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Prospective, Randomized Study on the Use of the Cardica PAS-Port Aortic Connector System in Off-Pump Coronary Artery Bypass Surgery

Jarmo Lahtinen, MD,[1] Fausto Biancari, MD, PhD,[1] Risto Ojala, MD, PhD,[2] Martti Mosorin, MD,[1] Riccardo Cresti, MD,[1] Pekka Rainio, MD, PhD, Vesa Anttila, MD, PhD, Martti Lepojärvi, MD, PhD, FECTS,[1] Tatu Juvonen, MD, PhD[1]

[1]Division of Cardiothoracic and Vascular Surgery, Department of Surgery, and [2]Department of Radiology, Oulu University Hospital, Oulu, Finland

ABSTRACT

Background. The use of aortic connector devices for proximal vein graft anastomosis has been shown to be associated with a relevant rate of early graft complications. Cardica PAS-Port is a new aortic connector whose preliminary clinical results seem promising. The safety and efficacy of this aortic connector device have been evaluated in this prospective, randomized study.

Material and Methods. Twenty-four patients were randomized to receive proximal aorta-vein graft anastomosis with either the Cardica PAS-port aortic connector or by the hand-sewn technique. Twenty-three patients underwent multidetector computed tomographic scan (MDCT) of the chest 6 months after surgery to evaluate graft patency.

Results. All aortic connector devices (18) were successfully deployed and 31 proximal anastomoses were performed by the hand-sewn technique. MDCT showed that 6-month freedom from vein graft complication was 22.2% in the PAS-Port group and 58.1% in the hand-sewn group (P = .04). Four vein grafts (22.2%) anastomosed with the PAS-Port and 2 hand-sewn vein grafts (6.5%) were occluded (P = .10). The use of the PAS-Port aortic connector was also predictive of any vein graft complication when adjusted for vein graft flow (P = .01; OR 8.64, 95% CI 1.66-45.00) and for peripheral resistance units (P = .02; OR 6.14, 95% CI 1.33-28.43).

Conclusions. The results of this prematurely stopped, prospective, randomized study suggest that the use of PAS-Port aortic connector device is associated with a higher rate of early vein graft complications than the hand-sewn technique.

INTRODUCTION

Although theoretically attractive, the use of the St. Jude Medical Symmetry aortic connector for proximal vein graft anastomosis has been abandoned because of well-documented immediate and early graft complications [Traverse 2003; Bergsland 2004; Cavendish 2004; Lahtinen 2004; Melero 2004]. Besides possible fatal complications related to this device [Lahtinen 2004], the main problem is the development of severe ostial stenosis/occlusion in a relevant number of vein grafts [Traverse 2003; Bergsland 2004; Cavendish 2004; Melero 2004]. Furthermore, the documented lack of reduction of embolic load associated with the use of the aortic connector as compared with the hand-sewn technique [Martens 2004] does not favor its use even in patients with diseased ascending aorta.

Recently, a new aortic connector device, the Cardica PAS-Port system (Guidant, Santa Clara, CA, USA), has been developed and introduced for clinical use to reduce the graft failure associated with previous aortic connector devices. The Cardica PAS-Port system is rather easy to use; the endothelium of the vein graft is left untouched by the device and metal exposure to the blood has been avoided in the orifice of the anastomosis and has been minimized inside the aorta. We sought to evaluate the safety and efficacy of this device in a randomized trial, but its production was terminated a few months after the start of the study. Herein, we report the results of this small randomized study on the use of the Cardica PAS-Port aortic connector device in primary, off-pump coronary artery bypass surgery (OPCAB).

MATERIAL AND METHODS

From July to November 2004, a series of 24 patients, 20 men and 4 women with a mean age of 67.1 years (range, 54.6-76.6 years), gave their consent and were enrolled in a prospective, randomized study evaluating the early results of a new proximal aortic anastomotic device compared with the conventional hand-sewn technique in primary OPCAB. Hand-sewn anastomoses were accomplished by 6-0 polypropylene running suture. This study was stopped because of unavailability of this anastomotic device, which was not cleared by the Food and Drug Administration [Maisel 2005]. At the completion of the procedure, flow was measured in 45 vein grafts by a transit time flow-meter (Medi-Stim, Oslo, Norway). Peripheral resistance units were calculated by dividing mean radial artery pressure by mean vein graft flow.

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Address correspondence and reprint requests to: Fausto Biancari, MD, PhD, Division of Cardiothoracic and Vascular Surgery, Department of Surgery, Oulu University Hospital, PO Box 21, 90029 Oulu, Finland; 358 8 315 2813/358 40 7333973; fax: 358 8 315 2577 (e-mail: faustobiancari@yahoo.it).

Table 1. Preoperative Variables in the Study Groups*

Risk Factor	Hand-Sewn Proximal Anastomosis Group, 14 Patients (%)	PAS-Port Proximal Anastomosis Group, 9 Patients (%)	*P*
Age, y	68.2 ± 6.5	66.5 ± 7.1	.64
Gender, M:F	11 (79):3 (21)	8 (89):1 (11)	1.00
Body mass index	27.3 ± 3.6	26.8 ± 2.3	.69
Extracardiac arteriopathy	2 (14)	3 (33)	.34
Pulmonary disease	2 (14)	1 (11)	1.00
Recent myocardial infarction	4 (29)	1 (11)	.61
Left ventricular ejection fraction 30-50%	3 (21)	0	.25
Left ventricular ejection fraction <30%	0	0	—
Unstable angina pectoris	3 (21)	1 (11)	1.00
Urgent operation	6 (43)	2 (22)	.40
Emergent operation	0	0	—
Critical preoperative status	0	0	—
Preoperative serum concentration of creatinine	75.6 ± 16.4	72.1 ± 14.3	.69
Preoperative cardiac index (L/min/m^2)	2.89 ± 0.64	2.92 ± 0.16	.73
Additive EuroSCORE	4.1 ± 2.2	3.4 ± 1.8	.48

*Risk factors are reported according to the EuroSCORE criteria. Continuous variables are reported as mean ± standard deviation.

Heparin (2.5 mg/kg) was given intravenously after sternotomy to maintain activated clotting time more than 400 seconds, and it was neutralized at the end of the procedure by protamin sulphate (2.5 mg/kg). Acetylsalicylic acid (100 mg/day) was given to all patients. No patient postoperatively received Clopidogrel. Heparin was postoperatively administered only in cases of atrial fibrillation.

These patients underwent multidetector computed tomographic scans (MDCT) of the chest (Aquilion Multi, Toshiba, Tokyo, Japan) about 1 week and 6 months after surgery to evaluate graft patency. Scanning parameters were 120 kV and 300 mAs, 500-ms rotation time, 4 × 1.0-mm section collimation and 3-mm table feed per rotation. Images were reconstructed at 0.5 mm intervals. All patients received 90 mL of a non-ionic contrast medium (Ultravist 370 mg/mL; Schering, Berlin, Germany) infused through an intravenous antecubital catheter at a flow rate of 4.5 mL/s for the first 22 mL and then 3.2 mL/s for the last 68 mL. The contrast agent was flushed with 30 mL of saline (3.2 mL/s). Sure start-automatic contrast medium detection software was used to determine the delay of the scan. Images were evaluated from axial image data and with the use of multiplane reconstruction and maximum intensity projection.

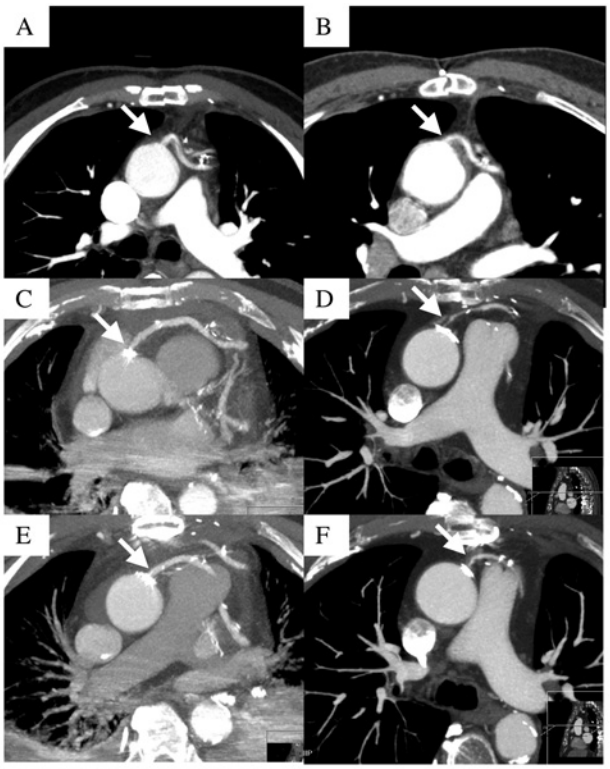
Statistical analysis was performed using SPSS statistical software (SPSS v. 10.0.5; SPSS, Chicago, IL, USA). Continuous variables are reported as mean ± standard deviation. The Fisher exact test and the Mann-Whitney test were used for univariate analysis. Binary logistic regression with the help of backward selection was used for multivariate analysis. A $P < .05$ was considered statistically significant.

RESULTS

One patient in the PAS-Port group refused to come to the 6-month follow-up control, but he was otherwise asymptomatic. He had all vein grafts patent at 7-day postoperative MDCT. Thus, 23 patients were included in the 6-month follow-up analysis. The study groups were comparable (Table 1). In all but 1 case, the left internal mammary artery was anastomosed to the left descending coronary artery. Vein graft was employed in all cases and was used in a sequential anastomotic fashion in only 1 patient. The radial artery was employed in 4 cases. The automatic anastomotic device was successfully employed in 9 patients (39.1%) for a total of 18 proximal anastomoses. No device deployment failure occurred in this series. Thirty-one vein grafts were anastomosed by the hand-sewn technique. A mean of 3.5 ± 0.5 distal anastomoses were carried out in the PAS-Port group, compared to 3.1 ± 0.3 in the hand-sewn group ($P = .11$). Forty-eight saphenous vein grafts were employed.

The mean in-hospital stay was 7.9 days. One patient experienced sepsis and 3 patients (13.0%) experienced atrial fibrillation. No other major morbidity or mortality was encountered in this series. One vein graft, which had a hand-sewn proximal anastomosis, was occluded as showed by MDCT 1 week after surgery. In 6 patients (26.1%), signs of pulmonary embolism were detected on MDCT performed 1 week after surgery. Pulmonary embolism was bilateral in 2 patients. Three of these patients (21.4%) had proximal saphenous vein anastomoses done by the automatic anastomotic device and 3 by hand-sewn technique (33.3%, $P = .64$). None of these patients had symptoms and signs of either pulmonary embolism or deep venous thrombosis.

At 6-month follow-up, all patients were alive and asymptomatic. MDCT showed that pulmonary embolism signs were resolved in all but 1 patient. MDCT showed some complications in 14 out of 18 vein grafts (77.8%) anastomosed with the PAS-Port and in 11 out of 31 hand-sewn vein grafts (41.9%) (Figure), thus the 6-month freedom rates from graft complication were 22.2% versus 58.1%, respectively ($P = .04$). Proximal vein graft stenosis was observed in 10 vein grafts (55.6%) anastomosed with the PAS-Port and in 11 hand-sewn vein grafts (35.5%, $P = .17$). Four vein grafts (22.2%) anastomosed with the PAS-Port and 2 hand-sewn vein grafts (6.5%) were occluded ($P = .10$).



(A) Patent hand-sewn proximal vein graft anastomosis on the 7th postoperative day and (B) 6 months after surgery. (C) Proximal mild vein graft stenosis anastomosed with the PAS-Port aortic connector on the 7th postoperative day, (D) with severe progression of the stenosis 6 months later. (E) Patent proximal anastomosis of the other vein graft on the 7th postoperative day, (F) with marked stenosis 6 months later. Note the metal artefacts at the aortic connector-made anastomosis site. Maximum intensity projection, 10-mm axial slabs. Arrows indicate vein graft at the site of proximal anastomosis.

Low saphenous vein graft flow (33.3 ± 24.5 mL/min versus 47.2 ± 19.5 mL/min, P = .01) and increased peripheral resistance units (3.3 ± 2.6 versus 1.7 ± 0.8, P = .02) were significantly associated with late graft complications. Low saphenous vein graft flow (33.3 ± 24.2 mL/min versus 44.4 ± 21.7 mL/min, P = .048), but not peripheral resistance units (3.0 ± 2.3 versus 2.3 ± 2.0, P = .9), was significantly associated with an increased risk of late graft stenosis. Vein graft occlusion was more likely in cases of low vein graft flow (33.2 ± 28.5 mL/min versus 40.3 ± 22.9 mL/min, P = .39) and increased peripheral resistance units (4.5 ± 3.7 versus 2.4 ± 1.9, P = .35), but the difference did not reach statistical significance (Table 2). The use of the PAS-Port aortic connector was predictive of any vein graft complication when adjusted for vein graft flow (P =.01; OR 8.64, 95% CI 1.66-45.00) and for peripheral resistance units (P = .02, OR 6.14, 95% CI 1.33-28.43).

DISCUSSION

Two studies, whose results have been reported only in abstract format, showed promising results with the use of the Cardica PAS-Port aortic connector system [Gummert 2005; Harringer 2005]. Data on 109 prospectively evaluated patients who underwent coronary artery bypass surgery with this aortic connector device have been submitted to support device clearance by the Food and Drug Administration. Failure to successfully deploy this aortic connector occurred in 12 patients (11%). In 77 patients who underwent control angiography, 6-month graft patency was 91%. In the remaining patients, graft patency was assessed by magnetic resonance imaging, computed tomography, and stress electrocardiogram. In 3 patients, the absence of symptoms was considered evidence of patency. The lack of angiographic data in all these patients was questioned by the Food and Drug Administration, which has recognized the importance of the use of such a device as well as the importance to adequately assess its safety and efficacy [Maisel 2005].

In the present study, we chose to evaluate vein graft patency by MDCT because it has recently been shown to have a sensitivity and specificity approaching 100% as compared with angiography in detecting severe graft stenosis and occlusion [Burgstahler 2003; Schlosser 2004; Chiurlia 2005; Moore 2005; Salm 2005; Song 2005]. Indeed, control angiography is not feasible in our institution in asymptomatic patients. However, this imaging method has recognized limits in detecting graft stenosis <50% [Moore 2005], artefacts can be caused by metal clips and, likely, the connector device, and distal anastomoses cannot be reliably visualized. Furthermore, grading of severe proximal anastomotic stenosis is not reliable.

Table 2. Clinical Data of Patients with Vein Graft Occlusion at 6-Month Follow-up as Detected by Multidetector Computed Tomography*

Patient	Proximal Anastomosis	Single Vein Graft	Distal Anastomosis	Stenosis of Grafted Coronary Artery	Lumen of Grafted Coronary Artery	Mean Graft Flow	Peripheral Resistance Units	Pulsatile Index
A	Hand-sewn	+	DG1	90%	2.0 mm	70 mL/min	0.74	1.6
B	Hand-sewn	+	RIVP	80%	1.5 mm	—	—	—
C	PAS-Port	+	RIVP	50 %	2.0 mm	16 mL/min	4.1	2.7
C	PAS-Port	+	OM	50 %	2.0 mm	9 mL/min	8.9	2.6
D	PAS-Port	+	RPD	95%	2.0 mm	58 mL/min	1.3	1.7
D	PAS-Port	+	RIVP	90%	2.0 mm	13 mL/min	7.7	2.4

*DG1 indicates first diagonal branch of the left anterior descending coronary artery; RIVP, right interventricular posterior descending coronary artery; OM, obtuse marginal coronary artery; RPD, right posterior descending coronary artery.

With the limitations of MDCT in mind, we have herein observed a rather high rate of early complications in vein grafts anastomosed with the PAS-Port aortic connector. The analysis of these cases is limited by the small size of a prematurely stopped study and by the multifactorial nature of graft occlusion. However, hemodynamic data obtained at completion of the procedure suggest that the use of this aortic connector device is implicated in the development of early graft complication. A 6-month freedom rate from graft complication of 22% versus 58% in the hand-sewn vein grafts does not support its use in coronary artery bypass surgery. Despite the minimal metal-to-blood exposure of the PAS-Port aortic connector device, a relevant number of proximal stenoses have still been detected by MDCT. It is possible that this device does not lead to accelerated intimal hyperplasia as observed with the use of the St. Jude Medical Symmetry connector [Melero 2004], but rather to graft kinking due to vein takeoff at a 90° angle. The problem of vein graft kinking is certainly lessened but still somewhat in existence with the hand-sewn technique.

In conclusion, the results of this prematurely stopped, prospective, randomized study suggest that the use of the PAS-Port aortic connector device is associated with a higher rate of early vein graft complication than the hand-sewn technique.

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