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Evaluation of Myocardial Flow Reserve Using Pharmacological Stress Thallium-201 Single-Photon Emission Computed Tomography: Is There a Difference between Total Arterial Off-Pump Coronary Artery Bypass Grafting and Conventional Coronary Artery Bypass Grafting?

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ABSTRACT

Background: The advantage of total arterial off-pump coronary bypass grafting (OPCAB) over conventional on-pump coronary artery bypass grafting with 1 internal thoracic artery and veins (CCAB) in terms of myocardial flow reserve has not been studied. We studied these procedures using thallium-201 perfusion single-photon emission computed tomography (Tl-201 perfusion SPECT).

Methods: Between 1997 and 2001, 152 patients were recruited from our database (OPCAB, n = 100; CCAB, n = 52). All patients underwent pharmacological stress Tl-201 perfusion SPECT 3 to 12 months after bypass surgery. Myocardial perfusion was analyzed semiquantitatively with a 5-point scoring system in a 20-segment model (0, normal, to 4, absence of uptake). Summed stress (SSS), rest (SRS), and difference score (SDS) of the entire myocardium as well as average scores (ASS, ARS, ADS) of individual walls (anterior, septal, lateral, and inferior) were compared by Student *t* test as well as by repeated-measures analysis of variance with Bonferroni correction.

Results: The SSS, SRS, and SDS of OPCAB versus those of CCAB were 6.86 ± 0.72 versus 7.17 ± 0.92, 3.95 ± 0.57 versus 3.75 ± 0.73, and 2.91 ± 0.47 versus 3.42 ± 0.74 ($P > .05$). However, the lateral wall showed lower scores in OPCAB (ASS, 0.18 versus 0.41, $P = .015$; ARS, 0.12 versus 0.20, $P = .168$; ADS, 0.06 versus 0.21, $P = .031$). The septal wall had higher scores in OPCAB (ASS, 0.33 versus 0.12, $P = .003$; ARS, 0.18 versus 0.07, $P = .037$; ADS, 0.14 versus 0.04, $P = .030$). The anterior and inferior walls were not different between the 2 groups.

Conclusions: OPCAB led to results similar to those of CCAB. The better results in the lateral wall have been the effect of grafting radial artery rather than vein. The similarity in myocardial reserve in the inferior wall between the 2 groups needs further study. There was no deleterious effect of off-pump as opposed to on-pump CAB.

INTRODUCTION

Because saphenous vein graft (SVG) failure is a major drawback of coronary artery bypass grafting (CABG), surgical techniques that involve minimal use of SVGs have been attempted [Lytle 1992]. The shift from routine use of left internal thoracic artery (LITA) with supplementary vein (SVG) to use of bilateral ITAs with supplementary artery has been ongoing since investigators at the Cleveland Clinic found better survival with bilateral arteries [Lytle 1999]. Furthermore, use of T anastomosis as well as sequential anastomoses and exclusive use of arterial conduit raised concerns about distal flow compromise [Jegaden 1998, 1999].

Off-pump CABG (OPCAB) is a less-invasive coronary bypass procedure, along with minimally invasive direct CABG and port-access CABG [Eagle 1999]. The intraoperative, perioperative, and early postoperative benefits of this approach have been well demonstrated in several studies [Puskas 1999, Hirose 2001, Bittner 2002, Kim 2002, Shennib 2002].

Thallium-201 myocardial perfusion single-photon emission computed tomography (Tl-201 perfusion SPECT) has had a role in numerous studies [Ichikawa 1997, Khoury 1997, Taki 1997, Ishino 2000]. In most of the studies, investigators analyzed reversibility on a patient or territory basis. None of the studies compared myocardial flow reserve between total arterial OPCAB and traditional on-pump CABG with 1 ITA

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and veins (CCAB). We used Tl-201 perfusion SPECT 3 to 12 months after coronary revascularization to evaluate the flow capacities of myocardium.

MATERIALS AND METHODS

Patient Population

Between November 1992 and December 2001, a total of 249 consecutive patients with the diagnosis of coronary artery disease underwent CABG by the same surgeon at Asan Medical Center. One hundred twenty-one of the patients underwent OPCAB (92 men and 29 women; mean age, 62 ± 8 years), and 128 underwent CCAB (84 men and 44 women; mean age, 66 ± 8 years). To compare 3- to 12-month postoperative Tl-201 myocardial perfusion SPECT findings, a total of 152 patients were recruited from 1997 to 2001 (OPCAB, n = 100,178 ± 47 days; CCAB, n = 52,164 ± 57 days). Preoperative, perioperative, postoperative data were documented in the medical record.

Definitions

The definitions used in the study have been described previously [Cameron 1988]. Coronary artery stenosis was considered clinically important if there was visually estimated luminal narrowing of at least 50% of the diameter of the left main coronary artery or at least 50% of any other coronary artery segment. Clinically important stenosis of the left main coronary artery was considered constituting double-vessel disease.

Surgical Procedures

All procedures were performed by the same surgeon (J.W.L.) with 2 surgical techniques. In the OPCAB group, the incision was made through a median sternotomy. The patients were heparinized with an initial dose of 1.5 mg/kg of heparin and periodically received supplemental doses to maintain an activated clotting time of more than 300 seconds. Deep pericardial traction sutures and a suction-based stabilizing system were used to facilitate exposure. The strategy for graft selection for specific coronary arteries was changed during the study period. In the early period, skeletonized LITA was selected for the left anterior descending artery (LAD), and radial artery (RA) was anastomosed in a T/Y fashion to the diagonal and obtuse marginal branches of the right coronary artery. In some cases of high-grade obstruction of the right system, right gastroepiploic artery (RGEA) was used as another arterial inflow if its size was adequate. After 1 or 2 episodes of string sign of the distal part of the LITA of the T anastomosis, we adopted the use of skeletonized right internal thoracic artery (RITA) to LAD, and skeletonized LITA was used as the source of blood flow to the anterior, lateral, and posteroinferior aspects of the heart. In the CCAB group, conventional cardiopulmonary bypass techniques were applied using a membrane oxygenator with moderate hemodilution under normothermia. For myocardial protection, an oxygenated cardioplegic solution was administered by combined antegrade/retrograde perfusion after aortic cross-clamping. The strategy for grafting was sequential or single grafts of LITA or RITA to LAD and of SVG to the anterolateral and posteroinferior aspects of the heart.

Stress/Rest Tl-201 Myocardial Perfusion SPECT

The administered dose of dipyridamole (n = 10) was 0.56 mg/kg per minute for a total of 4 minutes and that of adenosine (n = 142) was 140 μg/kg per minute for a total of 6 minutes into a peripheral antecubital vein through a pump-controlled infusion system. The indications for adenosine included evaluation of typical (n = 10 + 10), atypical (n = 22 + 15), or nonanginal chest pain (n = 29 + 5) and periodic checkup (n = 39 + 22). Three minutes after the start of drug administration, a bolus of 3 mCi Tl-201 was injected into the adenosine infusion and was followed by rapid flushing with 10 mL of normal saline solution.

Tomographic imaging was performed immediately (within 10 minutes) after pharmacological stress, and rest images were obtained 4 hours later. Image acquisition was achieved with a small field-of-view, single-crystal, rotating gamma camera (Adac high-resolution collimator [Phillips Medical Systems, Andover, MA, USA]; Triad 88 general purpose collimator [Trionix, Twinsburg, OH, USA]). Image acquisition was performed over a 360-degree arc at 6-degree intervals for 40 seconds per frame. Adac reconstruction was done with a back-projection technique with a Butterworth (order of 5; cutoff stress, 0.43; rest, 0.45) high-pass filter and a low-pass window. Triad 88 reconstruction was done with Hamming filter technique with Nyquist 1.404 (stress high-cut frequency, 0.700; rest. 0.65). Reconstructed tomographic sections were then reoriented into the standard short, horizontal long, and vertical long axes.

Image Interpretation

The reconstructed sections were reviewed by 2 nuclear physicians who had no prior knowledge of the angiographic findings. Discrepancies were resolved by consensus. The images were analyzed semiquantitatively with a 5-point scoring system in a 20-segment model as described in previous studies [Berman 1995, Zellweger 2001] (0, normal; 1, equivocal; 2, moderate; 3, severe reduction of radioisotope; 4, apparent absence of Tl-201 uptake). A summed stress score (SSS) was obtained by adding the scores for the 20 segments of the stress images. A summed rest score (SRS) was obtained similarly by adding the scores of 20 segments of the rest images. To assess defect reversibility, a summed difference score (SDS) was calculated by subtracting the SRS from the SSS. An average stress score (ASS) was also obtained by summing the scores of segments belonging to each myocardial wall (anterior, septal, lateral, and inferior) and dividing by number of the constituent segments. An average difference score (ADS) was calculated by subtracting the average rest score (ARS), obtained in the same manner as SDS in rest images, from the ASS.

Patient Follow-up

Follow-up was performed by review of medical records. Cardiac death (confirmed by review of death certificate or

Table 1. Preoperative, Operative, and Perioperative Data*

Variables	OPCAB (n = 100)	CCAB (n = 52)	*P*
Preoperative data			
Age, y	62 ± 8	65 ± 7	<.05
Sex, male, %	76	69	NS
Diabetes, %	39	40	NS
Hypertension, %	49	42	NS
Hyperlipidemia, %	43	40	NS
Current smoker, %	27	25	NS
Previous PCI, %	23	22	NS
Preoperative LVEF, %	57 ± 10	59 ± 12	NS
Three-vessel disease, %	67	68	NS
Left main disease, %	26	25	NS
Operative data			
Emergency operation, n	1	2	
Surgical time, min	256 ± 46	288 ± 47	<.05
Cross-clamp time, min		101 ± 21	
Total bypass time, min		122 ± 28	
Grafts/patient, n	2.7 ± 0.5	2.0 ± 0.0	<.001
Distal anastomoses/patient, n	3.63 ± 0.84	4.52 ± 0.96	<.001
Perioperative data			
Postoperative LVEF, %	56 ± 12	56 ± 12	NS
ICU length of stay, d	2.3 ± 0.77	3.0 ± 0.95	NS
Preoperative IABP, %	0	2	NS
Perioperative IABP, %	0	4	NS

*OPCAB indicates off-pump coronary bypass grafting; CCAB, conventional on-pump coronary artery bypass grafting with 1 internal thoracic artery and veins; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; ICU, intensive care unit; IABP, intraaortic balloon pump.

hospital chart) and post-CABG bypass surgery or percutaneous coronary intervention (PCI) were checked as in previous studies [Berman 1995].

Statistical Analysis

Comparisons between patient groups were performed with the Student *t* test for continuous variables and a chi-square test for categorical variables. Comparisons between myocardial walls in the same group were done by repeated-measures analysis of variance with Bonferroni correction. All continuous variables were described as mean ± SD. $P < .05$ was considered statistically significant.

RESULTS

Baseline Clinical Characteristics

Demographics and preoperative data are summarized in Table 1. The mean age of the patients was 62 years; 74% of patients were male, and 29% had an ejection fraction less than 50%. All baseline clinical characteristics showed no significant difference between OPCAB and CCAB except for age.

Operative and Perioperative Characteristics

Operative and perioperative data are also summarized in Table 1. Surgical time was shorter in the OPCAB group. The number of grafts was greater, and the number of distal anastomoses was smaller in that group. As shown in Table 2, our preference has been to place the ITAs to the anterior wall, although the ITAs were occasionally anastomosed to other myocardium while the RA was used to graft the branches of the lateral wall and then taken over the branches of the right coronary system. The RGEA was anastomosed to the inferior myocardium as needed.

Table 2. Distribution (n) of Arterial Conduits in the Off-Pump Coronary Bypass Grafting Group*

	Conduit				
Vessel Grafted	LITA	RITA	RA	RGEA	Total
LAD	39	64			103
Diagonal	44	7	8		59
Ramus intermedius	8		5		13
Circumflex branch	10	2	85	1	98
PDA/PL	1	1	74	7	83
Total	102	74	172	8	356

*LITA and RITA indicate left and right internal thoracic arteries; RA, radial artery; RGEA, right gastroepiploic artery; LAD, left anterior descending artery; PDA, posterior descending artery; PL, posterolateral artery.

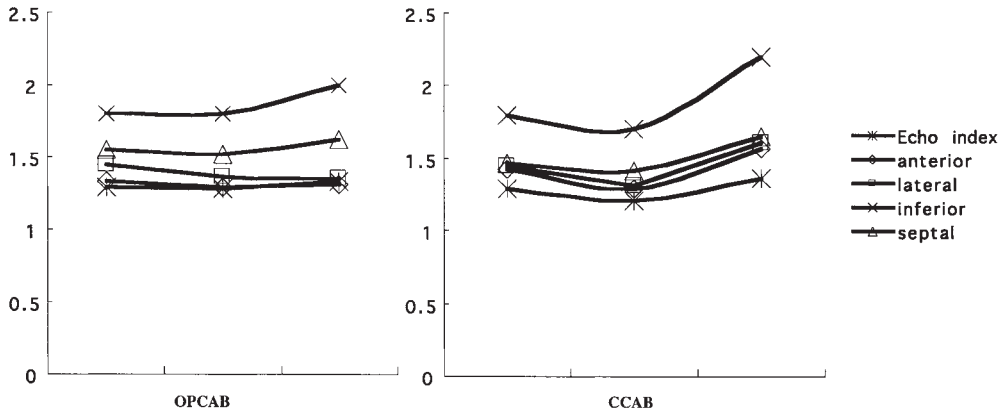
Echocardiography and Coronary Angiography

Preoperative echocardiography was performed in 150 patients 27 ± 35 days (range, 0-175 days) before surgery and postoperative echocardiography in 152 patients 8 ± 15 days (range, 4-195 days) after surgery. Wall motion index and segmental wall motion of each segment were analyzed between the 2 groups and compared with postoperative wall motion (Figure). Eighty-four patients in the OPCAB group underwent angiographic follow-up studies 83 ± 241 days (range, 2-1260 days) after surgery. Graft failure was defined as occlusion or at least 70% stenosis. As shown in Table 3, 307 (99.3%) of all 309 grafts studied were patent. One LIMA graft and 1 RIMA graft anastomosed to the LAD having a diffuse lesion were occluded. Nine RA grafts were revealed to have less than 70% stenosis. Seven of them were grafts anastomosed to the distal branches of the right coronary artery and 2 to the obtuse marginal branches.

Tl-201 Myocardial SPECT

SSS, SRS, and SDS were not significantly different between the OPCAB and CCAB groups (Table 4). However, the OPCAB group had significantly lower ASS and ADS in the lateral wall than the CCAB group ($P < .001$). On the contrary, all 3 scores for septal wall after OPCAB were higher than those after CCAB ($P < .001$).

In patients who underwent OPCAB, ASS and ADS for the lateral wall were significantly lower than those for the anterior ($P = .006$) and inferior walls ($P = .006$). In the CCAB group, scores for the septal wall were significantly lower than those for the lateral ($P = .042$), anterior ($P = .006$), and inferior walls ($P = .018$) (Table 5). Causes of increased septal stress score in the OPCAB group are summarized in Table 6.



Echocardiographic wall motion index and segmental wall motion of each segment between the 2 groups. Immediately postoperative left ventricular ejection fraction (wall motion index) was more compromised with more progressive recovery in the off-pump coronary bypass grafting group

The occurrence of diffuse/long lesions of the LAD was significantly higher in that group (15% versus 3.8%, $P = .05$). Preoperative infarction in the LAD area was present more frequently in the OPCAB group, although the difference was not statistically significant (16% versus 11.5%). The rate of graft stenosis/occlusion was not significant between the 2 groups (3% versus 3.8%).

Follow-up Data

Postoperative PCI was performed in 3 patients in the OPCAB group and 2 patients in the CCAB group. There were no confirmed operative or late deaths among the study population.

DISCUSSION

Since the benefit of the arterial conduit and the feasibility of OPCAB in myocardial revascularization became known, the area of total arterial OPCAB is widening in the CABG world. However, Tl-201 SPECT has not been used to compare the advantage of total arterial OPCAB over CCAB in regard to myocardial perfusion reserve. Our results showed that overall flow capacities between the OPCAB and CCAB groups did not differ when assessed 3 to 12 months after CABG. These results seem comparable to the results obtained by Doppler guide wire [Akasaka 1995]. However, the different flow capacities of the lateral and septal walls between OPCAB and CCAB are notable. The better perfusion reserve of the lateral wall in OPCAB over CCAB is shown in Table 5. During a period of change from CCAB to OPCAB in our experience, the flow of the lateral wall was supplied by the T/Y-fashioned RA in the OPCAB group and reversed SVGs in the CCAB group. This change of vein graft to a better arterial graft resulted in better flow reserve in the lateral area even in the early postoperative period. Although it was not possible to confirm superiority of the patency of the arterial graft because of a lack of follow-up angiographic data in the CCAB group, a remarkable angiographic result in the OPCAB group suggested this finding. Taki et al [1997] compared flow capacities between arterial and venous grafts as well as between the 3 coronary territories. In that study, Tl-201 SPECT was performed 1 month

Table 3. Postoperative Coronary Angiographic Data in the Off-Pump Coronary Bypass Grafting Group*

	LITA			RITA			RA			RGEA			
Target	Graft studied, n	Graft Patent, n	Patency Rate, %	Graft studied, n	Graft Patent, n	Patency Rate, %	Graft studied, n	Graft Patent, n	Patency Rate, %	Graft studied, n	Graft Patent, n	Patency Rate, %	Total
LAD	35	34	97.1	51	53	96.2							97.1
Diagonal	38	38	100	6	6	100	6	6	100				100
RI	6	6	100				5	5	100				100
Circumflex	13	13	100	2	2	100	71	71†	100	1	1	100	100
PDA/PL	1	1	100	1	1	100	64	64‡	100	7	7	100	100
Total	92	93	98.9	60	62	96.7	146	146	100	8	8	100	99.3

*LITA and RITA indicate left and right internal thoracic arteries; RA, radial artery; RGEA, right gastroepiploic artery; LAD, left anterior descending artery; RI, ramus intermedius; PDA, posterior descending artery; PL, posterolateral artery.

†Two grafts showed less than 70% stenosis, for a perfect patency rate of 97.1%.

‡Seven grafts showed less than 70% stenosis, for a perfect patency rate of 89%.

Table 4. Post–Coronary Artery Bypass Thallium-201 Single-Photon Emission Computed Tomographic Findings between the Off-Pump Coronary Bypass Grafting (OPCAB) and Conventional Coronary Bypass Grafting (CCAB) Groups*

Variable	OPCAB	CCAB	*P*
SSS	6.86 ± 0.72	7.17 ± 0.92	.794
SRS	3.95 ± 0.57	3.75 ± 0.73	.834
SDS	2.91 ± 0.47	3.42 ± 0.74	.545

*Values are mean ± SE. SSS indicates summed stress score; SRS, summed rest score; SDS, summed difference score.

after the operation, and this interval was too short for evaluation of adapted graft flow status. Nevertheless, the left circumflex territory showed the best postoperative perfusion reserve in the arterial group, and both left circumflex and LAD territories did so in the venous group. We judiciously suggest that this finding supports our results. But because Taki et al did not specify the graft technique, further comparison is meaningless. At the same time, in the OPCAB group, the designated flow to the septal and anterior walls may have deviated to the lateral wall. The result was less satisfactory flow reserve in this area compared with single ITA anastomosis to the LAD in the CCAB group. This concern and 1 case of LAD PCI after a T-graft string to the LAD resulted in a change in our strategy for total arterial bypass. The original technique of LITA to LAD and T-graft RA from the LITA to the anterior and lateral walls was changed to RITA to LAD and LITA to diagonal or proximal obtuse marginal artery and T-grafted RA to more distal obtuse marginal and right coronary branches. Jegaden et al [1998] had intentions similar to ours. However, that group noted the possible negative effect of extended use of arterial graft and observed no modification of left ventricular function in the arterial group in contrast to significant improvement in the vein group. Our echocardiographic data disagreed with the findings of Jegaden et al. Immediately postoperative left ventricular ejection fraction (wall motion index) was more compromised as recovery progressed in the OPCAB group, as shown in the Figure. Although there was improvement on the lateral wall with arterial grafting, the right coronary artery system needs more discussion. There are disagreements about the graft of choice to the right coronary artery. Because the right coronary artery distribution frequently supplies a smaller area of healthy myocardium that requires less flow than the LAD and circumflex distributions, the relatively poorer arterial graft patency to targets of the right coronary system has been demonstrated by several investigators [Mehta 1975, Shennib 2002]. Maniar et al [2003] recently showed that RA patency to targets of the right coronary system was poorer than patency of the LAD and circumflex territories regardless of the site of the proximal anastomosis. Lev-Ran et al [2003] also found that the use of RGEA for revascularization of the right coronary system does not confer clinical benefit over SVG after midterm follow-up. Our results obtained with angiographic and Tl-201 SPECT studies also did not reveal a difference in the two groups.

Other conditions considered for evaluation with Tl-201 SPECT are previous infarction, graft stenosis/occlusion, and diffuse and long LAD lesions. The higher incidence of preoperative infarction in the LAD territory in the OPCAB group was not different from that in the CCAB group, but this infarct may have had more negative impact on RITA or T-grafted LITA grafts in the OPCAB group than a traditional single LITA to LAD graft in the CCAB group. The rates of graft stenosis/occlusion in both groups also were not different. This finding again confirmed that RITA is comparable to LITA as a graft to the LAD in terms of patency. The incidence of diffuse and long LAD lesions was significantly higher in the OPCAB group than in the CCAB group among the patients with abnormal Tl-201 SPECT findings in the septum, as shown in Table 6. We believe this finding was the main cause of worse or unimproved flow reserve in the septal and anterior walls in our OPCAB patients.

The preoperative, intraoperative, perioperative data on our study population did not differ greatly with those in other reports, ie, the OPCAB group was younger, the surgical time was shorter, and the number of distal anastomoses was smaller than in the CCAB group. However, our study population had a remarkable male prevalence in the OPCAB group than was found in other studies. Comorbid conditions were similar in the two groups, as they were in other studies. There were no significant differences regarding diabetes mellitus. The diabetic group had results similar to those in the nondiabetic group, a finding that seems evident as in previous reports [Webster 1997].

The greatest limitation of our study was the complexity of our study population. Other variables such as single versus double ITA graft and arterial versus vein graft were combined with the off-pump versus on-pump situation.

Table 5. Post–Coronary Artery Bypass Thallium-201 Single-Photon Emission Computed Tomographic Findings in Each Myocardial Wall between Off-Pump Coronary Bypass Grafting (OPCAB) and Conventional Coronary Bypass Grafting (CCAB)*

	Anterior			Lateral			Inferior			Septal		
Variable	OPCAB	CCAB	*P*	OPCAB	CCAB	*P*	OPCAB	CCAB	*P*	OPCAB	CCAB	*P*
ASS	0.44 ± 0.07	0.56 ± 0.11	.347	0.18 ± 0.04	0.41 ± 0.08	.015	0.52 ± 0.07	0.45 ± 0.11	.598	0.33 ± 0.06	0.12 ± 0.03	.003
ARS	0.23 ± 0.05	0.30 ± 0.10	.457	0.12 ± 0.03	0.20 ± 0.06	.168	0.31 ± 0.06	0.23 ± 0.08	.414	0.18 ± 0.04	0.07 ± 0.03	.037
ADS	0.22 ± 0.05	0.26 ± 0.06	.574	0.06 ± 0.02	0.21 ± 0.06	.031	0.21 ± 0.04	0.22 ± 0.06	.851	0.14 ± 0.04	0.04 ± 0.02	.030

*Values are mean ± SE. ASS indicates average stress score; ARS, average rest score; ADS, average difference score.

Table 6. Causes of Thallium-201 Single-Photon Emission Computed Tomographic Abnormality in the Septum, n (%)*

Cause	OPCAB	CCAB	*P*
Diffuse/long LAD lesion	15 (15)	2 (3.8)	.05
Preoperative LAD infarct	16 (16)	6 (11.5)	.55
Graft stenosis/occlusion	3 (3)	2 (3.8)	.74

*OPCAB indicates off-pump coronary bypass grafting; CCAB, conventional on-pump coronary artery bypass grafting with 1 internal thoracic artery and veins; LAD, left anterior descending artery.

CONCLUSION

Total arterial OPCAB showed myocardial flow reserve similar to that of CCAB. Furthermore, the better results on lateral wall in the OPCAB group may be the effect of RA grafting rather than vein grafting in the CCAB group. However, the same myocardial reserve in the inferior wall in the 2 groups needs further study. There were no deleterious effects of off-pump as opposed to on-pump CAB.

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