in comparison with 'open' surgery, as confirmed by two recent comparative studies.

As evidenced in the previous articles, we are currently working to develop new laparoscopic instruments to simplify these techniques and to decrease the long learning curve. This study aims to establish the feasibility and efficacy of a new clampless and sutureless device for end-to-side aorto-prosthetic anastomosis. We decided to perform this feasibility study initially with a conventional open surgery, prior to the laparoscopic approach.

Material and Methods

The Clampless® device (Figs. 1 and 2)

The device used in this study is under development within the framework of a partnership between the 'Université de la Méditerranée' and Protomed, a company headquartered within our Faculty of Medicine. This device is a unit composed of a vascular implant, named Clampless®, and a specific ancillary. More precisely, the implant is used to perform a side-to-end aorto-prosthetic anastomosis and its ancillary introduces and positions the implant in the receiving artery and carries out anastomosis on the level of this artery. The Clampless® device is composed of a vascular graft and a connector.

In 25- to 33-kg pigs, the diameters of the infra-renal aorta and iliac arteries are, respectively, 7–8 mm and 4–5 mm (Table 1). To fit these diameters, the Clampless® prototype implant is composed of:

- a 7-mm dedicated connector, an expandable balloon and a stainless steel mesh covered with a polytetra-fluoroethylene (PTFE) graft (this part of the implant will remain inside the aorta); this is a tubular connector and has a side opening to release a large lumen with blood circulation into the bypass;
- a straight 5-mm PTFE vascular graft sutured to the side of the connector using 7/0 polypropylene thread;
- a specific 7-mm balloon, which is included in the device and which allows inflating the up- and downstream parts of the connector simultaneously, ensures that it is sealed between the aortic wall and the graft, forming the end-to-side bypass anastomosis. After deflation, the balloon is withdrawn through the 5-mm PTFE graft lumen;
- A 20 French (Fr.) ancillary introduction catheter that allows introducing and delivering the Clampless® device into the receiving artery. This allows placing the distal and proximal parts of the connector upstream and downstream of the puncture point, respectively, and allows using the connector to secure the
anastomosis using the specific 7-mm balloon at the level of the artery puncture.

The Clampless® device aims to create a vascular bypass without cross-clamping and suturing. Simplified anastomosis, no cross-clamping and reduced procedure time may reduce the perioperative and/or postoperative risks and complications. However, the system must be compatible with traditional laparotomy, mini-laparotomy and complete laparoscopic access.

**In vivo animal experimental study**

Eight 3-month-old female pigs, of a mean weight of 29 kg (range: 25–33 kg), underwent implantation of an aorta–left iliac artery bypass using the Clampless® device.

**Surgical protocol**

Animal care procedures complied with animal experimentation legislation. The institutional Animal Use and Care Committee reviewed and approved all the procedures and protocols used in this study. All the pigs were operated under general anaesthesia with endotracheal intubation. A conventional transperitoneal surgical approach to the abdominal aorta was performed with dissection of the first 5 cm of the left iliac artery. An intravenous injection of 100 UI kg⁻¹ of heparin was administered and the Clampless® device was implanted: after a single infra-renal aortic puncture, a stiff guide wire was placed retroperitonially, gradually introducing a 20 Fr. sheath into the 7- to 8-mm-diameter aorta. The Clampless® device was then inserted and deployed through its ancillary, after removing the sheath and guide wire. The flow through the 5-mm PTFE graft implanted laterally was checked, as well as a continuing pulse in the aorta below the graft. The graft was then clamped and the ostium of the left iliac artery was occluded with two clips. An end-to-end distal anastomosis was performed conventionally between the graft and the left iliac artery using a 7/0 polypropylene thread. An angiogram was performed systematically at the end of the procedure by direct puncture of the aorta above the Clampless® implantation. Finally, the retroperitoneal layer and the abdominal wall were closed using running sutures. A wound dressing was put into place and the animal was allowed to emerge from anaesthesia under the care of a veterinarian. During the postoperative period, each animal received analgesic medication, antibiotics for 10 days and a daily subcutaneous injection of 3000 IU/0.3 ml of low-molecular-weight heparin.

After 2, 4 or 6 weeks, the animals were sacrificed under general anaesthesia. A re-do open transperitoneal approach to the aorta was performed following another angiogram, as previously described. The aorta (from above the renal arteries to the iliac trifurcation) and the whole PTFE graft including the distal anastomosis were carefully removed and sent for pathological analysis. At the end of the experiment, the animals were euthanased by administering potassium chloride or KCl (40 mEq) intravenously.

**Morphological analysis**

All the samples were fixed in 4% formalin for 48 h. The aorta, PTFE graft and Clampless® device were opened along their great axis, and macroscopic images were taken. The metallic component of the Clampless® device was carefully removed. Specimen samples were taken along the PTFE-covered portion of the aorta, in the aorto-prosthetic ostium region and on the different anastomoses. Samples were embedded in paraffin, and 5-μm sections were cut and stained with haematoxylin and eosin (H&E).

**Results**

**The intra-operative period**

**Feasibility**

In the first pig, the Clampless® device was not completely inserted before removal of the introducer, which was responsible for a tear in the aorta, with no possibility of reintroducing the device. The animal was sacrificed and, secondarily, a specific landmark was placed on the

<table>
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<tr>
<th>Pig #</th>
<th>Intra-operative data</th>
<th>Data at sacrifice</th>
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<tr>
<td></td>
<td>Weight (Kg)</td>
<td>Aortic diameter (mm)</td>
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<tr>
<td>1</td>
<td>26</td>
<td>7</td>
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<tr>
<td>2</td>
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<td>8</td>
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</tr>
<tr>
<td>Mean</td>
<td>29</td>
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² ID: intra-operative death due to a graft misplacement.
³ PG: patent graft without stenosis.
⁴ unrelated death caused by a pneumonopathy on D4.
Clampless® device (on the part outside the introducer) to prevent this problem. The seven other implantations were uneventful with a mean operative time of 101 min (range: 81–115 min), and an anastomosis time of 3.35 min (range: 2.25–4.25 min), with good blood flow outside the PTFE graft and a good pulse distally on the aorta (Table 1). All the distal anastomoses on the left iliac artery were performed conventionally without anomalies.

Impermeability
Spontaneous impermeability was satisfactory with no leakage, except in one case, in which a 6/0 Prolene® stitch was necessary at the front part of the anastomosis, without cross-clamping. Mean blood loss was 152 ml (range: 30–235 ml) for the whole procedure.

Patency and angiographic control (Fig. 2)
The systematic angiogram performed at the end of the procedure showed no blood leakage and a patent aorto-left iliac bypass in all cases. No stenosis was noted either on the Clampless® implantation on the aorta or on the left iliac artery, despite two cases of distal spasm with spontaneous disappearance.

The surveillance period
All seven pigs had a normal postoperative recovery, except one (#4), for whom the recovery period was long and difficult. In the following days, this pig remained prostrated without any ischaemic hindleg and good femoral pulses. On the fourth postoperative day, this pig presented with whole body tremor, a cold snout, hypothermia with an abnormal auscultation of both lungs and died when brought to the operating table. No control angiogram was then possible but the whole abdominal aorta, the Clampless® device and the bypass were patent. The six other pigs had a normal surveillance period, with a growth of a mean of 6, 11 and 17 kg, before the sacrifice of two of them at 2, 4 or 6 weeks, respectively.

Euthanasia and graft removal
No peri-aortic haematoma or false aneurysm was noticed in any of the remaining six pigs during the abdominal re-intervention. An angiogram was systematically performed and showed no blood leakage and a patent aorto-left iliac bypass in all cases, as well as both renal and iliac arteries, and the inferior mesenteric artery. No stenosis was noted either on the Clampless® implantation on the aorta or on the left iliac artery. However, due to the growth of the animals, the diameter of the aorta increased and a progressive discrepancy could be noticed between the proximal and distal aorta compared to the intra-aortic part of the Clampless® device (Fig. 3).

Macroscopic examination
After removal of the aorta and the aorto-iliac bypass, no anomaly was observed. There were no clots and thromboses and the Clampless® device was well inserted into the aortic wall.

Microscopic examination
The tissue covering the intraluminal stent evolved over time: at 2 weeks, this tissue was inconsistent and was composed of fibrin associated with some endothelial cells; at 4 weeks, it became a fragile tissue of variable thickness; and at 6 weeks, the tissue was thick and continuous. There were no visible signs of endothelial proliferation and inflammation.

In the aortic wall under the stent graft, a localised intimal necrosis with some calcifications, but without modifications of the external layers, was noted at 2 weeks. This fibrinous necrosis was progressively replaced at 4 weeks by a loose conjunctive tissue, with mild inflammation at 4 and 6 weeks. A macrophagic giant cell reaction was noted in the periphery of the calcifications. A foreign body granuloma had developed close to the PTFE graft along its aortic wall without diffusion to the rest of the aortic wall (Fig. 4).

Discussion
Patients presenting with the most severe forms of aorto-iliac occlusive disease (TASC C and D lesions) and are also generally elderly patients with severe risk factors and poor cardio-respiratory conditions. As these patients, in line with the TASC recommendations, are not good candidates for endovascular techniques, there are a certain number of

Figure 3  Angiograms of the Clampless® device (arrow) performed during the initial procedure (A) and after 6 weeks (B).
contradictions involved in proposing the most aggressive surgical treatment to the most fragile patients. To decrease this aggressiveness, our team, with other authors, has tried to develop minimally invasive video-assisted techniques.4

Our goal is to use a minimally invasive surgical approach to minimise both large fluid shifts and hypothermia and to avoid the aortic cross-clamping time, which induces tissue ischaemia and cardiac stress. However, these two goals are not compatible, as recently mentioned in two comparative studies: in 2005, in the series by Rouers et al.,9 operative and clamping times were significantly different in the group of 28 patients who underwent conventional surgery for AIOD compared to 30 patients treated with total laparoscopic surgery, with a mean aortic cross-clamp time increasing from 17 to 66 min ($p < 0.0001$). This was confirmed in the study by Kolvenbach et al. with a significant increase in the mean cross-clamping time (from 25 to 45 min, $p < 0.05$) when comparing 187 patients treated with the laparoscopy-assisted technique with a mini-laparotomy and 105 patients who underwent a total laparoscopic technique.9

Since Carrel’s pioneering work on vascular anastomosis, a variety of alternative techniques have been developed to perform an ideal anastomosis.13 As mentioned in a previous article,12 rings, staples, clips, stents, adhesives or welding have been tested as substitutes for needles and thread, but most of these have had no clinical application.14–17 In the present experimental study, the Clampless® device allowed to perform the same side-to-end aorto-prosthetic anastomosis with a mean implantation time of 3.35 min, and without aortic cross-clamping. The aortic dissection is also simplified as there is no need to control the aorta above and below the anastomotic site, but only to expose several centimetres of the anterior part of the infra-renal aorta to make possible both a puncture and the penetration of the 20 Fr. introducer. Interestingly, none of the angiograms performed intra-operatively and during sacrifice showed any graft thrombosis or stenosis, and the macroscopic and microscopic examination after removal revealed good graft implantation. Despite an aortic diameter up to 42% (from 7 to 10 mm) in 6 weeks, neither aortic bleeding nor false aneurysm was noted.

Our study nevertheless deserves a certain amount of criticism: first, the intra-operative death of the first pig was due to insufficient spotting of the graft during implantation; the addition of specific landmarks on the Clampless® device prevented this complication in the other seven pigs. Second, the pigs’ rapid growth, with concomitant increase in the native aortic diameter during the surveillance period, was responsible for a progressive discrepancy with the implanted stent at 2, 4 and 6 weeks; another animal model, such as adult sheep, would have maintained the same aortic diameter throughout the study. Finally, developing this first prototype was not compatible with a laparoscopic implantation, which remains our ultimate goal; in the initial protocol, we wanted to be able to rapidly control any bleeding, and also to choose the angle for introducing the device into the aorta. In the future, we expect this device to simplify the performance of a bypass on a visceral artery or a unilateral aorto-femoral bypass. Hopefully, further development of a bifurcated graft will allow an aorto-bifemoral bypass to treat patients with severe AIOD. To adapt Clampless® to clinical use, the main body of these new grafts will need to cover a range from 12 to 16 mm with branches measuring 6–8 mm, and the delivering catheter will probably need to be used through a 24 Fr. introducer, in a 3- to 4 cm-long non-circumferentially calcified segment of the infra-renal aorta. Furthermore, a laparoscopic implantation will need improvements in delivering the catheter to secure its use through a 12 mm trocar and to prevent blood loss with a lower profile.18

Figure 4 Microscopic analysis of the tissue covering the intraluminal stent evolves over time: A- at 2 weeks, fibrin associated with some endothelial cells, B- at 4 weeks, there is a fragile tissue with a variable thickness, C- at 6 weeks, there is thick and continuous tissue.
Conclusion

We present a new clampless and sutureless device to perform an end-to-side aorto-prosthetic anastomosis. The present experimental study on eight pigs showed that the implantation procedure was safe and efficient, with no angiographic, macroscopic and microscopic anomalies after a surveillance period of 2, 4 and 6 weeks. Further developments are needed for laparoscopic implantation to be possible on larger aortas.

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The company Covidien awarded the authors the Covidien prize for this work at the 2008 meeting of the Association Française de Chirurgie (French surgery association).

Disclosure Statement

- Yves Alimi is a shareholder in Protomed. He is one of the inventors and holds a patent for this device.
- Vincent Garitey and Frederic Mouret are employees of PROTOMED.
- The other authors have no potential conflicts of interest with the company.

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