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European Journal of Cardio-thoracic Surgery 23 (2003) 925–934

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

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Evaluation of a novel 2 mm internal diameter stainless steel saphenous vein to coronary artery connector: laboratory studies of on-pump and off-pump revascularization☆

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Received 3 September 2002; received in revised form 24 February 2003; accepted 3 March 2003

Abstract

Objective: A second generation, 'easy-load', 2 mm internal diameter (ID), stainless steel, distal anastomotic device has been developed, and design improvements facilitate rapid connector loading with minimal magnification. The reduced size should allow application to most distal coronary vessels currently grafted. This technology may be useful in off-pump and minimally invasive surgical approaches to coronary revascularization. **Methods**: Two distinct models were used to evaluate the distal connector. In the first model, a single saphenous vein graft (SVG)-to-LAD procedure ($n = 18$) was used to evaluate long-term patency of the 2 mm ID, stainless steel, distal connector in a chronic canine model. Cardiopulmonary bypass was initiated through an anterolateral thoracotomy. Aortosaphenous vein anastomoses were created using suture. In the second model, an acute off-pump feasibility study of SVG-to-LAD bypass fashioned with both proximal and distal connectors ($n = 15$) was conducted. Aortosaphenous vein anastomoses were performed using a FDA approved vascular connector. Device loading and deployment times, graft blood flow following native LAD ligation, and device-related complications were compared. In the chronic model, the grafts were examined by angiography and gross and microscopic examination at animal sacrifice. **Results**: All 33 animals survived the procedures. All grafts were widely patent after a minimum 30 ($n = 8$), 90 ($n = 5$), and 180 days ($n = 5$) in the chronic model. Distal graft loading and deployment times, graft blood flow rates, and device-related complications were similar in both procedures. In the off-pump feasibility study, total grafting time including loading and deployment was 10:54 ± 2:54 min. **Conclusions**: Sutureless SVG-to-coronary artery bypass is feasible, rapid, and reproducible with on- and off-pump surgical techniques using a 2 mm ID, stainless steel, distal connector. In this model, early graft patency was 100% with either procedure, and grafts performed on-pump were widely patent at 30, 90, and 180 days. Few device-related complications occurred, each easily managed without compromising graft integrity, and the incidence of events was similar whether on- or off-pump techniques were employed. This or similar technologies may become an important addition to the management of coronary artery disease, particularly in off-pump or minimally invasive approaches.

Keywords: Off-pump coronary artery bypass; Minimally invasive surgical procedures; Surgical anastomosis; Suture techniques; Surgical equipment

1. Introduction

Recently, novel, metallic vascular connector devices and delivery systems (Anastomotic Technology Group, St. Jude Medical, Inc., Minneapolis, MN) have been developed that can be used to construct aortosaphenous vein and saphenous vein graft (SVG)-to-coronary artery anastomoses. Initial laboratory and clinical results appear to be equivalent to those created by suture [1–3]. The connector system may be ideally suited for 'off-pump' coronary artery bypass. Unlike clips or staples employed previously for vascular anastomoses [4,5], this system is applicable with atherosclerotic arteries since penetration or eversion of the calcified walls is not required for optimal intimal apposition.

A first generation of proximal aortosaphenous vein graft connectors (Symmetry Bypass System Aortic Connector®,

☆ Presented at the 16th Annual Meeting of the European Association for Cardio-thoracic Surgery, Monte Carlo, Monaco, September 22–25, 2002.

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[1] Dr Bonilla and Messrs Berg, Cornelius, and Hindrichs disclose that they have a financial relationship with St. Jude Medical, Inc.

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doi:10.1016/S1010-7940(03)00151-9

Anastomotic Technology Group, St. Jude Medical, Inc., Minneapolis, MN) has been used clinically in over 30 000 anastomoses performed throughout Europe and North America. Immediate results of proximal vein graft anastomoses have demonstrated rapid connector deployment (less than 10 s) with instantaneous hemostasis in 62 of 65 anastomoses [1]. The system failures were easily corrected by device removal and sutured revision. All grafts were patent at procedure's end. Long-term results are pending.

Likewise, promising results have been attained with the first generation distal SVG-to-coronary artery connector. In pre-clinical animal studies, a comparison of this device versus suture ($n = 12$) in an on-pump canine model showed no significant inter-group differences in vessel diameters, intraoperative graft flows, graft patency, and histology following 30-day sacrifice [2]. No mechanical failures occurred, and immediate hemostasis was obtained at all connector-fashioned anastomoses. Mean time for anastomotic performance with connectors was 3 min compared to 8.4 min for sutures ($P < 0.0001$). In a longer-term chronic study, a similar dog model found comparable results following 30-, 90-, and 180-day survival [3]. All grafts were patent on presacrifice angiography and there were no significant histologic differences between connector and sutured anastomoses at all time points. Remarkably, intimal overgrowth of connectors did not appear to substantially progress over time when comparing survival groups. One significant downside to the first generation distal connector was the requirement to load the vein onto the connector using a 10× operating microscope. This proved cumbersome and was time consuming.

Evolution in distal connector technology has produced a second generation, 'easy-load', 2 mm internal diameter (ID), stainless steel, anastomotic device with design improvements that facilitate rapid connector loading under minimal magnification (2×). Size reduction should allow application to most distal coronary vessels currently grafted. The purpose of this study was to evaluate this novel second generation distal connector in two distinct experimental models. First, to examine the long-term patency of the bypass graft in a standard on-pump chronic canine model, and second, to determine the acute feasibility of an off-pump SVG-to-LAD bypass performed with both proximal and distal connector devices.

2. Materials and methods

2.1. Connector designs and delivery technique

A stainless steel connector (Anastomotic Technology Group, St. Jude Medical, Inc., Minneapolis, MN) was designed to create side-to-side SVG-to-coronary artery anastomoses. Side-to-side technique was chosen because it allows accommodation of the connector to different conduit sizes, produces a uniform anastomosis diameter equivalent to the coronary artery diameter, and provides an optimal takeoff angle to prevent kinking. The connector contains external fingers that secure the SVG and internal fingers that engage the coronary artery internal lumen. A nose cone covers the internal fingers to prevent coronary artery endothelial trauma during intubation. The connector mounts on a balloon catheter (Fig. 1A), which, when pressurized, expands the connector creating the anastomosis while simultaneously reducing its length, firmly apposing the two vessels to create a hemodynamic seal. The connector body remains in place and adds structure to the anastomosis.

An opening is made in the vein wall approximately 1 cm from the distal end of the graft with a preformed 1.25 mm cutting device and a 1.5 mm Teflon-coated dilator (DuPont, Parkersburg, WV). The delivery system is passed through the distal end of the vein, and the external connector fingers engage the graft endothelium as the nosecone emerges from the new ostium (Fig. 1B).

At the appropriate target site in the bypassed vessel, an arteriotomy is made with the same preformed cutting device and dilator. The delivery system is then introduced axially through the arteriotomy until the new graft ostium intimately apposes the coronary artery wall (Fig. 2A). With the artery intubated, the nosecone is advanced uncovering the internal fingers, and the delivery system is repositioned perpendicular to the long axis of the coronary artery. The balloon is then inflated, radially expanding the connector to a uniform cylindrical configuration (Fig. 2B). Following connector expansion, the delivery system is removed and the distal vein graft stump ligated sufficiently close to the anastomosis to avoid a large cul-de-sac without compromising the vein-anastomosis lumen (Fig. 2C).

A FDA approved, commercially available proximal connector (Symmetry Bypass System Aortic Connector®, Anastomotic Technology Group, St. Jude Medical, Inc.,

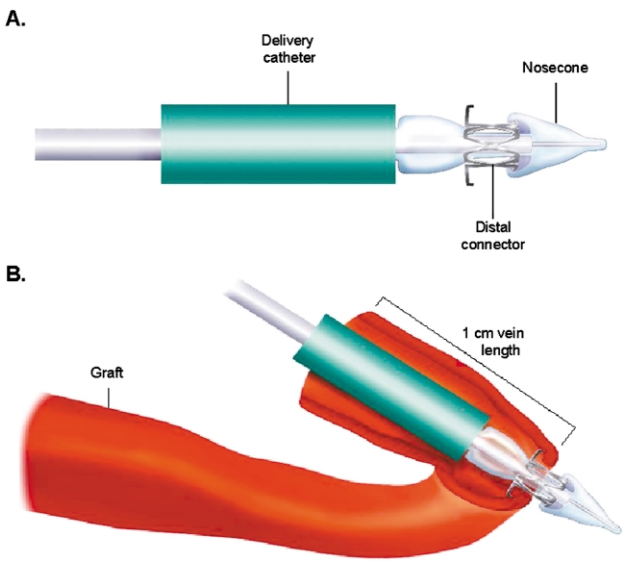

Fig. 1. (A) Connector and delivery system. (B) Connector and delivery system loaded into the graft.

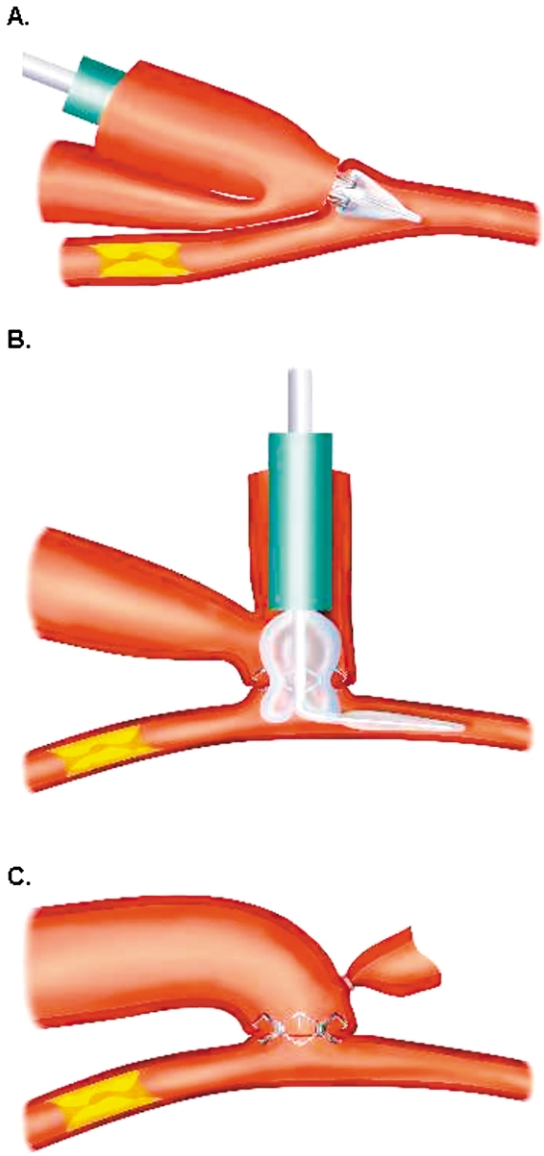

Fig. 2. The connector and delivery system are introduced axially through the arteriotomy (A); and balloon inflation radially expands and shortens the connector (B). Once the delivery system is removed, the distal vein stump is ligated close to the anastomosis to avoid a large cul-de-sac without compromising the vein-anastomosis lumen (C).

Minneapolis, MN) was used for aortosaphenous vein anastomoses in acute off-pump feasibility studies. This aortic connector system consists of a nickel-titanium (nitinol) connector, a delivery system, and an atraumatic aortic cutter with a rotatable blade to create a precisely sized, round hole without the need of an aortic partial occlusion clamp. Proximal connector loading and deployment was performed as previously described by Eckstein and colleagues [1].

2.2. Surgical procedure

Chronic distal connector studies were performed in conjunction with the Experimental Surgical Services Laboratory, University of Minnesota, Minneapolis, MN. Acute off-pump feasibility studies were performed in conjunction with the Division of Cardiovascular Surgery, Mayo Clinic, Rochester, MN.

Thirty-three adult male canine subjects (weight 26–34 kg) were used, eighteen for chronic studies and fifteen for acute. All animals were obtained from licensed suppliers and treated in accordance to the principles stated in the 'Guide for the Care and Use of Laboratory Animals' published by the National Institute of Health (NIH publication 85-23, revised 1985). The Animal Care and Use Committee of Mayo Clinic and Mayo Foundation and the University of Minnesota approved all procedures and protocols. Mayo Clinic and the University of Minnesota comply with the Animal Welfare Act of 1–66 (PL 89–544) and the Animal Welfare Act amendment of 1985 (PL 99–198).

Animals underwent induction of anesthesia with sodium thiopental (15 mg/kg to effect). After orotracheal intubation, the animals were ventilated mechanically and anesthesia maintained with halothane (1–1.5%). The electrocardiogram and blood pressure through a femoral arterial line were monitored continuously throughout the procedure. Chronic animals received Cefazolin (1 gm IV) during induction of anesthesia. Initial muscle relaxation was obtained with a solitary injection of pancuronium bromide (0.05–0.1 mg/kg).

Procedures were performed under sterile conditions in chronic animals. Animals were placed in the supine position, and both saphenous veins were harvested. The proximal and distal outer diameter (OD) of the veins were measured. To facilitate loading of the distal connector device, veins with a minimum OD of 4 mm were chosen as grafts. Veins were loaded with both proximal and distal connectors in acute studies and with distal connectors in chronic studies. After animals were repositioned, the heart was exposed through a left fourth intercostal space thoracotomy, and systemic anticoagulation was obtained with heparin (300 U/kg).

In chronic animals, an arterial perfusion cannula was placed in the right femoral artery and a venous return cannula was inserted through the right atrial appendage for extracorporeal circulation. During normothermic cardiopulmonary bypass, fibrillatory arrest was induced to obtain a still field. The middle third of the LAD was dissected, and the OD of the vessel measured. Device modifications of the second generation distal connector allow anastomoses to coronary vessels with an ID of 2 mm or greater; therefore, a region of the LAD with an OD of 2.5 mm (estimated ID of 2 mm) was chosen as the anastomotic site.

Proximal and distal 4-0 Prolene (Ethicon, Somerville, NJ) snares were placed to control bleeding through the coronary artery during construction of anastomoses. Hearts were cardioverted following completion of distal anastomoses. Aortosaphenous vein graft anastomoses were performed with running 6-0 Prolene suture.

Chronic animals were weaned off bypass, and once normal hemodynamics were obtained, flow through the grafts were measured using a Doppler flow probe (Small Animal Blood Flow Meter T-206, Transonic Systems, Inc., Ithaca, NY) before and after ligating the native coronary arteries proximal to the graft anastomosis. Protamine sulfate (1 mg for each 100 U of heparin) was then given, and meticulous hemostasis was achieved. The pericardium was approximated, a small drainage tube was placed in the left pleural space, and the wound was closed in layers. After the animal satisfactorily recovered form anesthesia, the chest tube was removed.

Acute animals maintained their own native circulation off-pump throughout the procedure. The middle third of the LAD was dissected and proximal and distal 4-0 Prolene snares were placed as in chronic animals to control bleeding through the coronary artery during anastomosis construction. The upper descending aorta was then partially occluded with a side-biting clamp and the aortosaphenous vein graft anastomoses performed with the proximal connector system. SVG-to-LAD anastomoses were then performed on the beating heart with the distal connector and flows obtained as in the chronic animals.

2.3. Postoperative care

Chronic animals received Cephazolin (1 gm IV) every 8 h for the first 24 h. Buprenorphine Hydrochloride (0.005 mg/kg intramuscularly) was used for pain control. Aspirin (325 mg orally) and Dypiridamol (20 mg orally) were given once a day until the day of sacrifice.

2.4. Conclusion of survival period

Chronic animals were subdivided into three survival groups and maintained for a minimum 30, 90, or 180 days prior to sacrifice. At the end of the survival period, chronic animals underwent general anesthesia as during the surgical procedure and a coronary angiogram was obtained with standard technique. With the animal heparinized (10 000 units IV) and still under deep general anesthesia, an overdose injection of pentobarbital followed by 40 mEq of potassium chloride was given.

Following euthanasia, the heart, bypass grafts, and thoracic aorta were excised en bloc and pressure-perfused at physiologic pressures with 10% neutral-buffered formalin for a minimum of 2 h. The specimens were then sent for gross and microscopic evaluation. Sub-gross photographs of the distal connector were prepared. Sections from the proximal and distal anastomoses, vein grafts, and coronary arteries immediately distal to the anastomoses were examined.

The connectors were processed and embedded in methylmethacrylate, cut using a diamond band saw (Exakt™ System), and ground and surface stained with hematoxylin and eosin (H&E). The remainder of tissues were processed through graded alcohols, embedded in paraffin, and stained with H&E, Masson's trichrome, and Verhoeff's elastic stains. The entire myocardium was examined grossly for the presence of infarction.

2.5. Statistical analysis

Continuous data are presented as mean plus or minus the standard deviation and range where indicated. Distal connector device loading and deployment times and graft blood flow following native LAD ligation were compared between off- and on-pump studies using Student's *t*-test (JMP Application 4.0.4, SAS Institute, Inc., Cary, NC). The incidence of intraoperative device-related complications for distal connectors, including device mechanical failure, leak, or rupture were compared between off- and on-pump procedures using Fisher's exact test. Two-tailed *P* values less than or equal to 0.05 were considered statistically significant. Chronic graft angiographic patency and distal anastomosis patency as determined from pathologic examination were descriptively reported.

3. Results

Chronic on-pump and acute off-pump results are summarized in Tables 1 and 2, respectively. All animals survived the procedures. In the chronic model, eighteen SVG-to-LAD procedures grafts were created on-pump with distal connectors and sutured aortosaphenous anastomoses. In the acute model, 15 beating heart SVG-to-LAD procedures were performed off-pump with both distal and proximal connectors. Mean proximal connector loading time was 248 ± 68 s (range 126–370 s) and deployment time was 56 ± 18 s (range 30–90 s). Total time for off-pump graft completion was 10:54 ± 2:54 min (range 5:54–15:40 min). No significant difference was noted between mean distal connector loading and deployment times in on- and off-pump procedures (mean loading time was 86 s for on-pump and 92 s for off-pump; mean deployment time was 205 s for on-pump and 194 s for off-pump, P = NS) (Fig. 3). Mean graft flow following native LAD ligation also did not differ significantly between on- and off-pump procedures (38.7 ml/min for on-pump and 35.5 ml/min for off-pump; P = NS) (Fig. 3).

Device-related complications were not encountered during deployment of any proximal connectors in off-pump procedures. However, three device-related complications were encountered with distal connector deployment for an overall incidence of 9% (Table 1). All of these events were observed in off-pump procedures. One distal connector was damaged upon removal of the delivery system in animal number 15, necessitating replacement with a second device. The second device was loaded in the chest and deployed without difficulty; loading, deployment, and off-pump coronary bypass times given in Table 1 reflect performance

Table 1
On-pump distal connector operative data

Animal No.	Loading time (s)	Deployment time (s)	Graft flow (ml/min)[a]	Complications
1	103	170	36	None
2	55	225	35	None
3	40	165	31	None
4	72	170	30	None
5	48	143	39	None
6	100	500	24	None
7	71	188	36	None
8	48	143	60	None
9	67	150	36	None
10	35	118	40	None
11	60	210	19	None
12	246	175	45	None
13	76	136	26	None
14	181	143	36	None
15	90	230	56	None
16	107	393	36	None
17	88	129	37	None
18	62	210	74	None
Mean	86	205	38.7	
(SD)	(52)	(97)	(13.3)	

[a] Graft flow measured following native LAD ligation; SD, standard deviation.

of the first device. Hemostasis was not instantaneous in animals 8 and 9, with a small leak developing that was easily corrected with a single suture. Though a trend towards more device-related complications was observed in off-pump procedures, this incidence did not differ statistically from on-pump procedures (20 versus 0%, respectively; $P = 0.08$).

All chronic animals survived to the minimum anticipated date of sacrifice ($n = 8$, $n = 5$, and $n = 5$ for 30, 90, and 180 days, respectively) (Table 3). Angiography performed prior to euthanasia demonstrated patent grafts in all cases (Fig. 4). All distal anastomoses were photographed after opening the opposite coronary artery wall longitudinally; representative photographs from each survival group are displayed in Fig. 5. Regardless of survival period, distal anastomoses were widely patent on gross examination in all animals except one animal within the 180-day survival group. In this case (animal number 17), the anastomosis was mild-to-moderately stenotic (5 mm ID diameter approximately), and the connector appeared compressed.

Representative photomicrographs from each survival group taken at the level of the distal anastomosis are also given in Fig. 5. Microscopic examination demonstrated a thin-to-moderate fibrous neointima covering distal connector lumenal surfaces in most specimens (Table 3). Three specimens (animal numbers 7, 9, and 11) displayed areas of thick neointima overlying the connector; however, neointimal formation did not compromise any of the anastomoses. Connectors were surrounded by fibrous connective tissue without any significant ongoing inflammation. Hemosiderophages were present within the neointima and surrounding fibrous tissue in a number of specimens consistent with the normal inflammatory reaction to acute hemorrhage occurring during connector deployment.

Table 2
Off-pump proximal and distal connector operative data[a]

Animal No.	Loading time (s)		Deployment time (s)		Total OPCB time (min)	Graft flow (ml/min)[b]	Complications
	Proximal	Distal	Proximal	Distal			
1	N/A	N/A	N/A	N/A	12.38	14	None
2	N/A	84	35	250	10.42	43	None
3	270	93	44	128	8.55	31	None
4	260	90	50	250	8.75	67	None
5	255	66	90	225	11.25	109	None
6	210	135	75	133	15.55	42	None
7	327	133	45	198	12.47	38	None
8	250	80	58	255	15.67	20	Distal anastomotic weep, suture controlled
9	208	80	58	102	5.87	26	Distal anastomotic weep, suture controlled
10	370	94	57	156	8.3	27	None
11	200	90	75	90	8.5	37	None
12	180	60	30	240	9	16	None
13	126	130	40	220	10.4	30	None
14	N/A	66	76	279	11.73	15	None
15	317	N/A	N/A	N/A	14.88	18	Distal connector damaged, replaced[c]
Mean	248	92	56	194	11	35.5	
(SD)	(68)	(25)	(18)	(64)	(3)	(24.7)	

[a] OPCB, off pump coronary artery bypass; N/A, information not available; and SD, standard deviation.
[b] Graft flow measured following native LAD ligation.
[c] OPCB time reflects initial connector deployment.

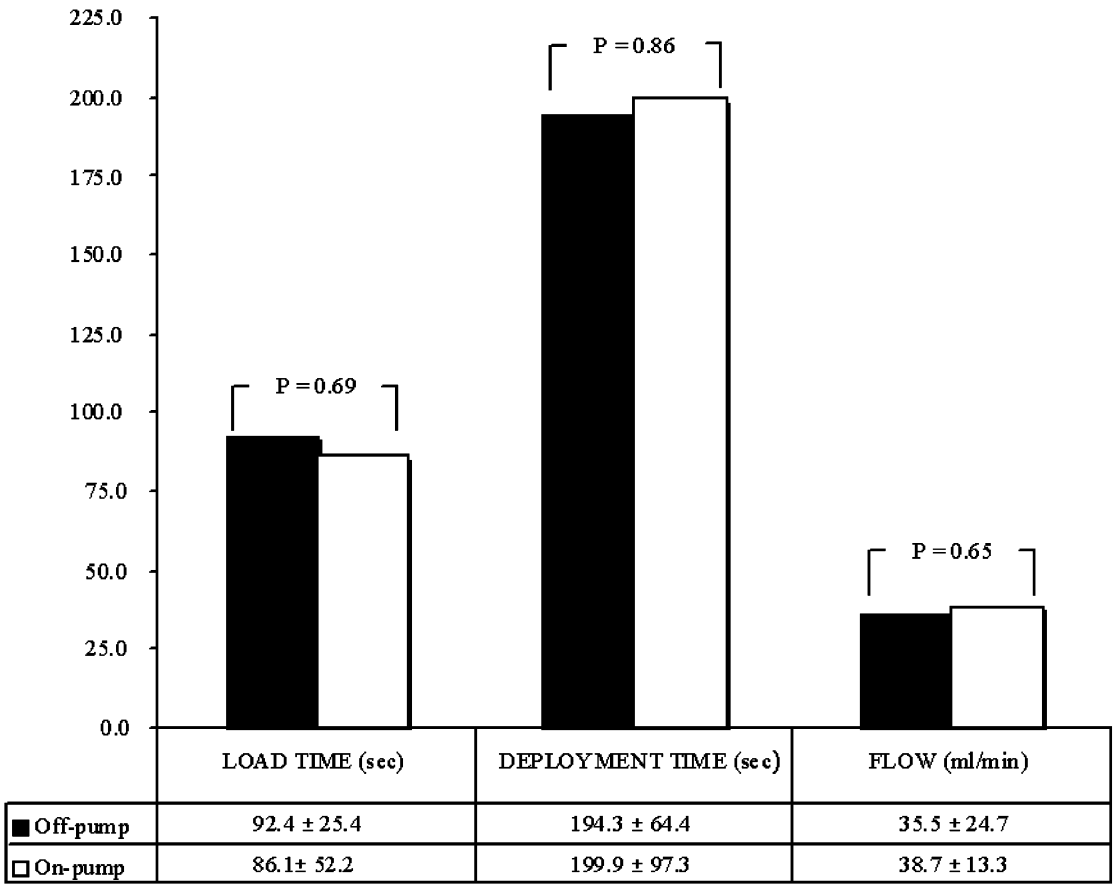

Fig. 3. Distal connector procedure and graft flow results. Deployment includes time from creation of coronary arteriotomy to ligation of the distal vein stump. Doppler blood flow was measured following ligation of the native LAD.

4. Discussion

To address concerns regarding the safety and efficacy [6–8] of minimal access and off-pump coronary artery bypass techniques, and the adequacy of distal graft anastomoses created during these procedures [9–12], the Anastomotic Technology Group at St. Jude Medical, Inc. have developed novel mechanical anastomotic devices for both aortosaphenous and SVG-to-coronary anastomoses. Initial results appear to be equivalent to those created by suture. Previous canine studies of SVG-to-coronary artery bypass performed with either a proximal or distal connector have shown excellent results with 100% graft patency at 180 days for proximal [Berg T, and Bonilla L, unpublished data] and 30 days for distal devices [2]. The first generation proximal connector, the Symmetry Bypass System Aortic Connector®, has also been employed clinically in Europe with 100% intraoperative patency, excellent graft flows, and no significant clinical events 3 months postoperatively [1]. These devices permit rapid creation of anastomoses, with reproducible results and minimal training.

Unlike previous preclinical investigations evaluating these devices, the acute phase of this study demonstrated the feasibility of a single SVG-to-coronary artery bypass on the beating heart, employing off-pump techniques, using the most current connector prototypes to fashion both graft anastomoses. Proximal anastomoses were performed on average in 56 s with no mechanical failures or anastomotic leaks. Average time for distal anastomotic completion was substantially longer, 194 s, but this reflects differences in connector design and delivery technique, not an increase in technical difficulty with anastomosis to a moving target. Indeed, off-pump distal anastomoses were performed just as rapidly as those created on-pump with no significant difference in deployment time noted between the two groups [$P = 0.86$]. More importantly, graft function was not sacrificed in this model as mean Doppler blood flow through these conduits following native LAD ligation proved to be equivalent to their on-pump counterparts [$P = 0.65$]. All the animals were hemodynamically stable during flow measurements and the blood pressure was not supported by inotropes. These flows are very similar to our previously published data comparing a hand sewn anastomosis to a larger 3 mm ID first generation distal device created anastomosis [2].

However, we did observe a trend towards an increased incidence of distal connector device-related complications during off-pump procedures [$P = 0.08$], which we defined

Table 3
Chronic distal connector outcome

Animal No.	Survival (days)	Angiogram	Anastomosis gross findings	Anastomosis histologic findings[a]
1	35	Widely patent	Widely patent	Thin fibrous neointima covering device
2	35	Widely patent	Widely patent	Thin fibrous neointima covering device
3	37	Widely patent	Widely patent	Thin fibrous neointima covering device
4	30	Widely patent	Widely patent	Thin fibrous neointima covering device
5	32	Widely patent	Widely patent	Thin fibrous neointima covering device
6	32	Widely patent	Widely patent	Thin fibrous neointima covering device (<70 μm) Minimal chronic inflammatory tissue surrounding device
7	33	Widely patent	Widely patent	Variable thickness fibrous neointima covering device (40–200 μm)
8	31	Widely patent	Widely patent	Thin fibrous neointima covering device (20–50 μm) Small number chronic inflammatory cells surrounding device
9	90	Widely patent	Widely patent	Variable thickness fibrous neointima covering device (60–300 μm) Few hemosiderophages in neointima and fibrous tissue surrounding device
10	91	Widely patent	Widely patent	Thin fibrous neointima covering device (40–70 μm) Few hemosiderophages in neointima and fibrous tissue surrounding device
11	90	Widely patent	Widely patent	Thick fibrous neointima covering device (>170 μm) Few hemosiderophages in neointima and fibrous tissue surrounding device
12	96	Widely patent	Widely patent	Variable thickness fibrous neointima covering device (20–120 μm) Mature fibrous tissue surrounding device
13	97	Widely patent	Widely patent	Variable thickness fibrous neointima covering device (10–130 μm) Few hemosiderophages in neointima and fibrous tissue surrounding device
14	195	Widely patent	Widely patent	Variable thickness fibrous neointima covering device (20–150 μm) Few hemosiderophages in neointima and fibrous tissue surrounding device
15	201	Widely patent	Widely patent	Thin fibrous neointima covering device Few hemosiderophages in fibrous tissue surrounding device
16	199	Widely patent	Widely patent	Thin fibrous neointima covering device (≤150 μm) Few hemosiderophages in fibrous tissue surrounding device
17	207	Widely patent	Mild-to-moderate stenosis External compression	Fibrous neointima covering device Few macrophages in fibrous tissue surrounding device
18	195	Widely patent	Widely patent	Thin fibrous neointima covering device Few macrophages in fibrous tissue surrounding device

[a] In cases where neointimal thickness is unspecified, the plane of sectioning did not permit accurate thickness measurement.

as mechanical failure or anastomotic leak or rupture. Two leaks developed immediately following device deployment; both were adequately controlled employing a single suture without disturbing the integrity of the anastomosis. In one instance, difficulty was encountered withdrawing the delivery system, resulting in irreparable damage to the connector. Simply removing the first device and replacing it with a second easily salvaged this anastomosis. This graft was successfully and rapidly loaded with a new connector and delivery system within the chest without disrupting the proximal anastomosis. We recognize that creating an anastomosis in a mobile field presents a technical challenge that may have been pivotal in these events, however, it is anticipated these results will improve once more experience is gained with these devices in off-pump procedures. In all three cases, intraoperative graft flow was not substantially affected, falling within one standard deviation of the off-pump group average.

Design modifications of this second generation, stainless steel distal connector permitted anastomoses to smaller caliber vessels and improved the ease of device loading compared to its predecessor, while maintaining the advantages of side-to-side technique, including distal graft ostium uniformity and avoidance of trauma to the endothelium within the graft body. Target sites on the LAD were chosen specifically for an ID of 2 mm in all cases, a downsizing of 0.5 mm from the earlier prototype [2]. We anticipate future generations of distal connectors will accommodate coronary artery diameters of 1.5 mm.

'Easy load' capabilities resulted in a sizable improvement in graft loading time, from 8.5 min (range 4–16 min) reported for the first generation device [2] to 1.5 min (range 0.6–4.1 min) for procedures in both groups, and loading time was similar whether off- or on-pump techniques were employed [$P = 0.69$]. Loading of the first generation distal device proved cumbersome. It required loading on the back table under microscopic magnification by an experienced assistant during exposure of the heart. However, the improved design made it possible for loading to be completed by the operating surgeon within the chest while minimally prolonging graft completion off-pump or aortic cross-clamp time in the on-pump procedures. In fact, the ability to re-load the graft rapidly within the chest without disrupting a previously fashioned proximal anastomosis was demonstrated in the one case in which a damaged distal connector was replaced.

Long-term graft patency appeared excellent at all time

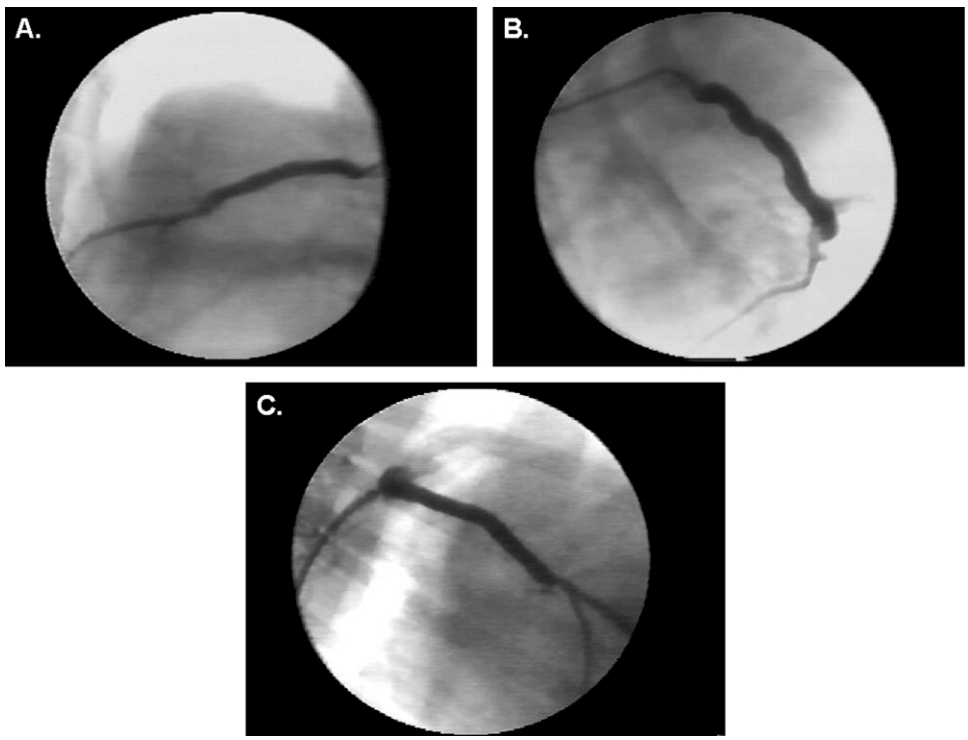

Fig. 4. Angiographic appearance of grafts at 30- (A); 90- (B); and 180-days postoperatively (C). Distal anastomoses are to the left in A and to the right in B and C.

intervals evaluated during the chronic phase of this study. Postoperative angiography demonstrated widely patent distal anastomoses. Effectively, the side-to-side anastomoses became smoothly tapered end-to-side grafts at 30, 90, and 180 days. There was no evidence of encroachment by thrombus from the blind end of the ligated vein graft. Pathologic examination confirmed these results, revealing a thin-to-moderate layer of neointima covering the endolumenal device surfaces. No substantial inflammatory or foreign body reaction to the stainless steel connectors was identified. Only one anastomosis was discovered to be stenotic on gross inspection, but the connector appeared ovoid and elongated as if externally compressed. This finding likely represented an artifact produced by damage

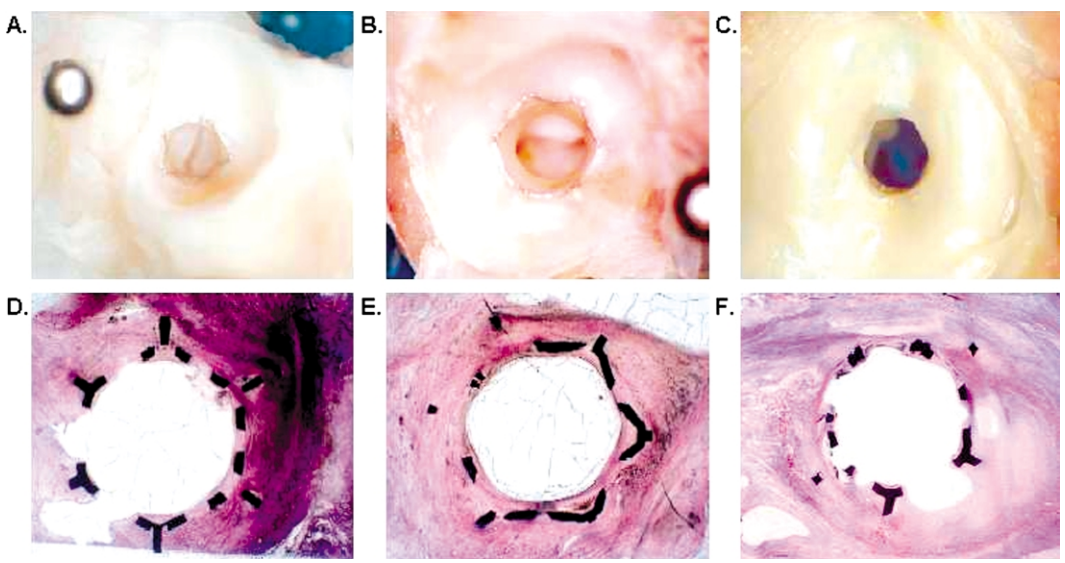

Fig. 5. Appearance of distal device-created anastomoses grossly and microscopically at 30- (A and D), 90- (B and E), and 180-days postoperatively (C and F). Devices are covered by fibrous neointima and surrounded by connective tissue (D–F). Gross photographs are taken through the opened posterior coronary arterial wall. (Magnification: A–C ×4; D–F ×40).

inflicted to the connector during graft harvesting as the corresponding postoperative angiogram showed a widely patent anastomosis. Overall, graft patency was essentially unchanged from that seen with the first generation distal connector [2], indicating that design modifications have not negatively altered device function.

All chronic animals received a standard prophylactic regimen of antiplatelet medications including Aspirin and Dipyridamol, prohibiting this study from drawing any meaningful conclusions regarding thrombogenicity of device anastomosis or methods for thrombus prevention. Certainly, this may become an important issue with longer periods of survival. Advances in antithrombotic management of coronary stents likely may be applicable to these connectors.

The omission of an off-pump group employing only manual suturing techniques did not allow for direct comparisons to be made between traditional and connector-fashioned anastomoses on the beating heart. However, based on our results and those published previously with similar devices, in an off-pump setting we would anticipate anastomoses created with connectors to provide a substantial time-savings for bypass grafting, while proving to be more easily reproducible, as durable, and equally functional to anastomoses fashioned with manual suturing techniques. Further study will be needed to evaluate these uncertainties.

Sutureless SVG-to-coronary artery bypass is feasible, rapid, and reproducible with on- and off-pump surgical techniques using a 2 mm ID, stainless steel, distal connector. In this model, early graft patency was 100% with either technique, while grafts performed on-pump were all patent on angiographic and pathologic examination at 30, 90, and 180 days. Few device-related complications occurred, each easily managed without compromising the graft integrity, and the incidence of these events was similar whether on- or off-pump techniques were employed. This or similar technologies may become an important addition to the armamentarium for the management of coronary artery disease, particularly in off-pump or minimally invasive approaches.

Acknowledgement

This study was funded in part by St. Jude Medical, Inc, Minneapolis, MN.

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Appendix A. Conference discussion

Dr A. Carpentier (*Paris, France*): Just one question. The cost.

Dr Zehr: Well, I don't think that cost has been released for the distal connectors. The cost is about $450 for the proximal connectors which attach the saphenous vein to the aorta. The distal connectors, are still in an investigatory mode, and I don't think any patients have been billed for them thus far.

Dr J. Bachet (*Paris, France*): Isn't it paradoxical to make big efforts to develop connectors for the saphenous vein when at the same time an enormous amount of papers try to prove that only arterial conduits work?

Dr Zehr: I agree with you a hundred percent if our efforts were to end with saphenous vein to coronary artery anastomoses. However, our goal is to develop connectors for arterial grafts. This is a work in progress. We have already begun work in the experimental laboratory with arterial conduits. We have been able to connect canine internal thoracic arteries to coronary arteries. In a similar way to this presentation, we come in the end of the artery with the device and create a side-to-side and then make it a functional end-to-side anastomosis by clipping the manipulated end of the artery. I believe that we can do this safely in radial arteries as well as internal thoracic arteries and avoid injuring the intima. This can possibly play a significant role for less invasive procedures, potentially thoracoscopic placement of saphenous vein and radial conduits and in conjunction with the use of the robot for a LITA to LAD.

Mr A. Murday (*Glasgow, United Kingdom*): It is a slightly cynical question, but what I want to ask is what assessments can you make to show that it's equal or better than a hand sewn anastomosis? It is a genuine question. How are you going to make that assessment?

Dr Zehr: Well, we have not made that assessment clinically. We have made this assessment experimentally in a previously published study evaluating the 3-0 distal connector. We looked at the difference between a hand sewn anastomosis and the connected anastomosis. In that study the flows were identical both before and after ligating the native coronary artery using either technique. In this experiment we did not have the same hand-sewn anastomosis as an internal control as all of the experiments were a single aorta to left anterior descending anastomosis. However, we examined the anastomoses of the chronic animals in this study by angiography, gross pathological examination, and histology. Intra-operatively we evaluated flows by transonic Doppler ultrasound in all experiments.

The flows were very similar to our historical hand-sewn control anastomoses. Clinically the gold standard is angiography and that is going to tell the story.

Mr Murday: Ultrasound of the animals?

Dr Zehr: Did we ultrasound these?

Mr Murday: Yes.

Dr Zehr: We did angiography on them. We did ultrasound at the time of the initial operation, and that is where the flows values came from, a transonic ultrasonic probe.

Dr G. Bloch (*Paris, France*): In your opinion is there a risk of stenosis in the long-term follow-up like restenosis in the stent in PTCA?

Dr Zehr: I think that whenever you put metal in any anastomosis there is concern about restenosis caused by pseudointimal hyperplasia. Clearly when we look at the first generation proximal, there have been incidences of occluded grafts and stenotic grafts, however, when we hand sew our anastomoses there is also an incidence of stenosis and occluded grafts. The longest term follow-up of a similar proximal connector device is by Dr Carlos Antona's group in Italy. They did angiography on 11 first generation proximals and found 10 of 11 to be widely patent at 1 year. The first generation distal connectors have also been shown to have excellent patency at 3 month evaluation. So I believe that the connectors can indeed have widely patent anastomoses at long-term follow-up, but clearly we need more long-term angiographic data to prove this to be an important technical advance.