Evaluation of a new device for quick sutureless coronary artery anastomosis in surviving sheep

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Abstract

Objective: A new device for performing quick sutureless vascular anastomosis by means of stent technology has recently been developed by Jomed International, Helsingborg, Sweden. The efficacy of this GraftConnector was studied in a sheep model. Methods: In adult sheep, a left anterior thoracotomy under the fourth rib extended across the sternum gave good access to the left anterior descending branch (LAD) and the right internal mammary artery (RIMA). On beating hearts, the GraftConnector group had the RIMA connected to the LAD by means of the new device, while the control animals had the same anastomoses sutured with continuous 7-0 polypropylene sutures. The time for completing the anastomosis (ischemic time) was recorded and the blood flow in the RIMA was recorded with the proximal LAD open and closed, respectively. An intra-operative fluoroscopy with contrast injection directly into the graft was done. Finally the proximal LAD was ligated. The surviving animals are to be followed up. Results: Seven (46%) of the 15 animals operated on with the traditional suturing technique and seven (63%) of the 11 GraftConnector sheep survived the procedures and are to be followed up. The 11 anastomoses done with the GraftConnector were completed in 2.41 ± 0.2 min, and the 14 anastomoses sutured with continuous suture were completed in 6.93 ± 0.419 min (P < 0.0001). The RIMA blood-flows in the two groups were comparable and are presented. All the surviving animals had open anastomoses at fluoroscopy. Conclusions: Quick coronary artery anastomoses without suturing on beating hearts can be completed with the new GraftConnector. The GraftConnector creates reproducible anastomoses in much less time than suturing, the per-operative mortality in the GraftConnector Group was accordingly lower. Long-time follow-up of the patency in surviving animals is pending. The presented device may ultimately permit quick anastomoses endoscopically. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Anastomosis; Sutureless; Stent; Animal; Coronary; Bypass

1. Introduction

A variety of procedures with different approaches towards minimal invasive coronary surgery (MICS) have been introduced during the last few years [1–10]. Many publications focus on stabilizing devices that facilitate the anastomosis when the surgery is done with the chest open [4,5,8], others describe minimal skin incisions through which traditional surgery is performed on patients with selected single vessel disease [3,11]. Baudet stated in the presidential address at the EACTS 1998 that ‘to be consistent, MICS would have to carry matters to an extreme, which is that totally thoroscopic surgery will be the only true microinvasive operation. These means are going to be supplied by robotics. One more step is then to use automatic suture stapling, one shot vascular anastomotic devices, laser welding or gluing the coronary artery to the arterial conduit anastomosis’ [12]. Some experimenting with gluing [13], stapling [14–16] and laser [17] have, in fact, been attempted. By means of modern stent technology, Jomed International AB, Helsingborg, Sweden, recently have developed a GraftConnector that allows quick suture-less anastomoses between blood vessels. The purpose of the present study was to evaluate the efficacy of the GraftConnector in conducting anastomoses between the internal mammary artery and the coronary artery on beating hearts without stabilizers in an animal model of surviving sheep.


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2. Material and methods

2.1. Design of the GraftConnector

A special coronary artery stent of Nitinol, a memory metal alloy of nickel and titanium, was designed for the GraftConnector. This stent represents the sleeve of the GraftConnector. Asymmetrically in this sleeve, the stent has an opening in the circumference closer to one end. The stent has a cover of extruded polytetrafluoroethylene (PTFE) that is 1/100 mm thick. A hole in this cover corresponds to the opening in the stent and a collar around the opening connects the stent cover with a side-branch of a 4-mm PTFE vascular graft (Fig. 1). This side branch, or tower as it is called, is where the conduit will be attached. The sleeve of the GraftConnector may be placed inside the receiving vessel, in this case the left anterior descending branch (LAD). The memory metal alloy of the sleeve exerts a radial force that tends to open the sleeve. This force is used to fixate the GraftConnector inside the artery once it is in place. Before insertion into the receiving vessel, the sleeve is crimped to an outer diameter of 1 mm, and held in this position by a thread that also fixes it to the handle that is used to insert the sleeve into the receiving vessel. This handle will fall off the GraftConnector once the release mechanism is activated and may be extracted in three pieces (Figs. 1 and 2). The asymmetrical position of the tower on the sleeve allows an insertion of the GraftConnector through an opening in a vessel the same way a foot is put into a shoe. The insertion is illustrated in Fig. 2. First, the long end, the toe, is inserted in the distal direction of the vessel, then in a reciprocating movement of the whole GraftConnector, the short end, the heel, is inserted into the other end of the opening. Once in this final position, the release mechanism is activated and the sleeve of the GraftConnector will expand inside the receiving vessel and fixate the GraftConnector and thereby the conduit to the receiving vessel. The conduit, in this case the right internal mammary artery, is fixed to the GraftConnector by means of a fixation ring of Nitinol, 4 mm in length and 2–2.5 mm in diameter. The conduit is passed through this ring, and the end is turned over the edges of the ring and everted over the outside of the ring. The ring and the conduit are put into the tower and fixed to the GraftConnector by means of a ligature outside (not shown in the picture). Thus, practically nothing of the PTFE in the tower is exposed to the blood, only the part in the collar closest to the opening in the sleeve and the covering sheet of the sleeve have contact with the blood. A T-shape of the GraftConnector was preferred in this first design in order to minimize blood to PTFE contact, and also to avoid the necessity of one left and one right design of the GraftConnector, since the handle is located at the side of the tower.

2.2. The surgical procedure

Healthy local sheep of the Najdi and Naimi breeds, 8–12 months in age, corresponding to a body weight of 40–55 kg were chosen and were obtained from the local market. They were taken to the animal quarter at the research center, and underwent a thorough physical examination and routine laboratory work-up, and were finally given prophylactic penicillin or cephalosporin. After a period of at least 2 weeks, when their health was determined to be satisfactory, they were used for experiments. The animals were fasted for 24–36 h with access to water until 8 h prior to surgery. Before the procedure, 1 g of intravenous Cefazolin sodium (Cefamexin) was given, followed by Gentamicin (Garamycin) 1 g/day, for 5 days. A central venous line was obtained by puncturing the left jugular vein, and the right carotid artery was openly accessed for monitoring of the arterial pressure and for obtaining blood for arterial blood gases. The arterial blood-gases were controlled every 30 min. Atropine sulfate (Atropisol), 0.2 mg/kg, was given pre-operatively and every 15–30 min during the procedure. For muscle relaxation, atracurium benzylate (Tracrium), 0.2 mg/kg, was given and for reversal neostigmine (Prostigmin) 2 + 1 ml. Propofol (Diprivan), 4 mg/kg, was used for induction and maintenance as required. Halothane (Fluothane) 0.8–1.5 vol.% was added after induction of anesthesia. For further monitoring, extremity EKG and pulse oximetry with a tongue probe were used. With the animal in supine position, a left anterior thoracotomy was made under the fourth rib. Depending upon the weight of the sheep, the incision was extended across the sternum, if the animal was very fat and the takedown of the right internal mammary artery (RIMA) was difficult. We later abandoned this extension, as we experienced recurrent and fatal chest wound infections in the extended incision.

![Image](image-url)
animals, due to the increased exposition of the wound to fecal contamination of the floor in the pen. The RIMA was dissected free and taken down without a pedicle. Thereafter, 100 IU/kg of Heparin and 1 mg/kg of Lidocaine were given intravenously as a bolus followed by Lidocaine at 0.1 mg/kg per min. Propranolol (Inderal), 1–6 mg, or Esmolol (Brevibloc), 0.5–1 mg, was given as needed to achieve a heart-rate below 80/min, since tachycardic animals proved to be more prone to ventricular fibrillation during ischemia. The LAD was then explored. The most common anatomy was the presence of two diagonal branches. Our aim was to make the anastomosis between these, or distal to, the second diagonal. A 4-0 polypropylene suture for snaring the LAD was placed around the proximal LAD, preferably just proximal to the anastomosis site, but very often it had to be placed proximal to the second diagonal due to lack of space. There were two groups of animals, one GraftConnector group and one control group that had the anastomoses completed with the traditional suture technique. According to the protocol, the experiments were to continue until we had six definite good survivors in each group. Only animals with detected blood flow in the RIMA and open anastomoses during fluoroscopy were considered candidates for survival. Due to a variable delivery of GraftConnectors, the animals were not randomized, and thus, the operations were performed with one or the other method depending on the supply of GraftConnectors. On beating hearts without any stabilizer, the LAD was cut open approximately 6 mm, the LAD was snared proximal and the RIMA was anastomosed to the LAD using the GraftConnector or suturing with 7-0 polypropylene continuous, respectively. The time for completing the anastomosis was recorded from when the snare on the proximal LAD was closed until it was opened again. After the release of the snare, the blood flow in the conduit was measured by a transit time flow meter (Transonic Systems Inc. Ithaca, NY) usually using a 2.5-mm probe. Two flows were measured, one with the proximal LAD open and one with the proximal LAD closed. A 24 G arterial cannula for direct contrast (Omnipaque, Nycomed, Oslo, Norway) injection into the RIMA was inserted into the RIMA and connected to an extension line. When the proximal RIMA was closed by means of a vascular clamp, an angiography was performed to prove the patency of the anastomosis. If the criteria for survival were fulfilled, the chest was closed after the insertion of a temporary chest tube for suction and injection of 10 ml of 1% Bupivacain hydrochloride as an intercostal nerve block. General anesthesia was terminated and the animal was allowed to wake up. The sheep was kept in the operating room area until it was standing up and drinking water. Thereafter, the animal was kept in a separate room in the research center overnight before returning to the pen. For anticoagulation, the sheep were given Ticlopidine (Ticlid), 250 mg, the evening before surgery and once daily for 1 month. Aspirin, 100 mg/day, was started in the morning the day of surgery and will be given continuously until the animals are sacrificed. All the animals received humane care in compliance with the European Convention on Animal Care. The protocol was approved by the Research Advisory Board Committee and the Ethics Committee for Animal Experiments of the Research Center. For statistical analysis of the results, a JMP (SAS) statistical software package was used. The results were analyzed using the Student’s t-test and the
Wilcoxon/Kruskal–Wallis test (rank sums) and expressed as means and standard error (SE).

3. Results

The procedure proved to be very challenging. Seven (46%) of 15 animals which were operated on with the traditional suture method survived and seven (63%) of 11 GraftConnector sheep survived the procedure. The reasons for per-operative mortality are summarized in Table 1. The extreme sensitivity of the sheep myocardium to ischemia was a recurring cause of death and an abrupt end to the experiments. The ischemic time before occurrence of ventricular fibrillation (VF) was very unpredictable and occurred as early as after 1.5 min in one case. For the same reason, we did not see many imperfect anastomoses on the angiogram, since such imperfection would immediately result in VF. Another common cause of ventricular fibrillation was the sensitivity to X-ray contrast. The myocardium did not tolerate an excess of 3–4 ml of contrast before VF occurred. In Table 2, the times for completion of the anastomosis in the two groups are presented. The significant difference in time is also reflected in the per-operative mortality since the occurrence of VF is directly related to the ischemic time. The shortest time for completion of the anastomosis in the GraftConnector group was 1.5 min and 4.5 min in the control group, respectively. The longest time for completing the anastomosis and survival in the GraftConnector group was 3.5 min, and 11 min in the control group. The sheep that had VF after 8 min in the control group actually first had one anastomosis sutured in 8 min that was occluded distally on angiogram. The revision took another 8 min, after which the VF occurred. From Table 2, we can see that the flows in the LAD with the proximal LAD open were higher in the control group, and with the proximal LAD closed equal. These data will be addressed in the discussion. In three animals we measured the native flow in the LAD at the typical anastomosis site in order to obtain something to relate our findings to. We found the flows to be 15, 15 and 18 ml/min, respectively; a surprisingly low flow even though the animals were under general anesthesia and must be considered to have been resting.

Fig. 3 depicts a completed anastomosis, the RIMA is coming off the LAD perpendicular and almost parallel to the heart surface. An angiogram by means of direct contrast injection into the RIMA is shown in Fig. 4.

4. Discussion

We have presented a new invention, the GraftConnector, for performing quick sutureless anastomoses between blood vessels. Recently, an enormous interest for off-pump [2–5,8,11], endoscopic [1,9,10] and the ultimate robotic virtual reality coronary artery bypass surgery [18–20] has been observed. For performing minimal invasive procedures utilizing smaller incisions and traditional suture

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**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>GraftConnector</th>
</tr>
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<tbody>
<tr>
<td>Peri-operative mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular fibrillation (1.5–8 min) (Induced by contrast injection 2)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Dissection of the RIMA</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Stenosis in the anastomosis</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Graft connector</th>
<th>Controls</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of anastomoses completed</td>
<td>11</td>
<td>14</td>
<td>NA</td>
</tr>
<tr>
<td>Time for the anastomoses in min (mean ± SE)</td>
<td>2.41 ± 0.200</td>
<td>6.93 ± 0.419</td>
<td>P &lt; 0.0001</td>
</tr>
<tr>
<td>Flow in RIMA, LAD open ml/min (mean ± SE)</td>
<td>9.45 ± 1.435b</td>
<td>17.89 ± 0.563b</td>
<td>P &lt; 0.02</td>
</tr>
<tr>
<td>Flow in RIMA, LAD closed ml/min (mean ± SE)</td>
<td>33.0 ± 3.898b</td>
<td>23.22 ± 3.685b</td>
<td>NS</td>
</tr>
</tbody>
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a The native flows in LAD in three animals were 15, 15 and 18 ml/min, respectively.

b n = 9.

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Fig. 4. Angiogram of the RIMA and the left anterior descending branch (LAD) by direct contrast injection into the RIMA. GC, GraftConnector.
techniques, one seems to manage without new devices; however, the number of cases eligible for this method is very limited, including the small minority with single vessel disease only [3,11]. Off-pump open procedures omitting extra corporeal circulation (ECC) have gained great popularity, utilizing a variety of stabilizers designed either by the industry or homemade [4,5,8]. During off-pump multi-vessel procedures, some vessels are difficult to reach, and for many surgeons it is a challenge to sustain consistent good anastomoses [21]. In a survey conducted by Shennib among 162 cardiac surgeons, as many as 62% of those surveyed considered the anastomotic quality to be inferior during off-pump surgery [22]. Untill very recently, the use of endoscopic technique in coronary artery bypass grafting (CABG) surgery has been restricted to the take-down of the LIMA since completion of anastomoses is too difficult [1,9,10]. Sporadic reports have recently been made about the progress in the field of conducting CABG by means of surgical robots. There are two surgical robotic systems available today, the ZEUS robotic surgical system (Computer Motion Inc, Goleta, CA) and the da Vinci Intuitive Surgical system (Intuitive Surgical Inc, Mountain view, CA). Both companies are active in the field of CABG surgery. However, the time for completion of an anastomosis is still very long, in the range of half an hour and more, and ECC is mandatory [18–20]. The rationale for developing the GraftConnector was therefore the obvious need for innovation when it comes to creating vascular anastomoses. For the testing of the GraftConnector, we chose the sheep as a suitable animal because of its size and resemblance to human anatomy. The previous good experience of Ali [23] in 180 operations of surviving sheep undergoing heart surgery encouraged us to use sheep. Our own experience with pigs in previous surviving experiments has not been encouraging, since the pig seems to be more prone to developing stress; while we found the sheep to be very durable and docile and definitely not prone to development of stress symptoms. The experience of Robinson [24] in performing coronary surgery on pigs also discouraged us from using pigs. We found, however, in our experiments that the sheep heart has the same extreme sensitivity to myocardial ischemia as the pig; even with the most careful pharmacology, ventricular fibrillation sometimes occurred only after 2–3 min, especially if the heart-rate was above 80/min. In previous pilot tests in non-surviving animals, good anastomoses were completed in less than 3 min by means of the GraftConnector; we therefore felt it unnecessary to involve ECC in the model, since ECC itself might increase morbidity. The insertion of the GraftConnector had a learning curve, thus to start with we needed 3.5 min to complete the anastomosis, in contrast the last three anastomoses which were completed in 1.5 min. With some improvements in technique and GraftConnector design, we expect the regular completion time for an anastomosis to be 1 min. The flow measurements revealed lower flows in the GraftConnector group when recording the flow with the proximal LAD open. These findings were in contrast to the angiogram which would show the best anastomosis in the vessels with low flow. We also found that anastomoses with problems of the heel showed good flows when the LAD was closed. The most likely explanation for this observation is a presence of competitive flow from the proximal LAD, which creates a low flow in the RIMA if the anastomosis is perfect in both the toe and the heel; the observations of Barnea [25] support this theory. The flows with the proximal LAD closed were similar, which seems natural since only the animals with good anastomoses survived. The measurement of the native flow in the distal LAD of the sheep of 15–18 ml/min was somewhat surprising, but served as a useful reference when it came to interpreting our findings after the completion of the anastomoses. We interpreted the observation of higher flows in the RIMA following proximal LAD-occlusion than the native flows in the LAD to be a result of increased flow during re-perfusion, since the flows were measured directly after ischemia during anastomosis completion. When it comes to the observation of long-term patency in this anastomoses, one should consider that these low flows make this animal model a challenging test for any device and other new techniques in coronary artery surgery.

The advantages of the new GraftConnector are several. Firstly, it has proven to create very fast anastomoses without any suturing on beating hearts. Also, the result seems to be very reproducible even without stabilizers, which might be an important point when it comes to totally endoscopic or robotic surgery. All vessels have a certain elasticity if not completely calcified, and therefore the GraftConnector will expand the receiving artery at the anastomosis. The built-in radial force in the stent of the GraftConnector will dilate the vessel to its maximum elasticity. When performing PTCA, the standard practice is to insert a stent 20–30% bigger than the vessel size on the angiogram. For these reasons, the anastomosis will be round rather than flat, as is the case when suturing the same. The possible disadvantages of this new device include its sensitivity to cover side-branches, and of course the introduction of foreign material. Only the long-term patency will reveal the future of this new device.

5. Conclusion

These experiments prove that coronary artery anastomoses with the new GraftConnector may be carried out in less than 3 min on beating hearts without stabilizers or any suturing. The method proved to be much faster than suturing with the traditional technique under identical conditions. Since the natural flow in the distal LAD of the sheep is low, this is a challenging model for long-term patency studies. The presented device may ultimately permit quick endoscopic anastomoses.
Acknowledgements

The authors wish to thank Dr Raafat El-Sayed for his dedicated work in anesthesia and animal care and Dr William Greer for his great help in getting the statistical analysis correct.

References

[7] Guliemos V, Knaut M, Cichon R, Matschke K, Kappert U, Brandt M, Boettcher Daswinkler C, Ahnert C, Finke D, Fries J, Ahrens G. Stenting of mammary artery intima pretty much averted and tied on by two circular encircling sutures onto a very rigid structure. That means, I believe, that the artery. I cannot tell you how that looks until we sacrifice the animals and send the specimens to the pathology that we will know how it is hooked up on a stent, has somewhat of a gap between it and the endo-thelium of the LAD. This is a very important concern in the design. So how do you propose that you would eliminate this major problem?
[8] Dr Solem: Yes, this is a disadvantage of the connector, you have to pick your site for the insertion so you don’t occlude, for instance, diagonal branches.
[9] Dr Hani Shennib (Montreal, Canada): I think this is an important step towards the consideration of catheter-assisted cardiac surgery in our field. I think it is one of the ways where we can advance enabling technologies and be able to compete as surgeons in the area of coronary revascularization.
[10] But if you look at your design, you have what everybody who does small vessel anastomosis recognizes, is that you put your stent, you use sutureless stent technique to small vessel anastomosis, but in this design, that has worked in the past in smaller animals for a long time, the stent is on the outside and not the inside. What your model proposes is that you have the LIMA with the stent on the outside, which is great, but then you have the stent on the other side inside the graft, which will induce major problems I suspect in the long term.
[11] There is also a step-down component in your design. The LIMA, which is hooked up on a stent, has somewhat of a gap between it and the endo-thelium of the LAD. This is a very important concern in the design. So how do you propose that you would eliminate this major problem?
[12] Dr Solem: I believe that you are focusing on the rim of PTFE, which is between the end of the LIMA inside, the side arm, and the endothelium of the artery. I cannot tell you how that looks until we sacrifice the animals and see how the healing process is at that spot. The only thing I know is that we didn’t see problems with thrombosis so far. So it will be when we sacrifice the animals and send the specimens to the pathology that we will know how this heals.

Appendix A. Conference discussion

Mr Philip Belcher (Glasgow, UK): Do you have any trouble occluding septal arteries? When the stent expands, it appears to be a solid device, do you occlude septal arteries and can this be a problem?

Dr Solem: Yes, this is a disadvantage of the connector, you have to pick your site for the insertion so you don’t occlude, for instance, diagonal branches.
would expect that part will die, just like any other stapled anastomosis in the
general surgery you do, the butt just fades off and necroses. I think you’ve
got to look at the pathology very soon to see if there are any early changes in
the intima. I am concerned about that isolated segment which is not viable.

**Dr Solem:** I think you have a good point there. We are prepared that if
we get disappointing results from this area, we are ready to do the connec-
tion between the connector and the conduit by suturing. This way you can
go all the way into the stent by suturing. I expect this will be the way that we
will do the anastomosis when we use veins, you can still prepare everything
outside the patient. If we are talking about endoscopic surgery, you can
have the conduit out through the port, you can prepare everything outside
the patient. So we are prepared, if we have problems here, we will have to
do suturing between the conduit and the connector.