Comparison of Five-Year Outcomes of Coronary Artery Bypass Grafting Versus Percutaneous Coronary Intervention in Patients With Left Ventricular Ejection Fractions ≤50% Versus >50% (from the CREDO-Kyoto PCI/CABG Registry Cohort-2)

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Coronary heart disease is a major risk factor for left ventricular (LV) systolic dysfunction. However, limited data are available regarding long-term benefits of percutaneous coronary intervention (PCI) in the era of drug-eluting stent or coronary artery bypass grafting (CABG) in patients with LV systolic dysfunction with severe coronary artery disease. We identified 3,584 patients with 3-vessel and/or left main disease of 15,939 patients undergoing first myocardial revascularization enrolled in the CREDO-Kyoto PCI/CABG Registry Cohort-2. Of them, 2,676 patients had preserved LV systolic function, defined as an LV ejection fraction (LVEF) of >50% and 908 had impaired LV systolic function (LVEF ≤50%). In patients with preserved LV function, 5-year outcomes were not different between PCI and CABG regarding propensity score–adjusted risk of all-cause and cardiac deaths. In contrast, in patients with impaired LV systolic function, the risks of all-cause and cardiac deaths after PCI were significantly greater than those after CABG (hazard ratio 1.49, 95% confidence interval 1.04 to 2.14, p = 0.03 and hazard ratio 2.39, 95% confidence interval 1.43 to 3.98, p <0.01). In both patients with moderate (35% < LVEF ≤ 50%) and severe (LVEF ≤35%) LV systolic dysfunction, the risk of cardiac death after PCI was significantly greater than that after CABG (hazard ratio 2.25, 95% confidence interval 1.15 to 4.40, p = 0.02 and hazard ratio 4.42, 95% confidence interval 1.48 to 13.24, p = 0.01). Similarly, the risk of all-cause death tended to be greater after PCI than after CABG in both patients with moderate and severe LV systolic dysfunction without significant interaction (hazard ratio 1.57, 95% confidence interval 0.96 to 2.56, p = 0.07 and hazard ratio 1.42, 95% confidence interval 0.71 to 2.82, p = 0.32; interaction p = 0.91). CABG was associated with better 5-year survival outcomes than PCI in patients with impaired LV systolic function (LVEF ≤50%) with complex coronary disease in the era of drug-eluting stents. In both patients with moderate (35% < LVEF ≤ 50%) and severe (LVEF ≤35%) LV systolic dysfunction, CABG tended to have better survival outcomes than PCI. (Am J Cardiol 2014;■:■–■)

Coronary artery disease is the most common cause of left ventricular (LV) systolic dysfunction and has increased with the growing incidence of associated mortality.[1–3] Several studies have shown improved outcomes after coronary artery bypass grafting (CABG) in patients with low LV ejection fraction (LVEF).[4,5] However, limited reports are available regarding the benefits of percutaneous coronary intervention (PCI) in patients with LV systolic dysfunction. Furthermore, in the drug-eluting stent (DES) era, few reports have compared the clinical outcomes of CABG and DES implantation in patients with LV systolic dysfunction, particularly in more complex coronary lesions such as 3-vessel or left main disease. In the present study, therefore, we mainly compared the 5-year outcomes between PCI and CABG in patients with preserved LV systolic function (LVEF >50%) or impaired LV systolic function (LVEF ≤50%) accompanying with 3-vessel and/or left main disease using a large observational database in Japan. As a subanalysis, we compared the outcomes between PCI and CABG in patients with

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See page 7 for disclosure information.

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moderate (35% < LVEF ≤ 50%) and severe (LVEF ≤35%) LV systolic dysfunction.

Methods

The Coronary REvascularization Demonstrating Outcome Study in Kyoto (CREDO-Kyoto) PCI/CABG Registry Cohort-2 is a physician-initiated, noncompany-sponsored, multicenter registry that enrolled consecutive patients undergoing first coronary revascularization in the 26 centers in Japan from January 2005 through December 2007.[6,7] The relevant ethics committees in all 26 participating centers (see Supplementary Data A) approved the research protocol. Because of retrospective enrollment, written informed consent from the patients was waived. However, patients who refused participation in the study when contacted for follow-up were excluded.

The study design and patient enrollment in the registry have been described in detail previously.[6] Of the 15,939 patients enrolled in the registry, patients who refused study participation, who had concomitant noncoronary surgery, who had acute myocardial infarction (MI), and who had single- or double-vessel disease were excluded. For the comparison of PCI with CABG, we selected 3,982 patients with 3-vessel and/or left main disease. Excluding 298 patients (10%) without LVEF data, the present study population consisted of 3,584 patients with 3-vessel and/or left main disease with known LVEF. There were 2,676 patients with preserved LV systolic function, defined as an LVEF of >50%, and 908 patients with impaired LV systolic function (LVEF ≤50%).

LVEF was measured by echocardiography or LV cine angiography. M-mode and/or 2-dimensional echocardiography was performed by experienced operators in each institution. M-mode LVEF was calculated using the Teichholz correction.[8] Two-dimensional echocardiographic LVEF was also evaluated by the Simpson biplane method of discs with manual planimetry of the endocardial border in end-diastolic (largest) and end-systolic (smallest) frames.[9] LV cine angiography was obtained in either a single-plane right anterior oblique view or biplane right and left anterior oblique views. LVEF was calculated using the built-in programs.

Demographic, angiographic, and procedural data were collected from hospital charts according to the prespecified definitions by experienced research coordinators in an independent research organization (Research Institute for Production Development, Kyoto, Japan; see Supplementary Data B). Definitions for clinical characteristics are presented in the Supplementary Data C.

The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score was calculated using the SYNTAX score calculator (available at: *http://www.syntaxscore.com*) by a dedicated SYNTAX score committee (see Supplementary Data D) in a blinded fashion to the clinical data. Intraobserver and interobserver variabilities of the SYNTAX score calculation in our group were previously reported.[10] Cut-off values for SYNTAX score tertiles (low <23, intermediate 23 to 33, and high ≥33) were defined according to the analysis in the SYNTAX trial.[11,12]

Collection of follow-up information was conducted mainly through review of inpatient and outpatient hospital charts by clinical research coordinators in the independent research organization. Additional follow-up information was collected through contact with patients, relatives, and/or referring physicians by sending mail with questions on vital status and additional hospitalizations. Death, MI, stent thrombosis, and stroke were adjudicated by the clinical event committee (see Supplementary Data E).

The primary outcome measure for the present analysis was death from any cause. Other prespecified end points included cardiac death, sudden death, stroke, MI, and any coronary revascularization. Death was regarded as cardiac in origin unless obvious noncardiac causes could be identified. Any death during the index hospitalization for coronary revascularization was regarded as cardiac death. Sudden death was defined as an unexpected death in previously stable patients. MI was defined according to the definition in the Arterial Revascularization Therapy Study.[13] Stroke during follow-up was defined as an ischemic or a hemorrhagic stroke requiring hospitalization with symptoms lasting >24 hours. Scheduled staged coronary revascularization procedures performed within 3 months of the initial procedure were not regarded as follow-up events but were included in the index procedure.

All continuous variables are expressed as the mean ± SD. Differences in baseline characteristics between the 2 groups were examined by the unpaired *t* test and Fisher's exact test. Cumulative incidence was estimated by the Kaplan-Meier method, and differences were assessed using the log-rank test. Propensity scores, which were the probabilities that a patient would undergo PCI, were estimated with multivariate logistic regression analyses including age, gender, body mass index, hypertension, dyslipidemia, diabetes mellitus, current smoker, heart failure, mitral regurgitation grade 3 or 4, previous MI, previous stroke, peripheral arterial disease, atrial fibrillation, chronic kidney disease, hemodialysis, anemia, platelet count, chronic obstructive lung disease, liver cirrhosis, malignancy, emergency procedure, number of diseased vessels, left main disease, target chronic total occlusion, target proximal left anterior descending coronary artery, and SYNTAX score as the covariates. These variables were consistent with previous reports from the present registry.[7,14] Continuous variables, except age, were dichotomized using clinically meaningful reference values or median values. We incorporated the 26 participating centers in the propensity score estimation as the stratification variable. The hazard ratios of PCI compared with those of CABG were estimated by the stratified Cox proportional hazard models; the models included PCI or CABG as the covariate and were stratified by the quartiles of propensity score and institute to adjust for confounding. Effects of PCI compared with those of CABG for individual end points are expressed as hazard ratios with 95% confidence intervals. All reported p values were 2-sided, and p values <0.05 were regarded as statistically significant.

All analyses were conducted by a statistician using SAS software, version 9.3 (SAS Institute Inc, Cary, NC), and S-Plus, version 7.0 (Insightful Corp, Seattle, Washington). The investigators had full access to the data and take responsibility for its integrity. All the investigators have read and agreed to the manuscript as written.

Results

Baseline clinical characteristics comparing the PCI with CABG groups in patients with preserved and impaired

Table 1
Baseline characteristics in patients with three-vessel and/or left main disease with preserved left ventricular systolic function (left ventricular ejection fraction >50%)

Variable	PCI n = 1432	CABG n = 1244	p Value
Age (years)	69.7 ± 9.7	68.5 ± 8.7	<0.001
>75	495 (35%)	338 (27%)	<0.001
Men	998 (70%)	914 (73%)	0.03
Ejection fraction (%)	65.0 ± 7.8	65.0 ± 8.5	0.89
Previous myocardial infarction	152 (11%)	178 (14%)	0.004
Heart failure	137 (10%)	135 (11%)	0.27
Atrial fibrillation	94 (7%)	229 (18%)	<0.001
Mitral regurgitation grade 3/4	52 (4%)	24 (2%)	0.08
Body mass index (kg/m^2)	24.0 ± 3.5	23.6 ± 3.1	0.02
>25	498 (35%)	390 (31%)	0.06
Hypertension	1236 (86%)	1057 (85%)	0.32
Diabetes mellitus	660 (46%)	627 (50%)	0.03
On insulin therapy	170 (12%)	197 (16%)	0.003
Current smoker	342 (24%)	280 (23%)	0.40
Previous stroke	207 (14%)	159 (13%)	0.21
Peripheral artery disease	170 (12%)	151 (12%)	0.83
Estimated glomerular filtration rate (ml/min/1.73 m^2)	62.3 ± 21.8	58.1 ± 23.7	<0.001
Hemodialysis	50 (3%)	67 (5%)	0.02
Anemia (hemoglobin <11.0 g/dl)	182 (13%)	220 (18%)	<0.001
Platelet count <100 × 10^9/L	22 (2%)	28 (2%)	0.17
Chronic obstructive pulmonary disease	40 (3%)	26 (2%)	0.24
Liver cirrhosis	47 (3%)	38 (3%)	0.74
Malignancy	178 (12%)	139 (11%)	0.32
Procedural characteristics			
Number of target coronary narrowings or anastomoses	2.0 ± 1.0	3.3 ± 1.1	<0.001
Emergency procedure	42 (3%)	40 (3%)	0.67
Percutaneous coronary intervention			
Stent use	1370 (96%)	—	n/a
Drug-eluting stent use	1039 (73%)	—	n/a
Coronary artery bypass grafting			
Left internal thoracic artery use	—	1202 (97%)	n/a
Bilateral internal thoracic artery use	—	381 (31%)	n/a
Off-pump coronary artery bypass grafting	—	832 (67%)	n/a
Number of coronary arteries narrowed:			
3 (Without left main disease)	1220 (85%)	783 (63%)	<0.001
Left main	212 (15%)	461 (37%)	<0.001
Proximal left anterior descending artery	879 (61%)	1073 (86%)	<0.001
Chronic total occlusion	251 (18%)	460 (37%)	<0.001
SYNTAX score	23.3 ± 9.3	29.6 ± 11.6	<0.001
Low (<23)	708 (50%)	318 (29%)	<0.001
Intermediate (23–32)	485 (35%)	401 (36%)	
High (≥33)	211 (15%)	384 (35%)	

Data are presented as mean ± SD or number of patients and percentage.

LV systolic functions are listed in Tables 1 and 2. LVEF was not different between PCI and CABG in both patients with preserved and impaired LV systolic functions. The SYNTAX score was higher in the CABG group in both patients with preserved and impaired LV systolic functions. The mean follow-up period was 4.74 years (median 5.12 years). Completeness of the follow-up for 3, 4, and 5 years was 95.8%, 94.4%, and 70.9%, respectively.

Kaplan-Meier analysis showed that cumulative incidence of all-cause death at 5 years was not different between PCI and CABG in patients with preserved LV systolic function (Figure 1). However, in patients with impaired LV systolic function, the cumulative incidence of all-cause death after PCI was significantly greater than that after CABG. Similarly, cumulative incidences of cardiac death and readmission for heat failure were not different between PCI and CABG in patients with preserved LV systolic function but were significantly greater after PCI in patients with impaired LV systolic function (Figure 1).

In patients with preserved LV systolic function, propensity score–adjusted risk of all-cause death, cardiac death, sudden death, readmission for heart failure, and stroke was not different between PCI and CABG (Table 3). The risk of MI and repeat revascularization after PCI was greater than that after CABG. In contrast, in patients with impaired LV systolic function, all-cause mortality after PCI

Table 2
Baseline characteristics in patients with three-vessel and/or left main disease with impaired left ventricular systolic function (left ventricular ejection fraction ≤50%)

Variable	PCI n = 464	CABG n = 444	p Value
Age (years)	70.1 ± 10.4	67.8 ± 9.7	<0.001
>75	186 (40%)	128 (29%)	<0.001
Men	354 (76%)	347 (78%)	0.50
Ejection fraction (%)	38.7 ± 8.7	39.2 ± 8.3	0.40
Previous myocardial infarction	202 (44%)	201 (45%)	0.60
Heart failure	251 (54%)	224 (50%)	0.27
Atrial fibrillation	57 (12%)	77 (17%)	0.02
Mitral regurgitation grade 3/4	66 (14%)	27 (6%)	<0.001
Body mass index (kg/m^2)	23.4 ± 3.5	22.7 ± 3.3	<0.001
>25	141 (30%)	100 (23%)	0.007
Hypertension	415 (89%)	378 (85%)	0.05
Diabetes mellitus	264 (57%)	249 (56%)	0.80
On insulin therapy	75 (16%)	94 (21%)	0.04
Current smoker	122 (26%)	134 (30%)	0.19
Previous stroke	84 (18%)	71 (16%)	0.40
Peripheral artery disease	60 (13%)	73 (16%)	0.13
Estimated glomerular filtration rate (ml/min/1.73 m^2)	52.6 ± 25.3	51.2 ± 24.6	0.40
Hemodialysis	51 (11%)	43 (10%)	0.52
Anemia (hemoglobin <11.0 g/dl)	104 (22%)	98 (22%)	0.90
Platelet count <100 × 10^9/L	7 (2%)	10 (2%)	0.41
Chronic obstructive pulmonary disease	17 (4%)	12 (3%)	0.41
Liver cirrhosis	12 (3%)	12 (3%)	0.91
Malignancy	38 (8%)	39 (9%)	0.75
Procedural characteristics			
Number of target coronary narrowings or anastomoses	2.1 ± 1.0	3.4 ± 1.0	<0.001
Emergency procedure	12 (3%)	17 (4%)	0.29
Percutaneous coronary intervention			
Stent use	420 (91%)	—	n/a
Drug-eluting stent use	347 (75%)	—	n/a
Coronary artery bypass grafting			
Left internal thoracic artery use	—	430 (97%)	n/a
Bilateral internal thoracic artery use	—	116 (26%)	n/a
Off-pump coronary artery bypass grafting	—	236 (53%)	n/a
Number of coronary artery narrowed:			
3 (Without left main disease)	389 (84%)	318 (72%)	<0.001
Left main	75 (16%)	126 (28%)	<0.001
Proximal left anterior descending artery	298 (64%)	403 (91%)	<0.001
Chronic total occlusion	147 (32%)	261 (59%)	<0.001
SYNTAX score	26.6 ± 9.8	32.5 ± 10.7	<0.001
Low (<23)	165 (36%)	80 (20%)	<0.001
Intermediate (23–32)	177 (39%)	133 (33%)	
High (≥33)	111 (25%)	187 (47%)	

Data presented as mean ± SD or number of patients and percentage.

was significantly greater than that after CABG. Similarly, the risk of cardiac death and sudden death after PCI was significantly higher after PCI than after CABG. The risk of stroke and MI was not different between the groups.

In both patients with moderate (35% < LVEF ≤ 50%) and severe LV systolic dysfunction (LVEF ≤35%), the risk of cardiac death was significantly greater after PCI than after CABG (Table 4). Similarly, the risk of all-cause death tended to be greater after PCI than after CABG in both patients with moderate and severe LV systolic dysfunctions without significant interaction. The risk of stroke and MI was not different between the groups in both patients with moderate and severe LV systolic dysfunctions.

Discussion

Although our study involved retrospective analyses, it is one of a few studies to report the clinical outcomes of patients with LV systolic dysfunction treated with PCI versus CABG in the DES era. In the present study, we compared the 5-year outcomes between PCI and CABG in Japanese patients with LV systolic dysfunction accompanying with 3-vessel and/or left main disease. We have reported the midterm outcomes of PCI versus CABG with a history of heart failure.[15] However, the study was insufficient because the study population included both patients with systolic and diastolic dysfunctions with less-complex coronary disease.

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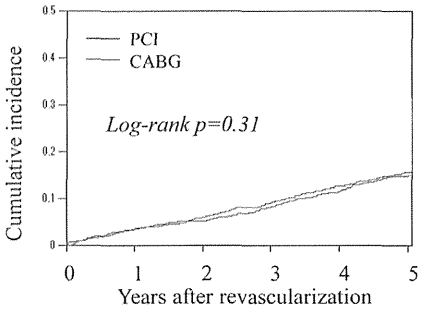
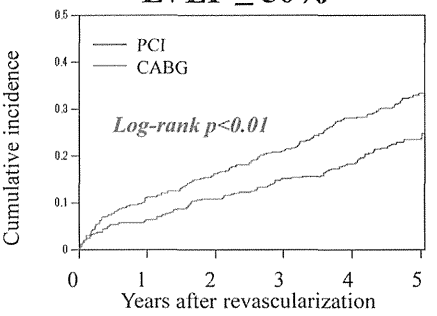


Interval (years)	0	1	3	5
PCI group				
No. of patients with events		50	128	210
No. of patients at risk	1432	1362	1260	773
Cumulative incidence (%)		3.5	9.1	15.6
CABG group				
No. of patients with events		42	98	174
No. patients at risk	1244	1172	1093	722
Cumulative incidence (%)		3.4	8.1	14.8



Interval (years)	0	1	3	5
PCI group				
No. of patients with events		51	95	144
No. of patients at risk	464	403	345	192
Cumulative incidence (%)		11.1	21.0	33.2
CABG group				
No. of patients with events		28	64	96
No. patients at risk	444	394	349	230
Cumulative incidence (%)		6.5	15.1	23.4

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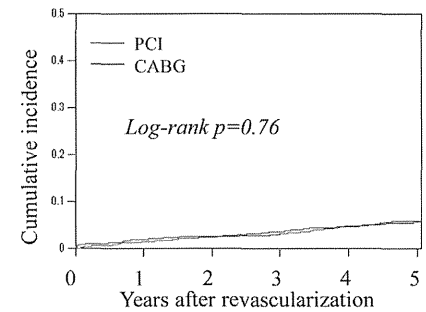
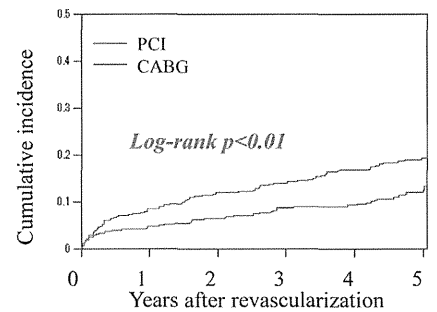


Interval (years)	0	1	3	5
PCI group				
No. of patients with events		18	40	71
No. of patients at risk	1432	1362	1260	773
Cumulative incidence (%)		1.3	3.0	5.5
CABG group				
No. of patients with events		22	42	65
No. patients at risk	1244	1172	1093	722
Cumulative incidence (%)		1.8	3.5	5.7



Interval (years)	0	1	3	5
PCI group				
No. of patients with events		39	62	81
No. of patients at risk	464	403	345	192
Cumulative incidence (%)		8.6	14.0	19.4
CABG group				
No. of patients with events		20	36	47
No. patients at risk	444	394	349	230
Cumulative incidence (%)		4.6	8.7	12.0

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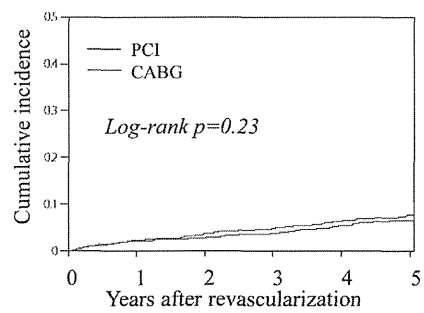
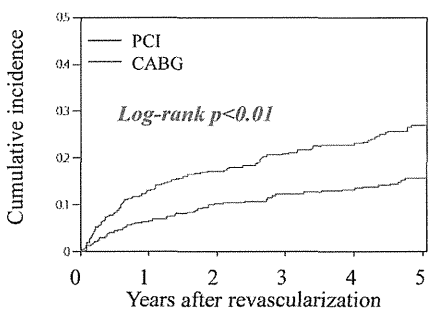


Interval (years)	0	1	3	5
PCI group				
No. of patients with events		31	66	97
No. of patients at risk	1432	1336	1212	721
Cumulative incidence (%)		2.2	4.9	7.6
CABG group				
No. of patients with events		26	44	72
No. patients at risk	1244	1150	1064	689
Cumulative incidence (%)		2.2	3.7	6.4



Interval (years)	0	1	3	5
PCI group				
No. of patients with events		56	87	106
No. of patients at risk	464	356	290	158
Cumulative incidence (%)		13.0	20.9	27.0
CABG group				
No. of patients with events		27	49	59
No. patients at risk	444	371	314	200
Cumulative incidence (%)		6.6	12.4	15.6

Figure 1. Five-year Kaplan-Meier curves comparing PCI with CABG in patients with preserved (LV ejection fraction >50%) and impaired (≤50%) LV systolic function. *(A)* All-cause death. *(B)* Cardiac death. *(C)* Readmission for heart failure.

Table 3
Propensity score–adjusted hazard ratios stratified by left ventricular ejection fraction in patients with three-vessel and/or left main disease

Variable	Number of Patients (Event/Total)		Comparison of PCI vs. CABG				
	PCI	CABG	Hazard Ratio*	95% Confidence Interval		p	Interaction p
Death							
LVEF >50%	24 (17%)	197 (16%)	0.98	0.76	1.28	0.91	0.12
LVEF ≤50%	155 (33%)	113 (25%)	1.49	1.04	2.14	0.03	
Cardiac death							
LVEF >50%	86 (6%)	72 (6%)	0.85	0.55	1.32	0.47	0.06
LVEF ≤50%	87 (19%)	53 (12%)	2.39	1.43	3.98	<0.01	
Sudden death							
LVEF >50%	37 (3%)	22 (2%)	1.77	0.87	3.61	0.12	0.61
LVEF ≤50%	28 (6%)	15 (3%)	2.45	1.01	5.95	0.05	
Readmission for heart failure							
LVEF >50%	108 (8%)	80 (6%)	1.39	0.92	2.09	0.11	0.24
LVEF ≤50%	113 (24%)	65 (15%)	2.22	1.42	3.46	<0.01	
Stroke							
LVEF >50%	113 (8%)	102 (8%)	0.78	0.54	1.14	0.20	0.23
LVEF ≤50%	37 (8%)	46 (10%)	0.75	0.41	1.38	0.36	
Myocardial infarction							
LVEF >50%	94 (7%)	30 (2%)	2.31	1.34	3.97	<0.01	0.32
LVEF ≤50%	36 (8%)	19 (4%)	2.20	0.96	5.04	0.06	
Any revascularization							
LVEF >50%	663 (46%)	182 (15%)	3.69	2.96	4.60	<0.01	0.07
LVEF ≤50%	189 (41%)	45 (10%)	4.42	2.87	6.81	<0.01	

Number of patients: ejection fraction >50%: PCI = 1,432, CABG = 1,244; ejection fraction ≤50%: PCI = 464, CABG = 444.
CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.
* Adjusted for age, gender, body mass index, hypertension, dyslipidemia, diabetes mellitus, current smoker, heart failure, mitral regurgitation grade 3 or 4, previous myocardial infarction, previous stroke, peripheral vascular disease, atrial fibrillation, chronic kidney disease, hemodialysis, anemia, platelet count, chronic obstructive lung disease, liver cirrhosis, malignancy, emergency procedure, number of diseased vessels, left main disease, target of chronic total occlusion, target of proximal left anterior descending coronary artery, SYNTAX score, and institute.

Thus, about 1/2 of the study population had normal LV systolic function. It is very important to obtain more consistent study population and to elucidate the long-term evidence limited to LV systolic dysfunction with more complex coronary disease; therefore, we conducted the present study.

Large observational studies demonstrated the benefit of CABG relative to PCI in patients with LV systolic dysfunction[16–18] (Table 5). Hannan et al[16] reported from the New York Registry database that CABG relative to PCI reduced the risk of death and MI in patients with LVEF <40%. Hlatky et al revealed that the risk of 5-year death after CABG was significantly less than that after PCI (51.7% vs 44.6%; hazard ratio 0.84, 95% confidence interval 0.79 to 0.88, $p < 0.001$) in patients with heart failure.[17] The subanalysis of the APPROACH database also demonstrated the survival benefits of CABG in patients with LVEF <35%.[18] In contrast, an observational study by Yang et al[19] comparing DES versus CABG in patients with LV dysfunction demonstrated that DES implantation provides comparable long-term clinical outcomes, except for repeat revascularization, to CABG (Table 5). Similarly, meta-analyses of Hlatky et al[20] and Kunadian et al[21] could not demonstrate the long-term survival benefits of CABG compared with PCI. However, their study included less-complex coronary lesions such as single- or double-vessel disease. As shown in the final 5-year outcomes of SYNTAX trial,[22] the advantage of CABG is more evident in more complex lesions such as 3-vessel and left main disease. Therefore, when analyzing registry data comparing PCI with CABG, it may be important to target patients with LV dysfunction with complex coronary lesions to minimize patient variations.

There is a lack of strong evidence regarding revascularization treatment options in patients with moderate-to-severe LV dysfunction secondary to coronary ischemia.[23] The current American Heart Association guidelines state that CABG is reasonable (class IIa, level B) in patients with moderate LV dysfunction (LVEF 35% to 50%) and may be considered (class IIb, level B) for patients with severe LV dysfunction (LVEF <35%) without significant left main disease. There are insufficient data to make a recommendation regarding the role of PCI in patients with LV dysfunction.[24] The European guidelines state that for patients having LVEF of ≤35% with anginal or heart failure symptoms, CABG is beneficial in the presence of left main or multivessel coronary artery disease (class I, level B).[25] There is conflicting and less well-established evidence for PCI, if anatomy is suitable (class IIb, level C).

In the present study, there is a markedly increased rate of MI and repeat revascularization with the PCI group, which may influence the overall cost after revascularization. Fanari et al[26] reported that despite greater initial costs, CABG is a highly cost-effective revascularization strategy compared with PCI using DES for patients with diabetes mellitus and multivessel coronary artery disease owing to more frequent repeat revascularization and greater outpatient medication costs. Similarly, the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease trial concluded that compared with PCI,

Table 4
Propensity score–adjusted hazard ratios in patients with impaired left ventricular systolic dysfunction with three-vessel and/or left main disease

Variable	Number of Patients (Event/Total)		Comparison of PCI vs. CABG				
	PCI	CABG	Hazard Ratio*	95% Confidence Interval		p	Interaction p
Death							
35% < LVEF ≤ 50%	101 (33%)	79 (26%)	1.57	0.96	2.56	0.07	0.91
LVEF ≤35%	54 (34%)	34 (25%)	1.42	0.71	2.82	0.32	
Cardiac death							
35% < LVEF ≤ 50%	54 (18%)	37 (12%)	2.25	1.15	4.40	0.02	0.43
LVEF ≤35%	33 (21%)	16 (12%)	4.42	1.48	13.24	0.01	
Sudden death							
35% < LVEF ≤ 50%	17 (6%)	11 (4%)	2.47	0.71	8.56	0.16	0.6
LVEF ≤35%	11 (7%)	4 (3%)	4.94	0.53	46.28	0.16	
Readmission for heart failure							
35% < LVEF ≤ 50%	62 (20%)	39 (13%)	2.72	1.39	5.34	<0.01	1
LVEF ≤35%	51 (32%)	26 (19%)	1.77	0.88	3.55	0.11	
Stroke							
35% < LVEF ≤ 50%	25 (8%)	35 (11%)	0.71	0.32	1.57	0.40	0.37
LVEF ≤35%	12 (8%)	11 (8%)	0.93	0.30	2.85	0.89	
Myocardial infarction							
35% < LVEF ≤ 50%	25 (8%)	17 (6%)	2.31	0.87	6.15	0.09	0.21
LVEF ≤35%	11 (7%)	2 (1%)	2.43	0.40	14.74	0.34	
Any revascularization							
35% < LVEF ≤ 50%	129 (42%)	27 (9%)	5.42	3.00	9.80	<0.01	0.21
LVEF ≤35%	60 (38%)	18 (13%)	1.73	0.76	3.95	0.20	

Number of patients: 35% < LVEF ≤ 50%: PCI = 306, CABG = 306; LVEF ≤35%: PCI = 158, CABG = 138.
CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.
* Adjusted for age, gender, body mass index, hypertension, dyslipidemia, diabetes mellitus, current smoker, heart failure, mitral regurgitation grade 3 or 4, previous myocardial infarction, previous stroke, peripheral vascular disease, atrial fibrillation, chronic kidney disease, hemodialysis, anemia, platelet count, chronic obstructive lung disease, liver cirrhosis, malignancy, emergency procedure, number of diseased vessels, left main disease, target of chronic total occlusion, target of proximal left anterior descending coronary artery, SYNTAX score, and institute.

Table 5
Reports of coronary revascularization in patients with left ventricular systolic dysfunction (PCI vs CABG)

	Year	LVEF	Number of Patients		Stent Type	Follow-Up	Main Outcomes
			PCI	CABG			
Observational study							
Hannan (subanalysis)[16]	2008	<40%	1059	1614	DES	18 months	High mortality in PCI
Hlatky (subanalysis)[17]	2013	n/a	6940	6572	n/a	5 years	High mortality in PCI
Nagendran[18]	2013	<35%	718	718	BMS/DES	5 years	High mortality in PCI
Yang[19]	2013	<50%	141	141	DES	3 years	No difference in mortality
Meta analysis (subanalysis)							
Hlatky[20]	2009	n/a	615	551	BMS	8 years	No difference in mortality
Kunadian[21]	2012	≤40%	455	502	n/a	>1 year	No difference in mortality

BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.

CABG is associated with less repeat revascularization, better quality of life, and improved survival rate in high-risk patients.[27] Although CABG is associated with greater costs, it is probably associated with a reasonable cost per quality-adjusted life year gained in many patients. Therefore, CABG will often be a cost-effective strategy, especially in patients with high angiographic complexity and/or diabetes.[27]

There are several important limitations to this study. First and the most importantly, the observational study design precluded definitive conclusions regarding the superiority of PCI or CABG because of selection bias and unmeasured confounders. Propensity score analysis may not adequately adjust for these biases. Second, the number of patients enrolled was still small, particularly in patients with moderate and severe LV systolic dysfunctions because only patients with 3-vessel and/or left main disease were selected to homogenize the patients' background. Third, we did not have data regarding the extent of myocardial ischemia, presence of hibernated myocardium, application of implantable cardioverter-defibrillator, and cardiac resynchronization therapy, which might influence the long-term outcomes of patient with LV systolic dysfunction.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2014.07.007.

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ORIGINAL ARTICLE

ADULT CARDIAC

Three-year outcomes after percutaneous coronary intervention and coronary artery bypass grafting in patients with heart failure: from the CREDO-Kyoto percutaneous coronary intervention/coronary artery bypass graft registry cohort-2†

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Abstract

OBJECTIVES: Ischaemic heart disease is a major risk factor for heart failure. However, long-term benefit of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) in those patients has not been well elucidated.

METHODS: Of the 15 939 patients undergoing first myocardial revascularization enrolled in the CREDO-Kyoto PCI/CABG Registry Cohort-2, we identified 1064 patients with multivessel and/or left main disease with a history of heart failure (ACC/AHA Stage C or D).

RESULTS: There were 672 patients undergoing PCI and 392 CABG. Preprocedural left ventricular ejection fraction was not different between PCI and CABG (46.6 ± 15.1 vs 46.6 ± 14.6%, $P = 0.89$), but the CABG group included more patients with triple-vessel and left main disease ($P < 0.01$ each). Three-year outcomes revealed that the risk of hospital readmission for heart failure was higher after PCI than after CABG (hazard ratio [95% confidence interval]; 1.90 [1.18–3.05], $P = 0.01$). More importantly, adjusted mortality after PCI was significantly higher than after CABG (1.79 [1.13–2.82], $P = 0.01$). The risk of cardiac death after PCI was also higher than after CABG (1.98 [1.10–3.55], $P = 0.02$). Stratified analysis using the SYNTAX score demonstrated that risk of death was not different between PCI and CABG in patients with low (<23) and intermediate (23–32) SYNTAX scores (2.10 [0.57–7.68], $P = 0.26$ and 1.43 [0.63–3.21], $P = 0.39$, respectively), whereas those with a high (≥33) SYNTAX score, the risk of death was far higher after PCI than after CABG (4.83 [1.46–16.0], $P = 0.01$).

CONCLUSIONS: In patients with heart failure with advanced coronary artery disease, CABG was a better option than PCI because CABG was associated with better survival benefit, particularly in more complex coronary lesions stratified by the SYNTAX score.

Keywords: Coronary artery bypass grafting • Percutaneous coronary intervention • SYNTAX score • Heart failure • Left ventricular dysfunction

INTRODUCTION

Coronary artery disease is the most common cause of heart failure and has increased with the growing incidence of associated mortality [1, 2]. Therefore, it is important to understand the clinical outcomes following myocardial revascularization in patients with heart failure with advanced coronary artery disease. Several studies have shown improved outcomes following coronary artery bypass grafting (CABG) in patients with left ventricular (LV) dysfunction [3–5]. However, limited reports have been available regarding the benefit of percutaneous coronary intervention (PCI), in patients with heart failure, particularly with drug-eluting stent (DES). In addition, 5-year outcomes of SYNTAX trial revealed that patients with more complex coronary lesions benefit more from CABG than from PCI [6]. Thus, it is desirable to investigate the impact of CABG compared with PCI on early and late outcomes in patients with heart failure with advanced coronary artery disease.

The CREDO-Kyoto (Coronary REvascularization Demonstrating Outcome Study in Kyoto) is a large multicentre registry in Japan enrolling over 25 000 patients undergoing first PCI or CABG. In the CREDO-Kyoto Registry Cohort-1, we have reported the outcomes

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comparing PCI with CABG in the era of bare-metal stent [7, 8]. The CREDO-Kyoto Registry Cohort-2 included patients undergoing PCI with DES [9, 10]. In the present study, therefore, we sought to investigate 3-year outcomes comparing PCI with CABG in patients with heart failure accompanied by multivessel and/or left main disease using the data from the CREDO-Kyoto registry Cohort-2.

PATIENTS AND METHODS

Study population

The CREDO-Kyoto PCI/CABG Registry Cohort-2 is a physician-initiated, non-company-sponsored, multicentre registry that enrolled consecutive patients undergoing first coronary revascularization in 26 centres in Japan from January 2005 through December 2007. The relevant ethics committees in all 26 participating centres (see Supplementary material S1A) approved the research protocol. Because of the retrospective enrollment, written informed consent from the patients was waived. However, patients who refused participation in the study when contacted for follow-up were excluded.

The study design and patient enrollment in the registry have been described in detail previously [11]. In the present study, we focused on patients with a history of heart failure (ACC/AHA Stage C or D) [2] with multivessel and/or left main disease. ACC/AHA heart failure Stage C denotes patients with current or past symptoms of heart failure associated with underlying structural heart disease (the bulk of patients with heart failure) and Stage D designates patients with truly refractory heart failure who might be eligible for specialized, advanced treatment strategies, such as mechanical circulatory support, procedures to facilitate fluid removal, continuous inotropic infusions or cardiac transplantation or other innovative or experimental surgical procedures, or for end-of-life care, such as hospice.

Of the 15 939 patients enrolled in the registry, we excluded those patients who refused study enrollment ($n = 67$), those with concomitant non-coronary surgery ($n = 609$), acute myocardial infarction (MI, $n = 4900$), single-vessel disease ($n = 3440$), those without a history of heart failure ($n = 5690$) and moderate-to-severe mitral regurgitation ($n = 169$). Subsequently, the study population for the present subanalysis of the registry consisted of 1064 patients with a history of heart failure accompanied by stable multivessel and/or left main disease without moderate-to-severe mitral regurgitation.

Data collection and definitions

Demographic, angiographic and procedural data were collected from hospital charts according to prespecified definitions by experienced research coordinators in an independent research organization (Research Institute for Production Development, Kyoto, Japan; see Supplementary material S1B). Definitions for clinical characteristics are presented in the Supplementary material S1C.

The SYNTAX score was calculated using the SYNTAX score calculator (available at: http://www.syntaxscore.com) by a dedicated SYNTAX score committee (see Supplementary material S1D) blinded to the clinical data. Intra- and interobserver variabilities of the SYNTAX score calculation in our group were previously reported [12]. Cut-off values for SYNTAX score tertiles (low <23, intermediate 23–33 and high ≥33) were defined according to analysis in the SYNTAX trial [13, 14].

Collection of follow-up information was conducted mainly through review of inpatient and outpatient hospital charts by clinical research coordinators in the independent research organization. Additional follow-up information was collected through contact with patients, relatives and/or referring physicians by sending mail with questions on vital status and additional hospitalizations. Death, MI, stent thrombosis and stroke were adjudicated by the clinical event committee (see Supplementary material S1E). Because final data collection for follow-up events was initiated on 1 July 2009, follow-up events were censored on this date.

End points

The primary outcome measurements for the present analysis were death from any cause. Other prespecified end points included cardiac death, readmission for heart failure, stroke, MI and repeat revascularization. Death was regarded as cardiac in origin unless obvious non-cardiac causes could be identified. Any death during the index hospitalization for myocardial revascularization was regarded as cardiac death. MI was defined according to the definition in the Arterial Revascularization Therapy Study [15]. Stroke was defined as ischaemic or haemorrhagic stroke requiring hospitalization with symptoms lasting >24 h. Repeat revascularization was defined as revascularization performed because of ischaemic symptoms, electrocardiographic changes at rest or positive stress test results. Scheduled-staged coronary revascularization procedures performed within 3 months of the initial procedure were not regarded as follow-up events but were included in the index procedure.

Statistical analyses

All continuous variables are expressed as the mean ± standard deviation. Differences in baseline characteristics across the two groups were examined by χ^2 test. Effects of PCI compared with CABG for individual end points were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). Propensity scores, which were the probabilities that a patient would undergo PCI, were calculated for each patient. The propensity scores were estimated with multivariable logistic regression. We used a non-parsimonious model, that is, all of the following confounding factors were included in the model age, sex, body mass index, hypertension, diabetes mellitus, current smoker, prior MI, prior stroke, peripheral arterial disease, atrial fibrillation, chronic kidney disease, haemodialysis, anaemia, platelet count, chronic obstructive lung disease, liver cirrhosis, malignancy, emergency procedure, number of diseased vessels, left main disease, target chronic total occlusion and target proximal left anterior descending coronary artery. These variables were consistent with previous reports from the current registry. Continuous variables except age were dichotomized using clinically meaningful reference values or median values. Harrell's *C*-statistic of the logistic regression for estimating propensity scores was 0.858. Outcomes after PCI and CABG were compared by Cox proportional hazard models. To adjust for confounding, these models were stratified to the tertiles of propensity scores and institutes. Propensity-score-adjusted HRs, 95% CIs and *P*-values are reported. All reported *P*-values were two-sided. We also performed subgroup analysis by tertiles of SYNTAX score and *P*-values for the interaction term between treatment and tertiles of SYNTAX score were reported additionally.

All analyses were conducted by a statistician (S.T.) with the use of the SAS version 9.2 (SAS Institute, Inc.) software and S-Plus version 7.0 (Insightful Corp). The authors had full access to the data and take responsibility for its integrity.

RESULTS

Among the 1064 patients with multivessel and/or left main disease with heart failure, 672 patients (63.2%) received PCI and 392 CABG. Baseline characteristics of the patients in the two groups are given in Table 1. Regarding the complexity of coronary artery anatomy, the CABG group included more patients with triple-vessel disease, left main disease, involvement of target of proximal left anterior descending artery and target of total occlusion. SYNTAX scores were available in patients with triple-vessel and/or left main disease ($n = 678$, 63.7%). The SYNTAX score was significantly higher in the CABG group ($P < 0.01$). Stent was used in 94.8% of patients in the PCI group and ≥1 DES was used in 75.1% patients. Left internal thoracic artery was used in 93.6% of patients in the CABG group. Prevalence of off-pump CABG was 58.4%. Median follow-up duration for surviving patients was 978 days.

Unadjusted 30-day and in-hospital mortality was not different between PCI and CABG (1.3 vs 2.0%, $P = 0.39$ and 3.0 vs 2.8%, $P = 0.87$, respectively). Similarly, 30-day incidences of stroke and MI were not different between the groups (1.0 vs 1.5%, $P = 0.48$ and 1.3 vs 1.0%, $P = 0.65$, respectively). Three-year follow-up rates were 87.0% in the CABG group and 80.2% in the PCI group.

Propensity score analysis showed that all-cause mortality adjusted for confounders was higher after PCI than after CABG (HR [95% CI]: 1.79 [1.13–2.82], $P = 0.01$, Table 2). The risk of cardiac death was also higher after PCI (1.98 [1.1–3.55], $P = 0.02$). The risk of repeat revascularization after PCI was much higher than after CABG (9.42 [4.35–20.4], $P < 0.01$). The risk of stroke was not different between PCI and CABG (1.44 [0.68–3.08], $P = 0.34$).

SYNTAX score was available in patients with triple-vessel and/or left main disease (Table 3). Clinical outcomes were compared between PCI and CABG among the three categories of coronary anatomical complexities stratified by the SYNTAX score. All-cause mortality was not different between PCI and CABG in patients with low and intermediate SYNTAX scores (2.1 [0.57–7.68], $P = 0.26$ and 1.43 [0.63–3.21], $P = 0.39$, respectively). However, all-cause mortality after PCI was far higher than after CABG in patients with a high SYNTAX score (4.83 [1.46–16.0], $P = 0.01$).

Table 1: Baseline characteristics

	PCI ($n = 672$)		CABG ($n = 392$)		*P*-values
Age (median)	71.3 ± 10.6	(73.0)	69.2 ± 9.5	(70.0)	<0.01
Age >75	296	44.0%	127	32.4%	<0.01
Male gender	448	66.7%	270	68.9%	0.46
Body mass index	23.3 ± 4.1	(23.0)	22.6 ± 3.3	(22.2)	<0.01
Body mass index ≥25	199	29.6%	90	23.0%	0.02
Hypertension	625	93.0%	351	89.5%	0.05
Diabetes mellitus	384	57.1%	234	59.7%	0.42
On insulin therapy	158	23.5%	101	25.8%	0.20
Current smoking	140	20.8%	95	24.2%	0.89
Ejection fraction	46.6 ± 15.1	(46.0)	46.6 ± 14.6	(46.0)	0.98
Previous myocardial infarction	257	38.2%	161	41.1%	0.36
Atrial fibrillation	108	16.1%	72	18.4%	0.34
Previous stroke	124	18.5%	60	15.3%	0.19
Peripheral artery disease	63	9.4%	42	10.7%	0.48
eGFR (ml/min/1.73 m^2) (median)	49.5 ± 25.1	(51.6)	47.3 ± 24.4	(49.1)	0.21
eGFR <30 ml/min/1.73 m^2 without hemodialysis	81	12.1%	60	15.3%	0.16
Haemodialysis	72	10.7%	38	9.7%	0.60
Anaemia (haemoglobin <11.0 g/dl)	192	28.6%	125	31.9%	0.25
Platelet count <100 × 10^9/l)	20	3.0%	11	2.8%	0.87
Chronic obstructive pulmonary disease	32	4.8%	9	2.3%	0.04
Liver cirrhosis	19	2.8%	13	3.3%	0.65
Malignancy	61	9.1%	42	10.7%	0.38
Procedural characteristics					
Number of target lesions or anastomoses (median)	1.8 ± 0.9	(2.0)	3.2 ± 1.0	(3.0)	<0.01
Extent of coronary artery disease					
Triple-vessel disease	312	46.4%	238	60.7%	<0.01
Left main disease	56	8.3%	122	31.1%	<0.01
Target of proximal left anterior descending artery	431	64.1%	357	91.1%	<0.01
Target of chronic total occlusion	171	25.4%	205	52.3%	<0.01
Stent use	637	94.8%	-		n/a
Drug-eluting stent use	515	76.6%	-		n/a
Left internal thoracic artery use	(-)		367	93.6%	n/a
Off-pump CABG	(-)		229	58.4%	n/a
Emergency procedure	39	5.8%	30	7.7%	0.24
SYNTAX score (median)	26.8 ± 10.0	(26.0)	32.2 ± 10.5	(31.0)	<0.01

Mean ± standard deviation, or number of patients and percentage.
eGFR: estimated glomerular filtration rate.

Table 2: Three-year outcomes after PCI and CABG in patients with heart failure

	Number of patients (event/total)				Comparison of PCI vs CABG			
	PCI (n = 672)		CABG (n = 392)		HR	95% CI		P-values
Death	143	21%	61	16%	1.79	1.13	2.82	0.01
Cardiac death	91	14%	34	9%	1.98	1.1	3.55	0.02
Readmission for heart failure	146	22%	46	12%	1.9	1.18	3.05	0.01
Stroke	45	7%	24	6%	1.44	0.68	3.08	0.34
Myocardial infarction	27	4%	12	3%	2.95	1	8.71	0.05
Repeat revascularization	127	19%	14	4%	9.42	4.35	20.41	<0.01

Adjusted for age, sex, Body mass index, hypertension, dyslipidaemia, diabetes mellitus, current smoker, heart failure, mitral regurgitation grade 3/4, prior myocardial infarction, prior stroke, peripheral vascular disease, atrial fibrillation, chronic kidney disease, haemodialysis, anaemia, platelet count, COPD, liver cirrhosis, malignancy, emergency procedure, number of diseased vessels, left main disease, target of chronic total occlusion, target of proximal left anterior descending coronary artery, institute.

Table 3: Three-year mortality after PCI and CABG in patients with heart failure stratified by tertiles of SYNTAX score

	Number of patients (event/total)				Comparison of PCI vs. CABG			
	PCI (n = 435)		CABG (n = 343)		HR	95% CI		P-value
Low (<23)	28	21%	9	16%	2.1	0.57	7.68	0.26
Intermediate (23–32)	35	23%	21	18%	1.43	0.63	3.21	0.39
High (≥33)	20	25%	19	13%	4.83	1.46	16.03	0.01

SYNTAX scores were available in patients with triple-vessel and/or left main disease (n = 678, 63.7%).
Adjusted for age, sex, Body mass index, hypertension, dyslipidaemia, diabetes mellitus, current smoker, heart failure, mitral regurgitation grade 3/4, prior myocardial infarction, prior stroke, peripheral vascular disease, atrial fibrillation, chronic kidney disease, haemodialysis, anaemia, platelet count, COPD, liver cirrhosis, malignancy, emergency procedure, number of diseased vessels, left main disease, target of chronic total occlusion, target of proximal left anterior descending coronary artery, institute.

DISCUSSION

Main findings

In the present study, we investigated the impact of CABG on early and 3-year outcomes after PCI with DES in Japanese patients with heart failure accompanied by multivessel and/or left main disease. Thirty-day outcomes were not different between PCI and CABG regarding the incidence of death, stroke and MI. Three-year outcomes revealed that CABG reduced the risk of all-cause death compared with PCI. Similarly, the risk of cardiac death was higher after PCI. The risks of MI and repeat revascularization after PCI were also much higher than after PCI. The risk of stroke was not different between PCI and CABG.

The survival benefit was more prominent in patients with more complex coronary lesions stratified by the SYNTAX score. Importantly, the risk of death was not different between PCI and CABG in patients with low and intermediate SYNTAX scores; however, the risk was far higher after PCI in patients with a high SYNTAX score. These outcomes indicate that in patients with heart failure with advanced coronary artery disease, CABG was better option than PCI because CABG was associated with better survival benefit, particularly in more complex coronary lesions stratified by the SYNTAX score.

Previously, CABG has been the preferred revascularization strategy for patients with LV dysfunction [16]. In the bare-metal stent era, a few previous studies have compared the clinical outcomes after PCI or CABG in patients with LV dysfunction [17, 18]. These studies demonstrated that the survival benefits of PCI were not inferior to those of CABG, despite the high incidence of repeat revascularization. The recent introduction of DES has broadened the indications for PCI to high-risk patients and complex lesions. In the DES era, few studies have compared the clinical outcomes of PCI and CABG in patients with LV dysfunction. Recently, however, subclass analyses of several large studies demonstrated the benefit of CABG in patients with heart failure with more complex coronary lesions.

FREEDOM trial randomized 1900 patients with diabetes and multivessel coronary disease to undergo either PCI with DES or CABG [19]. At 5 years, the primary composite end point of death/stroke/MI occurred more often in patients treated with PCI regardless of the SYNTAX score. In addition, CABG proved more beneficial than PCI in all prespecified subgroups such as those with renal insufficiency. Specifically, in patients with an LV ejection fraction of <40%, 5-year risk of composite of death/stroke/MI was significantly lower than that of PCI (62 vs 31%).

Large observational studies also demonstrated the benefit of CABG than PCI in patients with LV dysfunction [20, 21]. Hlatky *et al.* [20] revealed that the CABG advantage is strongest in patients with certain clinical characteristics, such as diabetes and heart failure. Five-year outcomes revealed that CABG reduced the adjusted risk of all-cause mortality compared with PCI (0.92 [0.90–0.95], $P < 0.001$). In patients with heart failure, the risk of 5-year mortality

was significantly lower than that with PCI (51.7 vs 44.6%; 0.84 [0.79–0.88], $P < 0.001$). Significant interaction P-value (<0.001) indicated the benefit of CABG was more prominent in patients with heart failure compared to those without heart failure.

The American College of Cardiology Foundation (ACCF) and the Society for Thoracic Surgery (STS) have established important national data registries for PCI and CABG [21]. The ASCERT study linked hospital data from the two registries collected from 2004 through 2007 to analyse long-term mortality, rehospitalization and resource utilization outcomes. Among patients older than 64 years with multivessel disease, 86 244 underwent CABG and 103 549 underwent PCI. At 4 years, there was lower mortality with CABG than with PCI (16.4 vs 20.8%; 0.79 [0.76–0.82]). Similar results were noted in multiple subgroups such as sex, age, presence or absence of diabetes, body mass index, presence or absence of chronic lung disease, ejection, fraction and glomerular filtration rate. In patients with an LV ejection fraction of <30%, 4-year mortality was significantly lower in the CABG group (0.70 [0.63–0.77]). These results indicate that CABG has greater long-term survival advantage than PCI in patients with heart failure with advanced coronary disease.

In the preset study, both the risks of all-cause and cardiac death after PCI were higher than after CABG. Several studies have reported that incomplete revascularization was associated with a greater risk of major cardiac events after PCI [22–24]. The clinical impact of angiographic complete and incomplete revascularization after PCI or CABG was evaluated in the 'all-comers' SYNTAX trial [23]. As a result, within the PCI and CABG arms of the all-comers SYNTAX trial, angiographically determined incomplete revascularization has a detrimental impact on long-term clinical outcomes, including mortality. A systematic review and meta-analysis of studies comparing complete revascularization versus incomplete revascularization in 89 883 patients with multivessel disease reported that incomplete revascularization was more common after PCI than after CABG (56 vs 25%), and that complete revascularization was associated with lower long-term mortality (0.71 [0.65–0.77], $P < 0.001$), MI (0.78 [0.68–0.90], $P = 0.001$) and repeat revascularization (0.74 [0.65–0.83], $P < 0.001$) [24]. In the preset study, the numbers of target/anastomotic sites were significantly lower in the PCI group. In addition, the risk of repeat revascularization after PCI was far higher than after CABG, which means that incomplete revascularization after PCI was seriously associated with cardiac mortality. Thus, complete revascularization should be obtained in patients with heart failure irrespective of the selection of PCI or CABG.

In the present study, the mean left ventricular ejection fraction (LVEF) preprocedure was not so bad possibly because we selected patients with a history of heart failure caused by both systolic and diastolic dysfunction. There are two types of heart failure. Systolic LV dysfunction (or systolic heart failure) occurs when the LV heart muscle does not contract with enough force (low LVEF). On the other hand, heart failure with preserved LV function (diastolic heart failure) occurs when the heart contracts normally, but the ventricles do not relax properly or are stiff and less blood enters the heart during normal filling. In this case, LVEF is often normal. In the current clinical practice, approximately half of patients with over congestive heart failure have diastolic dysfunction without reduced LVEF. Clinically, diastolic heart failure of ischaemic disease is associated with hypertension or atrial fibrillation. Although we did not have detailed data regarding diastolic failure in this registry, we believe that it is important to elucidate the impact of CABG in patients not only with systolic but also with diastolic heart failure.

The prevalence of diabetes mellitus in the present study was high compared with previous reports. In the overall population of our registry (both with and without heart failure), rate of diabetes was 40.2 for PCI and 50.6% for CABG. These values are not so different from those of previously reported studies that investigated myocardial revascularization in Japan. However, these values may be high compared with those from countries other than Japan. The reasons for high rate of diabetes in Asians including Japanese are unclear; however, several studies have reported high rates of diabetes in Asians including Japanese because of poor insulin secretion and sensitivity in Asians compared with Western Europeans [25].

There are several important limitations in this study. First and most importantly, the observational study design precluded definitive conclusions regarding the superiority of PCI or CABG because of selection bias and unmeasured confounders. Propensity-score analysis may not adequately adjust for these biases. Secondly, the number of patients enrolled was still small and SYNTAX score data were not available for all patients. Thirdly, the duration of follow-up might not be sufficient to evaluate the long-term outcomes of coronary revascularization.

CONCLUSIONS

In patients with heart failure accompanied by multivessel and/or left main disease, CABG is associated with better 3-year survival than PCI using DES, particularly in patients with higher SYNTAX score. CABG may be a favourable myocardial revascularization strategy in those patients. Further study with longer follow-up is necessary.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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APPENDIX: CONFERENCE DISCUSSION

***Dr M. Poullis** (Liverpool, UK)*: I just picked up from your talk that LIMA usage is just 59%; that's quite low I think. I have really two questions.

First of all, if all the patients were in heart failure, why was the mean ejection fraction 46%, which is quite good? I think that is an issue. I think the second question I wanted to ask partly alludes to that. 17.2% of people had grade 3 or 4 mitral regurgitation in the PCI group and 6.9% in the CABG group. Surely it would be better to eliminate all the people with mitral regurgitation grade 3 or 4 and then do your analysis. The end of the bed test I think is what's going on here: people who look bad have the PCI, people who look good have the surgery, and I think it is a major confounding issue.

Dr Marui: Regarding your first question, we didn't use the ejection fraction value in the present study. I should have used a cut-off point for ejection fraction of 30% or 40% in the present study, but we didn't do that because of the problem of sample size. So we used the history of heart failure instead of the value of ejection fraction. So as you say, 46% mean EF is much higher than in previous reports of heart failure comparing PCI with CABG. So it should be considered as a limitation of the present study.

Regarding the second question, the mitral regurgitation rate is higher in the PCI group, and the CABG group has approximately 7% of patients with mitral regurgitation. As you said, the high ratio of mitral regurgitation may affect the outcomes of the present study. Although we adjusted the ratio of mitral regurgitation, we should re-analyze the data excluding patients with mitral regurgitation and could adjust the difference of mitral regurgitation.

***Dr D. Bonneau** (Toronto, ON, Canada)*: This is a fantastic study and the message should be loud and clear, but recently we also know that stents were suboptimal for diabetic people. I wonder, and it's hindsight, of course, but if you removed the diabetics from the PCI series, would it affect the statistics? In other words, what we are seeing, is it due to congestive heart failure or the fact that diabetics were treated with stents?

Dr Marui: As you said, in the patients with diabetes, the outcome of CABG is better than in the non-diabetic population. So if we exclude the diabetic patients in the PCI group, there may be no difference between the PCI and CABG in the results. However, we did not compare the outcomes of the patients with or without diabetes in the present study. I would like to try the analysis in a future study.

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低左心機能例に対する血行再建 PCI vs CABG
—わが国でのレジストリーデータを含むこれまでのエビデンス—

丸井　晃，坂田　隆造

Akira Marui, Ryuzo Sakata: **Percutaneous versus surgical myocardial revascularization in patients with left ventricular systolic dysfunction: systematic review from the current evidences**. J Jpn Coron Assoc 2014; **20**: 67–74

I. はじめに

近年，SYNTAX 試験[1]を始めとする大規模ランダム化比較試験(RCT)や大規模観察研究・メタアナリシスによる新たなエビデンスが続々と報告され，安定狭心症に対する PCI または CABG についての至適治療選択のコンセンサスはほぼ完成された感がある．しかしながら虚血性心疾患を有する患者は様々なリスク因子を持つことが多く，そのような背景を持つ患者特有の PCI vs CABG の新たなエビデンスが必要となっている．

糖尿病に関しては 2012 年に大規模 RCT の FREEDOM 試験[2]により，複雑病変を有する糖尿病患者における CABG の長期優位性が報告されるに至った．しかし低左心機能症患者については，いまだ十分なエビデンスがあるとは言いがたく，実際，日本循環器学会の「慢性心不全治療ガイドライン(2010 年改訂版)」[3]においても，虚血性心疾患を合併した心不全患者に対する狭心症治療・冠血行再建については確立したエビデンスが存在しない，とされており，今後ますます重症化すると予想される本邦の虚血性心疾患の治療において，低左心機能患者に対する新たなエビデンスを確立していくことは非常に重要と思われる．ここでは左室収縮不全[左室駆出率(LVEF)低下]による低左心機能患者について，冠血行再建における現在までのエビデンスを検証する．

II. 低左心機能例における冠血行再建の海外のエビデンス

1. CABG vs 薬物治療

低左心機能患者における CABG と薬物治療の比較については古くより多くの報告がある．1994 年に Yusuf らは，7 つの RCT からの安定狭心症患者 2694 名を対象としたメタアナリシスを行い，CABG は薬物治療と比較して 5 年以上の追跡で生命予後改善効果を示し，左主幹部病変や低左心機能などのリスク因子が多い患者ほど CABG のメリットが大きいことを報告した[4]．

また観察研究としては，1983 年に Alderman らは，LVEF 36%未満の患者を対象に薬物治療を受けた 420 名と CABG を施行した 231 名を比較したところ CABG は有意に生命予後を改善し($p<0.05$)，かつその効果は LVEF 26%未満の患者でより顕著であったことを報告した(5 年生存率 43% vs 63%)[5]．2002 年に O'Connor らは LVEF 40%未満の 1052 名の薬物治療患者と 339 名の CABG 患者を比較し，10 年後の生存率は 13% vs 42%($p<0.0001$)と CABG で良好であることを報告した[6]．

しかしこれらの報告の時代に比べ現在は外科技術・薬物治療ともに飛躍的に進歩しており，十分なエビデンスであるとは言いがたかった．その後大規模 RCT である STICH 試験の結果が報告された[7-9]．STICH 試験は，低左心機能患者を対象として薬物治療・CABG 単独・CABG + 左室形成術を比較した RCT であり，2009 年に CABG 単独と CABG + 左室形成術の比較結果が報告され[7]，その後 2011 年に薬物治療と単独 CABG の比較が報告された[9]．LVEF 35%以下の患者 1212 名が薬物治療と CABG にランダムに割り付けられ，intension-to-treat をベースに 5 年追跡が行われた．5 年追跡による死亡率は，薬物治療 41%，CABG 36%であり，CABG の優位性を示すことができなかった($p=0.12$)．しかしながら追跡期間中に薬物治療群の 100 名(17%)が CABG を受けており(cross over)，実際に受けた治療による解析，いわゆる"as-treated"で解析を行ったところ，薬物治療に比べて CABG の死亡率が低いことが判明した[リスク比(95%信頼区間)：0.70 (0.58〜0.84)；$p<0.001$]．また 5 年追跡までの死亡率の傾向を見ると，さらなる長期追跡では本来の intension-to-treat による解析でも CABG が優位である可能性が指摘されており，現在継続追跡が行われている．

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Table 1 虚血性心疾患を有する低左心機能に対する冠血行再建の報告(PCI vs CABG)

報告者	報告年	LVEF	患者数		Stent	観察期間	主要結果 (PCI vs CABG)
			PCI	CABG			
RCT(サブ解析)							
Berger[15]	2001	50%未満	94	82	(-)	7年	3枝病変患者．有意差なし
観察研究							
O'Keefe[31]	1993	40%以下	100	100	(-)	5年	PCIで死亡率が高い傾向あり
Brener[32]	2004	30%以下	54	573	BMS	5年	PCIで死亡率が高い傾向あり
Sedlis[33]	2004	35%未満	152	140	未記載	36カ月	死亡で有意差なし
Gioia[34]	2007	35%以下	128	92	DES	2年	死亡で有意差なし
Hannan[16]	2008	40%未満	1059	1614	DES	18カ月	PCIで死亡，死亡/心筋梗塞が高い
Nagendran[17]	2013	35%未満	1599(718)*	1326(718)*	BMS/DES	5年	PCIで死亡率が高い
Yang[35]	2013	50%未満	402(141)*	551(141)*	DES	3年	死亡で有意差なし
Hlatky[18]	2013	未記載	6940	6572	未記載	5年	PCIで死亡率が高い
メタアナリシス							
Hlatky[19]	2009	未記載	615	551	BMS	8年	死亡で有意差なし
Kunadian[12]	2012	40%以下	455	502	未記載	1年以上	死亡で有意差なし

*プロペンシティマッチング患者数

2. PCI vs 薬物治療

虚血性心疾患を有する低左心機能患者に対するPCIと薬物治療の比較については，短期追跡での報告が散見されるが[10]，長期追跡データは極めて限られている．2006年にはAPPROACH databaseから，虚血性心疾患を有する心不全既往患者において，冠血行再建(PCIまたはCABG)を受けた患者と，薬物治療のみの患者を比較し，その7年追跡結果が報告された[11]．1690名が薬物治療を2538名が冠血行再建(52.5%がPCI)を受けた結果，冠血行再建群は薬物治療群に比して有意に死亡率が低く[0.50(0.44～0.57)]，さらにPCIは薬物治療に比して死亡率が低いことが報告された[0.58(0.49～0.69)]．一方2012年にKunadianらはLVEF 40%以下の患者を対象とした19研究・4766名のメタアナリシスの結果を報告したが，1年追跡ではPCIの薬物治療に対する優位性を証明することができなかった[12]．

3. PCI vs CABG

通常の安定狭心症患者に対するPCI vs CABGについては大規模RCTの結果が報告され，冠動脈疾患の重症度に応じた至適治療選択についてのガイドラインが確立されている[13, 14]．しかし低左心機能患者については，RCTという性質上対象患者が少なく，サブ解析を行うための十分なサンプルサイズが得られていない．2001年にBergerらにより報告されたBARI試験からの少数例のサブ解析では，3枝病変を有するLVEF 50%未満の患者176名の7年追跡結果が報告されているが，7年追跡の生存率がPCI群70%，CABG群74%で有意差を認めなかった(p=0.60)[15](Table 1)．

観察研究においてもバルーン血管形成やベアメタルステント時代では少数例の比較であり，統計的検出力が十分ではなかったが，最近では大規模観察研究によるサブ解析が報告されている．2008年のHannanらの報告[16]では，New York Registryに登録された17,400名の患者のうち，LVEF 40%未満のPCI施行患者1059名とCABG 1614名を対象とし18カ月の追跡を行ったところ，総死亡はCABG群で少なく[0.77(0.59～1.00)，p=0.05]，死亡または心筋梗塞の発症率についてもCABG群で低かった[0.67(0.53～0.84)，p<0.001]．またAPPROACH databaseからのサブ解析[17]では，LVEF 35%未満のPCI 1599名・CABG 1326名から718名ずつのプロペンシティマッチングを行った5年追跡結果で，やはりPCI群で死亡率が高かった[1.48(1.18～1.85)]．さらにHlatkyらによる大規模観察研究[18]では，1992～2008年までにPCIまたはCABGを受けた66歳以上の多枝病変を有するメディケア受給者251,553名を対象として，心不全を有する患者のプロペンシティマッチングによりサブ解析を行った．その5年追跡結果では生存率は44.6% vs 51.7%とCABGで高く[死亡リスク0.84(0.79～0.88)]，心不全のない患者に対しても有意に治療効果の差が見られた(交互作用p<0.001)．

メタアナリシスについては，2009年にHlatkyらはRCT 10研究の7812名を対象に，低左心機能患者(PCI 615名・CABG 511名)のサブ解析を報告しているが，5年生存率は有意差を認めなかった[0.93(0.73～1.18)][19]．また2012年のKunadianらの報告でも1年以上の追跡結果でPCIとCABGで死亡率の差がなかった[0.98(0.8～1.2)，p=0.83][12]．

以上のように，最近の大規模観察研究のサブ解析では虚血性低左心機能患者に対するCABGの長期優位性が示唆されているが，現時点では十分な統計学的検出力を持ったRCTは施行されていないため，エビデンスとしては十分とは言いがたく，今後の報告が待たれるところである．

Table 2 ESC/EACTS 2010 Guideline: Recommendations for patients with chronic heart failure and systolic left ventricular dysfunction (ejection fraction ≤35%), presenting predominantly with anginal symptoms[13]

Recommendations	COR	LOE	Ref.
CABG is recommended for:			
• Significant LM stenosis	I	B	22)
• LM equivalent (proximal stenosis of both LAD and LCx)			
• Proximal LAD stenosis with 2- or 3- vessel disease.			
CABG with SVR may be considered in patients with LVESV index >60 ml/m^2 and scarred LAD territory.	IIb	B	7, 36)
PCI may be considered if anatomy is suitable, in the presence of viable myocardium.	IIb	C	–

COR: Class of Recommendation, LOE: Level of evidence, CABG: coronary artery bypass grafting, LAD: left anterior descending, LCx: left circumflex, LM: left main, LVESV: left ventricular end-systolic volume, PCI: percutaneous coronary intervention, SVR: surgical ventricular reconstruction, Ref.: references

Table 3 ESC/EACTS 2010 Guideline: Recommendations for patients with chronic heart failure and systolic left ventricular dysfunction (ejection fraction ≤35%), presenting predominantly with heart failure symptoms (no or mild angina: Canadian Cardiovascular Society 1–2) [13]

Recommendations	COR	LOE	Ref.
LV aneurysmectomy during CABG is indicated in patients with a large LV aneurysm	I	C	–
CABG should be considered in the presence of viable myocardium, irrespective of LVESV.	IIa	B	37)
CABG with SVR may be considered in patients with a scarred LAD territory.	IIa	B	7, 36)
PCI may be considered if anatomy is suitable, in the presence of viable myocardium.	IIb	C	–
Revascularization in the absence of evidence of myocardial viability is not recommended.	III	B	37)

COR: Class of Recommendation, LOE: Level of evidence, CABG: coronary artery bypass grafting, LAD: left anterior descending, LCx: left circumflex, LM: left main, LVESV: left ventricular end-systolic volume, PCI: percutaneous coronary intervention, SVR: surgical ventricular reconstruction, Ref.: References

III. ガイドライン

本邦においては前述のとおり，日本循環器学会の「慢性心不全治療ガイドライン(2010年改訂版)」[3]において虚血性心疾患を有する低左心機能患者に対する冠血行再建選択の指針は記載されていない．「虚血性心疾患に対するバイパスグラフトと手術術式の選択ガイドライン(2011年改訂版)」[20]には低左心機能患者に対する記載はあるものの，CABGと左室形成術に関する適応に限られている．また「安定冠動脈疾患における待機的PCIのガイドライン(2011年改訂版)」[21]にも，慢性心不全患者に対する冠血行再建についての記載はない．

海外のガイドラインに目を向けてみると，2010年のESC/EACTS冠血行再建ガイドライン[13]では，左室収縮不全患者に対する冠血行再建については，2004年のACC/AHA CABGガイドライン[22]の内容およびSTICH試験[7]の結果から得られたエビデンスのみでガイドラインが作成されている(Table 2, 3)．このガイドラインでのクラスI推奨は，左主幹部病変などの複雑病変に対するCABGの適応や，左室瘤切除術の適応のみであり，PCIに関しては反映されるべきエビデンスはなく，ごく簡潔な記載に留まっている．そのためPCIとCABGの選択については，「冠動脈病変・冠血行再建の予測達成度・基礎疾患・併存する心臓弁膜症の有無などから総合的に判断する」，という記載にとどまっている．2012年のESC急性および慢性心不全に対する診断・治療ガイドライン[23]においてもクラスI推奨はCABGの適応に関してのみであり，PCIとCABGの選択については2010年ガイドラインと同様な記載となっている(Table 4)．

一方，2013年に報告されたACCF/AHA心不全のガイドライン[24]でのクラスI推奨は「ガイドラインに従った薬物治療を受けている心不全患者で，狭心症および治療適応となる冠動脈病変を有する場合はCABGまたはPCIの適応となる」となっている(Table 5)．この推奨は2012年のACCF/AHA安定虚血性心疾患治療ガイドライン[25]および2011年のACCF/AHA PCIおよびCABGのガイドライン[26, 27]が根拠となっているが，これらのガイドライン自体の根拠は前述のYusufらの報告がベースとなっており，エビデンスとしてはかなり古いものになる．またエビデンスレベルもCとなっており，十分なレベルがあるとは言い難い．クラスIIa推奨として，「軽度～中等度の左室収縮不全および有意な多枝・左前下行枝近位部病変を有する患者に対しては，心筋のviabilityが保たれていれば生命予後改善のためのCABGは妥当である」，「重度左室機能不全・心不全および有意な冠動脈疾患を有する患者に対しては，合併症率や死亡率を改善するためのCABGま

Table 4 ESC 2012 Guideline: Recommendations for myocardial revascularization in patients with chronic HF and systolic LV dysfunction[23]

Recommendations	COR	LOE	Ref.
CABG is recommended for patients with angina and significant left main stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of premature death.	I	C	–
CABG is recommended for patients with angina and two- or three-vessel coronary disease, including a left anterior descending stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of hospitalization for cardiovascular causes and the risk of premature death from cardiovascular causes.	I	B	9)
Alternative to CABG: *PCI may be considered as an alternative to CABG in the above categories of patients unsuitable for surgery.*	IIb	C	–
CABG and PCI are NOT recommended in patients without angina AND without viable myocardium.	III	C	–

CABG: coronary artery bypass graft, EF: ejection fraction, HF: heart failure, LV: left ventricular, PCI: percutaneous coronary intervention, COR: Class of recommendation, LOE: Level of evidence, Ref.: References

Table 5 ACCF/AHA 2013 Guideline: Recommendations for surgical/percutaneous/transcatheter interventional treatments of HF (selected)

Recommendations	COR	LOE	Ref.
Coronary artery revascularization via CABG or percutaneous intervention is indicated for patients (HFpEF and HFrEF) on GDMT with angina and suitable coronary anatomy, especially for a left main stenosis (>50%) or left main equivalent disease.	I	C	25–27,38)
CABG to improve survival is reasonable in patients with mild to moderate LV systolic dysfunction (EF 35% to 50%) and significant (≥70% diameter stenosis) multivessel CAD or proximal left anterior descending coronary artery stenosis when viable myocardium is present in the region of intended revascularization.	IIa	B	38–40)
CABG or medical therapy is reasonable to improve morbidity and cardiovascular mortality for patients with severe LV dysfunction (EF <35%), HF, and significant CAD	IIa	B	9, 41)
CABG may be considered with the intent of improving survival in patients with ischemic heart disease with severe LV systolic dysfunction (EF <35%) and operable coronary anatomy whether or not viable myocardium is present.	IIb	B	5, 9, 42)
Surgical reverse remodeling or LV aneurysmectomy may be considered in carefully selected patients with HFrEF for specific indications, including intractable HF and ventricular arrhythmias.	IIb	B	7)

CABG indicates coronary artery bypass graft, CAD: coronary artery disease, COR: Class of Recommendation, EF: ejection fraction, GDMT: guideline-directed medical therapy, HF: heart failure, HFpEF: heart failure with preserved ejection fraction, HFrEF: heart failure with reduced ejection fraction, LAD: left anterior descending, LOE: Level of Evidence, LV: left ventricular, Ref.: references

たは薬物治療は妥当である」となっており，CABGや薬物治療の推奨については述べられているが，PCIの具体的な適応については述べられていない．

以上からわかるように，虚血性心疾患を有する低左心機能患者に対する冠血行再建選択に関するガイドラインは現時点では十分なエビデンスに基づくものではなく，そのため2013年ACCF/AHA心不全ガイドライン[24]においても，血行再建法の至適選択については2010年ESC/EACTS冠血行再建ガイドライン[13]と同様に「冠動脈病変・基礎疾患の有無(糖尿病・CKDなど)・収縮不全の程度・患者選択・ハートチーム内でのディスカッションなどで総合的に決定すべき」，という結論にとどまっている．

IV. 本邦のエビデンス

本邦においても虚血性心疾患を有する低左心機能患者に対するPCI vs CABGの十分なエビデンスは現時点では存在しない．そこで我々は観察研究のサブ解析という位置づけではあるが，虚血性低左心機能患者におけるPCI vs CABGのエビデンスを2013年の日本循環器学会で報告した[28]．

CREDO-Kyotoは本邦最大の初回冠血行再建のレジストリであり，ベアメタルステント時代のCohort-1(2000〜2002年登録)[29]および，薬剤溶出ステント(DES)時代のCohort-2（2005〜2007年登録)[30]がある．Cohort-2は国内26施設から急性冠症候群および安定狭心症患者15,939名が登録されている．対象患者はCREDO-Kyoto Cohort-2に登録された患者のうち，多枝または左主幹部病変を有し，かつACC/AHAの心不全分類stage CまたはD(息切れなどの有症候群または治療抵抗性の心不全)の既往のある1,233名で，PCIが812名にCABGが432名に施行され

Table 6 Baseline characteristics of patients with heart failure (CREDO-Kyoto Registry Cohort-2)

	PCI n=812		CABG n=421		p value
Age	71.8±10.7		69.3±9.5		<0.01
Male gender	522	64.3%	286	67.9%	0.2
Hypertension	754	92.9%	375	89.1%	0.02
Diabetes mellitus	457	56.3%	254	60.3%	0.17
Ejection fraction	46.0±15.2		46.1±14.7		0.89
Previous myocardial infarction	321	39.5%	172	40.9%	0.65
Atrial fibrillation	136	16.7%	79	18.8%	0.38
Previous stroke	156	19.2%	64	15.2%	0.08
Hemodialysis	89	11.0%	43	10.2%	0.69
Chronic obstructive pulmonary disease	40	4.9%	10	2.4%	0.03
Malignancy	77	9.5%	47	11.2%	0.35
Number of target lesions or anastomoses	1.8±0.9		3.2±1.0		<0.01
Extent of coronary artery disease					
Triple-vessel disease	410	50.5%	331	78.6%	<0.01
Left main disease	76	9.4%	131	31.1%	<0.01
Target of proximal left anterior descending artery	519	63.9%	385	91.4%	<0.01
Target of chronic total occlusion	210	25.9%	223	53.0%	<0.01
Stent use	768	94.6%	n/a		
Drug-eluting stent use	610	75.1%	n/a		
Off-pump CABG	n/a		247	58.7%	
Emergency procedure	46	5.7%	33	7.8%	0.14
SYNTAX score	26.8±10.2		32.2±10.5		<0.01

Mean±standard deviation, or number of patients and percentage

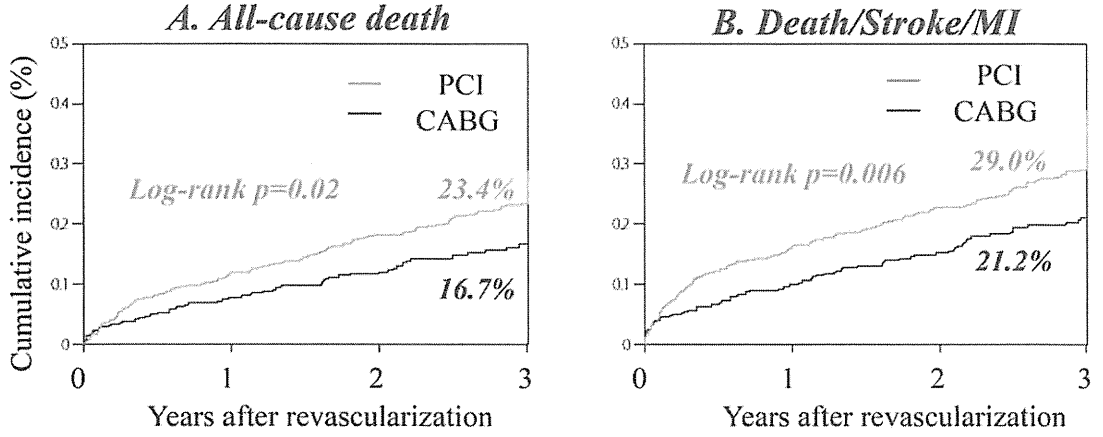

Fig. 1 Kaplan-Meier analyses comparing PCI with CABG in patients with heart failure.
A: All-cause death.
B: Composite of death, stroke, or myocardial infarction.
MI: myocardial infarction

A | B

た．患者背景を Table 6 に示した．術前の LVEF は差がなかったが(p=0.89)，CABG 群のほうが，3 枝や左主幹部などの複雑病変患者が多く，SYNTAX スコアも有意に高かった(p<0.01)．Kaplan-Meier による 3 年死亡率は PCI 群で有意に高く(23.4% vs 16.7%，p=0.02)，死亡 / 脳卒中 / 心筋梗塞の複合エンドポイントの発症も PCI 群で高かった(29.0% vs 21.1%，p<0.01)(Fig. 1A，B)．多変量解析の結果も，総死亡・複合エンドポイントともに PCI で有意に高かった[1.68(1.10〜2.56)，p=0.02 および 1.82(1.25〜2.66)，p<0.01，Table 7]．さらに心臓死亡，不整脈関連死亡や心不全入院・心筋梗塞・追加血行再建においても PCI で高率であった．脳卒中については有意差を認めなかっ