Impact of complete revascularization in coronary artery bypass grafting for ischemic cardiomyopathy

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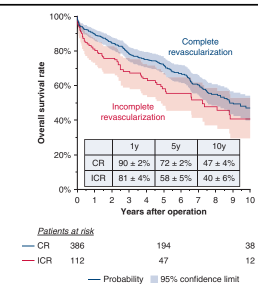
ABSTRACT

Objective: In patients with ischemic cardiomyopathy, coronary artery bypass grafting ensures better survival than medical therapy. However, the long-term clinical impact of complete revascularization remains unclear. This observational study aimed to evaluate the effects of complete revascularization on long-term survival and left ventricular functional recovery in patients with ischemic cardiomyopathy undergoing coronary artery bypass grafting.

Methods: We retrospectively reviewed outcomes of 498 patients with ischemic cardiomyopathy who underwent complete (n = 386) or incomplete (n = 112) myocardial revascularization between 1993 and 2015. The baseline characteristics were adjusted using inverse probability of treatment weighting to reduce the impact of treatment bias and potential confounding. The mean follow-up duration was 77.2 ± 42.8 months in survivors.

Results: The overall 5-year survival rate (complete revascularization, 72.5% vs incomplete revascularization, 57.9%, $P = .03$) and freedom from all-cause death and/or readmission due to heart failure (54.5% vs 40.1%, $P = .007$) were significantly greater in patients with complete revascularization than those with incomplete revascularization. After adjustments using inverse probability of treatment weighting, the complete revascularization group demonstrated a lower risk of all-cause death (hazard ratio, 0.61; 95% confidence interval, 0.43-0.86; $P = .005$) and composite adverse events (hazard ratio, 0.59; 95% confidence interval, 0.44-0.79; $P < .001$) and a greater improvement in the left ventricular ejection fraction 1-year postoperatively (absolute change: 11.0 ± 11.9% vs 8.3 ± 11.4%, interaction effect $P = .05$) than the incomplete revascularization group.

Conclusions: In patients with ischemic cardiomyopathy undergoing coronary artery bypass grafting, complete revascularization was associated with better long-term outcomes and greater left ventricular functional recovery and should be encouraged whenever possible. (JTCVS Open 2023;15:211-9)



	1y	5y	10y
CR	90 ± 2%	72 ± 2%	47 ± 4%
ICR	81 ± 4%	58 ± 5%	40 ± 6%

Complete revascularization was associated with greater survival rate after CABG for ICM.

CENTRAL MESSAGE

Complete revascularization might have a clinical impact on the overall survival and postoperative left ventricular functional recovery in patients with ischemic cardiomyopathy.

PERSPECTIVE

Complete revascularization might be desirable in patients with advanced ischemic cardiomyopathy undergoing coronary artery bypass grafting whenever possible. Complete revascularization was associated with improved long-term outcomes and affect postoperative left ventricular functional recovery.

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CI	= confidence interval
CR	= complete revascularization
HR	= hazard ratio
ICR	= incomplete revascularization
IPTW	= inverse probability of treatment weighting
IQR	= interquartile range
ITA	= internal thoracic artery
LAD	= left anterior descending artery
LCx	= left circumflex artery
LV	= left ventricular
SMD	= standardized mean difference

▶ Video clip is available online.

According to the current American College of Cardiology Foundation and the American Heart Association guidelines for coronary artery bypass grafting (CABG), CABG is recommended as the first choice of treatment for patients with ischemic cardiomyopathy.[1] This is supported by randomized controlled trials, which state that patients with advanced ischemic cardiomyopathy benefit more from CABG than from medical therapy in terms of reduced mortality and hospitalization due to heart failure.[2-4]

Complete revascularization (CR) is an important goal of CABG, indicating a survival benefit and lower frequency of repeat revascularization in patients with a wide range of difference in left ventricular (LV) systolic function who achieved CR.[5-8] However, whether CR leads to recovery of the LV function and subsequent survival benefit in patients with ischemic cardiomyopathy, in whom the myocardium is at least partially compromised due to scarring and/or the ischemic burden secondary to myocardial infarction, remains controversial. Furthermore, CR is not always possible in patients with ischemic cardiomyopathy due to complex coronary diseases and coexisting comorbidities. Presently, there is no consensus regarding the long-term clinical impact of CR in such patients. Therefore, our study aimed to elucidate the impact of CR on long-term survival and LV functional recovery in patients with ischemic cardiomyopathy undergoing coronary bypass grafting.

METHODS

The baseline characteristics and surgical data of patients were obtained from the surgical database of the Osaka Cardiovascular Surgery Research Group, which is a prospective database. A total of 504 patients with ischemic cardiomyopathy (defined as severely impaired LV systolic function with an ejection fraction of ≤40%) who underwent CABG between 1993 and 2015 were identified. Of these, those who underwent CABG followed by staged percutaneous coronary intervention (n = 6) were excluded. Finally, 498 patients were included in this study (Figure 1). The investigation conformed to the principles outlined in the Declaration of Helsinki. The final study protocol was approved by the Institutional Ethics Committee (Institutional review board of Osaka University Hospital, number 16105, approved November 2, 2016), and all participants provided written informed consent for publication of study data.

Definition of Complete Revascularization

Clinical lesions were defined as those that were >75% stenosed. Revascularization was considered complete when at least 1 bypass graft was placed for every diseased major coronary artery system, namely the left anterior descending artery (LAD), left circumflex artery (LCx), and right coronary artery regions.[9] Revascularization of left main trunk diseases was considered complete when grafts were placed for both the LAD and LCx. Patients were divided as follows: those in whom revascularization was complete (n = 386, CR group) and those in whom it was not (n = 112, incomplete revascularization [ICR] group).

Echocardiography

Two-dimensional and Doppler echocardiography were performed by expert echocardiographic examiners preoperatively (baseline), at 1 and 12 months postoperatively, and annually thereafter, to evaluate changes in LV function parameters, estimated systolic pulmonary artery pressure, and inferior vena cava diameter. The severity of mitral regurgitation was determined by the regurgitant volume and the ratio of color Doppler jet area to left atrial area in mid-systole and classified as none (0), trivial (1+), mild (2+), moderate (3+), or severe (4+).

Surgical Procedures

The off-pump revascularization technique was favored in high-risk patients and those with contraindications for cardiopulmonary bypass and aortic crossclamping (eg, extensive atherosclerotic disease of the ascending aorta). The on-pump technique was favored when manipulation of the heart was likely to induce hemodynamic instability. The in situ right or left internal thoracic artery (ITA) was used for bypass to the LAD when indicated. The use of bilateral ITAs was favored in younger patients when that was anatomically and clinically suitable. The decision to perform concomitant procedures, such as surgical ventricular restoration or mitral valve surgery, was generally based on the patient's clinical condition, coronary anatomy, extent of LV remodeling, and mitral regurgitation grade. However, the final decision was made at the discretion of the attending surgeon.

Clinical End Points and Follow-up

The clinical end points of this study were all-cause mortality during follow-up and adverse events of mortality and readmission due to exacerbation of heart failure. The diagnosis of postoperative recurrent heart failure was based on clinical symptoms, physical signs, or radiologic evidence of pulmonary congestion. Thirty patients could not be traced because of self-interruption of hospital visits. Those cases were censored at the date on which they were lost. Consequently, clinical follow-up examinations were completed in all patients with a mean follow-up period of 77.2 ± 42.8 months (interquartile range [IQR], 47.4-101.3 months) in survivors. The cumulative follow-up period was 2628 patient-years.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation or median with IQR, and categorical variables are expressed as numbers and frequencies (percentages). The comparison between the 2 groups was evaluated using the Mann–Whitney U test for continuous variables and the Fisher exact test or χ^2 test for categorical variables as appropriate.

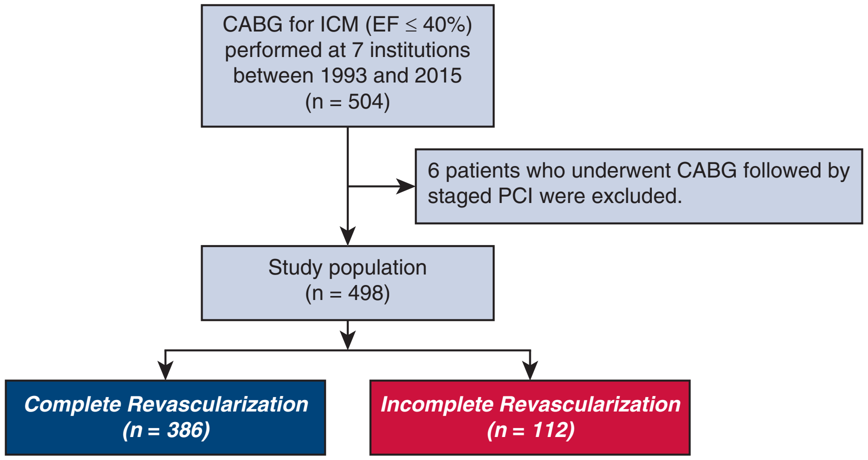

FIGURE 1. Patient selection flow diagram. *CABG*, Coronary artery bypass grafting; *ICM*, ischemic cardiomyopathy; *EF*, ejection fraction; *PCI*, percutaneous coronary intervention.

Longitudinal data of LV functional parameters were assessed using a mixed-effects model including factors for group, time, and interaction between group and time. The variance–covariance matrix of the observations in the linear mixed-effects models was assumed to be unstructured. The assessment time points were treated as categorical factors. Survival curves and freedom from composite events were constructed using the Kaplan–Meier method and were compared using the log-rank test. Hazard ratios (HRs) were reported with 95% confidence intervals (CIs). The interactions between the treatment group (CR and ICR) and each subgroup (with and without concomitant surgeries) were also investigated by the Wald test in the Cox proportional-hazards model.

To minimize the impact of potential confounding in this retrospective observational study, the adjustment for significant differences in patients' baseline and intraoperative characteristics was performed using weighted Cox proportional-hazards regression models with inverse probability of treatment weighting (IPTW).[10] In this technique, weights for patients receiving CR and ICR were the inverse of the propensity score and 1−propensity score, respectively. The probability of receiving CR (propensity score) for each patient was calculated using multivariate logistic regression analysis based on clinically relevant covariates that are listed in Table 1. To measure the covariate balance, we evaluated the standardized mean differences (SMDs) before and after IPTW. When the SMD was <0.25 (25%), we considered it to indicate a negligible imbalance between the 2 groups.[11] Statistical analyses were performed using JMP Pro 15.1.0 (SAS Institute Inc) and R version 3.5.3 (R Foundation for Statistical Computing).

RESULTS

Baseline Characteristics and Operation Data of Patients

Before adjustments, there were no intergroup differences in the patients' demographics European System for Cardiac Operative Risk Evaluation II (CR, 6.0 [IQR, 3.1-12.6]; ICR, 7.6 [IQR, 3.2-19.0], $P = .10$), LV functional parameters, and frequency of concomitant surgeries except for a greater prevalence of previous cardiac surgery in the ICR group.

Patients with CR tended to have a greater prevalence of left main coronary artery disease, whereas the prevalence of 3-vessel disease between the groups was not different. The number of target coronary vessels was 3.2 ± 1.1 and 3.3 ± 1.0 in the CR and ICR groups, respectively ($P = .25$), whereas the number of grafted vessels was 3.2 ± 1.1 and 2.2 ± 0.9 in the CR and ICR groups, respectively ($P < .001$). The bilateral ITAs were used more frequently in the CR group than in the ICR group.

In the ICR group, 119 diseased coronary artery systems were ungrafted. The right coronary artery (n = 57) and LCx (n = 53) were the most commonly ungrafted territories, followed by the LAD territory (n = 9). The main reason for ICR was the presence of infarcted territories (akinetic wall, thinned segment, or nonviable myocardium) (n = 47, 39%). Other reasons were a diffusely diseased and narrowed vessel that made it difficult to perform a bypass (n = 40, 34%), coronary artery inaccessible for grafting (eg, location in the atrioventricular groove, intramyocardial coronary artery) (n = 4, 3.4%), and the lack of usable grafts (n = 2, 1.7%). The reasons for ICR in the remaining 26 systems could not be identified.

After adjusting for the clinically relevant baseline and operative variables using IPTW, there were no intergroup differences, with the SMD for each of the variables being less than 0.25 (25%) (Table 1).

Short-Term and Long-Term Outcomes

The 30-day mortality in the CR and ICR groups was 3.4% and 5.4%, respectively ($P = .40$). During the follow-up period, there were 211 all-cause deaths and 128 readmissions for heart failure, and the overall 5-year and 10-year survival were 69.2% and 45.4%, respectively. The most common cause of death was heart failure (n = 57, 27%), followed by infection (n = 34, 16%), malignancy (n = 24, 11%), sudden death (n = 20, 9.5%), lethal arrhythmia (n = 16, 7.6%), stroke (n = 12, 5.7%), renal failure (n = 9, 4.3%), gastrointestinal complications (n = 5, 2.4%), acute myocardial infarction (n = 4, 1.9%), and others (n = 30, 14%).

TABLE 1. Patients' characteristics before and after adjustment using IPTW

	Original cohort				IPTW cohort			
Clinical variables	Complete revascularization (n = 386)	Incomplete revascularization (n = 112)	*P* value	SMD	Complete revascularization (n = 498)	Incomplete revascularization (n = 509)	*P* value	SMD
Preoperative variables								
Age, y	67.0 [60.0, 73.0]	69.0 [62.0, 75.0]	.10	.15	67.0 [60.8, 73.0]	67.8 [59.4, 73.0]	.70	.12
Male sex, n (%)	328 (85.0)	93 (83.0)	.73	.05	420 (84.3)	439 (86.2)	.63	.05
BSA, m^2	1.64 [1.54, 1.76]	1.62 [1.51, 1.74]	.23	.13	1.64 [1.53, 1.75]	1.66 [1.52, 1.80]	.55	.16
Preoperative IABP insertion, n (%)	41 (10.6)	18 (16.1)	.16	.16	59 (11.9)	55 (10.8)	.75	.03
Urgent or emergent operation, n (%)	59 (15.3)	22 (19.6)	.34	.12	80 (16.1)	76 (15.0)	.79	.03
Redo surgery, n (%)	12 (3.1)	11 (9.8)	.006	.28	25 (4.9)	24 (4.8)	.94	.008
Diabetes mellitus, n (%)	231 (59.8)	66 (58.9)	.95	.02	293 (58.9)	273 (53.7)	.42	.11
eGFR, mL/min/1.73 m^2	53.1 [34.7, 65.6]	48.2 [37.1, 61.1]	.33	.07	52.4 [34.2, 65.0]	54.0 [38.4, 61.4]	.65	.08
Previous PCI, n (%)	136 (35.2)	44 (39.3)	.50	.08	181 (36.3)	202 (39.7)	.60	.07
Previous MI, n (%)	315 (81.6)	93 (83.0)	.54	.04	409 (82.2)	430 (84.4)	.61	.06
Peripheral artery disease, n (%)	53 (13.7)	18 (16.1)	.64	.07	70 (14.1)	63 (12.3)	.63	.05
Previous stroke, n (%)	49 (12.7)	15 (13.4)	.97	.02	66 (13.2)	69 (13.5)	.93	.01
Three-vessel disease, n (%)	285 (73.8)	89 (79.5)	.28	.13	374 (75.0)	360 (70.8)	.52	.09
Left main disease, n (%)	66 (17.1)	8 (7.1)	.01	.31	74 (14.9)	87 (17.2)	.72	.06
LV ejection fraction, %	30.0 [25.0, 35.0]	30.0 [22.7, 36.0]	.38	.13	30.0 [25.0, 35.0]	32.0 [24.7, 38.0]	.22	.13
LV end-systolic diameter, mm	52.0 [47.0, 57.8]	52.0 [46.8, 56.3]	.63	.04	52.0 [47.0, 57.0]	52.0 [46.0, 57.0]	.86	.02
Operative variables								
Bilateral ITA grafting, n (%)	112 (29.0)	26 (23.2)	.28	.13	139 (27.8)	166 (32.6)	.45	.11
In situ ITA grafting, n (%)	327 (84.7)	83 (74.1)	.01	.27	411 (82.5)	421 (82.7)	.96	.005
Total arterial grafting, n (%)	106 (27.5)	44 (39.3)	.012	.25	151 (30.3)	189 (37.1)	.28	.15
Composite graft use, n (%)	70 (18.1)	20 (17.9)	>.99	.08	90 (18.0)	91 (17.9)	>.99	<.001
Concomitant MV procedure, n (%)	174 (45.1)	48 (42.9)	.75	.05	223 (44.8)	230 (45.2)	.95	.009
Concomitant SVR, n (%)	103 (26.7)	36 (32.1)	.28	.12	141 (28.3)	148 (29.1)	.87	.02

The frequencies after adjustment were rounded off after the decimal point. *IPTW*, Inverse probability of treatment weighting; *SMD*, standardized mean difference; *BSA*, body surface area; *IABP*, intra-aortic balloon pumping; *eGFR*, estimated glomerular filtration rate; *PCI*, percutaneous coronary intervention; *MI*, myocardial infarction; *LV*, left ventricle; *ITA*, internal thoracic artery; *MV*, mitral valve; *SVR*, surgical ventricular restoration.

In unadjusted comparisons, the CR group had significantly greater 5-year (72.5% vs 57.9%, respectively) survival rates than the ICR group ($P = .03$) (Figure 2, *A*). Likewise, freedom from composite adverse events was greater in the CR than in the ICR group (5-year survival, 54.5% vs 40.1%; $P = .007$) (Figure 2, *B*). After adjustments using IPTW, the CR group demonstrated a lower risk of all-cause death (HR, 0.61; 95% CI, 0.43-0.86; $P = .005$) and composite adverse events (HR, 0.59; 95% CI, 0.44-0.79; $P < .001$) than the ICR group. The adjusted outcomes of all-cause death and composite adverse events are summarized in Table 2 and this shows that the results were consistently in favor of the CR group in terms of long-term outcomes, before and after IPTW.

Moreover, considering the impact of the difference of the definition of CR, we analyzed the same cohort using a stricter definition of CR that stated that all diseased vessels be grafted, but the superiority of CR in terms of overall survival (HR, 0.70; 95% CI, 0.53-0.91; $P = .009$) and freedom from composite adverse events (HR, 0.70; 95% CI, 0.55-0.89; $P = .003$) remained.

In a subgroup analysis, an increased risk of mortality in patients with ICR was consistently observed regardless of whether concomitant surgeries were performed, with the *P* value for interaction based on a Wald test >.05 (Figure E1).

Longitudinal Changes in LV Function Parameters and Pulmonary Artery Pressure

Longitudinal echocardiographic assessment demonstrated significant changes 1-year postoperatively (Figure 3). Longitudinal echocardiographic assessment demonstrated significant improvements in LV ejection fraction (preoperative 29.4% → post-1-year 38.7%), LV end-systolic dimension (52.3 → 45.7 mm), systolic pulmonary arterial pressure (41.7 → 34.6 mm Hg), and inferior vena cava diameter 1 year (13.5 → 12.4 mm) postoperatively. Notably, the degree of improvement in the LV ejection fraction was greater in the CR than in the ICR group (CR 29.9 → 40.6% vs ICR 28.9 → 36.8%; *P* for interaction = .048).

DISCUSSION

The major findings of this study can be summarized as follows: (1) in patients with ischemic cardiomyopathy, surgery could be performed with an acceptable 30-day mortality, irrespective of the completeness of revascularization; (2) the overall survival rate and freedom from composite

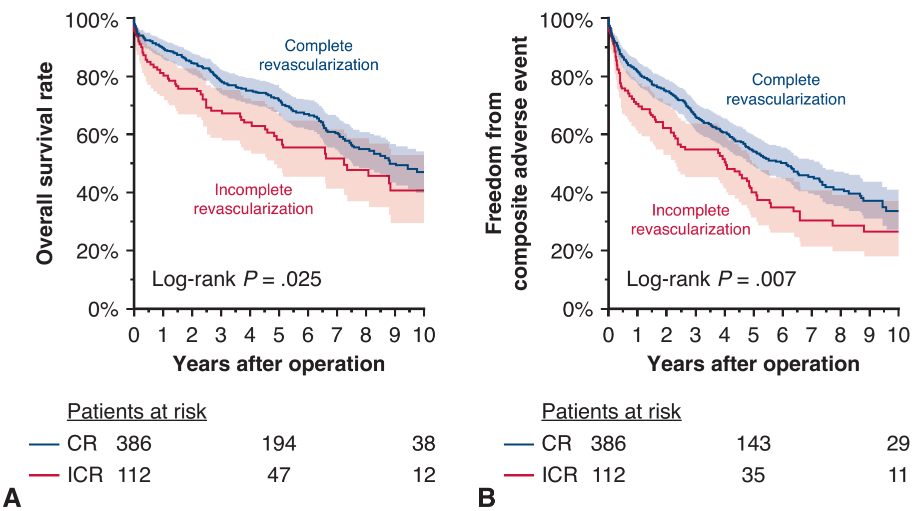

FIGURE 2. Kaplan–Meier curves for (A) overall survival rate and (B) freedom from composite events in the complete revascularization (*CR*) group and incomplete revascularization (*ICR*) group. *Shaded areas* represent 95% confidence limits.

adverse events were significantly superior in patients with CR than in those with ICR; (3) LV function parameters improved significantly irrespective of the completeness of revascularization; however, the degree of improvement in the LV ejection fraction was greater in the CR than in the ICR group; and (4) CR was identified as an independent protective factor for both mortality and composite adverse events, which was further confirmed after adjustments using the IPTW method (Video Abstract).

CR is associated with favorable outcomes following CABG, and it is recommended for surgeons to aim for CR whenever possible.[9,12] However, most patients enrolled in these studies had preserved LV systolic function; therefore, the aforementioned findings cannot be applied to patients with severely impaired LV function with severe coronary disease and greater myocardial damage because of the ischemic insult. It is controversial whether CR is associated with better long-term outcomes following CABG in such patients. In a single-center observational study with 111 patients, Lee and colleagues[13] compared outcomes of CR versus ICR (mean age (years): CR, 62.0 ± 9.3; ICR, 65.5 ± 10.4) with an LV ejection fraction ≤35% (mean: CR, 28.2% ± 4.5%; ICR, 27.9% ± 5.0%) and found better survival in patients with CR after a median follow-up period of 10.1 years (10-year survival, 62.1% vs 34.1%, $P = .02$) in the unadjusted analysis; however, the benefit was obliterated after adjusting the baseline demographics. They defined CR as the revascularization of all diseased vessels with a diameter of greater than 1.5 mm, and the main cause of ICR was the presence of diffusely diseased vessels. However, Kusunose and colleagues[14] retrospectively investigated the outcomes of 117 patients (mean age, 64.8 ± 10.4 years) with an LV ejection fraction ≤40% (mean, 23.0% ± 8.5%) who underwent CABG and concomitant mitral valve surgery and demonstrated that ICR significantly worsened overall survival (HR, 3.04; $P = .001$) during a median follow-up of 62 months. They defined CR as grafting for all diseased vessels perfusing the viable myocardium. These conflicting results regarding the clinical impact of CR might have been caused by differences in the definition of CR (ie, anatomical vs functional criteria), degree of LV dysfunction, number of cohorts enrolled, concomitant procedures (eg, mitral valve surgery), and the length of the follow-up period. Our data

TABLE 2. Unadjusted and adjusted HRs of all-cause death and composite events of the complete revascularization group compared with those of the incomplete revascularization group

Outcomes	HR (95% CI)	*P* value
All-cause death		
Crude (original cohort)	0.71 (0.52-0.96)	.03
IPTW	0.61 (0.44-0.86)	.004
All-cause death and/or readmission due to heart failure		
Crude (original cohort)	0.70 (0.54-0.91)	.007
IPTW	0.59 (0.44-0.79)	<.001

HR, Hazard ratio; *CI*, confidence interval; *IPTW*, inverse probability of treatment weighting.

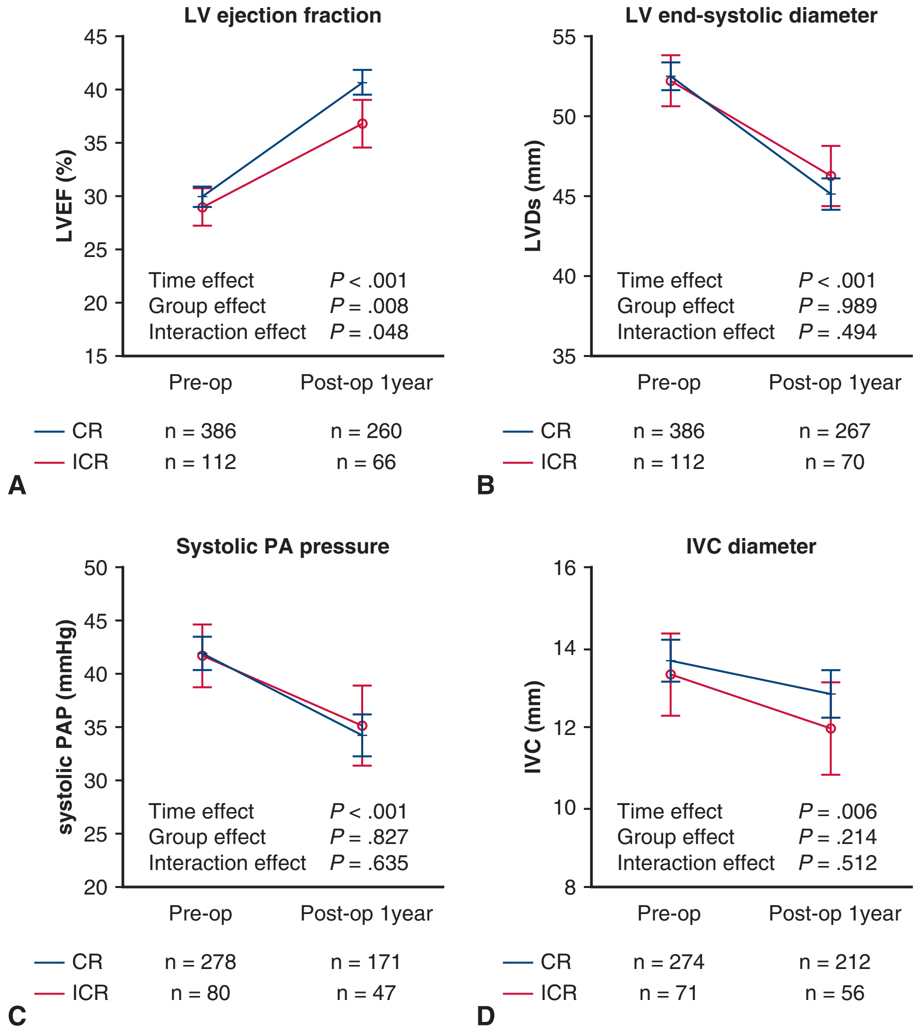

FIGURE 3. Longitudinal changes in (A) LVEF, (B) LV end-systolic diameter, (C) systolic PA pressure, and (D) IVC diameter in the CR and ICR groups. *LV*, Left ventricular; *CR*, complete revascularization; *ICR*, incomplete revascularization; *LVEF*, left ventricular ejection fraction; *Pre-op*, preoperative; *Post-op*, postoperative; *LVDs*, left ventricular end-systolic diameter; *PA*, pulmonary artery, *IVC*, inferior vena cava; *PAP*, pulmonary arterial pressure.

were partially consistent with those of the former study regarding the definition and positive impact of CR in the unadjusted analysis. Furthermore, the positive clinical impact of CR remained even after the adjustment of baseline characteristics in our study, and this was consistent with the findings of a latter study.

To date, recovery of the LV function following CABG has not been thoroughly evaluated according to CR or ICR, particularly in patients with ischemic cardiomyopathy, although postoperative LV reverse remodeling could affect prognosis in the specific cohort of patients. One of the novel findings of this study was that CR had a positive impact on the postoperative LV systolic function, as observed via longitudinal echocardiographic assessments. This can be attributed to the improvement in the coronary perfusion of the hibernating myocardium that lies along the infarcted territories. Revascularization of the hibernating myocardium has been reported to improve long-term outcomes,[15] and this might support our findings. These observations allow us to speculate that the superior outcomes observed in the CR group can be explained by the greater degree of improvement in the LV ejection fraction found in the CR than in the ICR group. These findings suggest that CR should be encouraged whenever possible in patients with advanced ischemic cardiomyopathy to improve long-term outcomes.

The main limitation of our study was its nonrandomized, retrospective nature. Due to the differences in baseline demographics between the patients in the CR group and those in the ICR group, a randomized control study was desirable. However, the conventional concept of treating stenotic lesions to the maximum makes planning a randomized study difficult. To minimize the potential bias related to patient selection, we excluded patients with a

TABLE 3. Predictors of all-cause death using the Cox proportional-hazards model

Clinical variables	Univariate		Multivariate	
	P value	HR (95% CI)	*P* value	HR (95% CI)
Age (per 10 y)	<.001	1.71 (1.46-2.02)	<.001	1.69 (1.42-2.01)
Male sex	.04	0.59 (0.49-0.98)	.51	
Preoperative IABP insertion	.005	1.71 (1.17-2.50)	.06	
Diabetes mellitus	.10			
On hemodialysis	<.001	3.19 (2.17-4.70)	<.001	3.35 (2.21-5.08)
Peripheral artery disease	.001	1.74 (1.25-2.42)	.03	1.47 (1.05-2.07)
Previous stroke	.04	1.49 (1.03-2.16)	.07	
Atrial fibrillation	.64			
Three-vessel disease	.56			
Previous MI	.71			
Previous PCI	.72			
Redo surgery	.009	2.01 (1.19-3.41)	.27	
Preoperative LV end-systolic diameter	.88			
Preoperative LV ejection fraction	.58			
Complete revascularization	.03	0.71 (0.52-0.96)	.02	0.69 (0.51-0.95)
Bilateral ITA grafting	<.001	0.53 (0.38-0.74)	.007	0.62 (0.44-0.88)
Concomitant MV procedure	.005	1.49 (1.13-1.96)	.43	
Concomitant SVR	.30			

HR, Hazard ratio; *CI*, confidence interval; *IABP*, intra-aortic balloon pumping; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *LV*, left ventricle; *ITA*, internal thoracic artery; *MV*, mitral valve; *SVR*, surgical ventricular restoration.

low degree of LV remodeling and restricted our analysis to those with advanced cardiomyopathy with an LV ejection fraction ≤40%. Although we adjusted the selection bias using IPTW, unrecognized confounding factors, such as myocardial viability, coronary anatomy, and surgical risks as well as the choices surgeons had to make at their own discretion may have influenced our results. Second, the myocardial viability assessment (ie, perfusion scintigraphy, cardiac magnetic resonance imaging, et al.) and functional assessment of coronary stenosis (ie, myocardial blood flow, fractional flow reserve, et al) were not routinely performed. In our cohort, only 35% of patients underwent myocardial viability study. The lack of these data made it difficult to discuss potential impacts of those factors on outcomes and clarify the mechanisms for the better prognosis in the CR group. Third, whether CR was performed or not would be decided based on particular conditions (the range of infarcted lesion, the property of target vessels and the harvested graft, the status of patients, etc). This selection bias could not be fully avoided and would limit the validity of the statistical analysis and results. Therefore, whether or not CR should be performed in patients with ischemic cardiomyopathy remained uncertain from the current findings. The observational nature just allowed us to determine whether CR was associated with improved outcomes, when CR was possible. Fourth, serial echocardiographic data of LV function after the second year could not be obtained. The data collection of much longer serial LV functional change might be more informative.

The definition of the CR varies according to previous studies and remains controversial.[16,17] Some would claim that patients with multiple lesions in 1 major coronary artery system in whom only 1 graft was placed to each major coronary artery and a diseased branch remained should have been placed in the ICR group. Although we analyzed the same cohort using a stricter definition of CR, which stated that all diseased vessels be grafted in order to address this issue, the superiority of CR in terms of overall survival and freedom from composite adverse events remained. Therefore, the differences in the definition of the CR did not alter the conclusion of our study.

Concomitant surgical procedures (ie, surgical ventricular reconstruction, restrictive mitral annuloplasty) might have also influenced the results, although such concomitant procedures are usually performed in patients with ischemic cardiomyopathy who present with severely deteriorated clinical and pathophysiological statuses. Furthermore, when the adjustment was further augmented by the concomitant surgery (Table 3), CR remained independently associated with better outcomes after CABG (HR, 0.66; 95% CI, 0.48-0.90; $P = .009$).

In conclusion, patients with ischemic cardiomyopathy in whom CR during CABG was achieved showed better survival rates and greater LV functional recovery than those with ICR. CR should be therefore encouraged whenever possible in those patients, but whether grafting the territory with nonviable myocardium improves outcomes remains to be fully elucidated. Importantly, a selection bias and a confounding-by-indication as to why the patients only underwent ICR inherent in this observational study limit the ability to determine whether or not CR should be performed in patients with ischemic cardiomyopathy. Therefore, further studies with more sophisticated design (randomization) including pre- and postoperative viability testing are warranted to validate our findings.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: ischemic cardiomyopathy, coronary artery bypass grafting, complete revascularization, long-term follow-up, left ventricular function

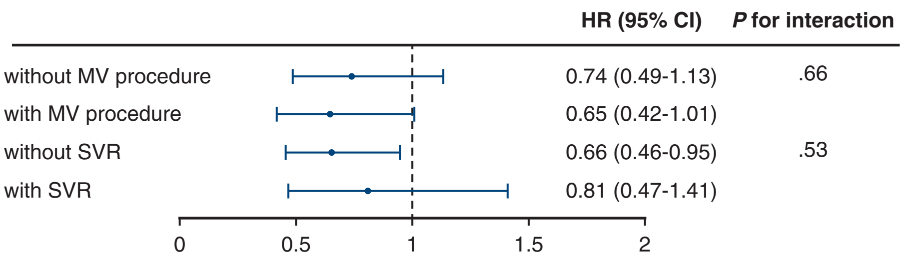

FIGURE E1. Subgroup analysis using Cox proportional hazard model for overall survival. *HR*, Hazard ratio; *CI*, confidence interval; *MV*, mitral valve; *SVR*, surgical ventricular restoration.