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ORIGINAL RESEARCH

Effect of Heart Failure on Long-Term Clinical Outcomes After Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Patients With Severe Coronary Artery Disease

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BACKGROUND: Heart failure might be an important determinant in choosing coronary revascularization modalities. There was no previous study evaluating the effect of heart failure on long-term clinical outcomes after percutaneous coronary intervention (PCI) relative to coronary artery bypass grafting (CABG).

METHODS AND RESULTS: Among 14 867 consecutive patients undergoing first coronary revascularization with PCI or isolated CABG between January 2011 and December 2013 in the CREDO-Kyoto PCI/CABG registry Cohort-3, we identified the current study population of 3380 patients with three-vessel or left main coronary artery disease, and compared clinical outcomes between PCI and CABG stratified by the subgroup based on the status of heart failure. There were 827 patients with heart failure (PCI: N=511, and CABG: N=316), and 2553 patients without heart failure (PCI: N=1619, and CABG: N=934). In patients with heart failure, the PCI group compared with the CABG group more often had advanced age, severe frailty, acute and severe heart failure, and elevated inflammatory markers. During a median 5.9 years of follow-up, there was a significant interaction between heart failure and the mortality risk of PCI relative to CABG (interaction P=0.009), with excess mortality risk of PCI relative to CABG in patients with heart failure (HR, 1.75; 95% CI, 1.28–2.42; P<0.001) and no excess mortality risk in patients without heart failure (HR, 1.04; 95% CI, 0.80–1.34; P=0.77).

CONCLUSIONS: There was a significant interaction between heart failure and the mortality risk of PCI relative to CABG with excess risk in patients with heart failure and neutral risk in patients without heart failure.

Key Words: coronary artery bypass grafting ■ coronary artery disease ■ heart failure ■ percutaneous coronary intervention

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CLINICAL PERSPECTIVE

What Is New?

- According to a Japanese observational all-comers registry database of patients who underwent first coronary revascularization for three-vessel or left main disease, the excess mortality risk of percutaneous coronary intervention (PCI) relative to coronary artery bypass grafting (CABG) was significant in patients with heart failure, whereas it was not significant in patients without heart failure, with significant interaction between heart failure and the mortality risk of PCI relative to CABG.
- There were substantial baseline differences between the PCI and CABG groups in patients with heart failure, while those were generally well balanced in patients without heart failure.

What Are the Clinical Implications?

- Considering the possible presence of selection bias for coronary revascularization modality in patients with heart failure, we should be cautious in interpreting the results from the observational studies suggesting the higher mortality risk of PCI relative to CABG in patients with heart failure.
- It was reassuring that the practice pattern in the present study was not associated with an excess long-term mortality risk of PCI relative to CABG in patients with severe coronary artery disease and without heart failure.

Nonstandard Abbreviations and Acronyms

3VD	three-vessel coronary artery disease
LMCAD	left main coronary artery disease
SYNTAX	Synergy between PCI with Taxus and Cardiac Surgery

Heart failure is a major public health burden worldwide in rapidly aging societies, and coronary artery disease (CAD) is one of the most common etiologies of heart failure. The STICHES (Surgical Treatment for Ischemic Heart Failure Extension Study) trial showed that coronary artery bypass grafting (CABG) compared with medical therapy only was superior in improving survival in patients with systolic dysfunction,[1] whereas there are currently no dedicated randomized controlled trials (RCTs) comparing percutaneous coronary intervention (PCI) versus medical therapy in patients with heart failure. The optimal revascularization strategy in CAD patients with heart failure is still controversial, because previous RCTs comparing PCI with CABG have excluded patients with heart failure, or included only a very small proportion of patients with heart failure.[2–7] In the observational studies, there is a report that PCI had comparable long-term survival outcomes to CABG in patients with multivessel disease and systolic dysfunction,[8] while other studies have suggested that CABG had significant survival benefit as compared with PCI in CAD patients with systolic dysfunction and/or heart failure.[9–11] At present, there was no previous study evaluating the effect of heart failure on long-term clinical outcomes after PCI relative to CABG. Therefore, we sought to evaluate the effect of heart failure on long-term clinical outcomes after PCI versus CABG in patients with severe CAD such as three-vessel coronary artery disease (3VD) or left main coronary artery disease (LMCAD) in a large observational database of patients undergoing first coronary revascularization in Japan.

METHODS

Study Design

The data that support the findings of this study are available from the corresponding author upon reasonable request. The CREDO-Kyoto (Coronary Revascularization Demonstrating Outcome Study in Kyoto) PCI/CABG registry Cohort-3 is a physician-initiated, noncompany-sponsored, multicenter registry enrolling consecutive patients who underwent first coronary revascularization with PCI or isolated CABG without combined noncoronary surgery among 22 Japanese centers between January 2011 and December 2013. Among 14 927 patients enrolled in the registry, we excluded those patients who refused study participation (N=60), acute myocardial infarction (N=5510), and one- or two-vessel disease (N=5977), and the current study population consisted of 3380 patients with severe CAD (3VD: N=2525, and LMCAD: N=855) (Figure 1). In this study, we compared long-term clinical outcomes between PCI and CABG stratified by the subgroup based on the status of heart failure. Heart failure was defined as having been diagnosed with heart failure at index hospitalization for coronary revascularization, and/or prior hospitalization for heart failure regardless of left ventricular ejection fraction. Heart failure at index hospitalization for coronary revascularization was defined as New York Heart Association (NYHA) class greater than or equal to II.

The relevant ethics committees in all the participating centers approved the study protocol. Because of the retrospective enrollment, written informed consents from the patients were waived; however, we excluded those patients who refused participation in the study when contacted for follow-up. This strategy

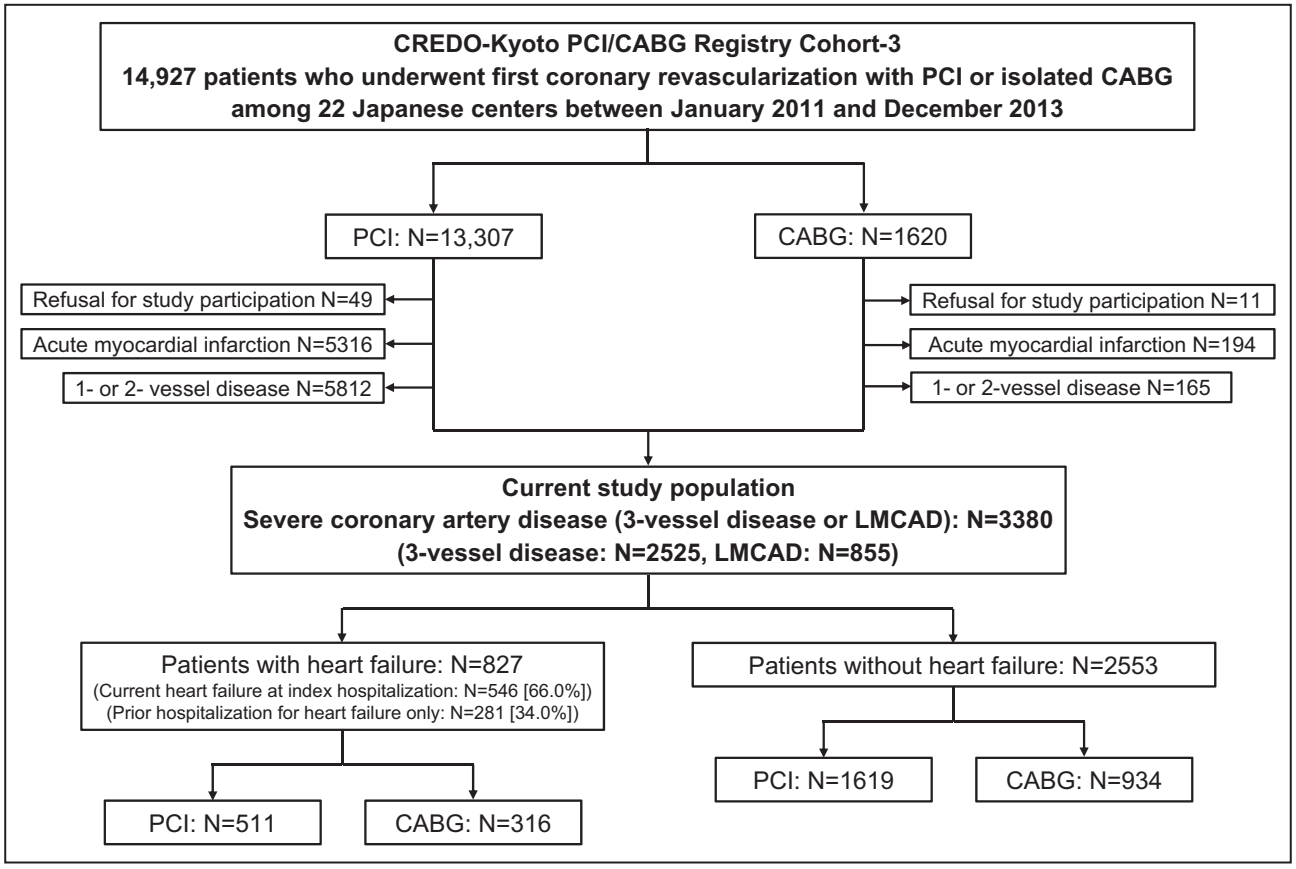


Figure 1. Study flowchart.
CABG indicates coronary artery bypass grafting; CREDO-Kyoto PCI/CABG Registry Cohort-3, Coronary Revascularization Demonstrating Outcome study in Kyoto PCI/CABG Registry Cohort-3; LMCAD, left main coronary artery disease; and PCI, percutaneous coronary intervention.

is concordant with the guidelines of the Japanese Ministry of Health, Labor and Welfare.

Outcome Measures

The primary outcome measure was all-cause death. The secondary outcome measures included cardiovascular death, noncardiovascular death, myocardial infarction, stroke, hospitalization for heart failure, major bleeding, and any coronary revascularization. Definitions of the outcome measures were described in Appendix S1.

Data Collection

Clinical, angiographic, and procedural data were collected from hospital charts or hospital databases according to the pre-specified definitions by the experienced clinical research coordinators belonging to an independent clinical research organization (Research Institute for Production Development, Kyoto, Japan). Follow-up data were collected from the hospital charts and/or obtained by contacting with patients, their relatives, or referring physicians. The clinical event committee adjudicated those events such as death, myocardial infarction, stroke, and major bleeding. Coronary anatomic complexity was evaluated according to the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score, which was evaluated by the experienced cardiologists (Appendix S1).

Statistical Analysis

Categorical variables were presented as number and percentage, and compared with the chi-square test. Continuous variables were expressed as mean±standard deviation or median and interquartile range (IQR). Continuous variables were compared with the Student *t* test or Wilcoxon rank sum test based on their distributions. Cumulative incidence of the outcome measures was estimated by the Kaplan-Meier method, and the differences were assessed with the log-rank test. The effects of PCI relative to CABG for the outcome measures were estimated by the Cox proportional hazard models, and were expressed as hazard ratios (HRs) and their 95% CIs. The adjusted

HRs were estimated by the multivariable Cox proportional hazard models adjusting for the 26 clinically relevant factors listed in Table. To avoid overfitting for the outcome measures with <100 patients with event, we constructed the parsimonious models with 7 risk-adjusting variables (age ≥75 years, men, diabetes mellitus, prior myocardial infarction, prior stroke, estimated glomerular filtration rate <30 mL/min per 1.73 m^2 or hemodialysis, and severe frailty). In patients with heart failure, the primary outcome measure was compared between PCI and CABG in the subgroups stratified by heart failure presentation (current heart failure at index hospitalization or prior hospitalization for heart failure only), NYHA classification, and left ventricular ejection fraction. In this analysis, the multivariable analysis was performed with the parsimonious model described above. As a sensitivity analysis, we performed the main analysis after excluding patients with surgical ineligibility. Moreover, as a sensitivity analysis, we performed the adjusted analysis including SYNTAX score as a continuous explanatory variable in the model in 3129 (92.6%) patients whom the SYNTAX score was available. Statistical analyses were performed with JMP 14.0 software (SAS Institute, Inc., Cary, NC). All statistical analyses were 2-tailed, and *P* values of <0.05 were considered statistically significant.

RESULTS

Study Population

In this study population of 3380 patients with severe CAD, there were 827 patients with heart failure (PCI: N=511, and CABG: N=316), and 2553 patients without heart failure (PCI: N=1619, and CABG: N=934) (Figure 1). The proportion of PCI/CABG was similar in patients with and without heart failure. Among 827 patients with heart failure, there were 546 patients with current heart failure at index hospitalization (PCI: N=399, and CABG: N=147), and 281 patients with prior hospitalization for heart failure only (PCI: N=112, and CABG: N=169). PCI was more often chosen in patients with current heart failure at index hospitalization, particularly in patients with severe current heart failure at index hospitalization (NYHA class III or IV) (Table S1).

Baseline Characteristics

Patients with heart failure were older, and more often women, and more often had comorbidities, frailty, surgical ineligibility, and complex coronary anatomy than in those without heart failure (Table S2).

In patients both with and without heart failure, the PCI group were older, and more often women than the CABG group. In patients with heart failure, the PCI group more often had current heart failure at index hospitalization and severe heart failure than the CABG group. The PCI group had higher inflammatory markers, and higher prevalence of frailty than the CABG group in patients with heart failure, but not in patients without heart failure. Interval from hospitalization to index procedure was significantly longer in the PCI group than in the CABG group in patients with heart failure, while it was significantly longer in the CABG group than in the PCI group in patients without heart failure. Regarding angiographic and procedural characteristics, the CABG group compared with the PCI group had greater number of target lesions or anastomoses, and higher coronary anatomic complexity regardless of heart failure (Table).

Baseline characteristics in patients with 3VD and LMCAD were consistent with those in the entire study population (Tables S3 and S4).

Regarding the baseline characteristics stratified by the current heart failure at index hospitalization or prior hospitalization only, the PCI group had higher inflammatory markers, and higher prevalence of advanced age, mitral regurgitation, prior myocardial infarction, and frailty than the CABG group in patients with current heart failure at index hospitalization, but not in patients with prior hospitalization for heart failure only. Interval from hospitalization to index procedure was significantly longer in the PCI group than in the CABG group in patients with current heart failure at index hospitalization, while it was significantly longer in the CABG group than in the PCI group in patients with prior hospitalization for heart failure only (Table S5).

Long-Term Follow-Up

Median follow-up for survivors was 5.9 (IQR: 5.1–6.8) years: (with heart failure: 5.8 [IQR: 4.8–6.6], and without heart failure: 5.9 [IQR: 5.1–6.8]). Complete 1-, 3-, and 5-year follow-up rates were lower in the CABG group than in the PCI group (with heart failure: 92.1% versus 96.5%, 90.2% versus 93.0%, and 79.4% versus 82.8%, and without heart failure: 92.6% versus 98.1%, 90.5% versus 95.7%, and 81.1% versus 83.6%).

Survival Outcomes

In patients with heart failure, the cumulative 5-year incidence of all-cause death was significantly higher in the PCI group than in the CABG group (37.7% versus 22.1%, log-rank *P*<0.001) (Figure 2). After adjusting confounders, the excess mortality risk of PCI relative to CABG remained significant (HR, 1.75; 95% CI, 1.28–2.42; *P*<0.001) (Figure 3). The PCI group compared with the CABG group was associated with higher adjusted risks for both cardiovascular and noncardiovascular death (Figure 3).

In the subgroup analysis stratified by heart failure presentation, the excess adjusted risk of PCI relative to

Table. Baseline Characteristics

	With Heart Failure (N=827)			Without Heart Failure (N=2553)		
	PCI (N=511)	CABG (N=316)	*P* value	PCI (N=1619)	CABG (N=934)	*P* value
Clinical characteristics						
Age, y	72.4±11.9	69.7±9.9	0.001	70.3±9.9	69.1±9.2	0.002
≥75*	248 (48.5)	117 (37.0)	0.001	589 (36.4)	275 (29.4)	<0.001
Men*	341 (66.7)	235 (74.4)	0.02	1225 (75.7)	743 (79.6)	0.02
Body mass index, kg/m^2	23.5±4.2	23.4±3.8	0.68	24.0±3.5	23.8±3.4	0.22
<25.0*	356 (69.7)	222 (70.3)	0.86	1066 (65.8)	628 (67.2)	0.47
Unstable angina	13 (2.5)	9 (2.8)	0.79	39 (2.4)	25 (2.7)	0.68
Blood pressure at index hospitalization, mm Hg						
Systolic	137±28	124±23	<0.001	136±20	129±19	<0.001
Diastolic	77±18	68±14	<0.001	74±13	70±12	<0.001
Heart rate at index hospitalization, bpm	85±21	75±16	<0.001	74±14	73±13	0.14
Hypertension*	448 (87.7)	281 (88.9)	0.59	1397 (86.3)	770 (82.4)	0.009
Diabetes mellitus*	295 (57.7)	204 (64.6)	0.051	756 (46.7)	450 (48.2)	0.47
On insulin therapy	95 (18.6)	96 (30.4)	<0.001	207 (12.8)	153 (16.4)	0.01
Current smoking*	101 (19.8)	68 (21.5)	0.54	344 (21.2)	140 (15.0)	<0.001
Prior hospitalization for heart failure	184 (36.0)	215 (68.0)	<0.001			
Current heart failure at index hospitalization	399 (78.1)	147 (46.5)	<0.001			
NYHA II	198 (38.7)	114 (36.1)	<0.001			
NYHA III	136 (26.6)	23 (7.3)				
NYHA IV	65 (12.7)	10 (3.2)				
LVEF	47.4±15.5	48.5±14.5	0.31	62.4±10.8	63.1±11.8	0.14
<40%	161 (34.6)	91 (30.4)	0.47	43 (3.1)	40 (4.5)	0.15
40–50%	101 (21.7)	71 (23.8)		122 (8.8)	88 (9.9)	
≥50%	203 (43.7)	137 (45.8)		1216 (88.1)	763 (85.6)	
Mitral regurgitation grade ≥3/4	86 (18.5)	42 (14.0)	0.1	55 (3.9)	42 (4.7)	0.38
Prior myocardial infarction*	217 (42.5)	110 (34.8)	0.03	255 (15.8)	181 (19.4)	0.02
Prior stroke*	99 (19.4)	60 (19.0)	0.89	269 (16.6)	158 (16.9)	0.84
Peripheral vascular disease*	62 (12.1)	41 (13.0)	0.72	245 (15.1)	113 (12.1)	0.03
eGFR <30 mL/min per 1.73 m^2 or hemodialysis	114 (22.3)	71 (22.5)	0.96	149 (9.2)	97 (10.4)	0.33
eGFR <30 mL/min per 1.73 m^2, without hemodialysis*	53 (10.4)	39 (12.3)	0.38	51 (3.2)	32 (3.4)	0.7
Hemodialysis*	61 (11.9)	32 (10.1)	0.42	98 (6.1)	65 (7.0)	0.37
Atrial fibrillation*	87 (17.0)	43 (13.6)	0.19	105 (6.5)	49 (5.2)	0.21
Hemoglobin <11.0 g/dL*	163 (31.9)	96 (30.4)	0.65	211 (13.0)	123 (13.2)	0.92
Platelet <100×10^9/L*	15 (2.9)	12 (3.8)	0.5	25 (1.5)	18 (1.9)	0.47
White blood cell, ×10^3 cells/μL	6.8 (5.5–8.7)	6.0 (5.0–7.3)	<0.001	6.0 (5.0–7.3)	6.0 (5.0–7.1)	0.62
CRP, mg/dL	0.43 (0.14–1.60)	0.20 (0.10–0.68)	<0.001	0.12 (0.06–0.3)	0.13 (0.06–0.33)	0.21
Chronic obstructive pulmonary disease*	27 (5.3)	27 (8.5)	0.07	53 (3.3)	50 (5.4)	0.01
Liver cirrhosis*	16 (3.1)	8 (2.5)	0.62	47 (2.9)	24 (2.6)	0.62
Malignancy	62 (12.1)	34 (10.8)	0.55	227 (14.0)	106 (11.3)	0.053
Active malignancy*	17 (3.3)	6 (1.9)	0.22	40 (2.5)	21 (2.2)	0.72
Severe frailty*,†	51 (10.0)	9 (2.8)	<0.001	42 (2.6)	14 (1.5)	0.07
Surgical ineligibility‡	54 (10.6)			66 (4.1)		
Procedural characteristics						
Number of target lesions or anastomoses	2.0±1.0	3.4±0.9	<0.001	2.1±1.0	3.4±0.9	<0.001
Target of proximal LAD*	326 (63.8)	275 (87.0)	<0.001	1045 (64.5)	816 (87.4)	<0.001

(*Continued*)

Table. Continued

	With Heart Failure (N=827)			Without Heart Failure (N=2553)		
	PCI (N=511)	CABG (N=316)	*P* value	PCI (N=1619)	CABG (N=934)	*P* value
Target of chronic total occlusion*	124 (24.3)	139 (44.0)	<0.001	311 (19.2)	355 (38.0)	<0.001
3-vessel disease	410 (80.2)	203 (64.2)	<0.001	1337 (82.6)	575 (61.6)	<0.001
LMCA disease	101 (19.8)	113 (35.8)	<0.001	282 (17.4)	359 (38.4)	<0.001
Isolated LMCA	7 (1.4)	0 (0)	<0.001	18 (1.1)	0 (0)	<0.001
LMCA+1-vessel disease	19 (3.7)	0 (0)		76 (4.7)	6 (0.6)	
LMCA+2-vessel disease	30 (5.9)	23 (7.3)		97 (6.0)	103 (11.0)	
LMCA+3-vessel disease	45 (8.8)	89 (28.2)		91 (5.6)	250 (26.8)	
SYNTAX score	26 (20–32)	31 (25–37)	<0.001	23 (17–29)	29 (23–35)	<0.001
Low <23	185 (36.5)	45 (18.0)	<0.001	777 (48.5)	175 (22.8)	<0.001
Intermediate 23–32	205 (40.4)	96 (38.4)		574 (35.8)	323 (42.0)	
High ≥33	117 (23.1)	109 (43.6)		252 (15.7)	271 (35.2)	
Total number of stents	2 (2–4)			3 (2–4)		…
Total stent length, mm	54 (33–87)			56 (31–90)		…
DES use	472 (92.4)			1482 (91.5)		…
New-generation DES use	463 (90.6)			1460 (90.2)		…
IVUS or OCT use	424 (83.0)			1353 (83.6)		…
Internal thoracic artery graft use		309 (97.8)			911 (97.5)	…
Off pump surgery		186 (58.9)			561 (60.1)	…
Interval from index hospitalization to procedure, d	6 (1–14)	3 (1–5)	<0.001	1 (0–3)	3 (2–5)	<0.001
Baseline medications						
Thienopyridine	510 (99.8)	76 (24.1)	<0.001	1608 (99.3)	194 (20.8)	<0.001
Aspirin	507 (99.2)	310 (98.1)	0.15	1608 (99.3)	922 (98.7)	0.12
Statins*	359 (70.3)	190 (60.1)	0.003	1214 (75.0)	600 (64.2)	<0.001
Beta-blockers*	275 (53.8)	171 (54.1)	0.93	501 (30.9)	493 (52.8)	<0.001
ACE-I/ARB*	368 (72.0)	111 (35.1)	<0.001	959 (59.2)	255 (27.3)	<0.001
Calcium channel blockers*	190 (37.2)	104 (32.9)	0.21	883 (54.5)	365 (39.1)	<0.001
Oral anticoagulants*	94 (18.4)	157 (49.7)	<0.001	103 (6.4)	487 (52.1)	<0.001
Proton pump inhibitors or histamine type-2 receptor blockers*	406 (79.5)	298 (94.3)	<0.001	1148 (70.9)	876 (93.8)	<0.001

Continuous variables were expressed as mean±standard deviation, or median (interquartile range). Categorical variables were expressed as number (percentage). Values were missing for LVEF in 344 patients, for mitral regurgitation in 319 patients, and for SYNTAX score in 251 patients. ACE-I indicates angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers; CABG, coronary artery bypass grafting; CRP, C-reactive protein; DES, drug-eluting stent; eGFR, estimated glomerular filtration rate; IVUS, intravascular ultrasound; LAD, left anterior descending coronary artery; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; and SYNTAX, SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery.

*Risk adjusting variables selected for the Cox proportional hazard models.

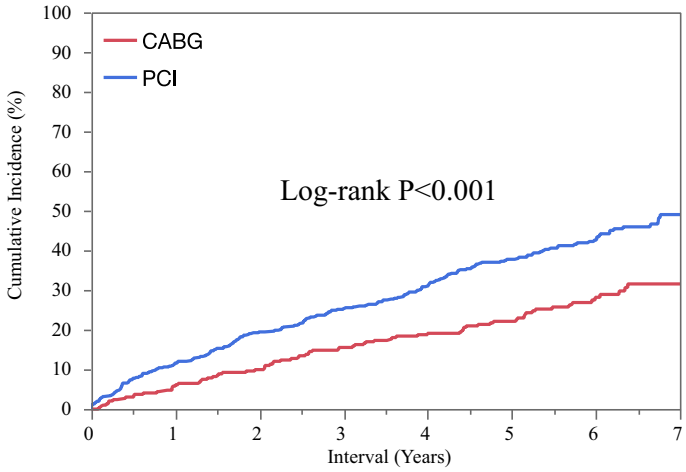
†Severe frailty was regarded as present when the inability to perform usual activities of daily living was documented in the hospital charts.

‡Surgical ineligibility was regarded as present when the term such as “contraindicated for surgery” or “too high risk for surgery” were documented in hospital charts.

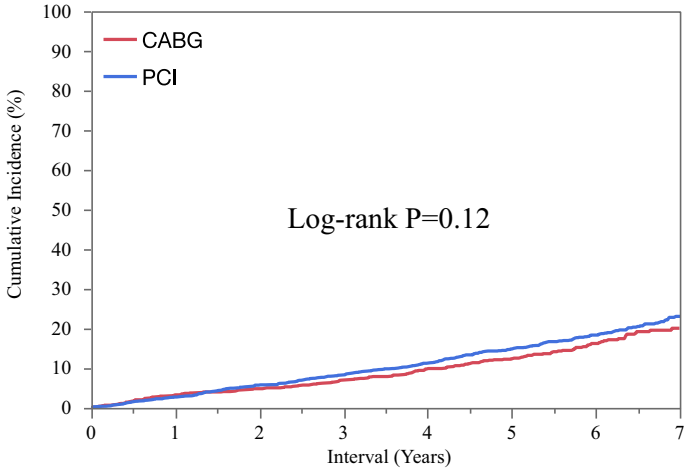
CABG was significant for all-cause death in patients with current heart failure at index hospitalization (HR, 2.07; 95% CI, 1.42–3.13; *P*<0.001), while it was not significant in patients with prior hospitalization for heart failure only (HR, 1.20; 95% CI, 0.78–1.82; *P*=0.4) (Figure 4 and Figure S1).

In patients without heart failure, the cumulative 5-year incidence of all-cause death was not significantly different between the PCI and CABG groups (14.9% versus 12.4%, log-lank *P*=0.12) (Figure 2). After adjusting confounders, the risk of PCI relative to CABG remained insignificant for all-cause death (HR, 1.04; 95% CI, 0.80–1.34; *P*=0.77) (Figure 3). There was significant interaction between heart failure and the effects of PCI relative to CABG for all-cause death (interaction *P*=0.009). Excess adjusted risk of PCI relative to CABG also was not significant for both cardiovascular and noncardiovascular death in patients without heart failure (Figure 3).

Survival outcomes in patients with 3VD and LMCAD were consistent with those in the entire study population (Tables S6 and S7). In the sensitivity analysis after



Interval	0 day	1 year	3 years	5 years
CABG group				
N of patients with event		18	45	63
N of patients at risk	316	274	241	188
Cumulative incidence		6.1%	15.5%	22.1%
PCI group				
N of patients with event		58	124	179
N of patients at risk	511	436	352	244
Cumulative incidence		11.6%	25.3%	37.7%



Interval	0 day	1 year	3 years	5 years
CABG group				
N of patients with event		29	62	105
N of patients at risk	934	837	784	653
Cumulative incidence		3.3%	7.2%	12.4%
PCI group				
N of patients with event		44	132	229
N of patients at risk	1619	1545	1417	1125
Cumulative incidence		2.8%	8.4%	14.9%

Figure 2. Kaplan-Meier event curves for all-cause death in patients (A) with heart failure, and (B) without heart failure.
CABG indicates coronary artery bypass grafting; CREDO-Kyoto PCI/CABG Registry Cohort-3, Coronary Revascularization Demonstrating Outcome study in Kyoto PCI/CABG Registry Cohort-3; LMCAD, left main coronary artery disease; and PCI, percutaneous coronary intervention.

Endpoints	PCI N of patients with event / N of patients at risk (Cumulative 5-year incidence)	CABG N of patients with event / N of patients at risk (Cumulative 5-year incidence)	Adjusted HR [95% CI]	P value	P value for interaction
All-cause death					
With heart failure	209/511 (37.7%)	82/316 (22.1%)	1.75 [1.28-2.42]	<0.001	0.009
Without heart failure	308/1619 (14.9%)	144/934 (12.4%)	1.04 [0.80-1.34]	0.77	
Cardiovascular death					
With heart failure	120/511 (23.3%)	48/316 (13.3%)	1.75 [1.16-2.69]	0.007	0.003
Without heart failure	125/1619 (5.9%)	77/934 (7.0%)	0.75 [0.51-1.08]	0.12	
Non-cardiovascular death					
With heart failure	89/511 (18.8%)	34/316 (10.2%)	1.67 [1.03-2.77]	0.04	0.35
Without heart failure	183/1619 (9.5%)	67/934 (5.8%)	1.42 [0.98-2.04]	0.06	
Myocardial infarction					
With heart failure	53/511 (11.1%)	18/316 (6.2%)	1.83 [1.08-3.22]*	0.02	0.85
Without heart failure	178/1619 (10.4%)	58/934 (6.3%)	1.75 [1.31-2.38]*	<0.001	
Stroke					
With heart failure	47/511 (11.1%)	23/316 (7.7%)	1.30 [0.79-2.19]*	0.31	0.25
Without heart failure	118/1619 (6.5%)	68/934 (6.4%)	0.96 [0.71-1.30]*	0.77	
Hospitalization for heart failure					
With heart failure	121/511 (26.6%)	62/316 (19.3%)	1.22 [0.84-1.79]	0.31	0.55
Without heart failure	130/1619 (7.1%)	62/934 (6.4%)	1.26 [0.84-1.90]	0.27	
Major bleeding (BARC type 3, 4, or 5)					
With heart failure	129/511 (29.2%)	151/316 (48.6%)	0.34 [0.26-0.47]	<0.001	0.42
Without heart failure	286/1619 (17.8%)	313/934 (32.4%)	0.45 [0.36-0.55]	<0.001	
Any coronary revascularization					
With heart failure	165/511 (36.6%)	35/316 (11.5%)	3.70 [2.42-5.65]	<0.001	0.57
Without heart failure	611/1619 (37.4%)	118/934 (12.8%)	3.52 [2.74-4.53]	<0.001	

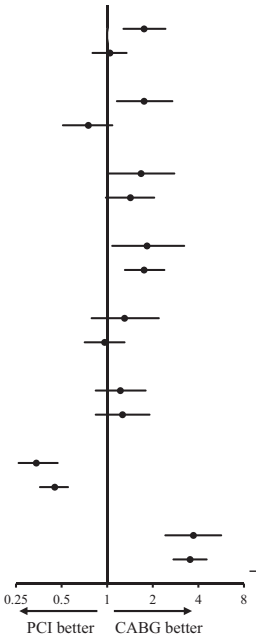


Figure 3. Forrest plots for the adjusted hazard ratios of PCI relative to CABG for clinical outcomes.
Number of patients with event was counted throughout the entire follow-up period, while the cumulative incidence was estimated at 5 years. BARC indicates Bleeding Academic Research Consortium; CABG, coronary artery bypass grafting; CREDO-Kyoto PCI/CABG Registry Cohort-3, Coronary Revascularization Demonstrating Outcome study in Kyoto PCI/CABG Registry Cohort-3; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LMCAD, left main coronary artery disease; and PCI, percutaneous coronary intervention.

excluding patients with surgical indelibility, the results were fully consistent with those in the main analysis (Table S8). In the sensitivity analysis of the model including SYNTAX score as an explanatory variable, the results were fully consistent with those in the main analysis (Table S9). In the subgroup analysis stratified

Subgroups	PCI N of patients with event / N of patients at risk (Cumulative 5-year incidence)	CABG N of patients with event / N of patients at risk (Cumulative 5-year incidence)	Adjusted HR [95% CI]	P value	P value for interaction
Heart failure presentation					
Current heart failure at index hospitalization	167/399 (38.7%)	30/147 (20.3%)	2.07 [1.42-3.13]	<0.001	0.1
Prior hospitalization for heart failure only	42/112 (34.2%)	52/169 (23.8%)	1.20 [0.78-1.82]	0.4	
NYHA					
NYHA II	65/198 (29.0%)	23/114 (21.1%)	1.66 [1.03-2.74]	0.04	0.5
NYHA III or IV	102/201 (48.5%)	7/33 (16.9%)	2.26 [1.12-5.40]	0.02	
LVEF					
<40%	75/161 (41.4%)	32/91 (24.8%)	1.43 [0.93-2.23]	0.1	
40<= - <50%	51/101 (47.1%)	20/71 (25.2%)	2.20 [1.29-3.89]	0.003	0.69
>=50%	63/203 (31.0%)	25/137 (17.5%)	1.56 [0.99-2.55]	0.055	

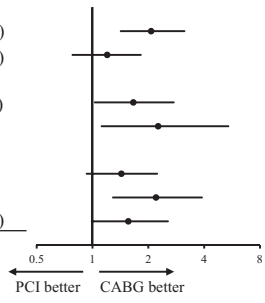


Figure 4. Subgroup analysis for all-cause death in patients with heart failure.
Values were missing for LVEF in 344 patients. Number of patients with event was counted throughout the entire follow-up period, while the cumulative incidence was estimated at 5 years. BARC indicates Bleeding Academic Research Consortium; CABG, coronary artery bypass grafting; CREDO-Kyoto PCI/CABG Registry Cohort-3, Coronary Revascularization Demonstrating Outcome study in Kyoto PCI/CABG Registry Cohort-3; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LMCAD, left main coronary artery disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and PCI, percutaneous coronary intervention.

by NYHA classification and left verntricular ejection fraction in patients with heart failure, there were no significant interactions between the subgroup factors and the effect of PCI relative to CABG for all-cause death (Figure 4 and Figure S2).

Other Clinical Outcomes

In patients both with and without heart failure, the excess adjusted risk of PCI relative to CABG was significant for myocardial infarction, and any coronary revascularization, while it was not significant for stroke, and hospitalization for heart failure. There was a significantly lower risk of PCI relative to CABG for major bleeding in patients both with and without heart failure. There was no significant interaction between heart failure and the effects of PCI relative to CABG for all the outcome measures other than survival outcomes (Figure 3).

DISCUSSION

The main finding of this study comparing PCI with CABG in patients with severe CAD was that there was a significant interaction between heart failure and the mortality risk of PCI relative to CABG with excess risk in patients with heart failure and neutral risk in patients without heart failure.

In this study, PCI compared with CABG was associated with a significant excess mortality risk in patients with heart failure, whereas the mortality risk was neutral in patients without heart failure. One of the reasons for the different mortality risk of PCI relative to CABG might be related to the difference of baseline clinical characteristics between those with and without heart failure. In this study, patients with heart failure more often had systolic dysfunction and high SYNTAX score compared with those without. CABG might be more suitable in patients with heart failure with complex coronary anatomy and/or systolic dysfunction, because in previous reports, CABG was associated with lower mortality risk compared with PCI in patients with systolic dysfunction, or high SYNTAX score.[9,10,12] However, there were substantial baseline differences between the PCI and CABG groups in patients with heart failure, while those were generally well balanced in patients without heart failure. In patients with heart failure, the PCI group compared with the CABG group had higher prevalence of advanced age, frailty, acute and severe heart failure, and elevated inflammatory markers. The interval from hospitalization to index procedure was longer in the PCI group than in the CABG group, suggesting that there were substantial proportion of patients who could not undergo PCI quickly due to severe hemodynamic or respiratory condition, and/or infection at index hospitalization in the PCI group. In this study, more than 60% of the patients were treated with PCI in the entire cohort, while more than 70% of the patients with acute heart failure, and more than 80% of the patients with severe acute heart failure were treated with PCI as the coronary revascularization modality, even though the current clinical guidelines recommend CABG as the revascularization modality in patients with heart failure.[13,14] Therefore, we cannot rule out the possibility of selection bias toward choosing PCI in sicker patients in this study, although the higher mortality risk of PCI relative to CABG in patients with heart failure was consistent with previous studies.[9–11] The excess adjusted risk of PCI relative to CABG for noncardiovascular death in patients with heart failure might also suggest the presence of selection bias. Indeed, there was no excess mortality risk of PCI relative to CABG in patients with prior hospitalization for heart failure only, whose baseline characteristics were relatively better balanced between the PCI and CABG groups than in those with current heart failure at index hospitalization. Considering the possible presence of selection bias for coronary revascularization modality in patients with heart failure, we should be cautious in interpreting the results from the observational studies suggesting the higher mortality risk of PCI relative to CABG in patients with heart failure.

It is noteworthy that there was no excess mortality risk of PCI relative to CABG in patients without heart failure in this study. In a meta-analysis of individual patient data from RCTs in patients with multivessel disease, there was no significant mortality risk of PCI relative to CABG in patients with low SYNTAX score, while PCI had higher mortality risk than CABG in patients with intermediate or high SYNTAX score.[12] In a meta-analysis of individual patient data from RCTs in patients with LMCAD, the mortality risk was similar between PCI and CABG, although the mortality risk trended to be higher in PCI than in CABG in those with high SYNTAX score.[12] Based on these results, the current clinical guidelines recommend that CABG remains standard revascularization modality for patients with severe CAD, although PCI is recommended as a good alternative to CABG only in patients without diabetes mellitus, with low SYNTAX score in patients with 3VD, and only in patients with low or intermediate SYNTAX score in patients with LMCAD.[13,14] In this study reflecting real clinical practice, PCI was chosen in more than 60% of patients with severe CAD and without heart failure, although patients treated with PCI had less complex coronary anatomy than those treated with CABG. The baseline characteristics were better balanced between the PCI and CABG groups in patients without heart failure than in patients with heart failure, suggesting that selection bias toward sicker patients in the PCI group was less apparent in patients without heart failure than in patients with heart failure. It

was reassuring that the practice pattern in the present study was not associated with an excess long-term mortality risk of PCI relative to CABG in patients with severe CAD and without heart failure.

Study Limitations

There were several important limitations in this study. First, patients were not randomly allocated to each coronary revascularization strategy. Analysis with propensity score might be an option to take into account the differences in baseline characteristics and the potential selection bias. However, even analysis with propensity score could not address unmeasured confounders, and the sample size was limited in the current study population to provide a plausible propensity score, particularly in the subgroup of heart failure. Hence, we conducted some multivariable models as sensitivity analyses. Especially in patients with heart failure, we could not deny the presence of the unmeasured confounders and some ascertainment bias, although we conducted extensive multivariable adjustment for the known confounders. In fact, patients with heart failure more often had surgical ineligibility than in patients without heart failure. The results after excluding patients with surgical ineligibility were consistent with the main results, although the seemingly very low prevalence of inoperable patients would suggest imperfect ascertainment of inoperable status in this retrospective study. In addition, we evaluated severe frailty defined as documentation of the inability to perform usual activities of daily living in the hospital charts. However, we could not deny ascertainment bias for severe frailty, because the prevalence of severe frailty in the present study was lower than those reported in previous studies.[15] Furthermore, due to the retrospective study design, we could not assess other important factors such as moderate frailty and cognitive impairment, which might have great influence on the choice between PCI and CABG, as well as on clinical outcomes. In patients without heart failure, patient selection and intervention biases should also be considered as the baseline patient or lesion characteristics were different between PCI and CABG, which could prevent generalization of the results and decision making in daily practice. Second, we might not have adequate statistical power in this subgroup analysis stratified by heart failure. However, we had enough number of patients with all-cause death to make extensive multivariable adjustment, and found a positive interaction between heart failure and the mortality risk of PCI relative to CABG. Third, the follow-up rate was suboptimal, and complete follow-up rate was lower in the CABG group than in the PCI group. The incidences of adverse event might have been underestimated in the CABG group. Fourth, as we excluded acute myocardial infarction patients in this study, the results of this study cannot be applied to those with non-ST-segment elevation myocardial infarction as well as ST-segment elevation myocardial infarction. Finally, the assessment of lesion-specific ischemia by fractional flow reserve was performed only in a small proportion of patients in the PCI group, which were different from the current clinical practice. Moreover, it was unknown whether the patients underwent complete or incomplete revascularization as the residual SYNTAX scores were not obtained.

CONCLUSIONS

There was a significant interaction between heart failure and the mortality risk of PCI relative to CABG with excess risk in patients with heart failure and neutral risk in patients without heart failure.

ARTICLE INFORMATION

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Supplementary Material

Appendix S1
Tables S1–S9
Figures S1–S2
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SUPPLEMENTAL MATERIAL

Appendix

List of Participating Centers and Investigators for the CREDO-Kyoto PCI/CABG Registry Cohort-3

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List of the SYNTAX Score Committee Members

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Definitions for Outcome Measures

Death was regarded as cardiac in origin unless obvious non-cardiac causes could be identified. Death of unknown cause and any death during the index hospitalization for coronary revascularization were regarded as cardiac death. Cardiovascular death included cardiac death, and other vascular death related to stroke, renal disease, and vascular disease. Myocardial infarction was adjudicated according to the ARC definition.[16] Stroke was defined as ischemic or hemorrhagic stroke with neurological symptoms lasting >24 hours. Hospitalization for heart failure was defined as hospitalization due to worsening heart failure requiring intravenous drug therapy. Bleeding was

defined according to the Bleeding ARC (BARC) classification.[17] BARC type 3, 4, or 5 bleeding were regarded as major bleeding. Any coronary revascularization was defined as either PCI or CABG for any reason. Scheduled staged coronary revascularization procedures performed within 3 months of the initial procedure were not regarded as follow-up events, but included in the index procedure.

Table S1. Proportion of PCI and CABG.

		3VD+LMCAD	3VD	LMCAD
Entire study population: N=3380	PCI	63.0%	69.2%	44.8%
(3VD: N=2525, and: LMCAD=855)	CABG	37.0%	30.8%	55.2%
Patients without heart failure: N=2553	PCI	63.4%	69.9%	44.0%
(3VD: N=1992, and LMCAD: N=641)	CABG	36.6%	30.1%	56.0%
Patients with heart failure: N=827	PCI	61.8%	66.9%	47.2%
(3VD: N=613, and LMCAD: N=214)	CABG	38.2%	33.1%	52.8%
Prior hospitalization for heart failure only: N=281	PCI	39.9%	44.4%	27.0%
(3VD: N=207, and LMCAD: N=74)	CABG	60.1%	55.6%	73.0%
Current heart failure at index hospitalization: N=546	PCI	73.1%	78.3%	57.9%
(3VD: N=406, and LMCAD: N=140)	CABG	26.9%	21.7%	42.1%
Current heart failure at index hospitalization (NYHA II): N=312	PCI	63.5%	69.2%	49.4%
(3VD: N=221, and LMCAD: N=91)	CABG	36.5%	30.8%	50.6%
Current heart failure at index hospitalization (NYHA III-IV): N=234	PCI	85.9%	89.2%	73.5%
(3VD: N=185, and LMCAD: N=49)	CABG	14.1%	10.8%	26.5%

CABG=coronary artery bypass grafting; LMCAD=left main coronary artery disease; NYHA=New York Heart Association; PCI=percutaneous coronary intervention; 3VD=three-vessel coronary artery disease.

Table S2. Baseline Characteristics and Management during the Index Hospitalization in Patients With and Without Heart Failure.

	With heart failure (N=827)	Without heart failure (N=2553)	P value
(A) Clinical characteristics			
Age (years)	71.4±11.3	69.9±9.7	<0.001
Age >=75 years	365 (44.1)	864 (33.8)	<0.001
Men	576 (69.6)	1968 (77.1)	<0.001
Body mass index (kg/m^2)	23.4±4.1	23.9±3.4	0.001
Body mass index <25.0 kg/m^2	578 (69.9)	1694 (66.4)	0.06
Unstable angina	22 (2.7)	64 (2.5)	0.81
Blood pressure at index hospitalization			
Systolic (mmHg)	132±27	133±20	0.33
Diastolic (mmHg)	74±17	73±13	0.06
Heart rate at index hospitalization (bpm)	81±20	73±13	<0.001
Hypertension	729 (88.1)	2167 (84.9)	0.02
Diabetes mellitus	499 (60.3)	1206 (47.2)	<0.001
on insulin therapy	191 (23.1)	360 (14.1)	<0.001
Current smoking	169 (20.4)	484 (19.0)	0.35
Prior hospitalization for heart failure	399 (48.3)	-	-
Current heart failure at index hospitalization	546 (66.0)	-	-
NYHA II	312 (57.1)	-	
NYHA III	159 (29.1)	-	-
NYHA IV	75 (13.7)	-	
LVEF	47.8±15.1	62.7±11.2	<0.001
<40%	252 (33.0)	83 (3.7)	
40<= - <50%	172 (22.5)	210 (9.2)	<0.001
>=50%	340 (44.5)	1979 (87.1)	
Mitral regurgitation grade >=3/4	128 (16.7)	97 (4.2)	<0.001
Prior myocardial infarction	327 (39.5)	436 (17.1)	<0.001
Prior stroke (symptomatic)	159 (19.2)	427 (16.7)	0.1
Peripheral vascular disease	103 (12.5)	358 (14.0)	0.25
eGFR <30 mL/min/1.73m^2 or hemodialysis	185 (22.4)	246 (9.6)	<0.001
eGFR <30 mL/min/1.73m^2, without hemodialysis	92 (11.1)	83 (3.3)	<0.001
Hemodialysis	93 (11.2)	163 (6.4)	<0.001
Atrial fibrillation	130 (15.7)	154 (6.0)	<0.001
Anemia (Hemoglobin <11.0 g/dL)	259 (31.3)	334 (13.1)	<0.001

Thrombocytopenia (Platelet <100 × 10^9/L)	27 (3.3)	43 (1.7)	0.006
WBC (× 10^3 cells/μL)	6.4 (5.2-8.2)	6.0 (5.0-7.2)	<0.001
CRP (mg/dL)	0.30 (0.10-1.12)	0.12 (0.06-0.30)	<0.001
Chronic obstructive pulmonary disease	54 (6.5)	103 (4.0)	0.003
Liver cirrhosis	24 (2.9)	71 (2.8)	0.85
Malignancy	96 (11.6)	333 (13.0)	0.28
Active malignancy	23 (2.8)	61 (2.4)	0.53
Severe frailty*	60 (7.3)	56 (2.2)	<0.001
Surgical ineligibility†	54 (10.6)	66 (4.1)	<0.001
(B) Procedural characteristics			
Number of target lesions or anastomoses	2.6±1.2	2.5±1.2	0.59
Target of proximal LAD	601 (72.7)	1861 (72.9)	0.9
Target of chronic total occlusion	263 (31.8)	666 (26.1)	0.001
Emergency procedure	44 (5.3)	130 (5.1)	0.8
3-vessel disease	613 (74.1)	1912 (74.9)	0.66
LMCA disease	214 (25.9)	641 (25.1)	0.66
Isolated LMCA	7 (3.3)	18 (2.8)	
LMCA + 1-vessel disease	19 (8.9)	82 (12.8)	0.08
LMCA + 2-vessel disease	54 (25.2)	200 (31.2)	
LMCA + 3-vessel disease	134 (62.6)	341 (53.2)	
SYNTAX score	28 (21-35)	25 (19-31)	<0.001
Low <23	230 (30.4)	952 (40.1)	
Intermediate 23-32	301 (39.8)	897 (37.8)	<0.001
High >=33	226 (29.9)	523 (22.1)	
Total number of stents	2 (2-4)	3 (2-4)	0.35
Total stent length (mm)	54 (33-87)	56 (31-90)	0.59
PCI	511 (61.8)	1619 (63.4)	0.4
Stent use	498 (97.5)	1579 (97.5)	0.93
DES use	472 (92.4)	1482 (91.5)	0.55
New-generation DES use	463 (90.6)	1460 (90.2)	0.78
IVUS or OCT use	424 (83.0)	1353 (83.6)	0.75
CABG	316 (38.2)	934 (36.6)	0.4
Internal thoracic artery graft use	309 (97.8)	911 (97.5)	0.8
Off pump surgery	186 (58.9)	561 (60.1)	0.71
Interval from index hospitalization to procedure (days)	4 (1-10)	2 (1-4)	<0.001
(C) Baseline medications			
Antiplatelet therapy			
Thienopyridine	586 (70.9)	1802 (70.6)	0.88

Aspirin	817 (98.8)	2530 (99.1)	0.43
Cilostazol	28 (3.4)	97 (3.8)	0.58
Other medications			
Statins	549 (66.4)	1814 (71.1)	0.01
Beta-blockers	446 (53.9)	994 (38.9)	<0.001
ACE-I/ARB	479 (57.9)	1214 (47.6)	<0.001
Calcium channel blockers	294 (35.6)	1248 (48.9)	<0.001
Oral anticoagulants	251 (30.4)	590 (23.1)	<0.001
Proton pump inhibitors or histamine type-2 receptor blockers	704 (85.1)	2024 (79.3)	<0.001

Continuous variables were expressed as mean ± standard deviation, or median (interquartile range). Categorical variables were expressed as number (percentage). Values were missing for LVEF in 344 patients, for mitral regurgitation in 319 patients, and for SYNTAX score in 251 patients.

*Severe frailty was regarded as present when the inability to perform usual activities of daily living was documented in the hospital charts.

†Surgical ineligibility was regarded as present when the term such as “contraindicated for surgery” or “too high risk for surgery” were documented in hospital charts

ACE-I=angiotensin converting enzyme inhibitors; ARB=angiotensin II receptor blockers; CABG=coronary artery bypass grafting; CRP=C-reactive protein; DES=drug-eluting stent; eGFR=estimated glomerular filtration rate; IVUS=intravascular ultrasound; LAD=left anterior descending coronary artery; LMCA=left main coronary artery; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; OCT=optical coherence tomography; PCI=percutaneous coronary intervention; SYNTAX=SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery; WBC=white blood cell; 3VD=three-vessel coronary artery disease

Table S3. Baseline Characteristics and Management during the Index Hospitalization in Patients With 3VD.

	With heart failure (N=613)			Without heart failure (N=1912)		
	PCI (N=410)	CABG (N=203)	P value	PCI (N=1337)	CABG (N=575)	P value
(A) Clinical characteristics						
Age (years)	72.0±12.2	68.8±10.3	0.001	70.0±10.1	68.5±9.3	0.002
Age >=75 years	196 (47.8)	69 (34.0)	0.001	473 (35.4)	163 (28.3)	0.003
Men	272 (66.3)	150 (73.9)	0.06	1006 (75.2)	452 (78.6)	0.11
Body mass index (kg/m^2)	23.6±4.2	23.6±4.0	0.98	24.0±3.5	23.9±3.4	0.3
Body mass index <25.0 kg/m^2	286 (69.8)	140 (69.0)	0.84	862 (64.5)	379 (65.9)	0.55
Unstable angina	8 (2.0)	6 (3.0)	0.43	34 (2.5)	7 (1.2)	0.07
Blood pressure at index hospitalization						
Systolic (mmHg)	138±28	124±22	<0.001	136±20	128±19	<0.001
Diastolic (mmHg)	78±17	69±15	<0.001	75±13	70±12	<0.001
Heart rate at index hospitalization (bpm)	85±21	77±17	<0.001	74±14	73±13	0.1
Hypertension	362 (88.3)	188 (92.6)	0.1	1167 (87.3)	479 (83.3)	0.02
Diabetes mellitus	241 (58.8)	133 (65.5)	0.11	647 (48.4)	291 (50.6)	0.37
on insulin therapy	78 (19.0)	63 (31.0)	0.001	173 (12.9)	106 (18.4)	0.002
Current smoking	86 (21.0)	48 (23.6)	0.45	291 (21.8)	94 (16.3)	0.007
Prior hospitalization for heart failure	147 (35.9)	144 (70.9)	<0.001	-	-	-
Current heart failure at index hospitalization	318 (77.6)	88 (43.4)	<0.001	-	-	-
NYHA II	153 (37.3)	68 (33.5)		-	-	
NYHA III	115 (28.0)	13 (6.4)	<0.001	-	-	-
NYHA IV	50 (12.2)	7 (3.4)		-	-	
LVEF	47.1±15.5	47.5±14.7	0.74	62.2±10.7	61.8±12.4	0.5
<40%	131 (34.4)	62 (32.3)	0.81	32 (2.8)	30 (5.5)	0.003

40<= - <50%	85 (22.3)	47 (24.5)		103 (9.0)	66 (12.0)	
>=50%	165 (43.3)	83 (43.2)		1012 (88.2)	454 (82.6)	
Mitral regurgitation grade >=3/4	69 (18.2)	27 (14.0)	0.21	47 (4.0)	26 (4.7)	0.53
Prior myocardial infarction	171 (41.7)	70 (34.5)	0.08	225 (16.8)	133 (23.1)	0.001
Prior stroke (symptomatic)	82 (20.0)	39 (19.2)	0.82	220 (16.5)	97 (16.9)	0.82
Peripheral vascular disease	42 (10.2)	27 (13.3)	0.26	197 (14.7)	83 (14.4)	0.87
eGFR <30 mL/min/1.73m^2 or hemodialysis	94 (22.9)	47 (23.2)	0.95	126 (9.4)	69 (12.0)	0.09
eGFR <30 mL/min/1.73m^2, without hemodialysis	46 (11.2)	29 (14.3)	0.28	38 (2.8)	24 (4.2)	0.13
Hemodialysis	48 (11.7)	18 (8.9)	0.29	88 (6.6)	45 (7.8)	0.33
Atrial fibrillation	68 (16.6)	28 (13.8)	0.37	85 (6.4)	29 (5.0)	0.27
Anemia (Hemoglobin <11.0 g/dL)	130 (31.7)	64 (31.5)	0.96	174 (13.0)	82 (14.3)	0.46
Thrombocytopenia (Platelet <100 × 10^9/L)	12 (2.9)	9 (4.4)	0.33	19 (1.4)	8 (1.4)	0.96
WBC (× 10^3 cells/μL)	6.8 (5.5-8.3)	6.1 (5.1-7.5)	<0.001	6.0 (5.1-7.3)	6.0 (5.0-7.1)	0.29
CRP (mg/dL)	0.40 (0.13-1.51)	0.20 (0.09-0.69)	<0.001	0.13 (0.06-0.30)	0.12 (0.05-0.30)	0.63
Chronic obstructive pulmonary disease	24 (5.9)	18 (8.9)	0.16	45 (3.4)	28 (4.9)	0.12
Liver cirrhosis	13 (3.2)	4 (2.0)	0.39	42 (3.1)	16 (2.8)	0.67
Malignancy	48 (11.7)	22 (10.8)	0.75	186 (13.9)	58 (10.1)	0.02
Active malignancy	13 (3.2)	4 (2.0)	0.39	31 (2.3)	15 (2.6)	0.7
Severe frailty[*]	40 (9.8)	7 (3.4)	0.006	33 (2.5)	8 (1.4)	0.14
Surgical ineligibility[†]	38 (9.3)	-	-	41 (3.1)	-	-
(B) Procedural characteristics						
Number of target lesions or anastomoses	2.0±1.0	3.6±0.9	<0.001	2.1±1.0	3.5±0.9	<0.001
Target of proximal LAD	274 (66.8)	183 (90.1)	<0.001	892 (66.7)	548 (95.3)	<0.001
Target of chronic total occlusion	108 (26.3)	104 (51.2)	<0.001	275 (20.6)	276 (48.0)	<0.001
Emergency procedure	17 (4.1)	8 (3.9)	0.9	61 (4.6)	11 (1.9)	0.005
SYNTAX score	25 (19-31)	30 (24-36)	<0.001	22 (17-28)	29 (23-34)	<0.001
Low <23	160 (39.4)	29 (18.2)	<0.001	689 (52.0)	106 (22.4)	<0.001

Intermediate 23-32	172 (42.4)	74 (46.5)		471 (35.6)	214 (45.2)	
High >=33	74 (18.2)	56 (35.2)		165 (12.5)	154 (32.5)	
Total number of stents	2 (2-4)	-	-	3 (2-4)	-	-
Total stent length (mm)	53 (33-84)	-	-	56 (30-89)	-	-
Stent use	399 (97.3)	-	-	1299 (97.2)	-	-
DES use	378 (92.2)	-	-	1218 (91.1)	-	-
New-generation DES use	370 (90.2)	-	-	1197 (89.5)	-	-
IVUS or OCT use	330 (80.5)	-	-	1093 (81.8)	-	-
Internal thoracic artery graft use	-	199 (98.0)	-	-	561 (97.6)	-
Off pump surgery	-	128 (63.1)	-	-	344 (59.8)	-
Interval from index hospitalization to procedure (days)	7 (1-15)	3 (2-5)	<0.001	1 (0-3)	4 (2-5)	<0.001
(C) Baseline medications						
Antiplatelet therapy						
Thienopyridine	409 (99.8)	49 (24.1)	<0.001	1327 (99.3)	117 (20.3)	<0.001
Aspirin	406 (99.0)	197 (97.0)	0.07	1330 (99.5)	569 (99.0)	0.2
Cilostazol	14 (3.4)	9 (4.4)	0.53	50 (3.7)	15 (2.6)	0.21
Other medications						
Statins	284 (69.3)	125 (61.6)	0.06	1002 (74.9)	381 (66.3)	<0.001
Beta-blockers	225 (54.9)	115 (56.7)	0.68	432 (32.3)	320 (55.7)	<0.001
ACE-I/ARB	299 (72.9)	82 (40.4)	<0.001	808 (60.4)	151 (26.3)	<0.001
Calcium channel blockers	150 (36.6)	74 (36.5)	0.97	745 (55.7)	220 (38.3)	<0.001
Oral anticoagulants	80 (19.5)	105 (51.7)	<0.001	85 (6.4)	308 (53.6)	<0.001
Proton pump inhibitors or histamine type-2 receptor blockers	323 (78.8)	187 (92.1)	<0.001	942 (70.5)	532 (92.5)	<0.001

Continuous variables were expressed as mean ± standard deviation, or median (interquartile range). Categorical variables were expressed as number (percentage). Values were missing for LVEF in 255 patients, for mitral regurgitation in 235 patients, and for SYNTAX score in 161 patients.

*Severe frailty was regarded as present when the inability to perform usual activities of daily living was documented in the hospital charts.

†Surgical ineligibility was regarded as present when the term such as “contraindicated for surgery” or “too high risk for surgery” were documented in hospital charts

Abbreviations are as in Table S2.

Table S4. Baseline Characteristics and Management during the Index Hospitalization in Patients With LMCAD.

	With heart failure (N=214)			Without heart failure (N=641)		
	PCI (N=101)	CABG (N=113)	P value	PCI (N=282)	CABG (N=359)	P value
(A) Clinical characteristics						
Age (years)	74.0±10.5	71.2±9.1	0.04	71.6±9.3	69.9±9.1	0.02
Age >=75 years	52 (51.5)	48 (42.5)	0.19	116 (41.1)	112 (31.2)	0.009
Men	69 (68.3)	85 (75.2)	0.26	219 (77.7)	291 (81.1)	0.29
Body mass index (kg/m^2)	23.0±4.3	23.0±3.4	0.92	23.7±3.2	23.7±3.4	0.93
Body mass index <25.0 kg/m^2	70 (69.3)	82 (72.6)	0.6	204 (72.3)	249 (69.4)	0.41
Unstable angina	5 (5.0)	3 (2.7)	0.38	5 (1.8)	18 (5.0)	0.03
Blood pressure at index hospitalization						
Systolic (mmHg)	135±28	124±24	0.003	134±20	131±19	0.02
Diastolic (mmHg)	75±19	67±12	<0.001	73±12	69±13	0.001
Heart rate at index hospitalization (bpm)	83±20	73±14	<0.001	71±12	72±13	0.3
Hypertension	86 (85.1)	93 (82.3)	0.57	230 (81.6)	291 (81.1)	0.87
Diabetes mellitus	54 (53.5)	71 (62.8)	0.17	109 (38.7)	159 (44.3)	0.15
on insulin therapy	17 (16.8)	33 (29.2)	0.03	34 (12.1)	47 (13.1)	0.7
Current smoking	15 (14.9)	20 (17.7)	0.57	53 (18.8)	46 (12.8)	0.04
Prior hospitalization for heart failure	37 (36.6)	71 (62.8)	<0.001	-	-	-
Current heart failure at index hospitalization	81 (80.2)	59 (52.2)	<0.001	-	-	-
NYHA II	45 (44.6)	46 (40.7)		-	-	
NYHA III	21 (20.8)	10 (8.8)	0.01	-	-	-
NYHA IV	15 (14.9)	3 (2.7)		-	-	
LVEF	48.8±15.7	50.3±13.9	0.48	63.2±11.3	65.1±10.5	0.03
<40%	30 (35.7)	29 (27.1)	0.44	11 (4.7)	10 (2.9)	0.38

40<= - <50%	16 (19.1)	24 (22.4)		19 (8.1)	22 (6.5)	
>=50%	38 (45.2)	54 (50.5)		294 (87.2)	309 (90.6)	
Mitral regurgitation grade >=3/4	17 (20.0)	15 (14.0)	0.27	8 (3.4)	16 (4.7)	0.44
Prior myocardial infarction	46 (45.5)	40 (35.4)	0.13	30 (10.6)	48 (13.4)	0.29
Prior stroke (symptomatic)	17 (16.8)	21 (18.6)	0.74	49 (17.4)	61 (17.0)	0.9
Peripheral vascular disease	20 (19.8)	14 (12.4)	0.14	48 (17.0)	30 (8.4)	0.001
eGFR <30 mL/min/1.73m^2 or hemodialysis	20 (19.8)	24 (21.2)	0.8	23 (8.2)	28 (7.8)	0.87
eGFR <30 mL/min/1.73m^2, without hemodialysis	7 (6.9)	10 (8.8)	0.6	13 (4.6)	8 (2.2)	0.09
Hemodialysis	13 (12.9)	14 (12.4)	0.92	10 (3.5)	20 (5.6)	0.23
Atrial fibrillation	19 (18.8)	15 (13.3)	0.27	20 (7.1)	20 (5.6)	0.43
Anemia (Hemoglobin <11.0 g/dL)	33 (32.7)	32 (28.3)	0.49	37 (13.1)	41 (11.4)	0.51
Thrombocytopenia (Platelet <100 × 10^9/L)	3 (3.0)	3 (2.7)	0.89	6 (2.1)	10 (2.8)	0.6
WBC (× 10^3 cells/μL)	7.4 (5.6-9.5)	5.7 (4.8-7.0)	<0.001	5.9 (4.8-7.1)	5.9 (5.1-7.1)	0.19
CRP (mg/dL)	0.59 (0.2-2.4)	0.20 (0.10-0.65)	<0.001	0.10 (0.05-0.30)	0.14 (0.07-0.42)	0.006
Chronic obstructive pulmonary disease	3 (3.0)	9 (8.0)	0.11	8 (2.8)	22 (6.1)	0.0502
Liver cirrhosis	3 (3.0)	4 (3.5)	0.82	5 (1.8)	8 (2.2)	0.68
Malignancy	14 (13.9)	12 (10.6)	0.47	41 (14.5)	48 (13.4)	0.67
Active malignancy	4 (4.0)	2 (1.8)	0.33	9 (3.2)	6 (1.7)	0.21
Severe frailty[*]	11 (10.9)	2 (1.8)	0.005	9 (3.2)	6 (1.7)	0.21
Surgical ineligibility[†]	16 (15.8)	-	-	25 (8.9)	-	-
(B) Procedural characteristics						
Number of target lesions or anastomoses	2.1±1.3	3.3±0.9	<0.001	2.1±1.2	3.1±0.9	<0.001
Target of proximal LAD	52 (51.5)	92 (81.4)	<0.001	153 (54.3)	268 (74.7)	<0.001
Target of chronic total occlusion	16 (15.8)	35 (31.0)	0.01	36 (12.8)	79 (22.0)	0.003
Emergency procedure	10 (9.9)	9 (8.0)	0.62	26 (9.2)	32 (8.9)	0.89
Extent of coronary artery disease						
Isolated LMCA	7 (6.9)	0 (0)	<0.001	18 (6.4)	0 (0)	<0.001

LMCA + 1-vessel disease	19 (18.8)	0 (0)		76 (27.0)	6 (1.7)	
LMCA + 2-vessel disease	30 (29.7)	24 (21.2)		97 (34.4)	103 (28.7)	
LMCA + 3-vessel disease	45 (44.6)	89 (78.8)		91 (32.3)	250 (69.6)	
SYNTAX score	29 (23-39)	35 (27-41)	0.02	27 (21-35)	29 (23-37)	0.02
Low <23	25 (24.8)	16 (17.6)		88 (31.7)	69 (23.4)	
Intermediate 23-32	33 (32.7)	22 (24.2)	0.09	103 (37.1)	109 (37.0)	0.04
High >=33	43 (42.6)	53 (58.2)		87 (31.3)	117 (39.7)	
Total number of stents	2 (1-4)	-	-	2 (1-4)	-	-
Total stent length (mm)	51 (24-112)	-	-	52 (28-88)	-	-
Stent use	99 (98.0)	-	-	280 (99.3)	-	-
DES use	94 (93.1)	-	-	264 (93.6)	-	-
New-generation DES use	93 (92.1)	-	-	263 (93.3)	-	-
IVUS or OCT use	94 (93.1)	-	-	260 (92.2)	-	-
Internal thoracic artery graft use	-	110 (97.3)	-	-	350 (97.5)	-
Off pump surgery	-	58 (51.3)	-	-	217 (60.5)	-
Interval from index hospitalization to procedure (days)	5 (1-12)	3 (1-4)	0.003	1 (0-3)	3 (2-6)	<0.001
(C) Baseline medications						
Antiplatelet therapy						
Thienopyridine	101 (100)	27 (23.9)	<0.001	281 (99.6)	77 (21.4)	<0.001
Aspirin	101 (100)	113 (100)	NA	278 (98.6)	353 (98.3)	0.8
Cilostazol	3 (3.0)	2 (1.8)	0.56	18 (6.4)	14 (3.9)	0.15
Other medications						
Statins	75 (74.3)	65 (57.5)	0.01	212 (75.2)	219 (61.0)	<0.001
Beta-blockers	50 (49.5)	56 (49.6)	0.99	69 (24.5)	173 (48.2)	<0.001
ACE-I/ARB	69 (68.3)	29 (25.7)	<0.001	151 (53.5)	104 (29.0)	<0.001
Calcium channel blockers	40 (39.6)	30 (26.5)	0.04	138 (48.9)	145 (40.4)	0.03

Oral anticoagulants	14 (13.9)	52 (46.0)	<0.001	18 (6.4)	179 (49.9)	<0.001
Proton pump inhibitors or histamine type-2 receptor blockers	83 (82.2)	111 (98.2)	<0.001	206 (73.0)	344 (95.8)	<0.001

Continuous variables were expressed as mean ± standard deviation, or median (interquartile range). Categorical variables were expressed as number (percentage). Values were missing for LVEF in 89 patients, for mitral regurgitation in 84 patients, and for SYNTAX score in 90 patients.

*Severe frailty was regarded as present when the inability to perform usual activities of daily living was documented in the hospital charts.

†Surgical ineligibility was regarded as present when the term such as “contraindicated for surgery” or “too high risk for surgery” were documented in hospital charts

Abbreviations are as in Table S2.

Table S5. Baseline Characteristics and Management during the Index Hospitalization in Patients With Current Heart Failure at Index Hospitalization and in Patients With Prior Hospitalization for Heart Failure Only.

	Current heart failure at index hospitalization (N=546)			Prior hospitalization for heart failure only (N=281)		
	PCI (N=399)	CABG (N=147)	P value	PCI (N=112)	CABG (N=169)	P value
(A) Clinical characteristics						
Age (years)	73.5±11.2	69.8±10.0	<0.001	68.7±13.5	69.6±9.9	0.53
Age >=75 years	204 (51.1)	56 (38.1)	0.007	44 (39.3)	61 (36.1)	0.59
Men	260 (65.2)	110 (74.8)	0.03	81 (72.3)	125 (74.0)	0.76
Body mass index (kg/m^2)	23.7±4.3	23.9±3.7	0.48	22.9±3.8	22.9±3.9	0.97
Body mass index <25.0 kg/m^2	272 (68.2)	94 (63.9)	0.35	84 (75.0)	128 (75.7)	0.89
Unstable angina	12 (3.0)	7 (4.8)	0.32	1 (0.9)	2 (1.2)	0.82
Blood pressure at index hospitalization						
Systolic (mmHg)	139±29	127±25	<0.001	132±25	122±21	<0.001
Diastolic (mmHg)	78±18	70±15	<0.001	73±14	67±13	<0.001
Heart rate at index hospitalization (bpm)	87±22	76±17	<0.001	76±13	75±14	0.59
Hypertension	348 (87.2)	131 (89.1)	0.55	100 (89.3)	150 (88.8)	0.89
Diabetes mellitus	231 (57.9)	81 (55.1)	0.56	64 (57.1)	123 (72.8)	0.007
on insulin therapy	73 (18.3)	41 (27.9)	0.01	22 (19.6)	55 (32.5)	0.02
Current smoking	74 (18.5)	29 (19.7)	0.75	27 (24.1)	39 (23.1)	0.84
Prior hospitalization for heart failure	72 (18.1)	46 (31.3)	0.001	112 (100)	169 (100)	NA
Current heart failure at index hospitalization	399 (100)	147 (100)	NA	-	-	-
NYHA II	198 (49.6)	114 (77.6)		-	-	
NYHA III	136 (34.1)	23 (15.7)	<0.001	-	-	-
NYHA IV	65 (16.3)	10 (6.8)		-	-	

LVEF	47.1±15.9	53.2±14.3	<0.001	48.3±14.1	44.7±13.4	0.04
LVEF <40%	136 (36.8)	26 (19.4)		25 (26.3)	65 (39.4)	
LVEF 40<= - <50%	79 (21.4)	26 (19.4)	<0.001	22 (23.2)	45 (27.3)	0.02
LVEF >=50%	155 (41.9)	82 (61.2)		48 (50.5)	55 (33.3)	
Mitral regurgitation grade >=3/4	74 (20.0)	11 (8.0)	0.001	12 (12.8)	31 (19.0)	0.2
Prior myocardial infarction	176 (44.1)	43 (29.3)	0.002	41 (36.6)	67 (39.6)	0.61
Prior stroke (symptomatic)	82 (20.6)	33 (22.4)	0.63	17 (15.2)	27 (16.0)	0.86
Peripheral vascular disease	41 (10.3)	18 (12.2)	0.51	21 (18.8)	23 (13.6)	0.25
eGFR <30 mL/min/1.73m^2 or hemodialysis	76 (19.0)	25 (17.0)	0.59	38 (33.9)	46 (27.2)	0.23
eGFR <30 mL/min/1.73m^2, without hemodialysis	43 (10.8)	14 (9.5)	0.67	10 (8.9)	25 (14.8)	0.15
Hemodialysis	33 (8.3)	11 (7.5)	0.76	28 (25.0)	21 (12.4)	0.007
Atrial fibrillation	71 (17.8)	17 (11.6)	0.08	16 (14.3)	26 (15.4)	0.8
Anemia (Hemoglobin <11.0 g/dL)	126 (31.6)	36 (24.5)	0.11	37 (33.0)	60 (35.5)	0.67
Thrombocytopenia (Platelet <100 × 10^9/L)	13 (3.3)	10 (6.8)	0.07	2 (1.8)	2 (1.2)	0.68
WBC (× 10^3 cells/μL)	7.1 (5.7-9.3)	6.3 (5.0-7.7)	<0.001	6.3 (5.2-7.7)	5.7 (5.0-6.9)	0.02
CRP (mg/dL)	0.50 (0.20-2.12)	0.23 (0.10-0.73)	<0.001	0.25 (0.10-0.76)	0.19 (0.07-0.60)	0.14
Chronic obstructive pulmonary disease	20 (5.0)	8 (5.4)	0.84	7 (6.2)	19 (11.2)	0.16
Liver cirrhosis	14 (3.5)	6 (4.1)	0.75	2 (1.8)	2 (1.2)	0.68
Malignancy	49 (12.3)	13 (8.8)	0.26	13 (11.6)	21 (12.4)	0.84
Active malignancy	13 (3.3)	1 (0.7)	0.09	4 (3.6)	5 (3.0)	0.78
Severe frailty[*]	45 (11.3)	4 (2.7)	0.002	6 (5.4)	5 (3.0)	0.31
Surgical ineligibility[†]	43 (10.8)	-	-	11 (9.8)	-	-
(B) Procedural characteristics						
Number of target lesions or anastomoses	2.0±1.0	3.4±0.9	<0.001	2.1±1.0	3.5±0.9	<0.001
Target of proximal LAD	254 (63.7)	122 (83.0)	<0.001	72 (64.3)	153 (90.5)	<0.001
Target of chronic total occlusion	93 (23.3)	65 (44.2)	<0.001	31 (27.7)	74 (43.8)	0.006
Emergency procedure	23 (5.8)	12 (8.2)	0.31	4 (3.6)	5 (3.0)	0.78

3-vessel disease	318 (79.7)	88 (59.9)	<0.001	92 (82.1)	115 (68.1)	0.009
LMCA disease	81 (20.3)	59 (40.1)	<0.001	20 (17.9)	54 (32.0)	0.009
Isolated LMCA	6 (1.5)	0 (0)		1 (0.9)	0 (0)	
LMCA + 1-vessel disease	14 (3.5)	0 (0)	<0.001	5 (4.5)	0 (0)	<0.001
LMCA + 2-vessel disease	25 (6.3)	18 (12.2)		5 (4.5)	6 (3.6)	
LMCA + 3-vessel disease	36 (9.0)	41 (27.9)		9 (8.0)	48 (28.4)	
SYNTAX score	25 (19-32)	31 (25-37)	<0.001	26 (21-32)	32 (24-37)	<0.001
Low <23	147 (37.1)	19 (16.4)		38 (34.2)	26 (19.4)	
Intermediate 23-32	154 (38.9)	50 (43.1)	<0.001	51 (46.0)	46 (34.3)	<0.001
High >=33	95 (24.0)	47 (40.5)		22 (19.8)	62 (46.3)	
Total number of stents	2 (2-4)	-	-	2 (1-4)	-	-
Total stent length (mm)	53 (32-86)	-	-	52 (30-89)	-	-
Stent use	391 (98.0)	-	-	107 (95.5)	-	-
DES use	371 (93.0)	-	-	101 (90.2)	-	-
New-generation DES use	364 (91.2)	-	-	99 (88.4)	-	-
IVUS or OCT use	329 (82.5)	-	-	95 (84.8)	-	-
Internal thoracic artery graft use	-	141 (95.9)	-	-	168 (99.4)	-
Off pump surgery	-	99 (67.3)	-	-	87 (51.5)	-
Interval from hospitalization to index procedure (days)	9 (1-16)	3 (1-4)	<0.001	1 (1-3)	3 (1-5)	<0.001
(C) Baseline medications						
Antiplatelet therapy						
Thienopyridine	398 (99.7)	39 (26.5)	<0.001	112 (100)	37 (21.9)	<0.001
Aspirin	396 (99.2)	145 (98.6)	0.51	111 (99.1)	165 (97.6)	0.36
Cilostazol	13 (3.3)	9 (6.1)	0.13	4 (3.6)	2 (1.2)	0.18
Other medications						
Statins	283 (70.9)	98 (66.7)	0.34	76 (67.9)	92 (54.4)	0.02

Beta-blockers	206 (51.6)	87 (59.2)	0.12	69 (61.6)	84 (49.7)	0.0498
ACE-I/ARB	284 (71.2)	46 (31.3)	<0.001	84 (75.0)	65 (38.5)	<0.001
Calcium channel blockers	147 (36.8)	40 (27.2)	0.04	43 (38.4)	64 (37.9)	0.93
Oral anticoagulants	75 (18.8)	56 (38.1)	<0.001	19 (17.0)	101 (59.8)	<0.001
Proton pump inhibitors or histamine type-2 receptor blockers	322 (80.7)	141 (95.9)	<0.001	84 (75.0)	157 (92.9)	<0.001

Continuous variables were expressed as mean ± standard deviation, or median (interquartile range). Categorical variables were expressed as number (percentage). Values were missing for LVEF in 63 patients, for mitral regurgitation in 62 patients, and for SYNTAX score in 70 patients.

*Severe frailty was regarded as present when the inability to perform usual activities of daily living was documented in the hospital charts.

†Surgical ineligibility was regarded as present when the term such as “contraindicated for surgery” or “too high risk for surgery” were documented in hospital charts

Abbreviations are as in Table S2.

Table S6. Survival Outcomes in Patients with 3VD.

Subgroups	PCI N of patients with event / N of patients at risk (Cumulative 5-year incidence)	CABG	Crude HR [95% CI]	P value	Adjusted HR [95% CI]	P value	P value for interaction
All-cause death							
With heart failure	162/410 (36.3%)	55/203 (21.9%)	1.60 [1.18-2.19]	0.003	1.71 [1.17-2.51]	0.006	0.4
Without heart failure	261/1337 (15.0%)	82/575 (10.2%)	1.35 [1.06-1.74]	0.02	1.23 [0.89-1.71]	0.21	
Cardiovascular death							
With heart failure	99/410 (23.7%)	38/203 (15.4%)	1.41 [0.98-2.07]	0.07	1.60 [1.00-2.61]	0.048	0.17
Without heart failure	111/1337 (6.4%)	50/575 (7.1%)	0.95 [0.68-1.33]	0.76	0.84 [0.54-1.32]	0.46	
Non-cardiovascular death							
With heart failure	63/410 (16.5%)	17/203 (7.6%)	2.02 [1.21-3.56]	0.006	1.84 [1.10-3.27]*	0.02	0.95
Without heart failure	150/1337 (9.2%)	32/575 (3.4%)	1.97 [1.36-2.93]	<0.001	1.93 [1.33-2.88]*	<0.001	

Number of patients with event was counted throughout the entire follow-up period, while the cumulative incidence was estimated at 5 years.

The effects of PCI relative to CABG for the outcome measures were estimated throughout the entire follow-up period by the Cox proportional hazard models, and were expressed as HRs and their 95%CIs. The adjusted HRs were estimated by the multivariable Cox proportional hazard models adjusting for the 26 clinically relevant factors listed in Table 1. *For the outcome measures of number of patients with event less than 100 in either heart failure or non-heart failure stratum, we selected parsimonious models with 7 risk-adjusting variables (age>=75, men, diabetes mellitus, prior myocardial infarction, prior stroke, eGFR <30 mL/min/1.73m^2 or hemodialysis, and severe frailty).

CABG=coronary artery bypass grafting; CI=confidence interval; HR=hazard ratio; PCI=percutaneous coronary intervention; 3VD=three-vessel coronary artery disease.

Table S7. Survival Outcomes in Patients with LMCAD.

Subgroups	PCI / CABG N of patients with event / N of patients at risk (Cumulative 5-year incidence)		Crude HR [95% CI]	P value	Adjusted HR [95% CI]	P value	P value for interaction
All-cause death							
With heart failure	47/101 (43.6%)	27/113 (22.6%)	2.30 [1.44-3.75]	<0.001	2.40 [1.45-4.04]	0.001	0.001
Without heart failure	47/282 (14.4%)	62/359 (16.1%)	0.87 [0.59-1.27]	0.48	0.81 [0.55-1.19]	0.28	
Cardiovascular death							
With heart failure	21/101 (21.2%)	10/113 (9.0%)	2.83 [1.36-6.30]	0.005	2.96 [1.35-6.90]	0.007	0.001
Without heart failure	14/282 (3.9%)	27/359 (6.7%)	0.60 [0.31-1.13]	0.11	0.52 [0.26-0.99]	0.047	
Non-cardiovascular death							
With heart failure	26/101 (28.5%)	17/113 (15.0%)	2.00 [1.09-3.75]	0.03	2.02 [1.05-3.98]	0.04	0.08
Without heart failure	33/282 (11.0%)	35/359 (10.1%)	1.08 [0.67-1.74]	0.75	1.04 [0.64-1.69]	0.88	

Number of patients with event was counted throughout the entire follow-up period, while the cumulative incidence was estimated at 5 years.

The effects of PCI relative to CABG for the outcome measures were estimated throughout the entire follow-up period by the Cox proportional hazard models, and were expressed as HRs and their 95%CIs. In the multivariable Cox proportional hazard models, we used the parsimonious models with 7 risk-adjusting variables (age>=75, men, diabetes mellitus, prior myocardial infarction, prior stroke, eGFR <30 ml/min/1.73m^2 or hemodialysis, and severe frailty) due to the small numbers of patients with event.

CABG=coronary artery bypass grafting; CI=confidence interval; HR=hazard ratio; LMCAD=left main coronary artery disease; PCI=percutaneous coronary intervention.

Table S8. Survival Outcomes After Excluding Patients with Surgical Ineligibility.

Subgroups	PCI	CABG	Crude HR [95% CI]	P value	Adjusted HR [95% CI]	P value	P value for interaction
	N of patients with event / N of patients at risk (Cumulative 5-year incidence)						
All-cause death							
With heart failure	178/457 (35.7%)	82/316 (22.1%)	1.63 [1.26-2.13]	<0.001	1.83 [1.31-2.56]	<0.001	0.03
Without heart failure	296/1553 (14.7%)	144/934 (12.4%)	1.17 [0.96-1.43]	0.12	1.04 [0.81-1.36]	0.74	
Cardiovascular death							
With heart failure	102/457 (22.0%)	48/316 (13.3%)	1.60 [1.14-2.27]	0.006	1.90 [1.23-2.98]	0.004	0.007
Without heart failure	120/1553 (5.8%)	77/934 (7.0%)	0.90 [0.67-1.20]	0.45	0.73 [0.51-1.06]	0.1	
Non-cardiovascular death							
With heart failure	76/457 (17.5%)	34/316 (10.2%)	1.67 [1.13-2.54]	0.01	1.63 [0.98-2.76]	0.06	0.52
Without heart failure	176/1553 (9.4%)	67/934 (5.8%)	1.48 [1.13-1.98]	0.005	1.46 [1.02-2.13]	0.04	

Surgical ineligibility was regarded as present when the term such as “contraindicated for surgery” or “too high risk for surgery” were documented in hospital charts. Number of patients with event was counted throughout the entire follow-up period, while the cumulative incidence was estimated at 5 years. The effects of PCI relative to CABG for the outcome measures were estimated throughout the entire follow-up period by the Cox proportional hazard models, and were expressed as HRs and their 95%CIs. The adjusted HRs were estimated by the multivariable Cox proportional hazard models adjusting for the 26 clinically relevant factors listed in Table 1.

CABG=coronary artery bypass grafting; CI=confidence interval; HR=hazard ratio; PCI=percutaneous coronary intervention.

Table S9. Survival Outcomes in the Model Including Syntax Score as a Continuous Explanatory Variable.

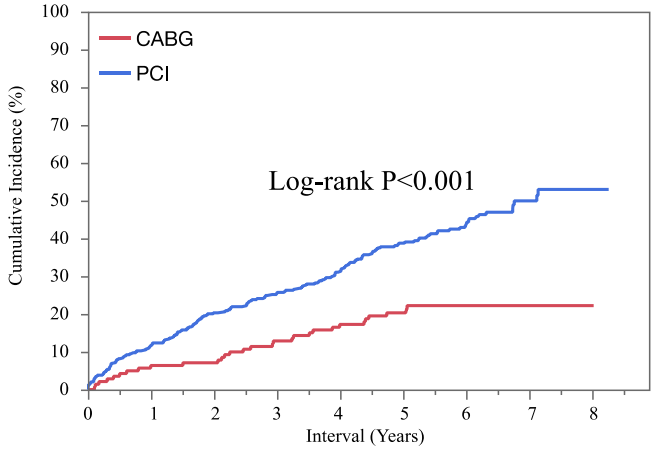
Subgroups	PCI / CABG N of patients with event / N of patients at risk (Cumulative 5-year incidence)		Crude HR [95% CI]	P value	Adjusted HR [95% CI]	P value	P value for interaction
All-cause death							
With heart failure	207/507 (37.5%)	68/250 (22.9%)	1.66 [1.27-2.20]	<0.001	1.76 [1.26-2.50]	0.001	0.01
Without heart failure	305/1603 (15.0%)	117/769 (12.6%)	1.18 [0.96-1.47]	0.12	1.09 [0.82-1.45]	0.54	
Cardiovascular death							
With heart failure	119/507 (23.1%)	43/250 (14.7%)	1.50 [1.07-2.16]	0.02	1.61 [1.04-2.50]	0.03	0.01
Without heart failure	124/1603 (6.0%)	61/769 (6.8%)	0.93 [0.69-1.27]	0.64	0.84 [0.56-1.25]	0.39	
Non-cardiovascular death							
With heart failure	88/507 (18.6%)	25/250 (9.6%)	1.93 [1.26-3.07]	<0.001	1.93 [1.13-3.41]	0.02	0.16
Without heart failure	181/1603 (9.5%)	56/769 (6.2%)	1.46 [1.09-1.98]	0.01	1.39 [0.94-2.07]	0.1	

Syntax score was available in 3129 (92.6%) patients. Number of patients with event was counted throughout the entire follow-up period, while the cumulative incidence was estimated at 5 years. The effects of PCI relative to CABG for the outcome measures were estimated throughout the entire follow-up period by the Cox proportional hazard models, and were expressed as HRs and their 95%CIs. The adjusted HRs were estimated by the multivariable Cox proportional hazard models adjusting for the 26 clinically relevant factors listed in Table 1.

CABG=coronary artery bypass grafting; CI=confidence interval; HR=hazard ratio; PCI=percutaneous coronary intervention

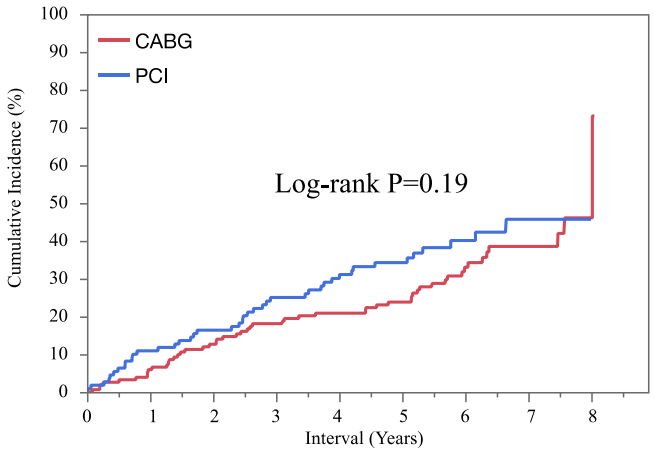
Figure S1. Kaplan-Meier Event Curves for All-cause Death in Patients (A) With Current Heart Failure at Index Hospitalization, and (B) With Prior Hospitalization for Heart Failure Only.

(A) With current heart failure at index hospitalization



Interval	0 day	30 days	1 year	3 years	5 years
CABG group					
N of patients with event		0	9	18	28
N of patients at risk	147	143	133	121	88
Cumulative incidence		0.0%	6.4%	12.9%	20.3%
PCI group					
N of patients with event		8	46	97	143
N of patients at risk	399	386	338	275	191
Cumulative incidence		2.0%	11.8%	25.4%	38.7%

(B) With prior hospitalization for heart failure only

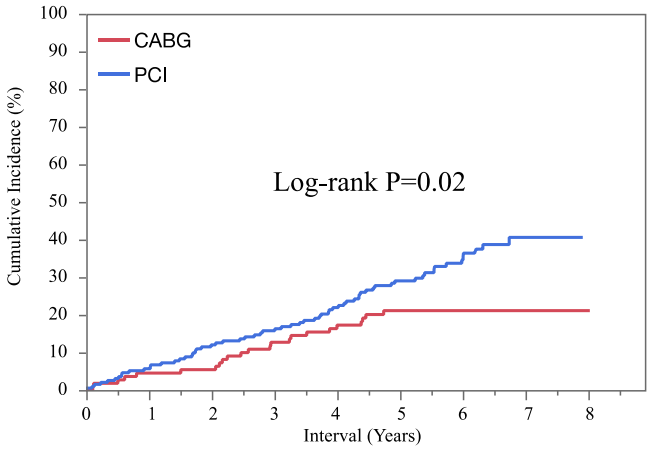


Interval	0 day	30 days	1 year	3 years	5 years
CABG group					
N of patients with event		0	9	27	35
N of patients at risk	169	163	142	121	100
Cumulative incidence		0.0%	5.9%	18.1%	23.8%
PCI group					
N of patients with event		2	12	27	36
N of patients at risk	112	110	99	78	53
Cumulative incidence		1.8%	10.9%	25.0%	34.2%

CABG=coronary artery bypass grafting; PCI=percutaneous coronary intervention.

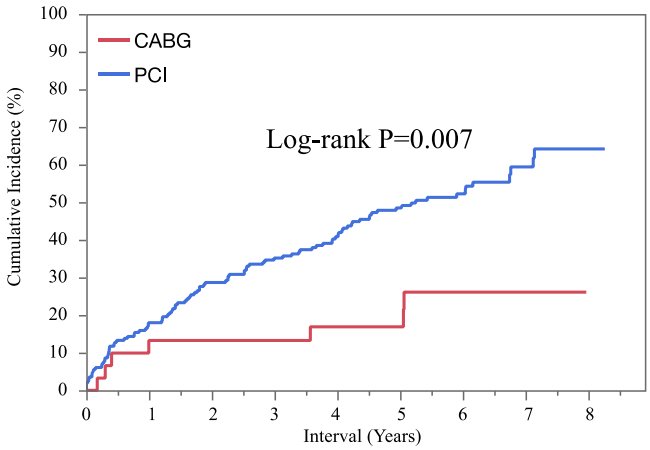
Figure S2. Kaplan-Meier Event Curves for All-cause Death in Patients (A) With NYHA class II, and (B) With NYHA class III or IV.

(A) All-cause death (NYHA II)



Interval	0 day	30 days	1 year	3 years	5 years
CABG group					
N of patients with event		0	5	14	23
N of patients at risk	114	112	107	97	69
Cumulative incidence		0.0%	4.5%	12.7%	21.1%
PCI group					
N of patients with event		1	11	30	53
N of patients at risk	198	196	181	155	110
Cumulative incidence		0.5%	5.7%	15.8%	29.0%

(B) All-cause death (NYHA III or IV)



Interval	0 day	30 days	1 year	3 years	5 years
CABG group					
N of patients with event		0	4	4	5
N of patients at risk	33	31	27	24	19
Cumulative incidence		0.0%	13.2%	13.2%	16.9%
PCI group					
N of patients with event		7	35	67	90
N of patients at risk	201	191	158	120	81
Cumulative incidence		3.5%	18.0%	35.1%	48.5%

CABG=coronary artery bypass grafting; NYHA=New York Heart Association; PCI=percutaneous coronary intervention.