Effects of the side of arteriovenous fistula on outcomes after coronary artery bypass surgery in hemodialysis-dependent patients

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Objective: The aim of the study was to determine whether using the in situ internal thoracic artery (ITA) graft ipsilateral to the arteriovenous fistula adversely affects the outcomes after isolated coronary artery bypass grafting (CABG) in the dialysis-dependent patients to answer the concerns of a possible steal and consequent myocardial ischemia.

Methods: We categorized 155 dialysis patients undergoing isolated CABG between January 1993 and December 2011 into 108 patients (70%, ipsilateral group) whose left anterior descending artery (LAD) was revascularized with the ITA ipsilateral to the arteriovenous fistula and 47 patients (contralateral group) whose LAD was grafted with the ITA opposite to the fistula, to compare their early and late outcomes.

Results: While 94% of the ipsilateral group had left fistula, 55% of the contralateral group had left fistulas. The LAD was grafted with the left ITA in 94% of the ipsilateral group, whereas it was grafted with left (49%) or right (51%) ITAs in the contralateral group. There was no significant difference in hospital mortality between the groups (ipsilateral 10.2% vs contralateral 10.6%). After follow-up for 55 ± 42 months, the overall survival (ipsilateral 58% vs contralateral 65% at 5 years) and cardiac event-free rates (ipsilateral 74% vs contralateral 68% at 5 years) were also similar between the groups by log-rank tests ($P = .90$ and $P = .07$).

Conclusions: Revascularization of the LAD using the in situ ITA graft ipsilateral to the arteriovenous fistula increases neither the operative mortality nor the risks of late death and cardiac events after isolated CABG in dialysis patients. (J Thorac Cardiovasc Surg 2014;147:619-24)

Cardiovascular disease is the principal cause of deaths in patients receiving hemodialysis (HD), more than two thirds of whom have symptomatic coronary artery disease.¹⁻³ Increased population with renal disease and extended life expectancy of HD patients result in more HD patients, especially with diabetes mellitus (DM) and advanced age, referred for coronary revascularization. For the HD patients with multivessel disease, coronary artery bypass grafting (CABG) may be selected on the basis of the guidelines and the previous studies demonstrating the superiority of CABG to percutaneous coronary intervention.⁴⁻⁷ As well as in non-HD patients, in situ internal thoracic artery (ITA) grafting to the left anterior descending artery (LAD) improves survival and freedom from major adverse cardiac events (MACE) in HD patients.⁸⁻¹¹

However, there are concerns of a possible steal in HD patients with a functioning ITA graft and an ipsilateral arteriovenous (AV) fistula or shunt of the upper extremity.¹²⁻¹⁵ Although no reports definitively document a coronary

artery steal with an ipsilateral AV fistula, there have been several reports of a steal and consequent myocardial ischemia during HD. The aim of the present study was to determine whether revascularization of the LAD using the in situ ITA graft ipsilateral to the AV fistula increases the risk of late death and MACE after isolated CABG in HD patients.

METHODS

The institutional review board approved this retrospective observational study, and the approval included a waiver of informed consent.

Study Patients

We performed isolated CABG in 159 patients with end-stage renal failure requiring HD (124 men and 35 women with a mean age of 63 ± 8 years) over an 18-year period between January 1993 and December 2011. They comprised 10.4% of all patients undergoing isolated CABG during the same period. They had a history of HD for 8.9 ± 8.1 years (range, 0.2-36 years). The major causes of end-stage renal failure included chronic glomerulonephritis ($n = 32$, 20%) and DM ($n = 86$, 54%), whereas the causes of disease in 17 (11%) patients were unknown.

Among them, after excluding 4 patients who did not undergo ITA grafting to the LAD, 155 patients were included in the study to compare 108 patients (69.7%, ipsilateral group) whose LAD was revascularized with the in situ ITA ipsilateral to the AV fistula and 47 patients (30.3%, contralateral group) whose LAD was revascularized with the in situ ITA opposite to the AV fistula.

CABG and Perioperative Renal Management

Surgical procedures of CABG were performed through a median sternotomy, after low-potassium (1.5 mEq/L) HD for the consecutive 2 days,

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Abbreviations and Acronyms

AV	= arteriovenous
CABG	= coronary artery bypass grafting
CI	= confidence interval
CPB	= cardiopulmonary bypass
DM	= diabetes mellitus
HD	= hemodialysis
HR	= hazard ratio
ITA	= internal thoracic artery
LAD	= left anterior descending coronary artery
LVEF	= left ventricular ejection fraction
MACE	= major adverse cardiac events

except for emergency cases, to obtain serum potassium of 3.0 mEq/L.¹⁶ In our strategy, in situ bilateral ITAs were preferred for revascularization of the left coronary territory whenever possible anatomically. Right ITAs were used to revascularize the LAD by crossing the midline if necessary. However, the use of bilateral ITAs was avoided in the HD patients with DM owing to the concerns of postoperative mediastinitis. The gastroepiploic artery (GEA) was mostly used for revascularization of the right coronary arteries with more than 90% stenosis. The coronary arteries, for which ITAs and gastroepiploic arteries were not used, were bypassed using saphenous veins anastomosed with the ascending aorta.

Since 2003, CABG was preferably performed on the beating heart with off-pump technique and cardiopulmonary bypass (CPB) was used if necessary. When CPB was used, we performed only hemofiltration during CPB, as in non-HD patients. By means of a hemoconcentrator incorporated into the CPB circuit, serum potassium less than 4.0 mEq/L and blood hemoglobin greater than 10.0 g/dL were maintained at the end of CPB to prevent subsequent hyperkalemia.¹⁶ HD was resumed on the first postoperative day in most patients, except for those with hemodynamic instability or advanced hyperkalemia, who alternatively underwent continuous venovenous hemofiltration.

Data Collection and Follow-up

The ipsilateral and contralateral groups were retrospectively compared regarding the following primary end points: hospital mortality, late overall death, and late MACE. Hospital mortality was defined as death for any reason during the same hospitalization regardless of the length. Follow-up data were obtained from hospital charts or follow-up physicians and by means of direct telephone interviews with the patients or their families. The MACE was defined as cardiac death, myocardial infarction, hospital admission owing to congestive heart failure, and repeat revascularization. Cardiac death was defined as any death related to cardiac events, including sudden death.

Statistical Analysis

Continuous variables were expressed as means $\pm$ standard deviations and compared for differences between 2 groups with the Mann-Whitney *U* test. Categorical variables were expressed as percentages and analyzed using the χ^2 test or Fisher's exact test where appropriate. A multivariate logistic regression model was constructed to evaluate whether the side of the ITA was an independent predictor of hospital mortality. Long-term survival and MACE-free rate were estimated using the Kaplan-Meier method. Unadjusted comparisons of the 2 groups were made with a log-rank test. Cox proportional hazards models were also constructed to evaluate the effect of the side of ITA in the presence of potentially confounding covariates. All statistical analyses were performed with IBM SPSS Statistics version 19

(IBM Corporation, Armonk, NY), calculating hazard ratios (HR), 95% confidence intervals (CI), and levels of statistical significance.

RESULTS**Preoperative and Operative Characteristics**

As shown in Table 1, there were no significant differences in the patient characteristics, with the exception of the side of AV fistula, between the ipsilateral and contralateral groups. Whereas 94% of the ipsilateral group had left AV fistula, 55% of the contralateral group had left AV fistulas ($P < .001$). The locations and constructions of AV fistulas were similar between the 2 groups.

As shown in Table 2, the study patients underwent conventional ($n = 55$, 34%), on-pump beating heart ($n = 31$, 20%) or off-pump coronary artery bypass ($n = 71$, 46%) with distal anastomoses of 2.9 ± 0.9 per patient, with no significant differences between the 2 groups. With regard to the graft arrangements, in situ left ITAs were used in all patients of the ipsilateral group and were mainly grafted to the LAD. In contrast, left ITAs were used in 91% of the patients of the contralateral group and were mostly grafted to the LAD or left circumflex artery. Right ITAs were more frequently used in the contralateral group than the ipsilateral group (60% vs 24%; $P < .001$). Right ITAs were mainly anastomosed to the left circumflex artery in the ipsilateral group and to the LAD in the contralateral group. No free ITA grafts were used for the non-LAD coronary arteries. Consequently, bilateral in situ ITAs were used more frequently in the contralateral group than in the ipsilateral group (47% vs 24%; $P = .004$). There were no significant differences in the use of gastroepiploic artery and saphenous vein graft between the 2 groups.

Early Outcomes

Hospital mortality was 10.3% (16/155). The mortality improved over time: 16.2% (11/68) before 2003 and 5.7% (5/87) after 2003. The causes of hospital death included mediastinitis ($n = 5$), cardiac-related ($n = 4$), sepsis ($n = 3$), pneumonia ($n = 2$), gastrointestinal ischemia ($n = 1$), and stroke ($n = 1$). As shown in Table 3, there were no significant differences in the hospital mortality and the occurrence of postoperative complications, including mediastinitis and stroke, between the ipsilateral and contralateral groups. There were also no significant differences in the durations of intensive care unit stay and hospital stay between the survivors of the 2 groups.

A multivariate logistic regression analysis adjusting for 5 covariates, including left ventricular ejection fraction (LVEF) less than 40%, CPB use, bilateral ITA, and postoperative mediastinitis, revealed that ipsilateral ITA grafting to the LAD was no longer a predictor for hospital mortality (HR, 0.86; 95% CI, 0.49-1.50; $P = .59$). However, the variables of LVEF less than 40% (HR, 2.22; 95% CI, 1.23-7.12; $P = .03$) and CPB use (HR, 3.27; 95% CI,

TABLE 1. Patients characteristics of 155 HD patients undergoing isolated CABG according to the side of AV fistula and the side of ITA grafted with the LAD

	Ipsilateral (n = 108)	Contralateral (n = 47)	P value
Age, y	63 ± 8	63 ± 9	1.00
Male, n (%)	88 (81%)	34 (72%)	.12
HD duration, y	8.8 ± 7.6	9.1 ± 9.0	.83
Hypertension, n (%)	79 (73%)	35 (75%)	.86
DM, n (%)	59 (55%)	25 (53%)	.84
Hyperlipidemia, n (%)	41 (38%)	19 (40%)	.70
Smoking, n (%)	69 (64%)	29 (62%)	.89
PAD, n (%)	33 (31%)	15 (32%)	.72
Previous CVD, n (%)	18 (17%)	7 (15%)	.63
Previous MI, n (%)	35 (32%)	13 (28%)	.53
History of HF, n (%)	39 (36%)	15 (32%)	.56
LVEF, %	54 ± 15	54 ± 17	1.00
Side of AV fistula, n (%)			<.001
Right	6 (6%)	21 (45%)	
Left	102 (94%)	26 (55%)	
Location of AV fistula, n (%)			.57
Upper arm	11 (10%)	7 (15%)	
Forearm	97 (90%)	40 (85%)	
Construction of AV fistula, n (%)			.95
Direct anastomosis	94 (87%)	40 (85%)	
Prosthetic graft	14 (13%)	7 (15%)	

HD, Hemodialysis; CABG, coronary artery bypass grafting; AV, arteriovenous; ITA, internal thoracic artery; LAD, left anterior descending artery; DM, diabetes mellitus; PAD, peripheral artery disease; CVD, cerebrovascular disease; MI, myocardial infarction; HF, heart failure; LVEF, left ventricular ejection fraction.

1.18-7.85; $P = .04$) emerged as predictor of hospital mortality.

Late Outcomes

During the follow-up period of 55 ± 42 months (median, 4.2 years) for 139 survivors, 58 (42%) patients died and 42 (30%) had MACE. The causes of late death included cardiac ($n = 24$, 41%), gastrointestinal ($n = 8$, 14%), infection ($n = 8$, 14%), stroke ($n = 7$, 12%), exacerbation of peripheral artery disease ($n = 5$), cancer ($n = 5$), and unknown ($n = 1$). The overall actuarial survivals were 76.9% and 60.0% at 3 and 5 years, respectively. Median survival was 7.0 years. The MACE-free rates were 77.0% and 70.1% at 3 and 5 years, respectively. Among them, 102 (73%) patients, 97 (75%) in the ipsilateral group and 29 (70%) in the contralateral group, used the AV fistula of the same side during the follow-up period, whereas the others switched to HD through a contralateral side fistula. According to the side of AV fistula, overall survival estimates were similar between the ipsilateral and contralateral groups ($P = .90$), as shown in Figure 1. Also, there was no statistically significant difference in MACE-free rate between the 2 groups ($P = .07$), as shown in Figure 2.

A Cox proportional hazards model adjusting for 6 covariates, including age greater than 65 years, DM, peripheral

TABLE 2. Operative data

	Ipsilateral (n = 108)	Contralateral (n = 47)	P value
Emergency, n (%)	24 (22%)	11 (23%)	.93
CABG			.79
Conventional, n (%)	41 (38%)	12 (26%)	
On-pump beating, n (%)	18 (17%)	13 (27%)	
Off-pump, n (%)	49 (45%)	22 (47%)	
Anastomosis	2.8 ± 1.0	2.9 ± 0.9	.55
LITA use, n (%)	108 (100%)	43 (91%)	.002
To LAD, n (%)	101 (93%)	21 (45%)	<.001
To diagonal branch, n (%)	11 (10%)	10 (21%)	.10
To LCX, n (%)	8 (7%)	22 (47%)	<.001
Sequential, n (%)	16 (15%)	12 (24%)	.13
RITA use, n (%)	26 (24%)	28 (60%)	<.001
To LAD, n (%)	5 (5%)	22 (47%)	<.001
To diagonal branch, n (%)	1 (1%)	3 (6%)	.06
To LCX, n (%)	14 (13%)	5 (11%)	.46
To RCA, n (%)	7 (6%)	2 (4%)	.51
Sequential, n (%)	2 (2%)	6 (13%)	.004
GEA use, n (%)	27 (25%)	10 (20%)	.45
To LCX, n (%)	5 (5%)	1 (2%)	.41
To RCA, n (%)	25 (23%)	10 (20%)	.62
Sequential, n (%)	5 (5%)	2 (4%)	.84
SVG use, n (%)	66 (61%)	27 (53%)	.33
To diagonal branch, n (%)	9 (8%)	3 (6%)	.31
To LCX, n (%)	42 (39%)	11 (23%)	.06
To RCA, n (%)	52 (48%)	23 (45%)	.89
Sequential, n (%)	37 (34%)	10 (20%)	.09
Bilateral ITA use, n (%)	27 (25%)	22 (47%)	.004
All arterial conduits, n (%)	42 (39%)	24 (51%)	.15

CABG, Coronary artery bypass grafting; LITA, left internal thoracic artery; LAD, left anterior descending artery; LCX, left circumflex artery; RITA, right internal thoracic artery; RCA, right coronary artery; SVG, saphenous vein graft; ITA, internal thoracic artery; GEA, gastroepiploic artery.

artery disease, LVEF less than 40%, and postoperative mediastinitis, revealed that ipsilateral ITA grafting to the LAD was not a predictor for late death (Table 4). The variables of age less than 65 years, DM, and peripheral artery disease emerged as statistically significant predictors of late death. Also, after adjusting for 6 covariates, DM, LVEF less than

TABLE 3. Early outcomes

	Ipsilateral (n = 108)	Contralateral (n = 47)	P value
Hospital death, n (%)	11 (10.2%)	5 (10.6%)	.93
Cardiac	3	1	.63
Non-cardiac	8	4	
Mediastinitis, n (%)	13 (12.0%)	8 (17.0%)	.40
CVVH use, n (%)	16 (14.8%)	11 (23.4%)	.19
Stroke, n (%)	2 (1.9%)	1 (2.0%)	.96
Survivors			
ICU stay, d (median)	2.7 ± 6.5 (2)	3.1 ± 5.1 (2)	.67
Hospital stay, d (median)	28 ± 33 (18)	35 ± 42 (19)	.30

CVVH, Continuous veno-venous hemofiltration; ICU, intensive care unit.

FIGURE 1. Estimated overall survival in the Kaplan-Meier model for patients whose left anterior descending artery (LAD) was revascularized with the internal thoracic artery (ITA) ipsilateral to the arteriovenous fistula (ipsilateral group, dotted line) and patients whose LAD was grafted with the ITA opposite to the fistula (contralateral group, solid line).

40%, use of saphenous vein graft, ipsilateral ITA grafting to the LAD was not a predictor for late MACE. DM and LVEF less than 40% were the independent predictors of late MACE.

FIGURE 2. Estimated freedom from major adverse cardiac events (MACE) in the Kaplan-Meier model for patients whose left anterior descending artery (LAD) was revascularized with the internal thoracic artery (ITA) ipsilateral to the arteriovenous fistula (ipsilateral group, dotted line) and patients whose LAD was grafted with the ITA opposite to the fistula (contralateral group, solid line).

TABLE 4. Predictors for late death and MACE

	Hazard ratio	95% CI	P value
All-cause death			
Age >65 y	1.84	1.65-5.23	.035
Diabetes mellitus	3.14	1.51-6.53	.002
PAD	1.27	1.07-8.64	.042
LVEF <40%	0.99	0.98-1.01	.586
Postoperative mediastinitis	1.072	0.46-2.51	.873
Ipsilateral ITA graft to LAD	0.53	0.24-1.17	.227
MACE			
Diabetes mellitus	3.11	1.50-6.45	.004
LVEF <40%	2.46	1.18-8.43	.036
SVG use	0.93	0.47-1.82	.421
CPB use	1.08	0.38-2.51	.755
Ipsilateral ITA graft to LAD	0.73	0.24-1.84	.114

MACE, Major adverse cardiac events; CI, confidence interval; PAD, peripheral artery disease; LVEF, left ventricular ejection fraction; ITA, internal thoracic artery; LAD, left anterior descending artery; SVG, saphenous vein graft; CPB, cardiopulmonary bypass.

DISCUSSION

The key finding of this study was that revascularization of the LAD using the ITA graft ipsilateral to the AV fistula raises neither the operative mortality nor the risks of late death and MACE after isolated CABG in HD patients. We focused the surgical revascularization of the LAD, which is the most important for clinical outcomes of the HD patients, as well as of the non-HD patients. To our knowledge, this is the first report to assess the effects of the side of ITA graft, ipsilateral or contralateral to the AV fistula, on outcomes after CABG. Although no specific investigations of coronary steal were performed, our results may answer to the concerns of HD-induced reduction of ipsilateral ITA flow as a potential cause of poor outcomes in HD patients after CABG.^{12-15,17-19}

In HD patients, the ascending aorta is often subject to severe atherosclerotic changes, constituting a dangerous source of systemic emboli after proximal anastomosis.^{20,21} The use of in situ ITAs is strongly recommended to minimize aortic manipulation during CABG. However, Gaudino and colleagues¹⁴ showed hemodynamically evident ITA flow steal and consequent myocardial hypokinesia on transthoracic echocardiography during HD in 5 patients with ipsilateral AV fistula and ITA graft. In contrast, Rahbar and colleagues²² reported, in 15 HD patients, no significant changes in Doppler flow of either the ipsilateral or contralateral ITA with the AV fistula occluded and during HD. According to the previous reports of survival in HD patients after isolated CABG,^{12-15,17-19} the 5-year survivals were 50% to 60% and apparently lower than those in non-HD patients. Our study showed that such poor prognosis of HD patients is not associated with the side of the ITA graft to the LAD, which may be closely related to the concerned ITA flow steal on the same side as the AV fistula.

The high mortality after CABG in HD patients may result from more diffuse coronary artery disease with poor runoff. However, Wong and associates²³ quantitatively showed that HD patients undergoing CABG did not have a greater coronary artery atherosclerosis burden than matched controls. Therefore, the high mortality in HD patients may attribute to their extracardiac multiple comorbid disorders, including ventricular hypertrophy, cerebrovascular and peripheral artery disease, anemia, infection, electrolyte disturbances, cachexia, and increase in oxidative stress.²⁴

The first limitation of this study is a retrospective design with a small sample size and a single-center experience. This observational study has produced a negative finding and may be underpowered. A power analysis using Power and Sample Size Calculation version 3.0 at Vanderbilt University,²⁵ which may be downloaded for free, showed that a sample size of 159 and 333 patients would have a power of 0.8 and α value of 5% to detect a 2-year difference in overall survival and MACE, respectively. Therefore, this study was underpowered for MACE, but for survival. Larger prospective studies of HD patients undergoing CABG are needed to identify risk factors for potential AV fistula-ITA hemodynamic interference. Second, this study may not match the patients adequately. Nearly half of the contralateral group had bilateral ITA use. Our results may be affected by this difference in bilateral ITA utilization. However, our study was conducted on the premise that coronary steal of the LAD has a much more adverse effect on the late outcomes than that of the non-LAD arteries. In addition, we should note our finding that late outcomes of the ipsilateral group are similar to those of the contralateral group, which included more patients receiving bilateral ITAs. This finding suggests the less adverse effects of the ipsilateral ITA use on late outcomes. The third limitation is that approximately 30% of the study patients lost functionality of the AV fistula and consequently switched the side of the fistula over time. The changes of the side of the AV fistula may affect the results of the present study.

As suggested in this study, ITA flow steal may not occur during HD in a CABG patient with an ipsilateral ITA graft of average flow. However, we should recognize the risk factors known to predispose to ITA flow steal, such as altered ITA anatomy, subclavian stenosis, and anatomic location of the AV fistula. In addition, we should recognize that the blood flow through the AV fistula increases with time, associated with potential risk of ITA flow steal. Furthermore, when the long-term HD patients require additional AV fistulas, we must consider what kind of graft conduit is used. On the other hand, as Baciewicz and Harris¹² and Baciewicz alone¹⁵ recommend, an AV fistula with high flow volume, for example, a bridge fistula with a prosthetic graft or more proximal fistula in the upper extremity, should not be constructed in patients with ipsilateral ITA grafts.

In conclusion, revascularization of the LAD using an in situ ITA graft ipsilateral to the AV fistula increases neither the operative mortality nor the risks of late death and MACE after isolated CABG in HD patients. Our results may provide important information regarding the choice of CABG graft conduits and the management of the HD patients after CABG.

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