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Single Versus Multiple Inflow Source for Coronary Artery Bypass Surgery in Ischemic Cardiomyopathy

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AUTHOR'S SUMMARY

Despite advancements in surgical revascularization, the optimal grafting strategy for ischemic cardiomyopathy (ICMP) remains unclear. This study suggests that using multiple inflow sources may enhance long-term survival and cardiac function recovery, particularly in select patient groups. These findings provide new insights into refining surgical approaches for ICMP patients, emphasizing the potential role of additional inflow sources in optimizing outcomes. Further research is needed to validate these results and establish tailored strategies for high-risk patients.

ABSTRACT

Background and Objectives: The optimal grafting strategy for ischemic cardiomyopathy (ICMP) remains uncertain despite the growing heart failure population undergoing coronary artery bypass grafting (CABG). This study sought to explore the outcomes of CABG in ICMP patients according to the number of inflow sources.
Methods: A total of 447 patients with an ejection fraction (EF) of ≤35% who underwent isolated CABG from 2009 to 2020 were analyzed. Patients were categorized into either a single inflow source group (single group, n=203), in which unilateral in situ internal thoracic artery (ITA) served as the sole inflow, or a multiple inflow source group (multiple group, n=244), utilizing additional inflow sources from the aorta or contralateral ITA. The primary outcome was all-cause mortality, analyzed after adjustment using the inverse-probability-of-treatment-weighting method.
Results: There were no differences in the early outcomes between 2 groups. After adjustment, the single group exhibited significantly worse survival compared to the multiple group during a median follow-up of 5.3-years (adjusted hazard ratio, 1.88; 95% confidence interval, 1.26–2.80; p=0.001), particularly in the subgroup of patients without a recent myocardial infarction within 1 month (p=0.005) and those with an EF of ≥25% (p=0.007). At the last follow-up echocardiography (>6 months), the multiple group showed a significantly higher postoperative EF (p=0.009) and a smaller left ventricular end-systolic dimension (p=0.027) compared to the single group, which had not shown significant differences preoperatively.

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Conclusions: In ICMP patients, CABG using multiple inflow sources was associated with improved outcomes, particularly in those without recent or profound myocardial injury.

Keywords: Coronary artery bypass grafting; Myocardial ischemia; Myocardial revascularization; Survival; Heart failure

INTRODUCTION

Ischemic heart disease has been the leading cause of premature mortality globally, and this phenomenon is expected to continue in conjunction with the increasing prevalence of obesity, diabetes, and metabolic syndrome in this aging society.[1][2] Clinically significant ischemic heart disease can manifest in various ways, including acute coronary syndrome and ischemic cardiomyopathy (ICMP). Advances in the management of cardiovascular disease and acute coronary syndrome have led to a growing population of individuals with non-fatal ischemic heart disease who live with chronic disabilities, particularly ischemic heart failure.[1][2] Furthermore, the proportion of patients undergoing coronary artery bypass grafting (CABG) who suffer from heart failure has been steadily increasing.[3] While the causes of heart failure can be overlapping and multifactorial, it is apparent that ICMP is the single largest cause of heart failure among patients receiving CABG.[4][5]

While CABG in patients with ICMP is generally considered high-risk and technically challenging, it has proved clinical benefits regarding survival compared to optimal medical therapy.[6][7] However, there have been only a limited number of studies focusing on CABG performed in patients with ICMP or severe left ventricular (LV) dysfunction. Furthermore, no studies have sought to determine the optimal grafting strategy in this specific setting.[8]

In this study, under the assumption that the enlarged and hypertrophied myocardium in ICMP demands a greater blood supply compared to typical ischemic heart disease, we sought to explore the long-term outcomes of CABG according to the number of inflow sources.

METHODS

Ethical statement

This study was reviewed and approved by Yonsei University Health System, Severance Hospital, Institutional Review Board (study number: 2024-0230-001; approval date: April 7, 2024). Requirements for informed consent were waived due to the retrospective nature of the study as directed by the Institutional Review Board.

Study population and definition

This study reviewed the data of ICMP patients with LV ejection fraction (EF) of 35% or less who were treated with CABG between January 2009 and December 2020 in Severance Cardiovascular Hospital (Seoul, Korea). Isolated CABG cases were exclusively reviewed in this study, excluding cases with concomitant valve, aorta, or surgical ventricular restoration procedures. Patients undergoing concomitant mitral procedures to address severe ischemic mitral regurgitation were intentionally excluded to maintain a homogeneous study population and facilitate a straightforward analysis. In addition, single target vessel CABG or CABGs that did not use in situ internal thoracic artery (ITA) or in which acute myocardial

infarction (MI) within 1 week was judged to be the main cause of LV dysfunction at the time of surgery were excluded from this study.

The study subjects were grouped by the number of inflow sources for surgical revascularization. In the single group, a unilateral in situ ITA (left or right) directly bypassing the left anterior descending artery was used as a singular inflow source for the entire coronary system. For revascularization of lateral and inferior wall, the composite graft configuration was used, in which the right ITA, radial artery, or saphenous vein graft (SVG) was sourced from the singular inflow, unilateral in situ ITA (**Figure 1**).
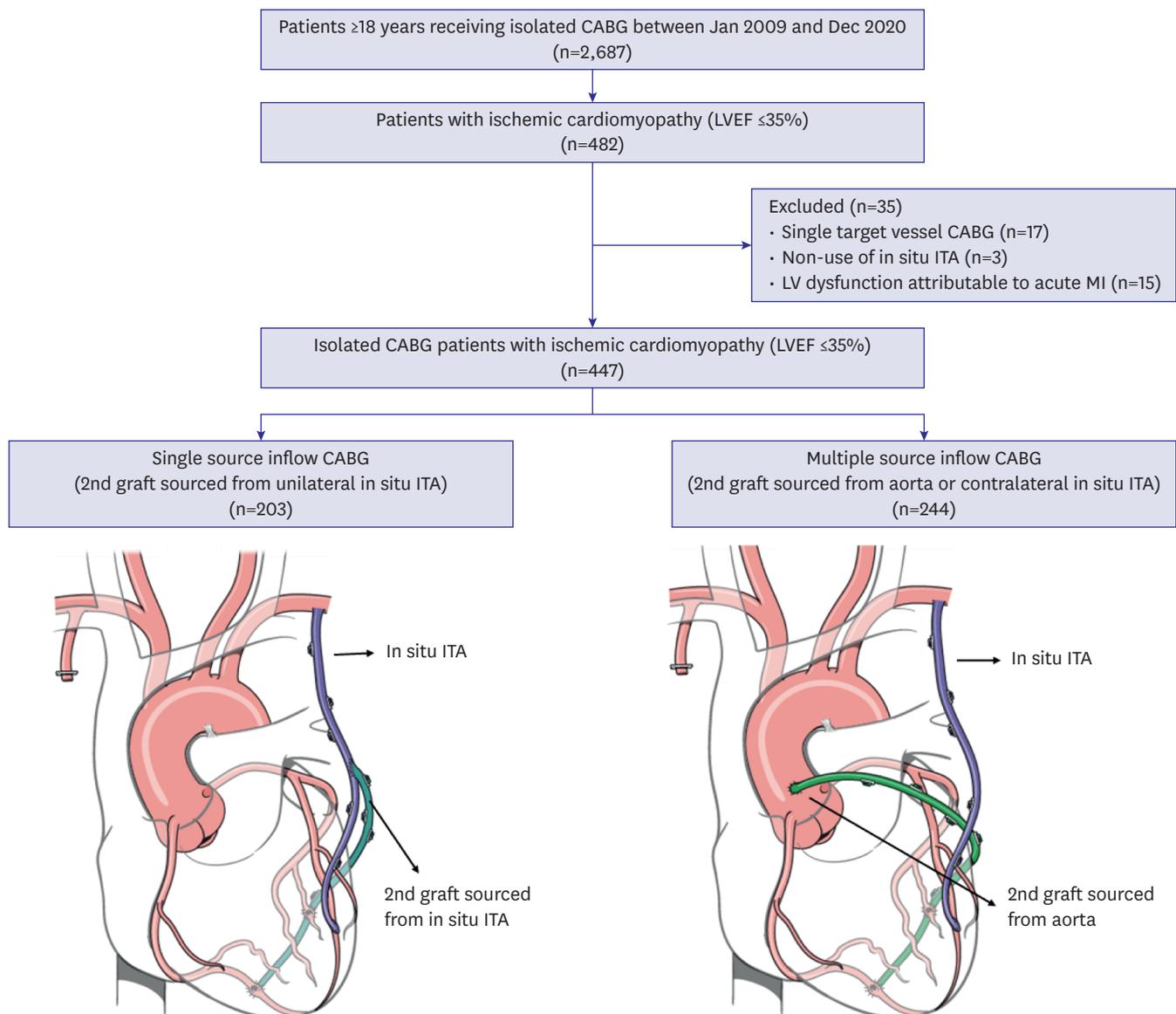
Figure 1. Patient selection diagram and schematic illustration of coronary artery bypass surgery in the single and multiple group. The flowchart outlines the patient selection process, while the schematic diagrams compare the grafting strategies, highlighting the differences in inflow sources and conduit configurations between the 2 groups.
CABG = coronary artery bypass grafting; ITA = internal thoracic artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

In the multiple group, at least one supplementary inflow source was utilized for coronary revascularization beyond the in situ ITA bypassing the left anterior descending artery. In these cases, the contralateral in situ ITA or a free graft (radial artery or SVG) sourced from the ascending aorta was used as a supplementary source.

Study end-points

The primary outcome was overall mortality after CABG. The secondary outcomes included cardiovascular death, major adverse cardiovascular events (MACE) and echocardiographic functional parameters including LVEF and LV end-systolic dimension (LVESD). MACE was defined as the composite of overall death, MI, or repeat revascularization. Data on vital status and cause of death (COD) were compiled and linked with data from Statistics Korea through 1-by-1 match-up using personal ID numbers. Statistics Korea annually collects vital status and COD information from death certificates and classifies COD according to the Korean Standard Classification of Diseases and Causes of Death, based on the International Classification of Diseases 10th Revision (ICD-10). Cardiovascular death was defined as ICD-10 codes for diseases of the circulatory system (I00–99).

For secondary outcomes including MI, repeat revascularization, and echocardiographic follow-up, the closing date of follow-up was set as December 31, 2021, to align with the mortality data obtained from Statistics Korea.

Operative techniques

In general, the majority of CABGs were performed in an off-pump manner. However, in a minority of cases, the elective decision to perform on-pump beating CABG was made in a shared decision process with the anesthesiology team. The default operative setting for off-pump CABG in Severance Cardiovascular Hospital has been described previously.[9] In brief, the Swan-Ganz catheter and the intraoperative transesophageal echocardiography were routinely applied for all patients. In off-pump coronary artery bypass (OPCAB) for ICMP patients with severe LV dysfunction, the effective communication and collaboration between the operating surgeon and the anesthesiology team are crucial, particularly in response to the worsening severity of mitral regurgitation and pulmonary artery pressure.[10] To ensure safe aortic manipulation, all cases involving aortic manipulation underwent epi-aortic ultrasound scan, and the Heartstring (Maquet Holding B.V. & Co. KG, Rastatt, Germany) was applied.

The grafting strategy was primarily determined at the discretion of the operating surgeon. When a second graft involved the use of an arterial conduit, such as the radial artery or right ITA, it was often utilized as a composite graft (sourced from left ITA) due to size and length constraints. When the SVG was used as the second conduit, the aorta was the usual and preferred inflow source. Throughout the entire study period, all vein grafts were harvested using the no-touch technique by experienced hands. However, in cases where aortic manipulation was difficult, such as with a porcelain aorta, the ITA was used as the inflow source.

In terms of conduit selection, arterial grafts were preferred as the second graft for younger patients. However, in cases with severe cardiomegaly or when multiple bypasses were required, vein grafts were prioritized to mitigate the risk of flow competition and address potential issues related to graft length shortage.

Statistical analysis

Categorical variables underwent comparison through either the χ^2 test or Fisher exact test and were reported as frequencies and percentages. Continuous variables, presented as mean and standard deviation, were subjected to comparison using the t-test. Multivariable Cox regression analysis was performed to identify independent predictors of overall mortality. Variables that were statistically significant in univariable analysis ($p<0.10$) were first selected, and stepwise backward elimination was conducted. In addition, clinically relevant variables—such as surgeon identity (operator), the number of distal anastomoses, and completeness of revascularization—were included in the final model regardless of univariable significance. The number of inflow sources, as the primary variable of interest, was also forced into the model.

To assess multicollinearity, we performed variance inflation factor (VIF) analysis. The VIF values for creatinine, end-stage renal disease (ESRD), and chronic kidney disease were 1.63, 2.53, and 2.31, respectively. To avoid redundancy, only creatinine and ESRD were retained in the model. For revascularization-related variables, the VIF values for number of distal anastomoses and ≥4 distal anastomoses were 3.94 and 3.84, respectively; only the continuous variable was included in the final model. The VIF for complete revascularization was 1.08. Surgeon identity and multi-arterial grafting (MAG) showed VIFs of 1.02, indicating no collinearity, and both were included in the model.

To minimize potential treatment-selection bias, we employed the inverse-probability-of-treatment-weighting (IPTW) method based on a propensity score model. To evaluate the discriminatory ability of the propensity score model, the concordance index was calculated, yielding a value of 0.801. This indicates good discrimination in predicting treatment assignment between the 2 groups. To mitigate the influence of extreme weights, stabilized inverse probability weights were applied and trimmed at fixed bounds (0.2 to 5). The propensity score incorporated all baseline variables and clinically relevant intraoperative variables listed in **Table 1**, except for MAG. Although MAG is a clinically important variable, it was strongly imbalanced between the groups and highly correlated with the treatment assignment (i.e., inflow strategy). Including MAG in the propensity score model resulted in extreme weights, instability in the IPTW estimates, and significant data loss due to necessary trimming. In accordance with methodological recommendations,[11] we excluded MAG from the propensity score model to preserve model stability and instead adjusted for MAG separately in the multivariable outcome model after IPTW correction. The distributions of propensity scores before and after IPTW were illustrated in **Supplementary Figure 1**. To verify the robustness of our findings, we also constructed an alternative IPTW-adjusted model that included MAG in the propensity score. The results were consistent with the main analysis and are presented as a sensitivity analysis in **Supplementary Table 1**.

After adjustment with the IPTW-method, the Cox-proportional hazard model was used to compare the risk of primary and secondary outcomes between the groups. The proportional hazards assumption was assessed using the Schoenfeld residual, which yielded no evidence to suggest rejecting the assumption. Subgroup analyses were performed across various subgroups. For these comparisons, the interaction between the number of inflow sources and each subgroup was evaluated in the IPTW-adjusted cohorts. In addition, a propensity score matching analysis was conducted as part of the sensitivity analysis to further reduce potential bias from extreme scores. One-to-one nearest-neighbor matching was performed using a caliper of 0.2 without replacement.

Table 1. Baseline and operative characteristics of patients before and after inverse probability weighting

Variables	Before adjustment			After adjustment		
	Single source (n=203)	Multiple source (n=244)	p value	Single source (n=202.5)	Multiple source (n=242.4)	SMD
Baseline profiles						
Age (years)	64.9±9.9	65.4±9.5	0.541	65.6±9.5	65.4±9.3	0.013
Female	43 (21.2)	47 (19.3)	0.700	46.6 (23.0)	51.2 (21.1)	0.046
Current smoker[*]	84 (41.4)	102 (41.8)	0.999	85.8 (42.4)	98.8 (40.8)	0.033
Hypertension	148 (72.9)	181 (74.2)	0.844	152.1 (75.1)	188.8 (77.9)	0.065
Diabetes	114 (56.2)	152 (62.3)	0.223	118.0 (58.3)	145.6 (60.1)	0.036
Stroke	34 (16.8)	33 (13.5)	0.401	28.4 (14.1)	35.7 (14.7)	0.019
Peripheral arterial occlusive disease	27 (13.3)	30 (12.3)	0.861	30.2 (14.9)	33.5 (13.8)	0.031
Chronic lung disease[†]	53 (35.1)	87 (44.8)	0.086	59.8 (37.0)	73.1 (40.0)	0.062
Previous PCI	11 (5.4)	10 (4.1)	0.665	10.3 (5.1)	11.6 (4.8)	0.014
Chronic kidney disease	27 (13.3)	47 (19.3)	0.119	32.2 (15.9)	42.6 (17.6)	0.045
End stage renal disease with dialysis	14 (6.9)	30 (12.3)	0.080	18.4 (9.1)	23.6 (9.7)	0.022
Creatinine (mg/dL)	1.81±3.70	1.77±2.33	0.885	1.79±3.08	1.68±2.26	0.042
Hemoglobin (g/dL)	12.4±2.2	12.3±2.2	0.562	12.4±2.2	12.4±2.1	0.006
Recent myocardial infarction <1 month	99 (48.8)	118 (48.4)	0.999	94.5 (46.7)	114.7 (47.3)	0.013
NYHA III or IV	43 (21.2)	72 (29.5)	0.058	49.6 (24.5)	60.1 (24.8)	0.007
Preoperative ECMO or IABP	2 (1.0)	9 (3.7)	0.126	2.4 (1.2)	5.6 (2.3)	0.086
Coronary artery disease			0.461			0.018
2-vessel disease	17 (8.4)	16 (6.6)		12.8 (6.3)	16.5 (6.8)	
3-vessel disease	186 (91.6)	228 (93.4)		189.6 (93.7)	225.9 (93.2)	
Preoperative atrial fibrillation	4 (2.0)	12 (4.9)	0.157	5.0 (2.5)	8.3 (3.4)	0.056
Preoperative echocardiography						
LV ejection fraction	28.1±5.2	27.6±4.9	0.380	27.8±5.1	27.7±4.8	0.009
LV end-systolic dimension (mm)	49.5±7.57	49.9±8.0	0.607	49.9±7.8	50.1±8.6	0.032
LV end-diastolic dimension (mm)	59.9±6.8	60.4±7.3	0.459	60.3±7.0	60.6±7.64	0.038
Mitral regurgitation (>grade II)	50 (24.9)	60 (24.8)	0.999	54.0 (26.8)	56.4 (23.4)	0.079
RV systolic pressure (>40 mmHg)	51 (33.6)	61 (37.0)	0.604	52.5 (36.5)	61.5 (36.3)	0.004
Intraoperative findings						
Surgeon factor			<0.001			0.108
Operator A	130 (64.0)	103 (42.2)		117.9 (58.3)	128.2 (52.9)	
Operator B	73 (36.0)	141 (57.8)		84.5 (41.7)	114.1 (47.1)	
Off-pump coronary bypass	201 (99.0)	240 (98.4)	0.853	201.3 (99.4)	238.3 (98.3)	0.103
Complete revascularization	181 (89.2)	233 (95.5)	0.018	186.1 (91.9)	221.1 (91.2)	0.026
Multi-arterial grafting	108 (53.2)	58 (23.8)	<0.001	96.6 (47.7)	59.7 (24.6)	0.494
Second grafts used in CABG						
Right ITA						
In situ	N/A	11 (4.5)				
Sourced from contralateral ITA	11 (5.4)	1 (0.4)				
Radial artery graft	97 (47.8)	56 (23.0)	<0.001			
Sourced from aorta	N/A	14 (5.7)				
Sourced from ITA	97 (47.8)	42 (17.2)				
Saphenous vein graft	96 (47.3)	231 (94.7)	<0.001			
Sourced from aorta	N/A	220 (90.2)				
Sourced from ITA	96 (47.3)	23 (9.4)				
Number of distal anastomoses	3.06±0.74	3.61±0.72	<0.001	3.35±0.87	3.38±0.73	0.036
2	41 (20.2)	11 (4.5)				
3	117 (57.6)	95 (38.9)				
4	38 (18.7)	118 (48.4)				
≥5	7 (3.5)	20 (8.2)				
Distal anastomosis ≥4	45 (22.2)	138 (56.6)	<0.001	76.1 (37.6)	98.4 (40.6)	0.062
Aorto-coronary bypass	N/A	233 (95.5)	<0.001			
On-pump conversion	2 (1.0)	0 (0)	0.400			

Data are mean ± standard deviation or number (%).

CABG = coronary artery bypass grafting; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; ITA = internal thoracic artery; LV = left ventricular; N/A = not available; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PFT = pulmonary function test; RV = right ventricular; SMD = standardized mean difference.

[*]Current smoker was defined as an individual who was actively smoking at the time of index hospital admission for surgery.

[†]Chronic lung disease was defined as physician-diagnosed chronic obstructive pulmonary disease or asthma with a preoperative PFT showing an forced expiratory volume in 1 second/forced vital capacity ratio <70%. PFT was routinely performed in all operable patients before surgery.

Echocardiographic comparisons were performed within the IPTW-adjusted cohort. Paired t-tests were used to compare pre- and post-operative values within each group, while unpaired t-tests were used to compare values between the single and multiple groups. All reported p values were 2-tailed, and p<0.05 was considered statistically significant. We used R software version 4.0.3 (R Project for Statistical Computing, Vienna, Austria) for statistical analyses.

RESULTS

Patients

From January 2009 to December 2020, a total of 3,188 patients received surgical coronary revascularization at Severance Cardiovascular Hospital, of which 2,687 patients underwent isolated CABG. After applying exclusion criteria, 447 patients with ICMP were included in the analysis. Among these patients, 203 received CABG with a single inflow source (single group), while 244 patients underwent CABG with multiple inflow sources (multiple group) (**Figure 1**). Among patients who were alive as of December 31, 2021, 77.9% had documented clinical follow-up data available within the defined follow-up period.

Table 1 summarizes the baseline demographic, clinical, and intraoperative profiles of the patients. There were no significant differences in baseline profiles between the groups. Concurrently, there were notable differences in operative profiles between the groups. The multiple group exhibited a significantly higher number of distal anastomoses (p<0.001). Significant distinctions were also observed in the utilization of the second graft. In the multiple group, SVG was the preferred second graft, while the frequency of radial artery and SVG use was similar in the single group. Consequently, there was a significantly higher frequency of MAG in the single group compared to the multiple group (p<0.001). Within the single group, all CABGs were performed without aortic manipulation, in contrast to the multiple group, where the aorta was utilized as a supplementary inflow source in 95.5% (233/244) patients. Following IPTW-adjustment, most covariates were well-balanced, except for the proportion of patients with MAG (**Table 1**).

Clinical outcomes

Early postoperative outcomes are detailed in **Tables 2** and **3**. Thirty-day mortality was observed in eight patients (1.8%), with no notable disparity between the groups (p=0.417), and this pattern persisted after IPTW-adjustment. Over a median follow-up duration of 5.3 years, 143 patients experienced overall mortality, and 64 faced cardiovascular death. Non-fatal MI occurred in 9 patients, and 18 individuals required repeat revascularization (**Tables 2** and **3**).

Table 2. Early clinical outcomes

Early adverse outcomes	Crude			IPTW-adjusted		
	Single source (n=203)	Multiple source (n=244)	p value	Single source (n=202.5)	Multiple source (n=242.4)	p value
In-hospital mortality	4 (2.0)	7 (2.9)	0.761	2.7%	2.2%	0.759
30-day mortality	2 (1.0)	6 (2.5)	0.417	1.4%	1.9%	0.715
Re-exploration for bleeding	0 (0.0)	3 (1.2)	0.316	0%	1.3%	0.165
Postoperative ECMO	1 (0.5)	3 (1.2)	0.749	0.4%	1.2%	0.333
New-onset dialysis	5 (2.5)	9 (3.7)	0.640	4.7%	4.5%	0.945
Stroke*	0 (0.0)	5 (2.0)	0.110	0%	4.1%	0.102
Tracheostomy	4 (2.0)	6 (2.5)	0.979	1.4%	3.0%	0.284

Values are presented as number of patients (%) or percentage (%) of patients.
ECMO = extracorporeal membrane oxygenation; IPTW = inverse probability of treatment weighting.
*Stroke was defined as permanent disabling stroke (confirmed by experienced neurologist or radiologic modalities).

Table 3. Overall clinical outcomes

Overall outcomes	Total (n=447)	Single source (n=203)	Multiple source (n=244)	Crude			IPTW-adjusted		
				HR	95% CI	p value	HR	95% CI	p value
Overall death	143 (32.0)	75 (36.9)	68 (27.9)	1.12	0.81–1.56	0.493	1.88	1.26–2.80	0.001
Cardiovascular death	64 (14.3)	37 (18.2)	27 (11.1)	1.41	0.85–2.33	0.179	2.06	1.18–3.59	0.011
MACE[*]	154 (34.5)	81 (39.9)	73 (29.9)	1.17	0.85–1.61	0.333	1.66	1.12–2.46	0.012
Non-fatal myocardial infarction	9 (2.0)	6 (3.0)	3 (1.2)	1.81	0.44–7.39	0.409	0.72	0.15–3.53	0.684
Repeat revascularization	18 (4.0)	10 (4.9)	8 (3.3)	1.26	0.49–3.22	0.631	1.35	0.47–3.89	0.577

Values are presented as number (%).
CI = confidence interval; HR = hazard ratio; IPTW = inverse probability of treatment weighting; MACE = major adverse cardiovascular event.
[*]MACE was defined as the composite of overall death, non-fatal myocardial infarction, or repeat revascularization.

Table 4. Univariable and multivariable analyses for overall mortality (unweighted model without IPTW)

Variables	Univariable			Multivariable		
	HR	95% CI	p value	aHR	95% CI	p value
Age	1.05	1.03–1.07	<0.001	1.05	1.03–1.08	<0.001
Female	1.50	1.03–2.18	0.034			
Hypertension	1.41	0.95–2.09	0.088			
Diabetes	1.85	1.29–2.66	0.001	1.43	0.97–2.11	0.071
Stroke history	1.46	0.96–2.21	0.075			
Peripheral arterial occlusive disease	1.85	1.20–2.86	0.005	1.75	1.12–2.73	0.013
Previous PCI	2.13	1.15–3.94	0.016			
Chronic kidney disease	2.93	2.02–4.25	<0.001			
Creatinine	1.07	1.04–1.10	<0.001	1.04	1.00–1.07	0.058
End stage renal disease	3.21	2.08–4.94	<0.001	1.91	1.08–3.36	0.026
Hemoglobin	0.77	0.71–0.83	<0.001	0.86	0.78–0.95	0.003
Recent myocardial infarction <1 month	1.01	0.73–1.41	0.944			
NYHA III or IV	1.05	0.71–1.53	0.822			
Preoperative atrial fibrillation	3.02	1.40–6.49	0.005	4.21	1.93–9.17	<0.001
Left ventricular ejection fraction <25%	1.15	0.82–1.62	0.413			
Mitral regurgitation (>grade II)	1.40	0.98–2.02	0.068			
Surgeon factor (operator A vs. B)	0.83	0.59–1.16	0.272	0.80	0.57–1.13	0.210
Multi-arterial grafting	0.37	0.25–0.55	<0.001	0.61	0.39–0.95	0.027
Number of distal anastomoses	0.85	0.70–1.06	0.148	1.09	0.84–1.42	0.500
Distal anastomosis ≥4	0.79	0.56–1.12	0.193			
Complete revascularization	0.60	0.37–0.97	0.037	0.82	0.46–1.44	0.482
Single source	1.12	0.81–1.56	0.493	1.73	1.18–2.56	0.006

The model was constructed without applying ITPW.
aHR = adjusted hazard ratio; CI = confidence interval; HR = hazard ratio; IPTW = inverse-probability-of-treatment-weighting; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.

The Cox-proportional hazard models, as presented in **Table 4**, disclosed several demographic, laboratory, and operative variables significantly associated with overall survival. Notably, as surgical factors, single inflow source was found to be associated with worse survival (adjusted hazard ratio [aHR], 1.73; 95% confidence interval [CI], 1.18–2.56; p=0.006), whereas MAG was associated with improved survival (aHR, 0.61; 95% CI, 0.39–0.95; p=0.027).

Single source versus multiple source

Before adjustment, there were no differences in survival between the groups (p=0.493) (**Supplementary Figure 2**). However, after adjustment, the single group showed significantly worse survival compared to the multiple group (aHR, 1.88; 95% CI, 1.26–2.80; p=0.001) (**Figure 2A**). Similarly, the single group demonstrated a significantly higher risk of cardiovascular death (aHR, 2.06; 95% CI, 1.18–3.61; p=0.011) and MACE (aHR, 1.66; 95% CI, 1.12–2.46; p=0.012) (**Figure 2B**, **Supplementary Figure 3**).
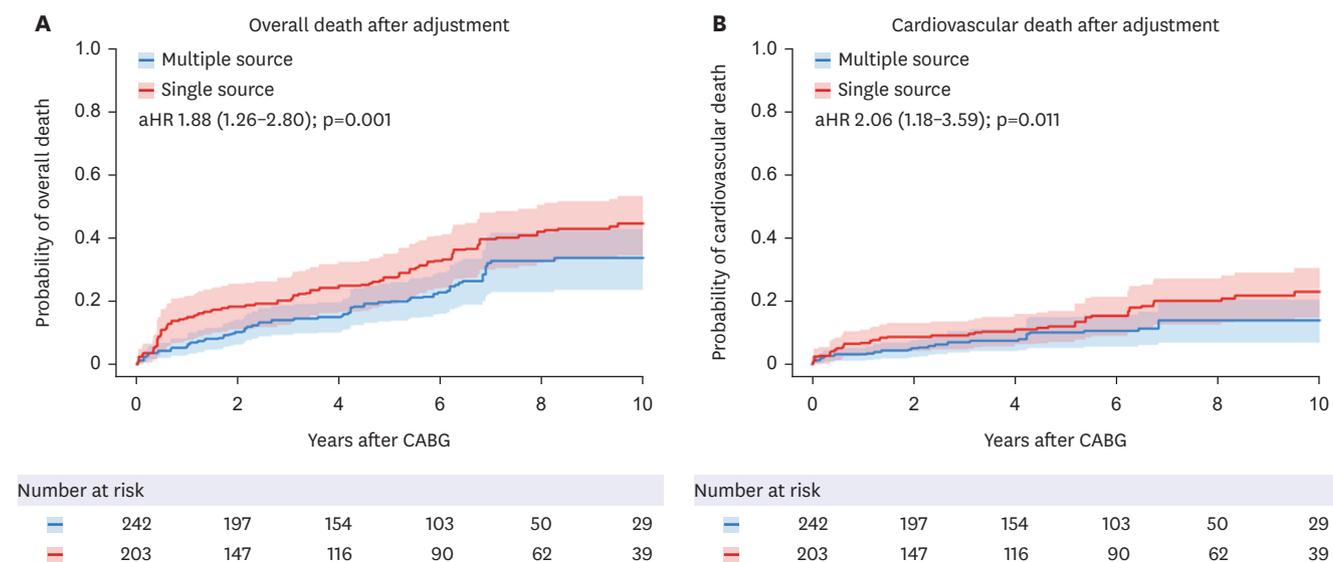
Figure 2. Survival Outcomes According to Inflow Source Number. Adjusted (A) overall death and (B) cardiovascular death according to the number of inflow sources after coronary artery bypass surgery. Kaplan-Meier survival curves depict the long-term outcomes of the single and multiple inflow groups, adjusted using the inverse-probability-of-treatment-weighting method.
aHR = adjusted hazard ratio; CABG = coronary artery bypass grafting.

Subgroup analysis revealed that the increased survival benefit of multiple inflow sources was consistent across most subgroups (**Figure 3**). Significant interaction was observed for recent MI within 1 month (p for interaction=0.042) and LVEF (p for interaction=0.036).

Survival benefits with multiple inflow sources were exclusively observed in the subgroups of patients without recent MI (aHR, 2.15; 95% CI, 1.26–3.67; p=0.005) and patients with LVEF of ≥25% (aHR, 1.94; 95% CI, 1.20–3.16; p=0.007). Among the original unweighted study population, 296 patients (66.2%) had an LVEF ≥25%, and 230 patients (51.4%) did not experience a MI within 1 month prior to surgery.

Echocardiographic results at last follow-up (>6 months)
Echocardiographic data since 6 months from the index surgery were available for 302 out of the 447 patients (67.6%). The median echocardiographic follow-up duration was 43.8 months (interquartile range, 25.3–71.4 months). Overall, echocardiographic functional parameters significantly improved at the last follow-up examination compared to the preoperative values (**Figure 4**).

After IPTW-adjustment, there were no significant differences in baseline echocardiographic parameters, including the mean echocardiographic follow-up duration (single group, 50.2±36.0 months; multiple group, 52.7±40.7 months; p=0.687). However, at the last follow-up examination, the multiple group showed significantly higher LVEF (p=0.009) and smaller LVESD (p=0.027) compared to the single group (**Figure 4**).

Sensitivity analysis
In a separate additional IPTW-adjusted cohort where MAG was included in the propensity score calculation (**Supplementary Table 1**), covariate balance between groups was achieved. Consistent with the main analysis, the single group demonstrated significantly worse survival compared to the multiple group (aHR, 1.60; 95% CI, 1.06–2.43; p=0.026) (**Figure 5**).
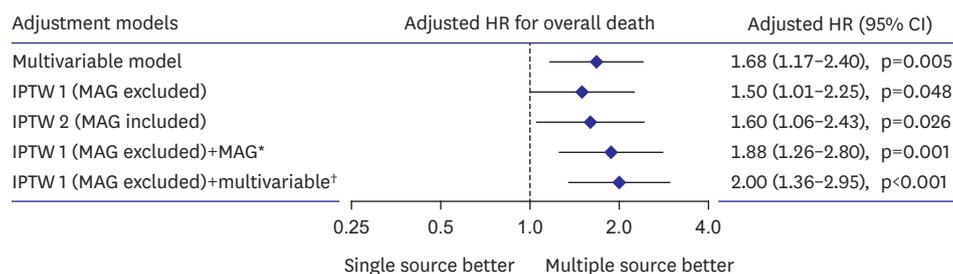
Number of patients		Adjusted HR for overall death	p value for interaction
Age			
<65 years	203		0.749
≥65 years	244		
Sex			
Male	357		0.461
Female	90		
Diabetes			
No	181		0.852
Yes	266		
ESRD			
No	403		0.221
Yes	44		
Multi-arterial grafting			
No	281		0.303
Yes	166		
Recent MI <1 month			
No	230		0.042
Yes	217		
LV ejection fraction			
<25%	151		0.036
≥25%	296		

0.1   1   10

Single source better   Multiple source better

Figure 3. Adjusted risks for overall mortality according to various subgroups. HRs with 95% confidence intervals are presented for different patient subgroups, comparing the single and multiple inflow groups.
ESRD = end-stage renal disease; HR = hazard ratio; LV = left ventricular; MI = myocardial infarction.

Figure 4. Echocardiographic results before and after coronary bypass. Changes in (A) LV ejection fraction, (B) LV end-systolic dimension, and (C) LV end-diastolic dimension are shown for the single and multiple inflow groups. Measurements were taken preoperatively and at the last follow-up (>6 months). Statistical significance is indicated for between-group comparisons.
LV = left ventricular.
[*]p<0.001, [†]p<0.001.

Adjustment models	Adjusted HR for overall death	Adjusted HR (95% CI)
Multivariable model		1.68 (1.17–2.40), p=0.005
IPTW 1 (MAG excluded)		1.50 (1.01–2.25), p=0.048
IPTW 2 (MAG included)		1.60 (1.06–2.43), p=0.026
IPTW 1 (MAG excluded)+MAG*		1.88 (1.26–2.80), p=0.001
IPTW 1 (MAG excluded)+multivariable†		2.00 (1.36–2.95), p<0.001

0.25   0.5   1.0   2.0   4.0

Single source better   Multiple source better

Figure 5. Adjusted risks for overall mortality in various statistical methods. HR with 95% CIs are shown for different adjustment models, including multivariable analysis and IPTW methods, with and without additional covariate adjustments. The results consistently indicate a survival benefit associated with multiple inflow source coronary artery bypass grafting.
CI = confidence interval; HR = hazard ratio; IPTW = inverse-probability-of-treatment-weighting; MAG = multi-arterial grafting.
*Additionally adjusted with MAG after IPTW correction.
†Additionally adjusted with all variables that were found to be significant in the multivariable model after IPTW correction.

Furthermore, as part of a sensitivity analysis, surgical period (as separated by early [2009–2014] and late period [2015–2020]) were also incorporated into the propensity score model to account for potential temporal bias related to advancements in surgical techniques or perioperative care over the study period. Even after this adjustment, the multiple group remained associated with significantly improved survival (aHR, 2.02; 95% CI, 1.14–3.58; p=0.015), reinforcing the robustness of our primary findings. The baseline characteristics after weighting with this extended model are presented in **Supplementary Table 2**.
As an additional sensitivity analysis, survival analysis using a propensity score–matched cohort (n=278; 139 pairs) demonstrated consistent results. The single group remained associated with significantly worse survival than the multiple group (aHR, 1.94; 95% CI, 1.26–3.00; p=0.002). Matched baseline characteristics and survival curves are provided in **Supplementary Table 3** and **Supplementary Figure 4**, respectively.

DISCUSSION

In this focused analysis for ICMP patients receiving coronary bypass surgery, the long-term outcomes were compared according to 2 different grafting strategies: single vs. multiple inflow sources in CABG. In the single group, unilateral in situ ITA was solely used as a singular source for inflow, while additional aortic grafts or contralateral ITA were used as a second inflow source in the multiple group. Before statistical adjustment, these 2 groups showed comparable long-term survival. However, after adjustment, the single group was found to have significantly worse long-term survival compared to the multiple group. The single group consistently showed worse outcomes compared to the multiple group regarding cardiovascular death, MACE, and echocardiographic functional outcomes.

Interestingly, the survival benefit associated with multiple inflow sources was not observed in patients with LVEF <25%, suggesting that the impact of grafting strategy may be attenuated in those with end-stage ventricular dysfunction. In this subgroup, the severely impaired myocardial reserve and limited extent of viable myocardium may reduce the potential for functional recovery, even after technically successful revascularization.[12][13] As a result, surgical revascularization alone may offer limited survival advantage in such patients. Preoperative viability assessment using myocardial perfusion imaging (e.g., MIBI scan)

or cardiac magnetic resonance imaging should therefore be considered essential to guide therapeutic decisions.[14] In cases where myocardial viability is minimal or absent, alternative treatment strategies such as durable LVAD implantation or heart transplantation may be more appropriate.[13] Similarly, in patients with recent myocardial injury, the clinical impact of the grafting strategy appears to be limited, likely because they have undergone less myocardial remodeling.

As well known, coronary artery disease is the most common cause of heart failure, and the proportion of ICMP patients being treated with CABG is continuously increasing.[1)3)5)] Surgical revascularization remains the sole proven treatment modality that surpasses optimal medical therapy for ICMP patients, whereas percutaneous revascularization has consistently failed to show its clinical benefit over conservative management.[5-7)15)] Therefore, the role of CABG in patients with ICMP will further expand in the upcoming aging society.[4)8)] However, there have been only limited number of studies focusing on CABG performed in patients with ICMP or severe LV dysfunction, in which pump strategy (on-pump vs. off-pump) was the primary focus rather than seeking the optimal grafting strategy.[16-18)] Instead, the issue of grafting strategy for ICMP patients has been indirectly addressed in few studies, where the primary focus was on comparing the long-term outcomes of multiple vs. single arterial CABG.[19-22)] Despite subgroup analyses conducted across the EF spectrum, it's crucial to note that the proportion of patients with low EF is very limited in these studies. To the best of our knowledge, this study represents the first direct investigation into the optimal grafting strategy for CABG specifically focusing on patients with ICMP.

The composite-Y graft configuration has been a time-honored faithful grafting strategy, when right ITA or radial artery used as a second graft. Despite multiple concerns regarding the composite-Y configuration, including potential insufficiency in flow capacity for the entire coronary system, it has demonstrated comparable graft patency and clinical outcomes when contrasted with the bilateral in situ configuration.[23)24)] Furthermore, the composite grafting strategy may offer an additional advantage as an an-aortic surgery, in terms of stroke. Despite the established merits of the composite grafting strategy, such advantages have not been consistently observed in patients with ICMP in the present study. The singular origin of flow may not have provided sufficient capacity for the enlarged and hypertrophied myocardium of ICMP.

The procedure involving the connection of a vein graft to the aorta, frequently employed in the multiple group, is not also exempt from potential concerns and limitations. Nonetheless, the use of the Heartstring device has been instrumental in minimizing the risk of potential stroke,[25)] and issues related to vein graft patency could be addressed through the application of no-touch harvesting technique, sequential grafting technique and postoperative adherence to strict antiplatelet medication regimens.[26)27)] For ICMP patients, performing sequential grafting on multiple target vessels often yields flowmeter readings exceeding 100 mL/min, and values approaching 200 mL/min are readily attainable at proximal portions. These excellent flow dynamics not only secure graft patency but also have the potential to offer sufficient flow to the enlarged and hypertrophied myocardium of ICMP.

In the final multivariable model, only 2 surgical factors, namely, the use of MAG and the number of inflow sources, were identified as significant determinants for survival. Notably, other potentially relevant surgical components, including achieving complete revascularization or the number of distal anastomoses, did not emerge as significant

determinants for long-term survival. The lack of statistical significance for complete revascularization should be interpreted with caution. In our cohort, the rate of incomplete revascularization was very low in both groups (10.8% in the single group and 4.5% in the multiple group), making it difficult to evaluate its independent impact on outcomes. Moreover, in most incompletely revascularized patients, the un-grafted vessels were likely small, diffusely diseased, or anatomically un-graftable, and therefore clinically less impactful. These factors may have attenuated the prognostic relevance of incomplete revascularization in this specific cohort.

Moreover, over the 12-year study duration, the majority of isolated CABG surgeries were consistently performed by 2 experienced and dedicated OPCAB surgeons, ensuring a high degree of data homogeneity. The low rate of incomplete revascularization and on-pump conversion may indirectly reflect the surgical expertise and proficiency of the operating surgeons. While such homogeneity of CABG procedures in this study may not be ideal for assessing the clinical impact of revascularization completeness on long-term survival following surgery, we posit that this consistent condition may provide a solid ground for a comparative analysis of two distinct grafting strategies, such as single versus multiple inflow sources.

The retrospective design of this study involves inherent limitations, such as potential selection bias and the inability to establish causal relationships. Although efforts were made to address confounding factors through propensity score weighting, residual confounding cannot be entirely ruled out and the study may still be susceptible to unmeasured confounders that could influence the observed outcomes. Factors not included in the analysis may have contributed to the reported associations. The study draws data exclusively from in a single tertiary center. The homogeneity of the patient population and procedural techniques may limit the generalizability of findings to diverse healthcare settings with varying patient demographics and surgical practices.

Another limitation of this study is the absence of quantitative data on the severity of coronary stenosis in individual target vessels, including the right coronary artery. While anatomical factors such as lesion severity may influence conduit selection—particularly in cases of moderate stenosis where competitive flow may be a concern—the clinical relevance of this issue is likely limited in our study population. The vast majority of patients in this ICMP cohort had diffuse multi-vessel disease and advanced coronary remodeling (e.g., arterial shrinkage, arteriosclerosis, heavy calcification, or chronic total occlusion), in which competitive flow is less likely to alter surgical planning. Moreover, conduit selection in such patients is guided by multiple intraoperative and anatomical considerations, and not by target vessel stenosis alone. Nevertheless, the lack of structured angiographic data precluded formal adjustment for this factor in our analysis.

In addition, this study could not incorporate direct assessment of graft patency using coronary CT angiography or conventional coronary angiography. Although postoperative echocardiographic improvement may indirectly reflect effective revascularization, it cannot fully substitute for direct patency data.

In CABG performed in patients with ICMP, the employment of multiple inflow sources was associated with improved clinical outcomes compared to CABG using a singular inflow source. This association was particularly significant in patients without recent MI within 1 month and in those with LVEF of ≥25%.

ACKNOWLEDGMENTS

SUPPLEMENTARY MATERIALS

Supplementary Table 1
Baseline and operative characteristics of patients after inverse probability weighting, multi-arterial grafting included

Supplementary Table 2
Baseline and operative characteristics of patients after inverse probability weighting, surgical period included

Supplementary Table 3
Baseline and operative characteristics of patients after propensity-score matching

Supplementary Figure 1
Distribution of propensity scores. (A) Before IPTW-adjustment and (B) after IPTW-adjustment.

Supplementary Figure 2
Unadjusted overall death according to the number of inflow source after coronary artery bypass surgery.

Supplementary Figure 3
Probability of major adverse cardiovascular event after coronary artery bypass surgery.

Supplementary Figure 4
Adjusted survival after propensity-score matching.

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