

Bilateral Internal Thoracic Artery Grafting in Hemodialysis Patients

Kohei Hachiro, MD; Takeshi Kinoshita, MD, PhD; Tomoaki Suzuki, MD, PhD; Tohru Asai, MD, PhD

Background: We compared postoperative outcomes in hemodialysis (HD) patients who underwent isolated coronary artery bypass grafting (CABG) for multivessel disease using either bilateral or single skeletonized internal thoracic artery.

Methods and Results: Among 1,486 patients who underwent isolated CABG between 2002 and 2020, 145 HD patients were retrospectively analyzed. After inverse probability of treatment weighting, there were no significant differences in the preoperative characteristics. No significant differences in 30-day mortality (P=0.551) or postoperative deep sternal wound infection (P=0.778) were observed. However, the bilateral internal thoracic artery grafting group had a lower postoperative stroke rate (0% vs. 4.0%, P=0.019). No significant differences in freedom from all-cause death (P=0.760) and cardiac death (P=0.863) were found. In the multivariate Cox proportional hazards models, bilateral internal thoracic artery grafting was not associated with all-cause death (P=0.246) or cardiac death (P=0.435).

Conclusions: Bilateral internal thoracic artery grafting in HD patients did not improve mid-term outcomes, but it was also not associated with worse postoperative outcomes. Use of the bilateral internal thoracic artery may be an important option in patients with limited conduits to prevent postoperative complications.

Key Words: Coronary artery bypass grafting; Deep sternal wound infection; Hemodialysis

B ilateral internal thoracic artery (BITA) grafting demonstrates a better survival benefit compared with single internal thoracic artery (SITA) grafting in patients with diabetes mellitus,¹ as well as in high-risk patients,² patients with low ejection fraction (EF),³ and patients with chronic kidney disease.⁴ However, the optimal treatment strategy for hemodialysis (HD) patients remains unclear.

Graft designs for HD patients undergoing coronary artery bypass grafting (CABG) are limited. Radial artery grafts are unavailable after vascular access surgery for HD, and saphenous vein grafts are often difficult to use because of peripheral artery disease. Additionally, HD patients often have atherosclerotic disease of the ascending aorta due to long-term renal impairment, which makes it difficult to anastomose the graft to the ascending aorta. Under such limited conduits, BITA grafting, which can reduce the frequency of ascending aorta contact, is a useful option. However, HD patients have a 3- to 4-fold higher risk of death in the long-term compared with other patients undergoing CABG,⁵ and BITA grafting can lead to deep sternal wound infection (DSWI). The present study aimed to compare postoperative outcomes in HD patients under-

Editorial p2011

going isolated CABG using BITA or SITA after adjusting for patients' background information, using weighted logistic regression analysis and inverse probability of treatment weighting (IPTW).

Methods

Patients

All patients previously provided informed consent to use their medical records for research purposes, and the Ethics Committee of Shiga University of Medical Science approved the study (Reg. No. 2019-144; approval date: July 11, 2019).

Between January 2002 and December 2020, 1,486 patients underwent isolated CABG and of them, 155 were HD-dependent using an arteriovenous fistula (AVF) before surgery. We excluded patients undergoing grafting without using the ITA (n=5), whose coronary anatomy presented only 1 target vessel in the left coronary artery system (n=4), and those who were converted to cardiopul-

Received March 24, 2021; revised manuscript received April 28, 2021; accepted May 20, 2021; J-STAGE Advance Publication released online June 25, 2021 Time for primary review: 34 days

Mailing address: Kohei Hachiro, MD, Division of Cardiovascular Surgery, Department of Surgery, Shiga University of Medical Science, Setatsukinowa, Otsu 520-2192, Japan. E-mail: starplatinum.1140@gmail.com

All rights are reserved to the Japanese Circulation Society. For permissions, please e-mail: cj@j-circ.or.jp ISSN-1346-9843



Division of Cardiovascular Surgery, Department of Surgery, Shiga University of Medical Science, Otsu, Japan

Table 1. Preoperative Patient Characteristics								
		Unweighted			Weighted			
	BITA (n=86)	SITA (n=59)	P value	ASMD	BITA (SoW=150.91)	SITA (SoW=136.26)	P value	ASMD
Age (years)	66.6±9.6	65.5±10.7	0.522	0.108	65.4±9.6	65.2±10.8	0.894	0.020
Sex (male)	68 (79.1%)	45 (76.3%)	0.692	0.067	122.31 (81.0%)	108.40 (79.6%)	0.751	0.035
BMI (kg/m ²)	22.9±2.9	23.5±4.3	0.329	0.164	23.1±3.0	23.2±4.1	0.816	0.028
Hypertension	69 (80.2%)	44 (74.6%)	0.423	0.134	119.89 (79.4%)	104.57 (76.7%)	0.582	0.065
DM	67 (77.9%)	45 (76.3%)	0.819	0.038	119.53 (79.2%)	106.55 (78.2%)	0.835	0.024
Dyslipidemia	45 (52.3%)	19 (32.2%)	0.015	0.416	62.99 (41.7%)	52.92 (38.8%)	0.618	0.059
Smoking history	42 (48.8%)	26 (44.1%)	0.575	0.094	72.24 (47.9%)	61.45 (45.1%)	0.640	0.056
Previous CVD	10 (11.6%)	11 (18.6%)	0.259	0.196	22.50 (14.9%)	19.87 (14.6%)	0.938	0.008
Previous PCI	40 (46.5%)	26 (44.1%)	0.773	0.048	69.67 (46.2%)	57.84 (42.4%)	0.528	0.077
PAD	12 (14.0%)	6 (10.2%)	0.501	0.117	18.57 (12.3%)	15.85 (11.6%)	0.861	0.022
LVEF <40%	12 (14.0%)	16 (27.1%)	0.061	0.329	36.33 (24.1%)	31.12 (22.8%)	0.806	0.031
3-vessel disease	51 (59.3%)	34 (57.6%)	0.842	0.035	86.88 (57.6%)	79.16 (58.1%)	0.929	0.010
LMT disease	36 (41.9%)	19 (32.2%)	0.238	0.202	51.08 (33.8%)	44.52 (32.7%)	0.834	0.023
HbA1c (%)	6.4±1.1	6.3±1.1	0.668	0.073	6.4±1.1	6.3±1.1	0.479	0.083
HD duration	4.0 (1.0-8.0)	4.0 (1.0-8.0)	0.419	0.132	4.8 (1.0-8.0)	3.0 (0.7–7.2)	0.966	0.006
Emergency operation	20 (23.3%)	20 (33.9%)	0.171	0.236	46.37 (30.7%)	40.26 (29.5%)	0.828	0.026
Acute MI	9 (10.5%)	10 (16.9%)	0.278	0.187	23.22 (15.4%)	19.24 (14.1%)	0.764	0.037
Side of AVF			0.260	0.196			0.836	0.026
Left	71 (82.6%)	44 (74.6%)			114.00 (75.5%)	104.36 (76.6%)		
Right	15 (17.4%)	15 (25.4%)			36.91 (24.5%)	31.90 (23.4%)		
Location of AVF			-	-			-	-
Forearm	86 (100%)	59 (100%)			150.91 (100%)	136.26 (100%)		
Upper arm	0 (0%)	0 (0%)			0 (0%)	0 (0%)		
STS score (%)	2.9 (2.1–4.8)	2.5 (1.3–6.2)	0.947	0.010	3.3 (2.2–5.1)	2.2 (1.3–5.6)	0.194	0.154
EuroSCORE II (%)	2.7 (1.9–4.2)	2.5 (1.4–7.5)	0.473	0.121	3.3 (1.9–5.4)	2.3 (1.4–5.7)	0.045	0.223

ASMD, absolute standardized mean difference; AVF, arteriovenous fistula; BITA, bilateral internal thoracic artery; BMI, body mass index; CVD, cerebral vascular disease; DM, diabetes mellitus; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HD, hemodialysis; LVEF, left ventricular ejection fraction; LMT, left main trunk; MI, myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; SITA, single internal thoracic artery; SoW, sum of weights; STS, Society of Thoracic Surgeons.

monary bypass during surgery (n=1). Finally, 145 patients were included in the study, and we retrospectively analyzed their postoperative outcomes.

Endpoints and Definitions

The endpoints were all-cause death and cardiac death. Cardiac death included death caused by myocardial infarction (MI), heart failure, or lethal arrhythmia. Causes of death were documented according to information obtained from witnesses, family members, death certificates, hospital records, and autopsy records.

Postoperative stroke was defined as newly developed central nervous system paralysis symptoms for \geq 72 h before discharge. Postoperative MI was defined according to the standard definition⁶ as an elevation of cardiac troponin >10-fold of the 99th percentile upper reference limit in patients with normal baseline values with at least one of the following elements: new pathological Q waves, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology, angiographic graft occlusion, or native coronary artery occlusion. DSWI was defined as any chest wound infection involving the sternum or mediastinal tissues during the follow-up period.

Surgical Treatment and Graft Arrangement

We noninvasively measured blood pressure simultaneously

in both upper arms preoperatively while the patient rested in the supine position. When there was a difference $\geq 20 \text{ mmHg}$ between blood pressure measurements, we did not use the ITA on the side with the lower value.

We used the off-pump technique in all patients. Details of surgical techniques, including graft harvest and graft arrangement, were published previously.^{2,7} The left anterior descending (LAD) artery was always revascularized using in situ grafting of the ITA. When the ITA was injured at its proximal portion or when the right ITA was too short for grafting to the LAD artery, we constructed a composite graft. We routinely performed computed tomographic scans and epiaortic ultrasonography to assess the severity and location of ascending aortic atherosclerosis to prevent complications related to manipulating the ascending aorta. When the surgeon judged that partial clamping of the ascending aorta carried a risk of embolism, a proximal anastomotic device, the Novare Enclose device (Novare Surgical Systems, Cupertino, CA, USA), was used. BITA grafting was preferred for revascularization of the left coronary territory whenever anatomically possible, even if the patient had poor blood sugar control before surgery or in emergency operations. We did not change the revascularization strategy when the LAD artery was revascularized using the ITA ipsilateral to the AVF.

Table 2. Operative and Postoperative Data								
Unweighted				Weighted				
	BITA (n=86)	SITA (n=59)	P value	ASMD	BITA (SoW=150.91)	SITA (SoW=136.26)	P value	ASMD
Operative data								
Operation time (min)	253.42±65.06	220.22±54.09	0.001	0.555	251.26±64.92	220.48±53.92	<0.001	0.516
Proximal anastomosis to aorta	26 (30.2%)	49 (83.1%)	<0.001	1.262	47.11 (31.2%)	114.80 (84.3%)	<0.001	1.275
Partial clamp	18 (20.9%)	39 (66.1%)	<0.001	1.024	35.90 (23.8%)	89.44 (65.6%)	<0.001	0.927
Anastomotic device	8 (9.3%)	10 (16.9%)	0.194	0.227	11.21 (7.4%)	25.36 (18.6%)	0.005	0.338
No. of distal anastomoses	3.35 ± 0.94	3.15±0.93	0.215	0.214	3.31±0.93	3.18±0.94	0.259	0.139
No. of grafts	2.67±0.52	2.17±0.38	<0.001	1.098	2.64±0.52	2.19±0.39	<0.001	0.979
Sequential grafting	48 (55.8%)	42 (71.2%)	0.058	0.324	83.43 (55.3%)	98.66 (72.4%)	0.002	0.362
GEA use	31 (36.0%)	16 (27.1%)	0.256	0.192	52.98 (35.1%)	38.16 (28.0%)	0.197	0.153
SVG use	26 (30.2%)	49 (83.1%)	<0.001	1.262	41.56 (27.5%)	114.80 (84.3%)	<0.001	1.395
Ipsilateral ITA graft to LAD	22 (25.6%)	38 (64.4%)	<0.001	0.847	40.86 (27.1%)	91.17 (66.9%)	<0.001	0.870
Postoperative data								
MI	0 (0%)	1 (1.7%)	0.321	0.186	0 (0%)	1.63 (1.2%)	0.203	0.156
DSWI	4 (4.7%)	3 (5.1%)	0.906	0.019	6.83 (4.5%)	5.25 (3.9%)	0.778	0.030
Stroke	0 (0%)	3 (5.1%)	0.083	0.328	0 (0%)	5.43 (4.0%)	0.019	0.289
Continuous hemodiafiltration	21 (24.4%)	17 (28.8%)	0.558	0.100	43.21 (28.6%)	35.21 (25.8%)	0.597	0.063
ICU stay >48 h	18 (20.9%)	18 (30.5%)	0.203	0.221	36.66 (24.3%)	34.15 (25.1%)	0.880	0.019
Ventilation >48h	5 (5.8%)	12 (20.3%)	0.015	0.441	15.41 (10.2%)	22.07 (16.2%)	0.138	0.178
30-day mortality	4 (4.7%)	4 (6.8%)	0.584	0.090	6.97 (4.6%)	8.47 (6.2%)	0.551	0.071

DSWI, deep sternal wound infection; GEA, gastroepiploic artery; ICU, intensive care unit; ITA, internal thoracic artery; LAD, left anterior descending artery; SVG, saphenous vein graft. Other abbreviations as in Table 1.

Statistical Analysis

Continuous variables are presented as mean±standard deviation or median and interquartile range, while categorical variables are presented as percentages. Comparisons of clinical characteristics between groups were performed using the unpaired t-test for normally distributed variables, the Mann-Whitney U test for skewed variables, and Pearson's χ^2 test for categorical variables. The estimated survival rates were calculated using the Kaplan-Meier method, and the log-rank test was used for comparisons. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of 30-day death and postoperative DSWI. Univariate and multivariate Cox proportional hazards regression analyses were performed to analyze the overall number of deaths and the number of cardiac deaths. Variables reaching a P value <0.050 in the univariate analysis or those that were considered clinically important were entered into the multivariate model. All statistical testing was two-sided, and results were considered statistically significant when P<0.050.

We adjusted patients' baseline characteristics using weighted logistic regression and IPTW to reduce the effect of selection bias and potential confounding factors. Weights for patients receiving BITA grafting were the inverse of propensity scores, and weights for patients receiving SITA grafting were the inverse of 1 – the propensity score. We used the following 18 adjustment variables to derive the propensity score: age, sex, body mass index (BMI), hypertension, diabetes mellitus, dyslipidemia, smoking history, previous cerebrovascular accident, history of percutaneous coronary intervention (PCI), peripheral artery disease, left ventricular (LV) EF <40%, 3-vessel disease, left main trunk disease, hemoglobin A1c, HD duration, emergency operation, acute MI, and side of AVF. The model was well calibrated (Hosmer-Lemeshow test, P=0.053), with reasonable discrimination (C-statistic, 0.707). Absolute standardized mean differences were calculated to compare the balance in baseline characteristics between the BITA and SITA groups in the unweighted cohort and the weighted cohort.⁸ An absolute standardized mean difference >0.100 was considered a meaningful imbalance. All statistical analyses were performed using SPSS, version 25.0 (IBM Corp., Armonk, NY, USA) and SAS, version 9.4 (SAS Institute, Cary, NC, USA).

Results

Right ITAs were too short to graft to the LAD artery in 2 patients, and left ITAs were injured at the proximal portion in 4 patients; therefore, composite grafts were constructed in all patients. There was a difference $\geq 20 \text{ mmHg}$ between upper arm blood pressure measurements in 5 patients; the ITAs on the side with the lower pressure were not used.

The mean age of the study population was 66.2 ± 10.1 years, and the population constituted 113 males (77.9%). Before adjustment, a greater number of patients in the BITA group compared with the SITA group had dyslipidemia (52.3% vs. 32.2%, respectively; P=0.015) (Table 1), but after adjustment using IPTW, the 2 groups were well balanced (Table 1).

Early Outcomes

Operative and postoperative data are shown in **Table 2**. The BITA group had longer operation times compared with the SITA group (251.26 ± 64.92 vs. 220.48 ± 53.92 min, respectively; P<0.001). No significant difference in the number of distal anastomoses was found between groups (P=0.259), but the BITA group had a greater number of grafts compared with the SITA group (2.64 ± 0.52 vs.

Table 3. Weighted Multivariate Logistic Regression Analyses for the Predictors of 30-Day Mortality and Postoperative DSWI							
Predictor	OR	95% CI	P value				
30-day mortality							
Age (year)	1.031	0.953-1.115	0.449				
BMI (kg/m²)	0.779	0.606-1.002	0.052				
Previous PCI	7.553	1.760-32.413	0.007				
LMT disease	5.679	1.227-26.283	0.026				
HD duration	0.852	0.676-1.075	0.176				
Emergency operation	7.376	1.710-31.826	0.007				
Acute MI	1.038	0.225-4.791	0.962				
BITA use	1.268	0.309-5.205	0.742				
DSWI							
BMI (kg/m²)	1.201	1.028-1.402	0.021				
Previous PCI	8.751	1.551-49.379	0.014				
BITA use	1.449	0.415-5.054	0.561				

CI, confidence interval; OR, odds ratio. Other abbreviations as in Tables 1,2.

Table 4. Causes of Overall Death									
	Unweighted					Weighted			
	BITA (n=86)	SITA (n=59)	P value	ASMD	BITA (SoW=150.91)	SITA (SoW=136.26)	P value	ASMD	
All-cause death	49 (57.0%)	22 (37.3%)	0.020	0.403	79.94 (53.0%)	48.71 (35.7%)	0.003	0.354	
Cardiac death	12 (14.0%)	7 (11.9%)	0.716	0.063	20.27 (13.4%)	16.51 (12.1%)	0.740	0.039	
MI	4 (4.7%)	5 (8.5%)	0.352	0.154	6.11 (4.0%)	11.93 (8.8%)	0.108	0.197	
Heart failure	7 (8.1%)	1 (1.7%)	0.061	0.300	12.59 (8.3%)	2.45 (1.8%)	0.010	0.300	
Lethal arrhythmia	1 (1.2%)	1 (1.7%)	0.789	0.042	1.57 (1.0%)	2.13 (1.6%)	0.696	0.053	
Noncardiac death	37 (43.0%)	15 (25.4%)	0.026	0.378	59.67 (39.5%)	32.2 (23.6%)	0.004	0.347	
Pneumonia	3 (3.5%)	2 (3.4%)	0.975	0.005	4.85 (3.2%)	6.30 (4.6%)	0.539	0.072	
Stroke	3 (3.5%)	0 (0%)	0.083	0.269	4.03 (2.7%)	0 (0%)	0.044	0.236	
Sepsis	15 (17.4%)	6 (10.2%)	0.206	0.210	24.02 (15.9%)	12.13 (8.9%)	0.070	0.214	
Cancer	1 (1.2%)	0 (0%)	0.409	0.156	1.32 (0.9%)	0 (0%)	0.252	0.135	
Others	15 (17.4%)	7 (11.9%)	0.361	0.156	25.45 (16.9%)	13.77 (10.1%)	0.093	0.200	

Abbreviations as in Table 1.

2.19 \pm 0.39; P<0.001), as well as lower rates of proximal anastomosis to the ascending aorta (31.2% vs. 84.3%, respectively; P<0.001), sequential grafting (55.3% vs. 72.4%, respectively; P=0.002), saphenous vein graft use (27.5% vs. 84.3%, respectively; P<0.001), and in situ ITA grafts ipsilateral to the AVF to revascularize the LAD artery (27.1% vs. 66.9%, respectively; P<0.001). A greater number of patients in the SITA group compared with the BITA group developed postoperative stroke (4.0% vs. 0%, respectively; P=0.019), which occurred just after operation in all affected patients. No significant differences in 30-day mortality (P=0.551) and DSWI (P=0.778) were found between groups, and no patients in either group developed symptoms associated with coronary steal, such as chest pain or lethal arrhythmia, during HD.

There were 4 deaths (4.9%) in the BITA group and 4 (8.2%) in the SITA group within 30 days after surgery (**Table 2**). The causes of death in the BITA group were lethal arrhythmia in 1 patient, sepsis in 2 patients, and pneumonia in 1 patient. The causes of death in the SITA group were acute MI in 3 patients and nonocclusive mesenteric ischemia in 1 patient.

Multivariate logistic regression analysis showed that the independent predictors of 30-day mortality were a history of PCI (odds ratio [OR]: 7.553, 95% confidence interval [CI]: 1.760–32.413; P=0.007), left main trunk disease (OR: 5.679, 95% CI: 1.227–26.283; P=0.026), and emergency operation (OR: 7.376, 95% CI: 1.710–31.826; P=0.007) (**Table 3**). The independent predictors of DSWI were BMI (OR: 1.201, 95% CI: 1.028–1.402; P=0.021) and a history of PCI (OR: 8.751, 95% CI: 1.551–49.379; P=0.014). Univariate logistic regression analysis revealed that LVEF <40% (OR: 10.414, 95% CI: 1.458–74.383; P=0.020) was the only predictor of postoperative stroke; therefore, we did not perform a multivariate logistic regression analysis for postoperative stroke. BITA grafting was not a predictor of 30-day mortality (P=0.742) or DSWI (P=0.561).

Mid-Term Outcomes

Follow-up was completed in 96.6% of patients (140/145), and the mean follow-up duration was 3.3 ± 3.1 years (maximum: 15.1 years). All causes of death are shown in **Table 4**. The adjusted 5-year estimated rates of freedom from all-cause and cardiac death, respectively, in the BITA group





Table 5. Weighted Multivariate Cox Hazard Proportional Models for the Predictors of All-Cause Death and Cardiac Death						
Predictor	HR	95% CI	P value			
All-cause death						
Age (years)	1.034	1.014-1.055	0.001			
Previous PCI	1.831	1.288-2.604	0.001			
GEA use	0.509	0.328-0.790	0.003			
Ipsilateral ITA graft to LAD	0.971	0.652-1.445	0.883			
BITA use	1.262	0.852-1.869	0.246			
Cardiac death						
Age (years)	0.993	0.950-1.037	0.750			
BMI (kg/m ²)	0.880	0.764-1.013	0.074			
Hypertension	0.601	0.285-1.267	0.181			
DM	4.954	1.281-19.163	0.020			
Previous PCI	2.045	0.991-4.220	0.053			
SVG use	1.869	0.656-5.326	0.242			
GEA use	0.608	0.205-1.803	0.370			
Ipsilateral ITA graft to LAD	1.985	0.905-4.355	0.087			
BITA use	1.395	0.605–3.218	0.435			

HR, hazard ratio. Other abbreviations as in Tables 1-3.

compared with the SITA group were 51.7% vs. 60.6% (Figure 1) and 86.5% vs. 86.9% (Figure 2); survival curves were not significantly different (P=0.760 and P=0.863, respectively).

Multivariate Cox proportional hazards regression analysis showed that independent predictors of mid-term death from all causes were age (hazard ratio [HR]: 1.034, 95% CI: 1.014–1.055; P=0.001), a history of PCI (HR: 1.831, 95% CI: 1.288–2.604; P=0.001), and gastroepiploic artery (GEA) grafting (HR: 0.509, 95% CI: 0.328–0.790; P=0.003) (**Table 5**). The only independent predictor of cardiac death was diabetes mellitus (HR: 4.954, 95% CI: 1.281–19.163; P=0.020). BITA grafting was not a predictor of overall death (P=0.246) or cardiac death (P=0.435).

Discussion

One of the major findings of the present study was that there was no significant difference in survival during a mean follow-up duration of 3.3 years between the BITA and SITA groups. Additionally, BITA grafting was not an independent predictor of overall mortality in the multivariate Cox proportional hazards analysis (HR: 1.262, 95% CI: 0.852–1.869; P=0.246; **Table 5**). Previous studies reported that the survival benefit of BITA grafting is only observed after long-term follow-up.⁹⁻¹² The 2014 United States Renal Data System reported that only 39.8% of patients survived 5 years after HD initiation.¹³ In the present study, adjusted 5-year estimated overall survival rates in the BITA and SITA groups were 51.7% and 60.6%, respectively (**Figure 1**). The life expectancy of HD patients undergoing CABG may be too short to affect late outcomes. Preoperative age was an independent predictor of overall death with the multivariate Cox proportional hazards analysis (HR: 1.034, 95% CI: 1.014–1.055; P=0.001), which may support this hypothesis. In other words, use of BITA, which is a challenging treatment for HD patients who are often immunocompromised,^{14,15} did not affect mid-term outcomes after CABG.

Previous studies report that BITA grafting during cardiac surgery increases the risk of postoperative DSWI.^{16,17} In the current study, BITA grafting was not a predictor of postoperative DSWI (P=0.561). Using the skeletonization technique when harvesting BITA grafts reduces wound infection rates compared with pedicled harvesting.^{18,19} In our study, all patients underwent CABG using the skeletonization technique, and our results suggest that skeletonization should be used to reduce sternal infection after CABG in both the general population and in HD patients.

No patients developed postoperative stroke in the BITA group (Table 2). Although there was no significant difference in the number of distal anastomoses (BITA: 3.31±0.93 vs. SITA: 3.18±0.94; P=0.259), the BITA group had fewer proximal anastomoses to the ascending aorta (BITA: 31.2% vs. SITA: 84.3%; P<0.001). HD patients often have severe calcification or atherosclerotic changes in the ascending aorta. In such patients, some methods, such as partial clamping and use of anastomotic devices for the ascending aorta, can lead to embolic events. In the current study, all 3 patients who developed postoperative stroke in the SITA group had had intraoperative partial clamping of the ascending aorta. However, partial clamping was not an independent predictor of postoperative stroke (P=0.933) in the univariate logistic regression analysis because of the small number of patients. In HD patients with a limited life expectancy, use of BITA grafts may be an important option to reduce the risk of postoperative early complications such as embolism and stroke.

There are concerns regarding coronary steal when using in situ ITA grafts ipsilateral to the AVF. However, no patients in either group demonstrated coronary steal postoperatively. Additionally, ipsilateral ITA grafting to revascularize the LAD artery was not a predictor of overall death (P=0.246) or cardiac death (P=0.435). We previously reported that coronary steal could be prevented by measuring blood pressure in both upper arms before surgery and not using the ITA on the side with the lower value when there is a difference $\geq 20 \text{ mmHg}$ between blood pressure measurements. We also showed that ipsilateral ITA to revascularize the LAD artery did not affect mid-term overall death and cardiac death.²⁰ In the present study, we performed CABG after the same measurements of both arms, which affected the results. Predicting whether coronary steal will occur when the ipsilateral ITA is used to revascularize the LAD artery is very important when designing grafts for HD patients, who often have severe calcification or atherosclerotic changes in the ascending aorta. Thus, it may be useful to measure blood pressure in both arms preoperatively.

Our multivariate Cox proportional hazards analysis revealed that a history of PCI (HR: 1.831, 95% CI: 1.288– 2.604; P=0.001) and GEA grafting (HR: 0.509, 95% CI: 0.328–0.790; P=0.003) were predictors of mid-term overall death (**Table 5**). A history of PCI was a predictor of 30-day death (OR: 7.553, 95% CI: 1.760–32.413; P=0.007) and postoperative DSWI (OR: 8.751, 95% CI: 1.551–49.379; P=0.014) (**Table 3**). PCI before CABG suggests that the patient has had coronary artery disease for a long period of time, which may have negative effects on multiple organs, including the sternum. GEA grafting to the right coronary area is associated with more survival benefit compared with saphenous vein grafting.^{21,22} Additionally, we previously reported good early patency with GEA grafting in HD patients.²³ Our results suggest that GEA grafting is associated with mid-term survival benefit, even in HD patients. Moreover, diabetes mellitus was the only predictor of cardiac death (**Table 5**). Patients with diabetes mellitus have a 3-fold higher risk of fatal coronary artery disease compared with patients without diabetes mellitus.²⁴ which may have affected our patients' mid-term outcomes.

The multivariate logistic regression analysis revealed that left main trunk disease (OR: 5.679, 95% CI: 1.227– 26.283; P=0.026) and emergency operation (OR: 7.376, 95% CI: 1.710–31.826; P=0.007) were predictors of 30-day death (**Table 3**). Left main coronary artery stenosis has historically been recognized as a risk factor for early death among patients undergoing CABG.^{25,26} Additionally, emergency CABG has been reported as one of the most important predictors of in-hospital death.²⁶ For HD patients who have a higher risk of cardiovascular surgery compared with the general population, emergency surgery, in which the whole body cannot be examined before surgery, may increase the risk.

In the present study, BMI was a predictor of DSWI in addition to a history of PCI (OR: 1.201, 95% CI: 1.028–1.402; P=0.021) (**Table 3**). Previous studies reported that BMI is a predictor of DSWI after CABG.^{27,28} Our results suggest that BMI should also be considered as a risk factor for postoperative DSWI after CABG in HD patients.

Study Limitations

This study had several limitations to note. First, the study had a retrospective design with intrinsic selection bias. Despite statistical adjustments with IPTW, unmeasured confounders might have affected the results. Second, all participants who underwent revascularization using the off-pump technique at a single center were Japanese patients, which limits the generalizability of the findings. Finally, lack of available coronary angiographic data meant that we could not evaluate whether the survival benefit of ITA grafting is related to graft patency.

Conclusions

In this study, BITA grafting did not improve mid-term outcomes in HD patients undergoing isolated off-pump CABG, but it was also not associated with worse postoperative outcomes. To prevent postoperative complications, use of BITA may be an important option in HD patients with limited conduits.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Disclosures

T.A. is a member of Circulation Journal's Editorial Team.

Ethics Approval

The Ethics Committee of Shiga University of Medical Science granted

approval for the study (Reg. No. R2019-144).

References

- Pevni D, Medalion B, Mohr R, Ben-Gal Y, Laub A, Nevo A, et al. Should bilateral internal thoracic artery grafting be used in patients with diabetes mellitus? *Ann Thorac Surg* 2017; 103: 551–558.
- Kinoshita T, Asai T, Suzuki T, Kambara A, Matsubayashi K. Off-pump bilateral versus single skeletonized internal thoracic artery grafting in high-risk patients. *Circulation* 2011; 124: S130–S134.
- Galbut DL, Kurlansky PA, Traad EA, Dorman MJ, Zucher M, Ebra G. Bilateral internal thoracic artery grafting improves longterm survival in patients with reduced ejection fraction: A propensity-matched study with 30-year follow up. *J Thorac Cardiovasc Surg* 2012; 143: 844–853.
- 4. Kinoshita T, Asai T, Suzuki T. Off-pump bilateral skeletonized internal thoracic artery grafting in patients with chronic kidney disease. *J Thorac Cardiovasc Surg* 2015; **150**: 315–321.
- Liu JY, Birkmeyer NJ, Sanders JH, Morton JR, Henriques HF, Lahey SJ, et al. Risks of morbidity and mortality in dialysis patients undergoing coronary artery bypass surgery: Northern New England Cardiovascular Disease Study Group. *Circulation* 2000; **102**: 2973–2977.
- Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). *Circulation* 2018; 138: e618–e651.
- Asai T, Suzuki T, Nota H, Kuroyanagi S, Kinoshita T, Takashima N, et al. Off-pump coronary artery bypass grafting using skeletonized in situ arterial grafts. *Ann Cardiothorac Surg* 2013; 2: 552–556.
- Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009; 28: 3083–3107.
- 9. Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R, et al. Two internal thoracic artery grafts are better than one. *J Thorac Cardiovasc Surg* 1999; **117**: 855–872.
- Berreklouw E, Rademakers PP, Koster JM, van Leur L, van der Wielen BJW, Westers P. Better ischemic event-free survival after two internal thoracic artery grafts: 13 years of follow-up. *Ann Thorac Surg* 2001; **72**: 1535–1541.
- Endo M, Nishida H, Tomizawa Y, Kasanuki H. Benefit of bilateral over single internal mammary artery grafts for multiple coronary artery bypass grafting. *Circulation* 2001; **104**: 2164–2170.
- nary artery bypass grafting. *Circulation* 2001; 104: 2164–2170.
 12. Lytle BW, Blackstone EH, Sabik JF, Houghtaling P, Loop FP, Cosgrove DM. The effect of bilateral internal thoracic artery grafting on survival during 20 postoperative years. *Ann Thorac Surg* 2004; 78: 2005–2014.
- Saran R, Li Y, Robinson B, Ayanian J, Balkrishnan R, Bragg-Gresham J, et al. US renal data system 2014 annual data report: Epidemiology of kidney disease in the United States. *Am J Kidney Dis* 2015; 66: Svii, S1–S305.
- de Marie S. Disease and drug-related interventions affecting host defence. *Eur J Clin Microbiol Infect Dis* 1993; 12: S36–S41.
- 15. Kato S, Chmielewski M, Honda H, Pecoits-Filho R, Matsuo S, Yuzawa Y, et al. Aspects of immune dysfunction in end-stage

renal disease. Clin J Am Soc Nephrol 2008; 3: 1526-1533.

- Deo SV, Shah IK, Dunlay SM, Erwin PJ, Locher C, Altarabsheh SE, et al. Bilateral internal thoracic artery harvest and deep sternal wound infection in diabetic patients. *Ann Thorac Surg* 2013; 95: 862–869.
- Urso S, Nogales E, Gonzalez JM, Sadaba R, Tena MA, Bellot R, et al. Bilateral internal thoracic artery versus single internal thoracic artery: A meta-analysis of propensity score-matched observational studies. *Interact Cardiovasc Thorac Surg* 2019; 29: 163–172.
- Peterson MD, Borger MA, Rao V, Peniston CM, Feindel CM. Skeletonization of bilateral internal thoracic artery grafts lowers the risk of sternal infection in patients with diabetes. *J Thorac Cardiovasc Surg* 2003; **126**: 1314–1319.
- De Paulis R, de Notaris S, Scaffa R, Nardella S, Zeitani J, Del Giudice C, et al. The effect of bilateral internal thoracic artery harvesting on superficial and deep sternal infection: The role of skeletonization. *J Thorac Cardiovasc Surg* 2005; **129**: 536–543.
- Hachiro K, Kinoshita T, Suzuki T, Asai T. Internal thoracic artery graft ipsilateral to the arteriovenous fistula in haemodialysis patients. *Interact Cardiovasc Thorac Surg* 2021; 32: 864–872.
- Suzuki T, Asai T, Matsubayashi K, Kambara A, Kinoshita T, Takashima N, et al. In off-pump surgery, skeletonized gastroepiploic artery is superior to saphenous vein in patients with bilateral internal thoracic arterial grafts. *Ann Thorac Surg* 2011; 91: 1159–1164.
- 22. Glineur D, D'hoore W, Price J, Dormeus S, de Kerchove L, Dion R, et al. Survival benefit of multiple arterial grafting in a 25-year single-institutional experience: The importance of third arterial graft. *Eur J Cardiothorac Surg* 2012; **42**: 284–290.
- Hachiro K, Kinoshita T, Suzuki T, Asai T. In situ skeletonized gastroepiploic artery grafting in hemodialysis patients. *Gen Thorac Cardiovasc Surg* 2020; 68: 1319–1324.
- Huxley R, Barzi F, Woodward M. Excess risk of fatal coronary heart disease associated with diabetes in men and women: Metaanalysis of 37 prospective cohort studies. *BMJ* 2006; **332:** 73–78.
- 25. Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, et al. ACC/AHA guidelines for coronary artery bypass graft surgery: executive summary and recommendations: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1991 guidelines for coronary artery bypass graft surgery). *Circulation* 1999; **100**: 1464–1480.
- Davierwala PM, Maganti M, Yasu TM. Decreasing significance of left ventricular dysfunction and reoperative surgery in predicting coronary artery bypass grafting-associated mortality: A twelve-year study. *J Thorac Cardiovasc Surg* 2003; **126**: 1335– 1344.
- 27. Benedetto U, Altman DG, Gerry S, Gray A, Lees B, Pawlaczyk R, et al. Pedicled and skeletonized single and bilateral internal thoracic artery grafts and the incidence of sternal wound complications: Insights from the Arterial Revascularization Trial. J Thorac Cardiovasc Surg 2016; 1152: 270–276.
- Rubens FD, Chen L, Bourke M. Assessment of the association of bilateral internal thoracic artery skeletonization and sternal wound infection after coronary artery bypass grafting. *Ann Thorac Surg* 2016; **101**: 1677–1682.