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An Automatic Sutureless Coronary Anastomotic Device: Initial Results of an Animal Study

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ABSTRACT

Background: The efficacy and long-term patency of a new distal anastomotic device (DAD) for the creation of rapid, sutureless end-to-side venous or arterial coronary artery bypass graft anastomoses were tested in a sheep model.

Methods: The DAD was used on the beating hearts of 34 sheep to create 20 anastomoses between saphenous veins (n = 9) or internal mammary arteries (n = 11) and various coronary arteries. Fourteen conventional hand-sutured anastomoses (7 veins; 7 internal mammary arteries) served as controls. The sheep were sacrificed 1 day, 1 week, and 1, 3, and 6 months after surgery.

Results: The immediate patencies of all anastomoses were proven by the rates and pattern of flow. There were no significant differences between the DAD and suture anastomosis groups in presacrifice pulsatility index and occlusion rate. The histomorphometric studies showed complete intimal bridging over the DAD with no significant differences between DAD and suture anastomoses with respect to tissue response, mural injury, inflammation, and adventitial fibrosis.

Conclusions: The DAD enables the creation of rapid, efficient, and sutureless venous or arterial coronary anastomoses. The long-term results of histomorphometric studies show that the results with the DAD are comparable with those of conventional hand-sutured anastomoses.

INTRODUCTION

Recently, Bypass Ltd (Hertzlia, Israel) designed and developed an anastomotic device that can be used to construct an end-to-side connection between venous or arterial grafts and coronary arteries. This device may be ideally suited for off-pump coronary artery bypass surgery, because it is designed for a very rapid connection, which will reduce myocardial ischemic time and shorten the time in which the heart has to be dislocated.

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The purpose of this study was to evaluate this new method of mechanically creating sutureless end-to-side coronary anastomoses using saphenous veins and internal mammary arteries by comparing it with the conventional suturing technique in terms of the times required to construct the anastomosis, immediate and long-term patency, leakage rate, and histopathology of the anastomosis.

MATERIALS AND METHODS

Design of the Device and the Delivery Technique

The distal anastomotic device (DAD) is an elliptical nitinol ring to which 8 pins are attached (Figure 1). The ring is capable of expanding and adjusting itself to the local coronary anatomy while the pins attach the graft and the vessel wall against the ring to create the anastomosis (Figure 2). Vessels with an outer diameter (OD) of 2 to 6 mm were accommodated by the design of 2 sizes of the DAD, one with internal diameters of 3.22 × 1.84 mm intended for grafted vessels of 2 to 3.5 mm OD and the other with internal diameters of 5 × 3 mm for vessels with an OD of 3 to 6.0 mm. Both sizes are intended for use in all target coronary arteries that are suitable for conventional suturing. The vein or artery graft is inserted through a side opening in the delivery capsule that harbors the DAD at its distal end and then pulled through the central opening in the DAD with a special snare (Figure 3). The beveled end of the graft is then flared with the aid of special forceps over the 8 circumferential pins that are designed to penetrate it. Turning a knob located at the base of the capsule advances the pins forward and converges them, enabling the device to be inserted through a small coronary arteriotomy (Figure 4). Following the completion of the loading procedure (which can be done after the proximal side of the vein has been connected to the aorta), the capsule is connected to a handle set that enables deployment. At the appropriate site on the vessel to be bypassed, an arteriotomy is made with a special "arteriotome" or by conventional means to a predetermined length measured by a sizer.

The converged pins are then introduced into the coronary artery. When it is certain that all pins are properly placed within the lumen, the handles are squeezed, and the pins diverge to approximate and fix the graft to the coronary artery (Figure 5).

Surgical Procedure

Thirty-four mature female sheep weighing 60 to 80 kg were used. Studies were conducted at Technion, Israel Institute

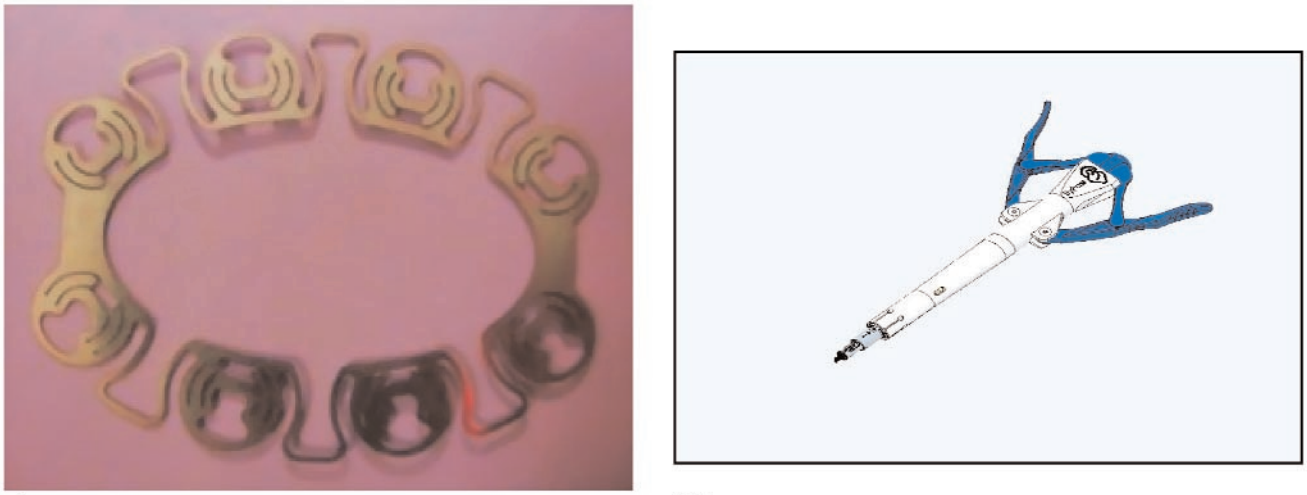

Figure 1. The Bypass distal anastomotic device. A, The compliant nitinol rings with 8 ports to accommodate the fixating pins. B, The delivery handle with the distal anastomotic device at its tip.

of Technology, Faculty of Medicine, Haifa, Israel, after obtaining approval from the institute's ethical committee for animal experiments. All proceedings complied with the Animal Welfare Act of 1966 (PL 89-544) as amended by the Animal Welfare Act of 1970 (PL 91-579) and 1976 (PL 94-279). The sheep were divided into 2 major groups. In the DAD group comprising 20 sheep, a saphenous vein (n = 9) or the right internal mammary artery (n = 11) was connected with the DAD to a coronary artery. In the control group comprising 14 sheep, a saphenous vein (n = 7) or the right internal mammary artery (n = 7) was anastomosed to a coronary artery by conventional sutures. Sheep were medicated with 325 mg/day aspirin 48 hours prior to intervention.

After premedication with 10 mg/kg ketamine and 0.2 mg/kg xylazine, general anesthesia was induced with 10 mg/kg thiopental sodium (Pentothal) and maintained with 1.5% isoflurane. Intravenous and arterial lines were inserted for fluid and drug administration and continuous blood pressure monitoring (Propaq 100 vital signs monitor; Welch Allyn Protocol, Beaverton, OR, USA), and electrocardiograms were obtained. Saphenous veins were harvested from the sheep's hind legs and immediately immersed in normal saline solution containing 5000 U heparin. All sheep were treated with slow intravenous administration of 150 mg amiodarone and 0.5 mg fentanyl, followed by an intravenous bolus of 75 mg lidocaine given immediately before manipulating the heart. An analgesic (0.6 mg buprenorphine) was given at the beginning of the procedure. A left anterolateral thoracotomy at the third or fourth intercostal space was performed, followed if needed by dissection of the right internal mammary artery with low-grade cautery. When venous grafts were used, their proximal ends were manually sutured (5-0 polypropylene) to the sheep's brachiocephalic trunk after its occlusion by a side-biting clamp. Heparin (10,000 IU) was intravenously injected in each animal, with additional amounts given to maintain the activated coagulation time (Hemotec; Medtronic Hemotec, Englewood, CO, USA) longer than 300 seconds until completion of the surgical procedure. On completion of the graft preparation and loading it onto the capsule, the pericardium was incised, and a coronary artery of a suitable size was chosen. A 5-0 polypropylene suture was placed around the artery for snaring. In the control group, a stabilizer (off-pump coronary artery bypass access system; CardioThoracic Systems, Cupertino, CA, USA) was used to stabilize the anastomotic area. Because sheep are prone to develop intractable ventricular fibrillation during prolonged ischemia, preconditioning (periods of 1, 2, and 4 minutes of coronary occlusion separated by reperfusion periods of 1 minute) was performed in the control group. In the DAD group, stabilizers were not used, and preconditioning was not performed. Grafts were then connected to the coronary artery with either the DAD or the conventional continuous-suture technique (polypro-

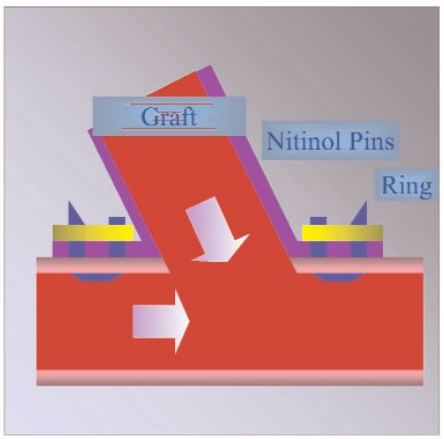

Figure 2. Schematic view of the graft connected to a coronary artery by the distal anastomotic device.

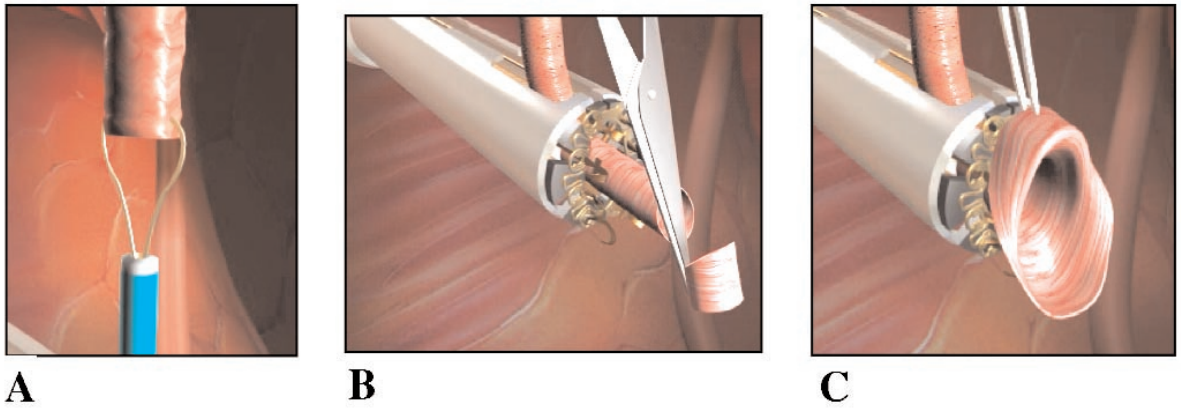

Figure 3. Graft loading. A, The graft is inserted through the device with a snare. B, The distal end of the graft is beveled. C, The graft is flared over the pins with a special penetrating tool.

pylene 7-0 suture). A carbon dioxide gas blower was used to improve visibility in the anastomotic area. The time for completing the anastomosis was defined as the time from the closure of the snare prior to arteriotomy to the time of its release. After the final ligation of the proximal coronary artery, the blood flow in the graft was measured with a transit-time flowmeter (Transonic model 106, probe CM4B or CM3B; Transonic Systems, Ithaca, NY, USA). The pericardium was then loosely reapproximated into position, a temporary chest tube was inserted, and the chest was closed. General anesthesia was terminated, and the sheep was extubated upon the resumption of vagal reflexes. Anticoagulation treatment was not reversed.

Postoperatively, the sheep were treated with antibiotics (1 g/day amoxycillin) for 7 days, analgesics for the first 3 days, and 325 mg/day aspirin until sacrifice.

Animals were scheduled for sacrifice after the operation at time intervals ranging from 24 hours to 6 months, as detailed in the Table. The sacrifice intervals were chosen to permit the evaluation of both acute and chronic tissue responses. Before sacrifice and following anesthesia and tracheal intubation, a rethoracotomy was performed. The graft was carefully dissected, and the anastomotic site was inspected. The blood flow through the grafts was measured in the same way as during the initial operation. The anastomoses were carefully harvested after the animals were killed.

Specimen Preparation

A 3 × 3 × 3–cm segment of the myocardium surrounding the anastomotic site was excised together with a graft segment 4 cm long. After a rinse with a 5% dextrose solution, the whole specimen was fixed in 10% neutral buffered formaldehyde. Radiographs of the specimen were taken to help locate the anastomosis as well as to evaluate the integrity of the device. The specimens were trimmed to the appropriate size and were dehydrated through graded alcohol solutions. The specimens were cleared with xylene and infiltrated with methyl methacrylate for polymerization at 37°C for 24 hours. Approximately 10 mm of the selected area of the plastic blocks was cut at 0.6-mm intervals with a low-speed rotary saw mounted with a diamond wafering blade. Sections 50 to 100 μm thick were further polished down in thickness and stained with a metachromatic stain. The sections were mounted on glass slides with immersion oil and examined with a Nikon Labphot II compound microscope (Nikon, Tokyo, Japan). Sections closest to the midaxis of the anastomosis were selected for data measurement.

Statistics

All data are presented as the mean ± standard deviation. The Student *t* test and the Fisher exact test were used for statistical analysis. A *P* value of less than .05 was considered statistically significant.

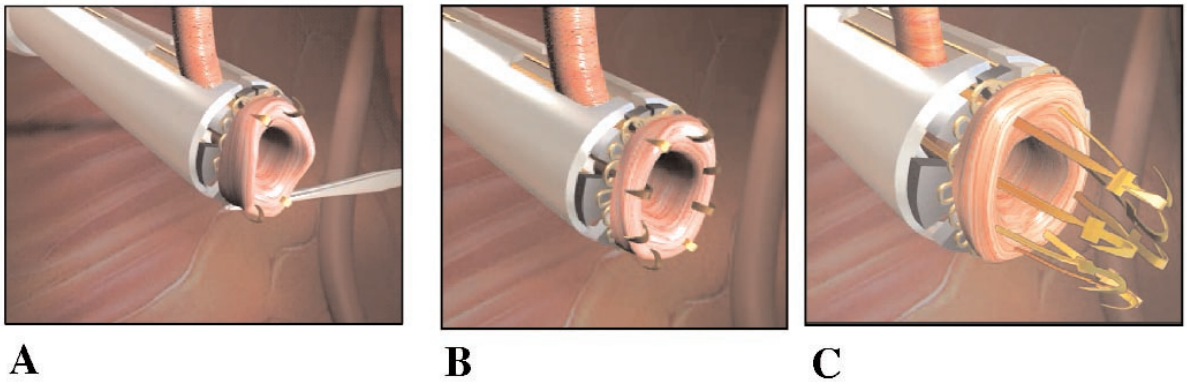

Figure 4. A, With a special forceps, each pin is made to penetrate the graft wall. B, View of the distal anastomotic device and the fully loaded graft. C, The pins are advanced forward to converge and become ready for deployment.

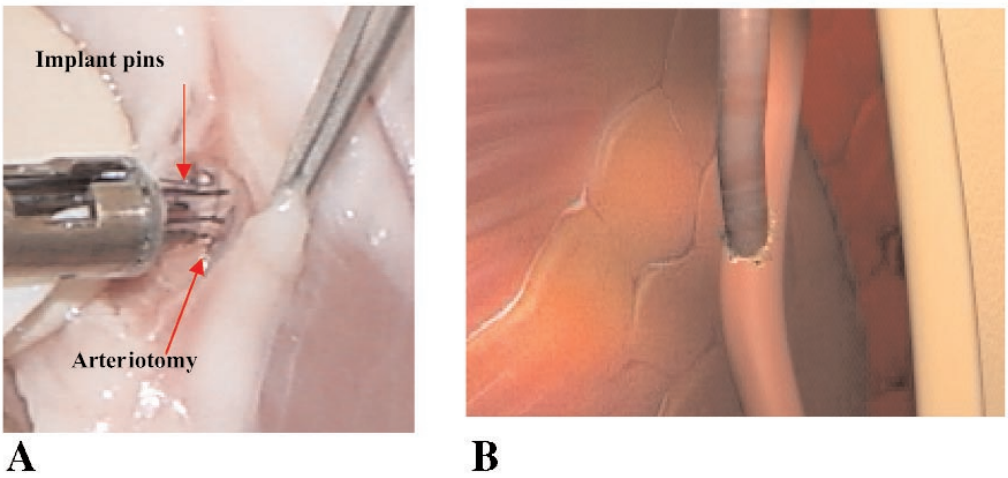

Figure 5. A, Insertion of the distal anastomotic device into the arteriotomy. B, The completed anastomosis.

RESULTS

Thirty-four anastomoses (20 DAD and 14 suture controls) were created, and the grafts (18 right internal mammary arteries, 16 saphenous veins) were connected to various coronary arteries in the DAD group (7 left anterior descending, 9 diagonal, and 4 marginal arteries) and the control group (1 left anterior descending, 8 diagonal, and 5 marginal arteries). Target coronary vessels were chosen for their suitable size (>1 mm) and ease of exposure.

The average time required for the construction of 19 of the 20 DAD anastomoses was 24 ± 7.4 seconds (range, 10-30 seconds), compared with 660 ± 198 seconds (11.1 ± 3.3 minutes) in the suture control group ($P < .0001$).

In one DAD case, an operator error (improper locking of the capsule into the delivery handle) caused the misfiring of the device. Lengthy corrective measures prolonged the anastomotic time to 160 seconds. This case was regarded as an outlier and not included in the statistical calculations.

Leakage was observed in 10 DAD and 2 sutured control anastomoses. Seven of these anastomoses (6 DAD, 1 control) required an additional stitch for hemostasis, whereas leakage in the remaining 5 anastomoses ceased with only the application of local pressure and without any additional surgical intervention.

All 34 anastomoses were patent immediately after their creation. The mean rate for the flow measured after proximal native coronary artery occlusion was 27.7 ± 22.3 mL/min for the DAD group, compared with 35.0 ± 37.9 mL/min for the suture control group (not significantly different). No significant differences in flow rates were found between internal mammary artery and vein grafts in either group. The pulsatility index was 3.7 ± 1.9 for the DAD group and 3.1 ± 1.2 for the control group (not significant).

All DAD-mediated grafts came off the coronary arteries in a smooth angularity with no kinks. Three of the 20 DAD anastomoses were found to be totally occluded before sacrifice (1 at 30 days and 2 at 180 days after surgery), compared with 2 of the 14 sutured anastomoses (7 days and 90 days after surgery). These results yielded a patency rate of 85% for the DAD group and 86% for the hand-sutured anastomoses (not significant).

Average presacrifice flow rates for the two groups were similar (DAD, 24.6 ± 21.4 mL/min; control, 28.9 ± 29.4 mL/min) and not significantly different, as were the average presacrifice pulsatility indices (DAD, 6.03 ± 2.42; control, 6.93 ± 3.92).

Histomorphometric Results

The separation of components or possible breaks were detected by radiography in 8 devices. These events were not associated with any significant hemorrhage or disruption of the anastomoses.

Acute thrombosis was seen in 8 samples (4 DAD and 4 controls), and an organized clot was seen in 5 DAD and 2 control samples. Neointima was seen bridging the anasto-

Sacrifice Schedule*

		DAD, n			Suture Controls, n		
Time to Sacrifice	Total, n	Total	SVG	RIMA	Total	SVG	RIMA
24 h	6	4	2	2	2	1	1
1 wk	6	4	1	3	2	1	1
1 mo	6	4	2	2	2	1	1
3 mo	8	4	2	2	4	2	2
6 mo	8	4	2	2	4	2	2
Total	34	20	9	11	14	7	7

*DAD indicates distal anastomotic device; SVG, saphenous vein graft; RIMA, right internal mammary artery.

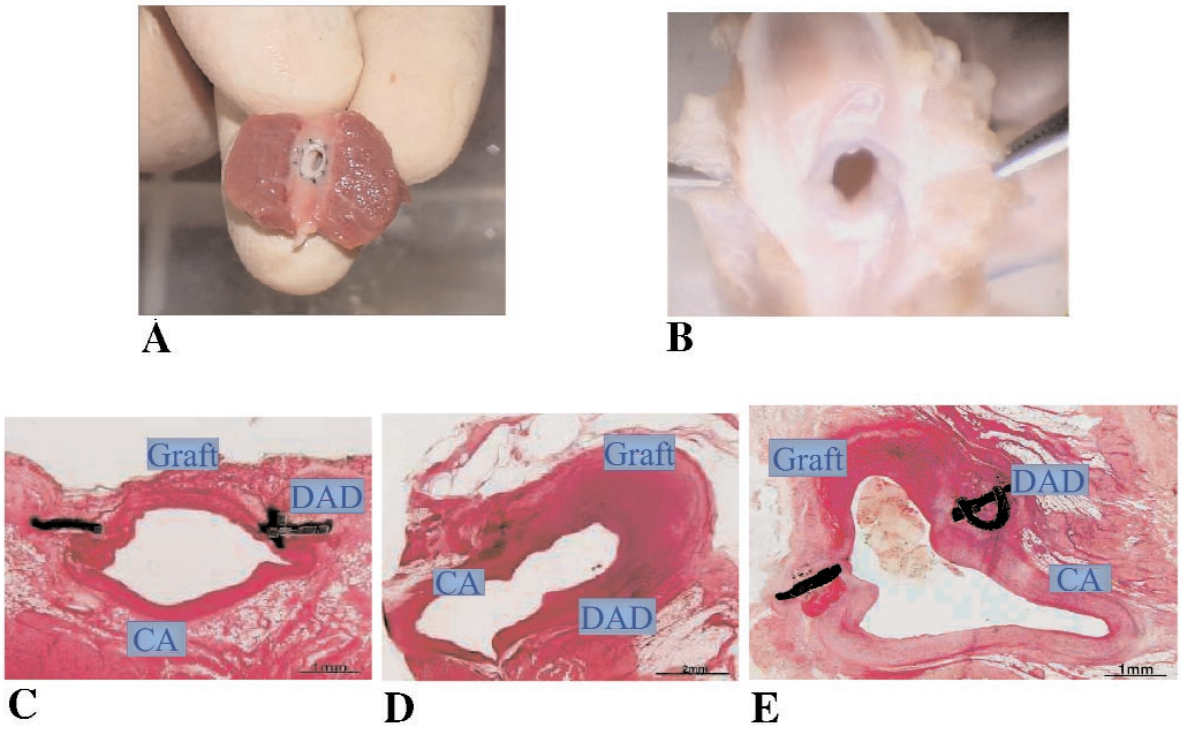

Figure 6. Appearance of the anastomosis created by the distal anastomotic device (DAD). Gross appearance immediately after anastomosis creation (A) and at 180 days postoperatively (B). Microscopic appearance at 7 days (C), 90 days (D), and 180 days (E) postoperatively. CA indicates coronary artery.

moses examined at 1, 3, and 6 months after surgery. The adventitia was sealed at the anastomosis by adventitial fibrosis. A thick intima of 400 μm (0.4 mm) or greater at the point of the anastomosis, which might be the cause of significant luminal stenosis, was seen in 9 DAD anastomoses and 6 controls (not significant). Four of these samples were in the 30-day group, 6 were in the 90-day group, and 5 were in the 180-day group. The thickness of the intimal bridging across the anastomosis was 0.53 ± 0.52 mm in the DAD group and 0.48 ± 0.52 mm in the controls (not significant).

Most of the examined samples (19/20 DAD and 11/14 controls; not significant) were found to have mural injuries to the graft as well as to the native coronary artery at or near the anastomosis. This damage is probably inherent in the procedure, regardless of the technique performed (Figure 6).

DISCUSSION

The increasing use of minimally invasive cardiac surgical procedures in which coronary artery bypass grafting is performed on the beating heart and through small access ports has been accompanied by a growing interest in new anastomotic techniques [Werker 1997, Shennib 2001, Subramanian 2002]. These techniques are intended to reduce the laborious and sometimes difficult conventional suturing approach, shorten the ischemic and cardiac dislocation times, and thus perhaps increase the safety of the procedures and improve outcomes.

In the present study, the first in a series of preclinical investigations testing the new DAD manufactured by Bypass, the immediate, midterm, and long-term patencies, complication rates, and tissue responses were evaluated and compared in a sheep model with those of conventionally hand-sutured anastomoses.

In 10 of the 20 DAD anastomoses, a perianastomotic leak was seen immediately after deployment. One of the important aspects of the DAD procedure is the precision of the adjustment between the length of the coronary arteriotomy and the size of the device. A short arteriotomy will hinder device insertion into the coronary artery, whereas a long arteriotomy might result in a perianastomotic leak. The optimal length of the arteriotomy was determined during the study period, and the leakage rate subsequently decreased.

Although the patency rates were found to be similar for the DAD and the sutured anastomoses, the finding that intimal thickening equally affected the DAD and the control sutured specimens was significant. This result may be due to factors such as local injury and/or inflammation, which have been described in several studies that have used nitinol for endovascular implants [Schurmann 1996, White 1998]. Moreover, the thickened intima probably can at least partially be attributed to the animal model used, because some species tend to form a thicker intima through smooth muscle migration and proliferation [Schwartz 1993, Wilensky 1995, Schwartz 1999]. In the future, adding a more aggressive antiplatelet therapy such as clopidogrel may prove to be beneficial for reducing the intima response in this model.

The high proportion of device breaks (8/20), although inconsequential, deserves attention. Some of the breaks are probably attributable to the manipulation of the device while removing it

after the sacrifice of the animal, but additional data and testing are required to reduce the frequency of device breaks.

With respect to the histomorphometric analyses, the DAD appears to provide a good seal with no significant hemorrhage at the point of anastomosis. Its performance is comparable with that of the conventional suture technique. The intima was sealed with neointima traversing the gap of the anastomosis, and the media plus adventitia showed healing by fibrosis.

This study has several limitations. Because one of the aims was to evaluate the tissue response during the healing process, only a few animals were followed up for periods exceeding 3 months. Thus, long-term patency (>3 months) cannot be definitely determined. A second major limitation is that all anastomoses were constructed on normal animal vessels, which are substantially different from rigid, diffusely atherosclerotic human arteries. To address the first limitation in future animal studies, we plan to include larger homogenous groups that will be followed up by angiography for longer periods. Planned clinical studies will address the second limitation.

The results of this initial animal study show that the patency rates of the DAD, both immediately and up to 180 days after surgery, are comparable with those of conventional hand-sutured anastomoses. No significant differences were noted between the two methods.

The DAD has several distinctive features that may make it a suitable alternative to the conventional suturing anastomotic technique. It enables a safe, efficient, angular, reproducible, and very rapid end-to-side connection of both venous and arterial grafts to coronary arteries. Confirmation of the initial results found in this study in future preclinical and clinical investigations probably will greatly influence the management of minimally invasive surgical approaches to coronary artery disease.

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