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Bilateral versus Single Internal Thoracic Artery Grafting in Dialysis Patients with Multivessel Disease

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ABSTRACT

Background: The purpose of our study was to compare mortality in dialysis patients undergoing bilateral internal thoracic artery (BITA) or single internal thoracic artery (SITA) grafting and to quantify the magnitude of the BITA grafting benefit for survival.

Methods: Between January 2002 and December 2008, 656 consecutive patients underwent isolated coronary artery bypass grafting (99.1% by an off-pump technique). Fifty-six of these patients with chronic dialysis and multivessel disease were retrospectively compared with respect to surgical technique: BITA (n = 32) or SITA (n = 23) grafting. End points were all-cause and cardiovascular mortality (mean follow-up duration, 2.5 years). In an attempt to minimize the selection bias, we created propensity scores based on 13 preoperative factors that would affect the surgeon's decision about operative strategy; these factors were used for regression adjustment (*C* statistic, 0.914).

Results: There were no significant differences between the 2 groups with respect to age, sex, left ventricular ejection fraction, prevalence of diabetes mellitus and peripheral arterial disease, and logistic EuroSCORE. All patients underwent revascularization with the off-pump technique, with no conversion to cardiopulmonary bypass. All arterial conduits were harvested with a skeletonization technique in all cases. Except for 1 patient who received a SITA, internal thoracic arteries were used as in situ grafts in both groups. Complete revascularization was achieved in all patients. The 1-, 3-, and 5-year survival rates free from all-cause mortality for BITA grafting versus SITA grafting were 94% versus 73%, 72% versus 42%, and 52% versus 28%, respectively ($P = .01$, log-rank test). For survival free from cardiovascular mortality, the respective rates were 100% versus 90%, 80% versus 77%, and 80% versus 58% ($P = .06$). After propensity score adjustment, BITA grafting was significantly associated with lower risks for all-cause mortality (hazard ratio, 0.27; 95% confidence interval, 0.09-0.81; $P = .02$) and cardiovascular mortality (hazard ratio, 0.20; 95% confidence interval, 0.04-0.93; $P = .04$).

Conclusion: In situ skeletonized BITA grafting provides better long-term survival in dialysis patients with multivessel disease.

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INTRODUCTION

Multiple studies have reported that bilateral internal thoracic artery (BITA) grafting provides better long-term results than single ITA (SITA) grafting, especially when BITA grafting to the left coronary system is used [Pick 1997; Schmidt 1997; Berreklouw 2001; Endo 2001; Taggart 2001; Tector 2001; Lytle 2004]. Several studies have reported the long-term results of coronary artery bypass grafting in dialysis patients [Blakeman

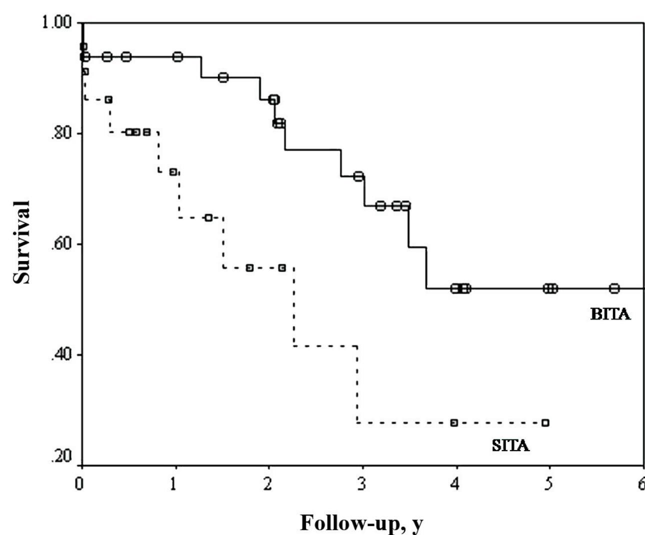

Figure 1. Kaplan-Meier curves for survival free from all-cause mortality. Numbers of patients at risk were 26, 15, and 7 for bilateral internal thoracic artery (BITA) grafting at 1, 3, and 5 years, respectively, and were 10, 3, and 2 for single internal thoracic artery (SITA) grafting. $P = .009$, log-rank test.

Table 1. Preoperative Characteristics*

	BITA Group (n = 32)	SITA Group (n = 23)	*P*
Age, y†	64.1 (7.2)	68.6 (10.0)	.06
Female sex, n (%)	4 (13)	5 (22)	.47
Hemodialysis duration, y†	5.2 (3.3)	7.3 (7.1)	.15
Hemodialysis >5 y, n (%)	14 (44)	14 (61)	.21
Body mass index, kg/m^2†	22.6 (3.3)	20.6 (3.5)	.03
Body surface area, m^2†	1.65 (0.15)	1.59 (0.20)	.20
Hypertension, n (%)	22 (69)	14 (61)	.38
Hyperlipidemia, n (%)	12 (38)	2 (9)	.10
Diabetes mellitus, n (%)	21 (66)	10 (44)	.55
Insulin dependent diabetes, n (%)	13 (41)	8 (35)	.66
Chronic obstructive pulmonary disease, n (%)	5 (16)	4 (17)	.99
Peripheral arterial disease, n (%)	11 (34)	5 (22)	.31
NYHA functional class†	2.2 (1.0)	2.6 (1.0)	.13
NYHA functional class 3 or 4, n (%)	11 (34)	13 (57)	.10
History of PCI, n (%)	12 (38)	8 (35)	.84
Previous myocardial infarction, n (%)	4 (13)	12 (52)	<.01
Congestive heart failure, n (%)	10 (31)	9 (39)	.54
Ejection fraction, %†	50.1 (11.3)	50.1 (13.0)	.99
Ejection fraction <40%, n (%)	7 (22)	5 (22)	.99
Left main trunk disease >50%, n (%)	12 (38)	9 (39)	.90
No. of systems with >75% stenosis†	2.69 (0.4)	2.57 (0.5)	.36
Double-vessel disease, n (%)	10 (31)	10 (44)	.35
Triple-vessel disease, n (%)	22 (69)	13 (57)	.35
Emergency, n (%)	7 (22)	6 (26)	.73
Logistic EuroSCORE‡	5.9 (3.7-8.6)	6.0 (4.4-24.5)	.12

*BITA indicates bilateral internal thoracic artery; SITA, single internal thoracic artery; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

†Data are presented as the mean (SD).

‡Data are presented as the median (interquartile range).

1990; Franga 2000; Dacey 2002; Beckermann 2006; Dewey 2006]. Dialysis patients undergoing BITA grafting have better long-term results with regard to cardiac-related events than SITA grafting [Kai 2007]. Not much has been done, however, to clarify long-term survival for dialysis patients following BITA grafting. The present study investigates whether BITA grafting provides better long-term survival in dialysis patients with multivessel disease, compared with SITA grafting.

PATIENTS AND METHODS

Study Population

Between January 1, 2002, and December 31, 2008, 656 consecutive patients underwent isolated coronary artery bypass grafting by a single surgeon at our institution. Except for 1 redo case and 5 salvage cases, all patients underwent myocardial revascularization with the off-pump technique. No patients were converted to cardiopulmonary bypass during their operation. Of these patients, 56 patients with end-stage renal failure who were maintained on chronic hemodialysis and had 2- or 3-vessel coronary disease were included in the present study. Patients were classified into one of 2 groups depending on whether they underwent BITA grafting (n = 32) or SITA grafting (n = 23). All of the patients had previously granted permission for use of their medical records for research purposes.

End Points

The end points were all-cause mortality and cardiovascular mortality. Follow-up data were obtained by reviewing medical records, by using a mailed questionnaire, or by telephone interview. Cardiovascular mortality included deaths by myocardial infarction, stroke, and sudden death. The patients' data were all prospectively collected and entered into our database.

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Table 2. Operative Data*

	BITA Group (n = 32)	SITA Group (n = 23)	*P*
No. of distal anastomoses†	3.3 (1.1)	3.1 (1.0)	.37
Gastroepiploic artery, n (%)	9 (28)	5 (22)	.59
Saphenous vein, n (%)	10 (31)	20 (87)	<.01
Complete revascularization, n (%)	32 (100)	23 (100)	—
Operation time, min†	283 (78)	269 (67)	.50

*BITA indicates bilateral internal thoracic artery; SITA, single internal thoracic artery.
†Data are presented as the mean (SD).

Surgical Technique

After a median sternotomy, the ITA and gastroepiploic artery were harvested by a skeletonization technique with an ultrasonic scalpel (Harmonic Scalpel; Ethicon Endo-Surgery, Cincinnati, OH, USA) in all cases [Higami 2000, 2001; Asai 2002, 2006]. A few superficial and deep pericardial sutures were placed to facilitate cardiac displacement. During anastomoses, a suction-type mechanical stabilizer (Octopus 4.3; Medtronic, Minneapolis, MN, USA) was used to immobilize the target site of the coronary artery. Distal myocardial perfusion was maintained with an intracoronary shunt tube (AnastaFlo; Edwards Lifesciences, Irvine, CA, USA).

The vein-to-aorta proximal anastomosis was performed with partial clamping or an anastomotic device. To prevent complications related to manipulation of the ascending aorta, we routinely performed computed tomography scanning and epiaortic ultrasonography evaluations to assess the severity and location of atherosclerosis of the aorta. When the surgeon judged that partial clumping of the ascending aorta increased the risk of embolism, a proximal anastomotic device (the Novare Enclose device [Novare Surgical Systems, Cupertino, CA, USA], the HEARTSTRING Proximal Seal System [Guidant Corporation, Santa Clara, CA, USA], or the Symmetry aortic connector system [St. Jude Medical, St. Paul, MN, USA]) was used.

Each graft was assessed with a transit-time flowmeter (CardioMed CM2005; MediStem, Oslo, Norway) with the patient in a stable hemodynamic condition just before sternal closure.

Graft Arrangement

The basic strategy for myocardial revascularization was in situ BITA grafting to the left coronary system with complementary saphenous vein and/or gastroepiploic artery grafting. In the majority of cases, the in situ right ITA was tunneled through the right pericardial incision and routed anterior to the aorta across the midline for grafting to the left anterior descending artery (LAD); the in situ left ITA was used for the diagonal branches and/or circumflex branches. To prevent complications related to resternotomy at the end of the procedures, we covered the right ITA with loosely attached mediastinal tissue before the sternum was reattached with wires. On rare occasions when the in situ right ITA was too short for grafting to the LAD, the in situ right ITA was grafted to the circumflex branches through the transverse sinus, and the in situ left ITA was grafted to the LAD. Routine use of composite grafts was avoided because it has been shown to be associated with an increase in morbidity [Legare 2004]; however, if the right ITA was injured at its proximal portion or was too short for grafting to the LAD and circumflex branches, a composite graft was constructed. In these cases, the in situ left ITA was anastomosed to the LAD, the free graft of the right ITA was anastomosed to the in situ left ITA in an end-to-side fashion, and its distal end was connected to the circumflex branches. The gastroepiploic artery was used as an in situ graft to revascularize the posteroinferior wall; however, in cases of a coronary stenosis that was less than critical, a saphenous vein was used. Complete revascularization was accomplished when at least 1 bypass graft was placed distal to a site of ≥75% narrowing in each diseased territory. Left main trunk stenosis would require bypass grafting to both the LAD and the circumflex territory to be considered complete.

Perioperative Medications

Antiplatelet and anticoagulant drugs were discontinued at least 5 days before the operation, and intravenous heparin administrations were continued for unstable patients with critical stenoses until 6 hours before the operation. Intravenous heparin administration was started 6 hours after the surgical intervention and was followed with oral administration of aspirin or clopidogrel. In our institution, most patients were extubated on the day of surgery, and oral administrations including a beta-blocker, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and statins were initiated on the first postoperative day. Dialysis was usually performed on postoperative day 1 after extubation.

Statistical Analysis

We compared the baseline characteristics and operative data for the 2 groups with the Pearson chi-square test for categorical variables and by the Student *t* test or the Mann-Whitney *U* test for continuous variables. The Kaplan-Meier method was used to describe all-cause and cardiovascular mortality, and the log-rank test was used to compare the groups. A Cox proportional hazards model was used for estimating hazard ratios. Potential independent predictors of all-cause and cardiovascular mortality were identified by univariate analyses, and these independent predictors were entered into the model.

Table 3. Combinations for Internal Thoracic Artery Graft Placement*

	Patients, n
BITA group (n = 32)	
In situ LITA-LAD, in situ RITA-CX	4
In situ RITA-LAD, in situ LITA-CX	26
In situ LITA-LAD, in situ RITA-RCA	2
SITA group (n = 23)	
>In situ LITA-LAD	21
In situ RITA-LAD	1
Composite LITA-LAD	1

*BITA indicates bilateral internal thoracic artery; SITA, single internal thoracic artery; LITA, left internal thoracic artery; LAD, left anterior descending artery; RITA, right internal thoracic artery; CX: circumflex artery; RCA, right coronary artery.

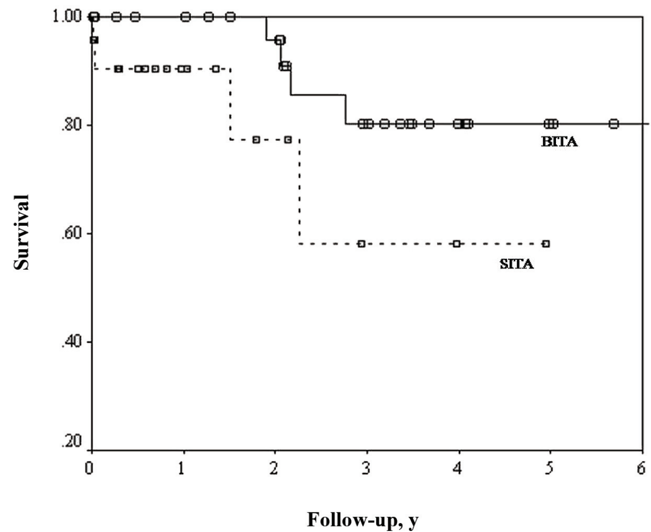

Figure 2. Kaplan-Meier curves for survival free from cardiovascular mortality. Numbers of patients at risk were 26, 15, and 3 for bilateral internal thoracic artery (BITA) grafting at 1, 3, and 5 years, respectively, and were 17, 6, and 1 for single internal thoracic artery (SITA) grafting. *P* = .061, log-rank test.

In an attempt to perform a fair group comparison, a propensity score was created to quantify the likelihood that a given patient would receive BITA grafting. We estimated propensity scores by a regression adjustment based on the following patient characteristics and major preoperative risk factors that would affect the surgeon's decision about operative strategy: age, sex, body mass index, body surface area, diabetes mellitus, peripheral arterial disease, New York Heart Association functional class, history of myocardial infarction, left ventricular ejection fraction, number of systems with >75% stenosis, left main trunk stenosis >50%, urgency of operation, and preoperative use of an intra-aortic balloon pump. Model discrimination was assessed with C statistics. Calibration was estimated with the Hosmer-Lemeshow goodness-of-fit test. Because the numbers of patients and events were small, we used the propensity score for regression adjustment. In regression adjustment based on the propensity score, both the comparison variable of interest (in this case, BITA grafting) and the propensity score were included in the model. The significance level for the *P* value was set at 5%. All statistical analyses were performed with the SPSS statistical package (version 11.0; SPSS, Chicago, IL, USA).

RESULTS

Preoperative Characteristics

Patients in the BITA group had a higher body mass index and a lower prevalence of previous myocardial infarction than the patients in the SITA group. There were no significant differences between the 2 groups with respect to other characteristics (Table 1).

Operative Data and Combinations for ITA Graft Placement

In both groups, all patients underwent myocardial revascularization with the off-pump technique without conversion to cardiopulmonary bypass during surgery (Table 2). Complete revascularization was achieved in all patients. There were no significant differences between the 2 groups with respect to the number of distal anastomoses, the use of the gastroepiploic artery, and operation time. In 1 case in the SITA group, flow in the harvested left ITA was weak, probably because of left subclavian artery stenosis. In this case, the saphenous vein was anastomosed to the circumflex artery, the free graft of the left ITA was anastomosed to the saphenous vein in an end-to-side fashion, and its distal end was connected to the LAD (Table 3). In all of the other cases, the ITA was used as an in situ graft. In 2 patients of the BITA group, the right ITA was anastomosed to the right coronary artery.

Postoperative Complications

The incidences of postoperative complications in the 2 groups were similar (Table 4).

Long-term Mortality

The collection of long-term outcomes was complete for 99.3% of the patients. Patients were followed up for a mean of 2.5 years (maximum, 6.1 years) after surgery. The 1-, 3-, and 5-year survival rates free of all-cause mortality for BITA grafting versus SITA grafting were 94% versus 73%, 72% versus 42%, and 52% versus 28%, respectively (*P* = .009, log-rank test) (Figure 1). For survival free from cardiovascular mortality, the respective rates were 100% versus 90%, 80% versus 77%, and 80% versus 58% (*P* = .061) (Figure 2).

Univariate and Multivariate Cox Proportional Hazards Model

In univariate analyses, chronic obstructive pulmonary disease, an ejection fraction <40%, peripheral arterial disease,

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Table 4. Postoperative Complications*

	BITA Group (n = 32), n (%)	SITA Group (n = 23), n (%)	*P*
Ventilation >24 h	13 (41)	7 (30)	.96
Atrial fibrillation	6 (19)	5 (22)	.79
Pneumonia	1 (3)	0	.99
Stroke	0	1 (4)	.42
Reexploration for bleeding	0	0	—
Perioperative myocardial infarction	0	0	—
Impaired chest wound healing	3 (9)	2 (9)	.99
Mediastinitis	0	0	—
Impaired leg wound healing	0	2 (9)	.17
30-Day mortality	2 (6)	3 (13)	.64

*BITA indicates bilateral internal thoracic artery; SITA, single internal thoracic artery.

Table 5. Hazard Ratios (HR) and 95% Confidence Intervals (CI) for Long-term Mortality

	All-Cause Mortality		Cardiovascular Mortality	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Unadjusted	0.31 (0.12-0.79)	.014	0.28 (0.10-1.15)	.078
Adjusted for all univariate predictors	0.25 (0.08-0.79)	.018	0.30 (0.07-1.35)	.117
Adjusted for propensity score	0.27 (0.09-0.81)	.020	0.20 (0.04-0.93)	.040

and New York Heart Association function class greater than 3 or 4 were significant univariate predictors of all-cause mortality. Previous myocardial infarction was only a potential univariate predictor of cardiac mortality. In multivariate Cox analyses including BITA grafting and all other significant univariate predictors, BITA grafting was significantly associated with a lower risk for all-cause mortality (hazard ratio, 0.25; 95% confidence interval, 0.08-0.79; $P = .018$), but not for cardiovascular mortality (hazard ratio, 0.30; 95% confidence interval, 0.07-1.35; $P = .117$) (Table 5).

Propensity Score Analysis

The C statistic for the propensity score model was 0.914 (Table 5). The Hosmer-Lemeshow goodness-of-fit chi-square test statistic was 8.88 ($P = .26$). After propensity score adjustment, BITA grafting was associated with a significantly lower all-cause mortality (hazard ratio, 0.27; 95% confidence interval, 0.09-0.81; $P = .020$) and cardiovascular mortality (hazard ratio, 0.20; 95% confidence interval, 0.04-0.93; $P = .040$).

DISCUSSION

The major finding of the present study was that among dialysis patients with multivessel coronary disease, use of in situ skeletonized BITA grafting without cardiopulmonary bypass provides better long-term survival than SITA grafting without a worsening of the early results.

Dialysis patients had multiple risk factors and high EuroSCOREs in our study (Table 1). They are regarded as high-risk patients because events that would be nonfatal in low-risk patients can easily cause fatal outcomes in these patients. We believe that this reason is why the survival benefit of BITA grafting became clear in our study after a relatively short follow-up.

Multiple studies have reported that BITA grafting provides better long-term results than SITA grafting, especially when BITA grafting to the left coronary system is used [Pick 1997; Schmidt 1997; Berreklouw 2001; Endo 2001; Taggart 2001; Tector 2001; Lytle 2004]. Our results concur with these studies and were borne out by the high resistance of the ITA to atherosclerosis, even in dialysis patients [Ura 2001]. Kai and colleagues investigated long-term outcomes in 76 dialysis patients who underwent BITA grafting and compared the results with those for 25 dialysis patients who underwent SITA grafting. To our knowledge, this study was the first available to compare the long-term outcomes of BITA grafting and SITA grafting. These investigators reported that long-term all-cause and cardiac-related mortality rates for BITA grafting were not different from those of SITA grafting but that BITA grafting provided better long-term results than SITA grafting with regard to cardiac-related events [Kai 2007]. Our results were not compatible with the study of Kai et al. There are several possible explanations for these differences. First, all of the arterial conduits in our study were harvested with the skeletonization technique in all cases, whereas this technique was used for only a limited number of arterial conduits in their study. Second, a Y composite graft constructed with

the free right ITA and the in situ left ITA were used in 27.6% of the patients in the BITA group in their study, whereas we used this technique in only 1 patient (4%). Third, we exclusively used the off-pump technique in all patients, whereas only a limited number of patients underwent off-pump coronary artery bypass surgery in the Kai et al study. Finally, we excluded patients with single-vessel disease from our study population, whereas Kai et al included 6 patients with single-vessel disease in their study.

One problem of BITA use is that a right ITA crossing the midline can be injured during the median sternotomy in redo coronary artery bypass surgery. Therefore, we attempted to decrease the likelihood of injuring the right ITA by covering it with loosely attached mediastinal tissue in the initial coronary artery bypass surgery before the sternum was repaired. In the follow-up period, of all the patients (n = 656), we carried out redo coronary artery bypass surgery in 3 patients in whom the right ITA crossed the midline; all 3 operations were performed successfully without injuring the ITA.

Some reports have described a reduction in wound infections when BITA were harvested with a skeletonization technique [Kramer 2000; Matsa 2001; Peterson 2003; De Paulis 2005]. On the other hand, Nakano and associates demonstrated that BITA use was a risk factor for wound infection in diabetic patients, even when the arteries were harvested with a skeletonization technique [Nakano 2008]. In our study, all arterial conduits were harvested with a skeletonization technique. No mediastinitis occurred. There was no statistical difference between the 2 groups in the occurrence of impaired wound healing. The SITA group, however, had a higher rate of impaired leg wound healing, probably because the SITA group featured greater use of the saphenous vein to achieve complete revascularization than the BITA group.

Limitations

There are several important limitations in the present study. First, even with propensity score adjustment, we could not truly evaluate the effect of BITA grafting as we could in a prospective randomized trial. Although the propensity score can adjust for confounding by indication and selection bias, we cannot eliminate residual confounding due to unobserved factors. Second, our study population was small, leading to insufficient statistical power. The limited number of early deaths did not allow the construction of a statistical model to assess the impact of BITA grafting on early mortality. Third, there were no available data on medications used after discharge, which could have affected outcomes, given that the patients received postoperative treatment from different hospitals.

CONCLUSION

Among dialysis patients with multivessel coronary artery disease, in situ skeletonized BITA grafting without cardiopulmonary bypass provides better long-term survival than SITA grafting without worsening the early results.

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