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Which Is First: Left Anterior Descending Artery Anastomosis or Right Coronary Artery Anastomosis in Off-Pump Coronary Artery Bypass Grafting?

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ABSTRACT

Objectives: The sequence of the distal anastomosis for revascularization in off-pump coronary artery bypass grafting (OPCABG) surgery is under debate. The hypothesis in this study was that an analysis of cardiac markers would reveal that anastomosing the left anterior descending coronary artery (LAD) before the right coronary artery (RCA) would decrease myocardial damage in OPCABG surgery for 2-vessel disease.

Methods: Forty patients with stable angina who underwent OPCABG surgery and who had LAD and RCA lesions were randomized into 2 groups of 20 patients each. The LAD was revascularized first in group 1, and the RCA was revascularized first in group 2. Cardiac troponin I, creatine kinase (CK), and CK myocardial band (CK-MB) were measured in the 2 groups before surgery and at 8, 24, and 48 hours after surgery.

Results: No mortality occurred in the 2 groups. The groups were similar with respect to sex, age, durations of anastomosis of the left internal thoracic artery to the LAD and of the saphenous vein graft to the RCA, and preoperative CK, CK-MB, and troponin I levels. Postoperative CK-MB levels were significantly higher in group 2 in the eighth and 24th postoperative hours than in group 1 (P = .009 and .041, respectively). Similarly, troponin I levels were significantly higher in group 2 in the eighth, 24th, and 48th hours than in group 1 (P = .003, .003, and .006, respectively).

Conclusions: Anastomosis to the LAD first in OPCABG surgery led to a slight reduction in myocardial enzyme release against the occlusion of the target vessels during anastomoses in patients with RCA and LAD stenoses.

INTRODUCTION

Off-pump coronary artery bypass grafting (OPCABG) offers the option of revascularization without the complications of extracorporeal support. Conventional bypass grafting with cardiopulmonary bypass is associated with the complications of cannulation of the heart and great vessels and with the complications of extracorporeal circulation. On the other hand, occlusion of the coronary artery flow in OPCABG to create a bloodless field for a comfortable distal anastomosis can produce temporary regional ischemia. To address this issue, cardiovascular surgeons have introduced intravascular coronary shunts into practice [Rivetti 1997; Baumgartner 1999]. The use of intracoronary shunts reduces postoperative troponin I levels and is suggested for patients thought to be susceptible to transient ischemia [Gürbüz 2006].

Some technical aspects of OPCABG are under debate. One of these issues is the sequence of the distal anastomoses for revascularization. Until now, no prospective randomized study has compared the effects of the sequence of distal anastomoses on myocardial ischemia. The present study is primarily concerned with this problem. The primary hypothesis in the present study was that an analysis of cardiac markers would reveal that anastomosing the left anterior descending coronary artery (LAD) before the right coronary artery (RCA) would decrease myocardial damage in OPCABG surgery for 2-vessel disease.

PATIENTS AND METHODS

Patients

During a 3-year period between June 2004 and May 2007, 40 patients were included in the study. The study population included patients with stable angina who underwent OPCABG surgery and who had isolated proximal LAD and RCA lesions (angiographic evidence of luminal diameter narrowing of >70%) with patent diagonals and circumflex branches. Intracoronary shunts were not used during the distal anastomosis. The patients were prospectively randomized into 2 groups. Group 1 consisted of 20 patients who underwent their OPCABG operation with anastomosis of the distal LAD before the distal RCA anastomosis, whereas in the control group (group 2), 20 patients underwent OPCABG in which the distal RCA anastomosis was done first. The exclusion criteria were 1- or 3-vessel disease, age >75 years, severe left ventricular dysfunction (ejection fraction of 30% by

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echocardiogram), reoperative operation, emergency operation, diabetes, elevated cardiac enzyme levels, and recent myocardial infarction (MI). The patients and healthcare providers (outside of the operating room) were blinded to the study. The local ethics committee approved the study, and informed consent was obtained from all patients before the operation. The same surgical team performed the operations in both groups.

Surgical Technique

The anesthesia technique was standard for all patients. General anesthesia and intratracheal intubation was done. The chest was opened via median sternotomy. Left internal thoracic artery (LITA) and saphenous vein grafts were prepared before the pericardiotomy. Systemic hypothermia was avoided by adjusting the operating room temperature. Alpha-stat acid-base management was adopted, and partial anticoagulation was accomplished with heparin (1 mg/kg body weight) until a target activated clotting time of 250 to 350 seconds was achieved. The heart rate, systemic arterial pressure, central venous pressure, pulmonary arterial pressure, and pulmonary capillary wedge pressure were monitored continuously. Medications including β-blockers and calcium-channel blockers were not used for heart rate control during the operation. The OPCABG technique was used in both groups. To exclude the effects of the ischemia period during the proximal anastomosis, we performed the proximal anastomosis of the conduit graft for the RCA first in both groups. In group 1, patients had their LITA-LAD bypass performed after exposure and stabilization of the LAD. Cardiac stabilizers were used during the distal anastomosis, and 7-0 polypropylene suture was used for the anastomosis. After the arteriotomy, a bulldog clamp was applied to the LAD just proximal to the arteriotomy to obtain a bloodless anastomotic field. The vessel was occluded throughout the anastomosis. A carbon dioxide blower was used to clear blood from the field and to open the arteriotomy during the anastomosis. Heparinized isotonic solution was used in the blower. The LAD was declamped after the last suture of the anastomosis. After the LITA-LAD anastomosis was completed, the anastomosis of the saphenous vein graft to the RCA was done. A cardiac stabilizer and a proximal bulldog clamp were applied to obtain a bloodless, immobile field. In group 2, the sequence of the distal anastomoses was changed, with the RCA distal anastomosis performed first, followed by the LAD anastomosis. Anastomosis duration was noted in both groups. Heparin was not neutralized with protamine sulfate at the end of the operation. The chest was closed in a standard fashion.

Table 1. Postoperative Data of the Patients by Group*

	Group 1 (n = 20)	Group 2 (n = 20)	*P*
Age, y	61.8 ± 9.0	60.6 ± 7.8	.507
Female sex, n	5	6	1.000
Hypertension, n	5	4	1.000
COPD, n	2	2	1.000
Peripheral vascular disease	1	2	1.000
LVEF, %	58 ± 7	57 ± 6	.532
EuroSCORE	1.72 ± 0.95	1.76 ± 1.27	.634
LAD anastomosis time, min	5.9 ± 1.1	6.0 ± 0.7	.943
RCA anastomosis time, min	6.8 ± 1.1	6.4 ± 1.1	.162
Inotropic support, n	4	4	1.000
Arrhythmia, n	2	3	1.000
Time to extubation, h	7.0 ± 3.3	7.5 ± 2.2	.234
ICU stay, d	1.7 ± 0.8	1.7 ± 0.7	.611
Postoperative hospital stay, d	6.9 ± 2.0	6.8 ± 1.7	.887

*Data are presented as the mean ± SD where indicated. COPD indicates chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; LAD, left anterior descending coronary artery; RCA, right coronary artery; ICU, intensive care unit.

Electrocardiography

All patients underwent standard 12-lead electrocardiography (ECG) assessment before the operation and daily after the operation. Clinical diagnostic criteria for perioperative MI were as follows: new Q waves >0.04 milliseconds or a reduction in R waves of >25% in at least 2 leads, or both; new ST segment elevation in at least 2 contiguous leads measuring >0.2 mV in leads V1 to V3 or >0.1 mV in all other leads; or a new left bundle branch block [French 2004].

Markers of Myocardial Damage

Cardiac troponin I, creatine kinase (CK), and CK myocardial band (CK-MB) were measured in 4 samples: half an hour before the operation and at 8, 24, and 48 hours after the operation. Serum CK and CK-MB levels were studied by enzymatic immunoassay (AU640e Chemistry Immuno Analyzer; Olympus America, Melville, NY, USA). Troponin levels were assessed by electrochemiluminescence in an immunoassay (Modular Analytics E 170; Roche Diagnostics, Basel, Switzerland). Reference-interval values for the cardiac markers were 0.00 to 0.04 ng/mL for cardiac troponin I, 30 to 200 IU/L for CK, and 0 to 25 IU/L for CK-MB. For differentiation of perioperative MI, we accepted troponin I cutoff values of 6.5 ng/mL at 8 hours, 9.8 ng/mL at 12 hours, and 11.6 ng/mL at 24 hours [Sadony 1998]. An increase in the CK-MB level of >100 IU/L was considered diagnostic of MI [Carrier 2000].

Statistical Analysis

Statistical analysis was performed with the SPSS 10.0 statistical software program (SPSS, Chicago, IL, USA). Randomization was done with this program. Patients who met the study-inclusion criteria were randomized prospectively to the 2 groups.

Categorical data were analyzed with the chi-square test. Data for continuous variables were expressed as the mean ± 1 SD and were compared with the Mann-Whitney *U* test. Because the data for biochemical markers troponin I, CK,

Table 2. Biochemical Results

	Preoperative	Postoperative Hour 8	Postoperative Hour 24	Postoperative Hour 48
Creatine kinase, IU/L				
Group 1	94.9 ± 53.9	608.7 ± 425.5	516.8 ± 407.8	305.8 ± 234.6
Group 2	79.5 ± 52.7	840.7 ± 691.2	770.4 ± 645.5	359.5 ± 326.4
P	.344	.323	.194	.715
Creatine kinase MB, IU/L				
Group 1	21.6 ± 5.3	61.7 ± 16.3	46.6 ± 12.5	32.5 ± 8.7
Group 2	23.3 ± 7.0	75.9 ± 16.2	55.7 ± 12.6	34.6 ± 9.0
P	.363	.009*	.041*	.378
Troponin I, ng/mL				
Group 1	0.0418 ± 0.0168	0.4560 ± 0.3037	0.3886 ± 0.2978	0.2406 ± 0.2017
Group 2	0.0365 ± 0.0191	0.9522 ± 0.5374	0.7671 ± 0.4179	0.4069 ± 0.2348
P	.291	.003*	.003*	.006*

*Statistically significant, Mann-Whitney *U* test.

and CK-MB were obtained serially, we also compared the groups with repeated-measures analysis of variance. *P* values <.05 were considered statistically significant.

RESULTS

There were no deaths in the study groups. The mean age of the patients was 61.8 ± 9.0 years in group 1 and 60.6 ± 7.8 years in group 2 (*P* = .507). There were 5 women in group 1 and 6 women in group 2 (*P* = 1.000). The 2 groups were similar with respect to sex and age. The durations of the distal anastomoses were similar in the 2 groups. Similarly, the 2 groups did not differ with respect to the use of inotropic support, arrhythmia (only temporary bradycardia occurred, with no hemodynamic deterioration), time to extubation, and lengths of stay in the intensive care unit and the hospital (Table 1).

The biochemical studies revealed no significant differences between the groups with respect to preoperative CK, CK-MB, and troponin I levels; however, the 2 groups did show some significant differences with respect to postoperative myocardial enzyme levels. Postoperative CK-MB levels in group 2 were significantly higher than in group 1 in the eighth and 24th postoperative hours (*P* = .009 and .041, respectively). Similarly, troponin I levels in group 2 were significantly higher than those in group 1 in the eighth, 24th, and 48th postoperative hours (*P* = .003, .003, and .006, respectively). The increases in the enzyme markers were within the reference limits for postoperative enzyme levels. None of the patients had hypotension or important rhythm disturbances when the heart was positioned for anastomosis. There was no ECG abnormality, severe CK-MB or troponin I elevation, or hemodynamic deterioration after the operation that would be consistent with perioperative MI. Table 2 summarizes the preoperative and postoperative enzyme levels in the patients.

Analysis of variance for the CK levels measured at the 4 different times showed that the groups were not significantly different (*P* = .230) with respect to the change in CK level with time; however, the 2 groups did show significant differences with respect to changes in CK-MB and troponin I levels with time (Table 3).

COMMENT

The primary postulation of the study was proved in this prospectively designed study; that is, distal anastomosis of the LAD before the RCA distal anastomosis in OPCABG surgery reduces myocardial ischemia–induced enzyme leakage.

Large increases in serum troponin I in the setting of coronary surgery indicate perioperative myonecrosis, as indicated by contrast-enhanced cardiovascular magnetic resonance imaging. However, some of the troponin leakage probably represents protein release from cytosolic pools that are not structurally bound, rather than true myocardial necrosis [Bleier 1998]. Neither of the groups in the present study had elevated marker levels or pathologic ECG tracings consistent with an MI. Both groups showed an increase in the troponin I level; however, performing the RCA anastomosis first produced a greater increase in troponin I. In addition to the troponin I increase, CK-MB levels were significantly higher at postoperative hours 8 and 24 when the RCA anastomosis was performed first. The increase in troponin I and CK-MB observed in the present study represents reversible myocardial damage, not irreversible necrosis.

Intracoronary shunts decrease postoperative troponin I leaks [Gürbüz 2006]. They also prevent regional myocardial dysfunction and hemodynamic deterioration during coronary anastomosis in OPCABG surgery [Yeatman 2001]. Insertion of intracoronary shunts during beating-heart surgery also may lead to endothelial damage in coronary arteries [Hangler 2004]. In addition to such damage, shunts may bring about some technical problems [Gürbüz 2006]. Therefore, many

Table 3. Variance Analysis of Biochemical Markers*

	Multivariate Tests	Within-Group Effects	Within-Group Contrasts		Between-Group Effects
CK	<.001†	<.001†	CK 8 h versus CK preop	<.001†	<.001†
			CK 24 h versus CK preop	<.001†	
			CK 48 h versus CK preop	<.001†	
CK versus group	.367	.097	CK 8 h versus CK preop	.179	
			CK 24 h versus CK preop	.122	
			CK 48 h versus CK preop	.438	
CK-MB	<.001†	<.001†	CK-MB 8 h versus CK-MB preop	<.001†	<.001†
			CK-MB 24 h versus CK-MB preop	<.001†	
			CK-MB 48 h versus CK-MB preop	<.001†	
CK-MB versus group	.062	.004†	CK-MB 8 h versus CK-MB preop	.016†	
			CK-MB 24 h versus CK-MB preop	.053	
			CK-MB 48 h versus CK-MB preop	.891	
Tro	<.001†	<.001†	Tro 8 h versus tro preop	<.001†	<.001†
			Tro 24 h versus tro preop	<.001†	
			Tro 48 h versus tro preop	<.001†	
Tro versus group	.012†	<.001†	Tro 8 h versus tro preop	.001†	
			Tro 24 h versus tro preop	.002†	
			Tro 48 h versus tro preop	.020†	

*CK indicates creatine kinase; preop, preoperative; CK-MB, CK myocardial band; tro, troponin I.

†Statistically significant (analysis of variance for repeated measures).

surgeons do not use intracoronary shunts in OPCABG surgery. To exclude a possible effect of shunt use on the postoperative outcome, we did not use shunts.

A common consensus is that a totally occluded collateralized vessel should be revascularized before a collateralizing vessel. The LAD is the preferred artery for the first anastomosis. This vessel is the easiest to expose and to access, and performing this anastomosis first allows revascularization of the septum and the anterior wall before other provocative maneuvers [Dewey 2003]. An exception to this strategy can occur if the LAD collateralizes a completely occluded RCA, thereby providing the sole blood supply to the septum and anterior and inferior walls. In this circumstance, the initial grafting of the RCA to limit the amount of myocardium made ischemic during occlusion of the LAD would be a reasonable approach [Dewey 2003]; however, damage to the LITA-LAD anastomosis or LITA stretching may be encountered while performing the other anastomosis if the LITA-LAD anastomosis is performed first. Therefore, there is no clear-cut consensus as to which artery to revascularize first. Initially anastomosing the LAD reduced enzyme leaks significantly in the present study.

The main RCA can be problematic to graft when a large, dominant, and moderately stenotic RCA is to be bypassed proximal to the crux. Proximal occlusion causes ischemia to the atrioventricular node, which thereby can manifest as bradycardia and heart block that can lead to ventricular distension and cardiovascular collapse [Dewey 2003]. We did not encounter such a problem during the procedure, although all of the RCAs were bypassed proximal to the crux. Therefore, the differences in enzyme levels should be due to the sequence of the anastomoses, not to hemodynamic fluctuations. Bradyarrhythmias and hemodynamic problems are seen infrequently with occlusion of the posterior descending artery, in contrast to the RCA [Dewey 2003]. To exclude any possible effect of positioning and hemodynamic problems on the enzyme levels, we did not include patients in the study who had a distal RCA lesion. Although there was no hemodynamic deterioration due to occlusion of the RCA, an increase in enzyme levels when the RCA anastomosis is done first may be due to anastomosis duration, because it was the only difference between these 2 techniques. Both groups had the same total ischemic times, however, so the only difference appears to be the sequence. The first ischemic period when the LAD was anastomosed first was less than that when the RCA was anastomosed first, owing to the technical difficulties of the RCA anastomosis. The time of the first myocardial ischemic period was 5.9 ± 1.1 minutes during the LAD anastomosis (group 1). On the other hand, the first ischemic period was 6.8 ± 1.1 minutes when the RCA was anastomosed first (group 2). Therefore, the patients who had the LAD anastomosis performed first were exposed to a shorter initial period

of ischemia. One may speculate that when the RCA is anastomosed after the LAD anastomosis, the probable collateral flow from the LAD to the right side of the posterior septum might have protected the myocardium, although collateralization is angiographically undetermined. The longer duration of the RCA anastomosis is probably performed under a better collateral flow. On the contrary, occlusion of the RCA first caused a longer initial ischemic period, probably with less collateral flow from the left side. Although unproved, this explanation may account for the difference in enzyme levels. Thus, other detailed studies are necessary to explain the possible mechanisms of this difference.

Patients with unobstructed RCAs who have ischemic preconditioning applied to the LAD have better postoperative contractility of the right ventricle, which is more vulnerable to ischemia. Such patients do not demonstrate changes in the right ventricular ejection fraction [Laurikka 2002]. This observation may explain the present results. Performing the LAD anastomosis first may have an effect of ischemic preconditioning on the right ventricle, because the RCAs were severely stenotic. Because the revascularized coronary arteries were immediately perfused after anastomosis, there may not be a postconditioning effect at these sites. When the RCA is anastomosed first, the right ventricle may face ischemia without this preconditioning effect. Nevertheless, this explanation is just a speculation, which needs to be proved.

An increased release of enzymes postoperatively, even in the absence of a clear clinical picture of MI, can influence intermediate- or long-term survival. Patients with greater CK-MB release show less freedom from cardiac-related events. The findings in the present study are therefore important, even in the case of subclinical myocardial damage [Calafiore 2003; Di Mauro 2005]. In conclusion, in this randomized trial that compared a strategy of revascularizing the LAD first against a strategy of revascularizing the RCA first without the use of intracoronary shunts, anastomosing the LAD first appears to have produced a slight reduction in myocardial enzyme release, although the results are of limited clinical significance.

LIMITATIONS

Although the differences between the groups with respect to the myocardial markers are statistically significant, the mechanisms for this result are not proved in this study. The sample size was small, which might have reduced the power of the study. The patient population selected represents a rather stable, low-risk group and is not indicative of the majority of patients who undergo CABG surgery. No studies were performed to test the patency or the adequacy of flow in the grafts, either with postoperative angiography or with a flow meter intraoperatively. Although the enzyme changes were statistically significant, they were not clinically significant, and future studies with patients at higher risk and with triple-vessel disease are necessary to confirm the present findings. Another limitation may be that the patients were not examined with echocardiography for postoperative wall-motion abnormalities, but such data would not have yielded additional information for the present study. Postoperative medications may have had minor effects on the biochemical measurements, considering that different medications might have been used according to the needs of the patients.

REFERENCES

Baumgartner FJ, Cheisssari A, Capouya ER, Panagiotides GP, Katouzian A, Yokoyama T. 1999. Technical aspects of total revascularization in off-pump coronary bypass via sternotomy approach. Ann Thorac Surg 67:1653-8.

Bleier J, Vorderwinkler KP, Falkensammer J, et al. 1998. Different intracellular compartmentations of cardiac troponins and myosin heavy chains: a causal connection to their different early release after myocardial damage. Clin Chem 44:1912-8.

Calafiore AM, Di Mauro M, Canosa C, Di Giammarco G, Iacò AL, Contini M. 2003. Myocardial revascularization with and without cardiopulmonary bypass: advantages, disadvantages and similarities. Eur J Cardiothorac Surg 24:953-60.

Carrier M, Pellerin M, Perrault LP, Solymoss BC, Pelletier LC. 2000. Troponin levels in patients with myocardial infarction after coronary artery bypass grafting. Ann Thorac Surg 69:435-40.

Dewey TM, Mack MJ. 2003. Myocardial revascularization without cardiopulmonary bypass. In: Cohn LH, Edmunds LH, eds. Cardiac surgery in the adult. 2nd ed. New York: McGraw-Hill. p 609-25.

Di Mauro M, Iacò AL, Contini M, et al. 2005. Reoperative coronary artery bypass grafting: analysis of early and late outcomes. Ann Thorac Surg 79:81-7.

French JK, White HD. 2004. Clinical implications of the new definition of myocardial infarction. Heart 90:99-106.

Gürbüz A, Emrecan B, Yilik L, et al. 2006. Intracoronary shunt reduces postoperative troponin leaks: a prospective randomized study. Eur J Cardiothorac Surg 29:186-9.

Hangler HB, Pfaller K, Ruttmann E, et al. 2004. Effects of intracoronary shunts on coronary endothelial coating in the human beating heart. Ann Thorac Surg 77:776-80.

Laurikka J, Wu ZK, Iisalo P, et al. 2002. Regional ischemic preconditioning enhances myocardial performance in off-pump coronary artery bypass grafting. Chest 121:1183-9.

Rivetti RA, Gandra SMA. 1997. Initial experience using an intraluminal shunt during revascularization of the beating heart. Ann Thorac Surg 63:1742-7.

Sadony V, Körber M, Albes G, et al. 1998. Cardiac troponin I plasma levels for diagnosis and quantitation of perioperative myocardial damage in patients undergoing coronary artery bypass surgery. Eur J Cardiothorac Surg 13:57-65.

Yeatman M, Caputo M, Narayan P, Ghosh AK, Ascione R, Angelini GD. 2001. Intracoronary shunts reduce transient intraoperative myocardial dysfunction during off-pump coronary operations. Ann Thorac Surg 73:1411-7.