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ORIGINAL ARTICLE

Long-term outcomes of three-vessel coronary artery disease after coronary revascularization by percutaneous coronary intervention using second-generation drug-eluting stents versus coronary artery bypass graft surgery

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Abstract

Studies on the outcomes of de novo three-vessel coronary artery disease (3VD) are limited. This study evaluated the outcomes after coronary revascularization in patients with 3VD treated by percutaneous coronary intervention (PCI) using second-generation drug-eluting stents (2ndDES) in comparison with coronary artery bypass grafting (CABG). We analyzed 853 patients undergoing either PCI or CABG for 3VD between 2010 and 2014. Of them, this study included 298 undergoing PCI with 2ndDES alone (PCI group) and 171 undergoing CABG (CABG group). The primary outcome measure was a composite of all-cause death, non-fatal myocardial infarction (MI), or stroke. The secondary outcome measures were cardiac death, MI, stroke, and target vessel revascularization (TVR). Propensity matching was used to adjust a cohort of patients with similar baseline characteristics. Between the PCI and CABG groups, no significant differences were found in the 3-year cumulative incidence of the primary outcome measure (14.9% vs. 12.9%, $p=0.60$). After propensity score matching, no significant differences were found in the incidences of primary outcome measure (13.0% vs. 12.8%, $p=0.95$), cardiac death, MI, and stroke (3.5% vs. 2.7%, $p=0.72$; 1.2% vs. 0.0%, $p=0.31$; and 4.9% vs. 3.1%, $p=0.35$), whereas that of TVR was significantly higher in the PCI group (24.5 vs. 7.1%, $p<0.01$). Compared with CABG, PCI with second-generation DES was not associated with higher risk of clinical outcomes, but was associated with a higher risk of TVR in the treatment of 3VD.

Keywords Coronary artery disease · Drug-eluting stent · Coronary artery bypass grafting

Introduction

The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) randomized trial was a cornerstone study, from which it has been reported that cardiovascular outcomes of patients with three-vessel coronary artery disease (CAD) after percutaneous coronary intervention (PCI) were significantly influenced by the angiographic complexity calculated by the SYNTAX score [1]. Various domestic and international guidelines recommended coronary artery bypass grafting (CABG) as the optimal treatment for patients with three-vessel CAD with intermediate and high SYNTAX scores [2–4]. Recently, second-generation drug-eluting stents (DES) have been developed and have shown to reduce the risks of clinically meaningful restenosis and definite stent thrombosis as compared with first-generation DES [5]. However, studies evaluating cardiovascular outcomes after PCI with second-generation DES in comparison with those of CABG in patients with three-vessel CAD are still limited [6]. In this study, we evaluated the long-term outcomes of patients with three-vessel

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CAD by comparing revascularization techniques between PCI with second-generation DES and CABG.

Methods

Patient population

Patients were eligible for this study if they had three-vessel CAD, which was defined as more than 50% stenosis in three major epicardial coronary arteries, and if they had undergone either PCI with second-generation DES, including everolimus-eluting cobalt chromium stents (Xience®, Abbott Vascular, Santa Clara, CA), everolimus-eluting platinum chromium stents (Promus Element®, Boston Scientific, Marlborough, MA), biolimus-eluting stents (Nobori®, Terumo Corporation, Tokyo, Japan), and zotarolimus-eluting stents (Endeavor Resolute® and Resolute Integrity®, Medtronic, Santa Rosa, CA) or CABG. The decision making regarding the revascularization technique was dependent on the physician and/or patient. The choice of the specific types of DES was dependent on the operator's decision. Surgical revascularization was performed using standard bypass techniques, and on-pump or off-pump surgery was performed at the surgeon's discretion. The exclusion criteria were as follows: previous CABG or PCI, PCI with stents other than second-generation DES, and ST segment elevation myocardial infarction (MI) within 24 h before the procedure. This study was approved by the institutional review committee.

Data collection

Demographic, angiographic, and procedural data were collected from hospital charts or databases. Follow-up data were obtained from hospital charts or by contacting patients. The European System for Cardiac Operative Risk Evaluation (EuroSCORE) was used to calculate the risk of death after cardiac surgery. The SYNTAX Score was used to evaluate the extensiveness of CAD.

Clinical outcome measures

The primary outcome measure was a composite of all-cause death, non-fatal MI, or stroke. The secondary outcome measures were cardiac death, non-fatal MI, stroke, and target vessel revascularization (TVR). Non-fatal MI was defined as MI that spontaneously occurred, with an increase in CK-MB levels above the upper limit of normal, ischemic changes on electrocardiograms, or a new pathological Q wave. Periprocedural MI after PCI was defined as an increase in CK-MB levels three times greater than the upper limit of normal, and periprocedural MI after CABG was defined as an increase in CK-MB levels five times greater than the upper limit of normal in patients with stable angina, according to the second universal definitions of MI [7]. Routine measurement of CK-MB levels was performed on all the patients undergoing PCI or CABG. Stroke was defined as ischemic or hemorrhagic stroke either occurring during hospitalization or requiring hospitalization for symptoms. TVR was defined as either PCI or CABG in the target vessel for any reasons. In the PCI group, routine follow-up coronary angiography was performed 8 and 20 months after the procedure. If PCI was performed on left main coronary artery lesions or chronic total occlusion lesions, routine follow-up coronary angiography was performed 3, 8, and 20 months after the procedure. In the CABG group, routine follow-up coronary angiography was performed within 1 month after surgery. If graft vessel occlusion occurred or ischemic changes developed, PCI in the target vessel was performed. Revascularization was performed if a significant stent restenosis or a significant coronary stenosis developed, irrespective of being either symptomatic (clinically driven) or asymptomatic (angiographically driven).

Statistical analysis

Categorical variables are presented as numbers and percentages and were compared using the Chi square test. Continuous variables are expressed as the mean with the standard deviation or the median with the interquartile range. Continuous variables were compared using unpaired Student's *t* test or the Mann–Whitney *U* test depending on their distributions. Cumulative incidences were calculated using the Kaplan–Meier method and were compared using the log-rank test. The effects of PCI relative to those of CABG for the individual endpoints are expressed as hazard ratios (HR) and their 95% confidence intervals (CI). We estimated the HR by Cox proportional hazard models adjusting for 7 clinically relevant factors listed in Table 1.

Given the differences in the baseline characteristics of the eligible patients between the PCI and CABG groups, propensity score matching was used to identify a cohort of patients with similar baseline characteristics. A logistic regression model was used to develop propensity scores with 15 independent variables potentially influencing the choice of mode of coronary revascularization (age ≥ 80 years, male, hypertension, diabetes, dyslipidemia, prior MI, prior stroke, peripheral arterial disease, LMT involvement, eGFR < 30, Hemodialysis, EuroSCORE ≥ 6, EF < 40%, unstable angina pectoris, SYNTAX score ≥ 33) listed in Table 1. To create a propensity score-matched cohort, patients in the CABG group were matched to those in the PCI group using a 1:1 greedy matching technique [8]. We conducted statistical analyses with JMP (SAS Institute, Cary, NC) or IBM SPSS statistics 23 (International Business Machines Corporation,

Table 1 Baseline patient characteristics

Variables	PCI ($n=298$)	CABG ($n=171$)	p value
Age, years	71.1 ± 11.4	68.1 ± 9.6	0.004
Age ≥ 80 years, n (%)[a]	62 (21)	22 (13)	0.03
Men, n (%)	217 (73)	192 (80)	0.08
Hypertension, n (%)	238 (80)	200 (84)	0.71
DM, n (%)	157 (53)	97 (57)	0.40
IDDM, n (%)[a]	40 (13)	35 (21)	0.045
Dyslipidemia, n (%)	221 (71)	126 (74)	0.51
Prior MI, n (%)	116 (39)	98 (29)	0.02
Prior stroke, n (%)	39 (13)	29 (17)	0.25
Peripheral arterial disease, n (%)	22 (7)	32 (19)	<0.001
LMT involvement, n (%)[a]	28 (9)	73 (43)	<0.001
eGFR (ml/min/1.73 m^2)	60.2 ± 26.1	57.2 ± 26.8	0.23
eGFR < 30, n (%)[a]	38 (13)	29 (17)	0.22
Hemodialysis, n (%)	20 (7)	14 (8)	0.55
EuroSCORE			
Mean score	5.6 ± 3.1	4.5 ± 3.0	0.001
≥ 6, n (%)[a]	146 (49)	57 (33)	0.001
LV dysfunction (EF < 40%), n (%)[a]	30 (10)	37 (22)	0.001
Unstable angina pectoris	79 (27)	36 (21)	0.19
SYNTAX score			
Mean score	28.3 ± 9.4	29.0 ± 7.9	0.42
≥ 33, n (%)[a]	111 (37)	53 (31)	0.16

PCI percutaneous coronary intervention, *CABG* coronary artery bypass grafting, *DM* diabetes mellitus, *IDDM* insulin-dependent diabetes mellitus, *MI* myocardial infarction, *LMT* left main trunk, *eGFR* estimated glomerular filtration rate, *EF* ejection fraction

The European System for Cardiac Operative Risk Evaluation (EuroSCORE) is a clinical model for calculating the risk of death after cardiac surgery

The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score is an angiographic model for evaluating the extensiveness of coronary artery disease

[a]Indicates potential independent risk-adjusting variables selected for Cox proportional hazards models

Armonk, NY). All the reported p values were 2-tailed, and p values < 0.05 were considered statistically significant.

Results

A total of 853 consecutive patients underwent PCI with second-generation DES or isolated CABG surgery for three-vessel CAD between January 2010 and December 2014. After excluding 384 patients who had performed coronary revascularization (previous PCI: $n=298$, previous CABG: $n=53$) and PCI with stents other than second-generation DES ($n=33$), this study included 298 patients undergoing PCI with only second-generation DES (PCI group) and 171 undergoing CABG (CABG group) for de novo three-vessel CAD. The study flow chart is shown in Fig. 1. The baseline characteristics of the patients are shown in Table 1. The PCI group was significantly older and had a higher rate of the history of MI and a significantly higher EuroSCORE. The prevalences of insulin-dependent diabetes mellitus, peripheral arterial disease, left ventricular dysfunction, and left main trunk disease were significantly higher in the CABG group. The average SYNTAX score was similar in

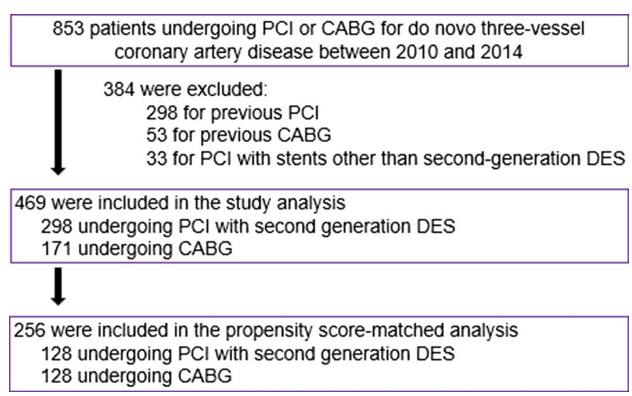


Fig. 1 Study flow chart. The method of patient selection is demonstrated. *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass grafting

the two groups. Thienopyridine agents and statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blocker were often prescribed in the PCI group than in the CABG group, and beta-blockers and warfarin, proton pump inhibitors were more prescribed in the CABG group than in the PCI group.

The procedural characteristics of the patients are shown in Table 2. In the PCI group, the average number of implanted stents per patient was 5.1 stents, and the average total length of stents per patient was 120.0 mm. Staged PCI was performed in 45% of the PCI group. In the CABG group, 81% of the patients underwent off-pump surgery and 95% of the patients received a left internal thoracic artery graft bypass. The rate of periprocedural MI was similar in the PCI and CABG groups (5.9% vs. 10.4%, $p=0.15$) (Supplementary Table S2).

Table 2 Baseline procedural characteristics

PCI group	Values, *n* (%)
No. of patients	298
No. of stents placed	5.1 ± 1.8
Stent diameter, mm	2.8 ± 0.4
Total length of stents placed, mm	120.0 ± 42.7
Total number of stents placed	1527
Types of second-generation DES	
CoCr-everolimus-eluting stents	610 (40%)
Biolimus-eluting stents	443 (29%)
PtCr-everolimus-eluting stents	362 (23%)
Zotarolimus-eluting stents	112 (7%)
PCI planning	
One staged PCI	165 (55%)
Two staged PCI	128 (43%)
Three staged PCI	5 (2%)
Stent-implanted sites	
LAD	270 (91%)
LCx	265 (89%)
RCA	251 (84%)
LMT	98 (32%)
CABG group	
No. of patients	171
No. of grafted vessels per patient	
Any	3.4 ± 0.8
Arterial graft	2.0 ± 0.8
Left internal thoracic artery graft	163 (95%)
Off-pump surgery	138 (81%)
Anastomotic sites	
LAD	168 (98%)
LCx	161 (94%)
RCA	146 (85%)
Dg of LAD	49 (29%)

PCI percutaneous coronary intervention, *CABG* coronary artery bypass grafting, *CoCr* cobalt chromium, *PtCr* platinum chromium, *LAD* left anterior descending artery, *LCx* left circumflex artery, *RCA* right coronary artery, *LMT* left main trunk, *Dg* diagonal

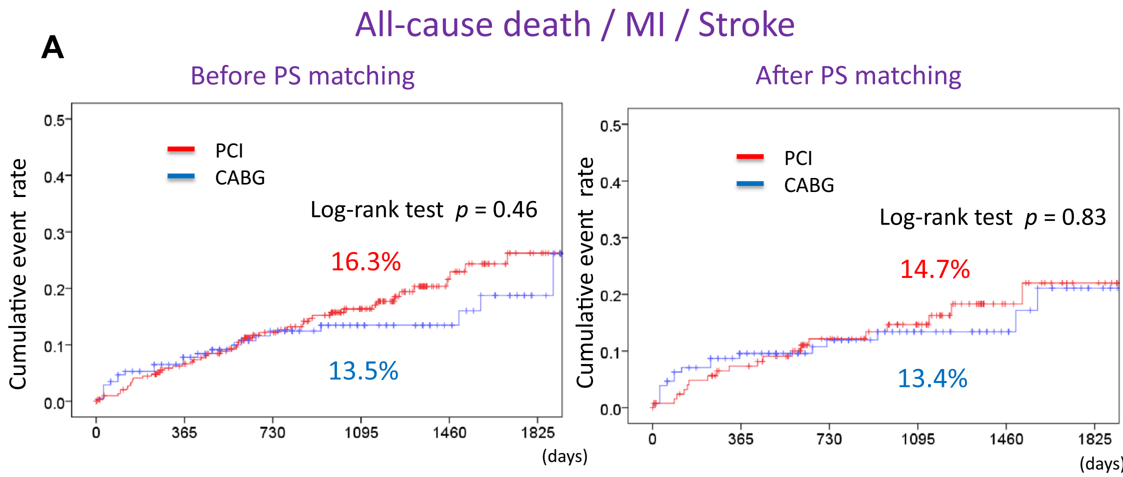
The median follow-up duration of the surviving patients was 998 days [interquartile range 589–1374 days]. The 3-year cumulative incidence of the primary outcome measure was similar in the PCI and CABG groups (16.3% vs. 13.5%; HR 1.20; 95% CI 0.75–2.01; $p=0.46$) (Fig. 2a). The 3-year cumulative incidences of all-cause death, cardiac death, non-fatal MI, and stroke were similar in the two groups (12.1% vs. 8.4%, $p=0.32$; 4.7% vs. 2.0%, $p=0.15$; 2.3% vs. 2.4%, $p=0.57$; and 3.9% vs. 4.2%, $p=0.56$, respectively) (Fig. 2b–e). Fifty-one patients died, 15 of whom died of a cardiac cause. The 3-year cumulative incidence of TVR was significantly higher in the PCI group than in the CABG group (23.2% vs. 5.9%, $p<0.01$) (Fig. 2f), whereas that of clinically driven TVR was similar in the two groups (4.7% vs. 4.8%, $p=0.71$) (Supplementary Table S1).

On the basis of propensity score matching, 128 patients in the PCI group were matched with 128 patients in the CABG group. After propensity score matching, no significant differences were observed in patient characteristics between the PCI and CABG groups (Table 3). Between the PCI and CABG groups, no significant differences were found in the 3-year cumulative incidence of the primary outcome measure (14.7% vs. 13.4%; HR 1.07; 95% CI 0.56–2.09; $p=0.83$) (Fig. 2a). There were no significant differences in the 3-year cumulative incidence of incidences of all-cause death, cardiac death, non-fatal MI, and stroke between two groups (11.2% vs. 7.7%, $p=0.41$; 3.5% vs. 2.7%, $p=0.72$; 1.8% vs. 3.1%, $p=0.65$; and 3.1% vs. 4.9%, $p=0.35$, respectively) (Fig. 2b–e). The 3-year cumulative incidence of TVR was significantly higher in the PCI group than in the CABG group (24.5% vs. 7.1%, $p<0.01$) (Fig. 2f), whereas that of clinically driven TVR was not higher in the PCI group than in the CABG group (2.9% vs. 6.4%, $p=0.43$).

Discussion

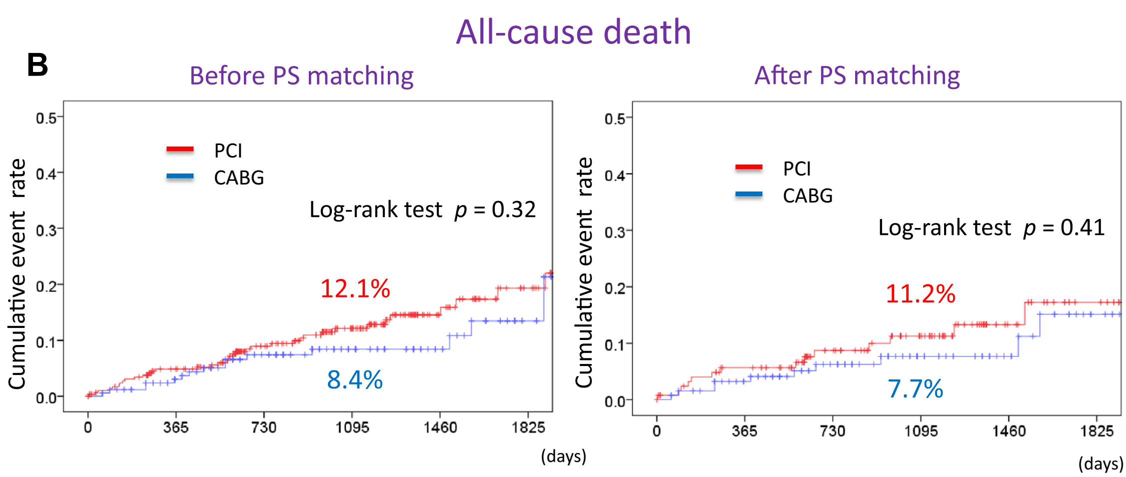
The main finding of this study was that PCI with second-generation DES was not associated with the long-term risk of the primary outcome measure compared with CABG in patients with de novo three-vessel CAD. A previous observational study comparing PCI with DES with CABG in patients with three-vessel CAD showed that CABG was associated with better long-term outcomes with lower incidences of death, MI, and stroke than PCI with DES [9], which was consistent with what the SYNTAX randomized trial revealed. However, because these studies were conducted with the use of first-generation DES, the superiority of CABG to PCI with second-generation DES is debatable.

In the first-generation DES era, a report from the CREDO-Kyoto PCI/CABG Registry cohort showed



Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		19	41	50
N of patients at risk	298	253	132	33
CABG Group				
N of patients with at least 1 event		13	19	22
N of patients at risk	171	140	101	12

Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		9	16	19
N of patients at risk	128	109	58	12
CABG Group				
N of patients with at least 1 event		12	15	17
N of patients at risk	128	101	47	7



Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		14	30	36
N of patients at risk	298	258	138	35
CABG Group				
N of patients with at least 1 event		5	12	14
N of patients at risk	171	148	70	13

Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		7	12	14
N of patients at risk	128	111	61	12
CABG Group				
N of patients with at least 1 event		4	8	10
N of patients at risk	128	109	51	9

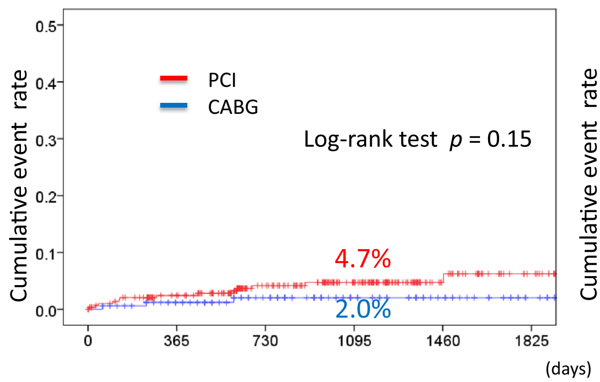
Fig. 2 Cumulative 3-year incidences. Comparisons between the PCI and CABG groups before and after propensity score matching are demonstrated: **a** primary outcome measure; **b** all-cause death; **c** cardiac death; **d** non-fatal myocardial infarction; **e** stroke; and **f** target vessel revascularization. Abbreviations are as in Fig. 1

that the 3-year cumulative incidence of all-cause death, non-fatal MI, stroke, and coronary revascularization were 11.7%, 5.0%, 5.7%, and 42.5%, respectively [10]. In comparison with the results from the CREDO-Kyoto PCI/CABG Registry cohort, the rates of non-fatal MI and TVR in this study were numerically lower. There were no

C

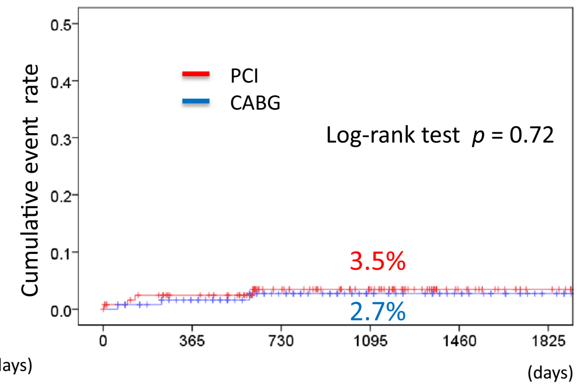
Cardiac death

Before PS matching



Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		7	12	13
N of patients at risk	298	258	138	35
CABG Group				
N of patients with at least 1 event		2	3	3
N of patients at risk	171	148	70	13

After PS matching

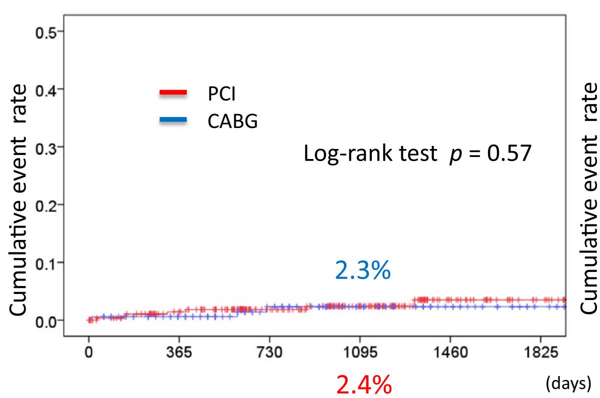


Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		3	4	4
N of patients at risk	128	111	61	12
CABG Group				
N of patients with at least 1 event		2	3	3
N of patients at risk	128	109	51	9

D

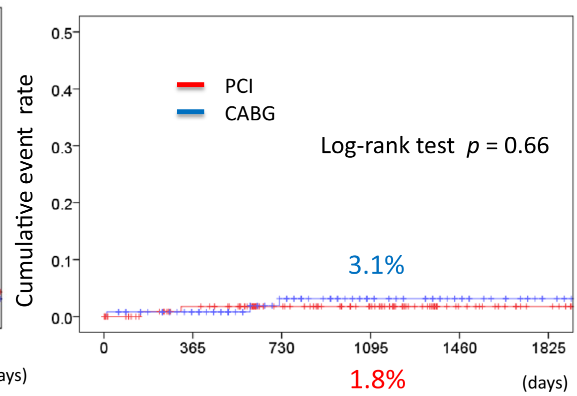
Non-fatal myocardial infarction

Before PS matching



Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		4	6	7
N of patients at risk	298	255	134	33
CABG Group				
N of patients with at least 1 event		1	3	3
N of patients at risk	171	147	67	12

After PS matching

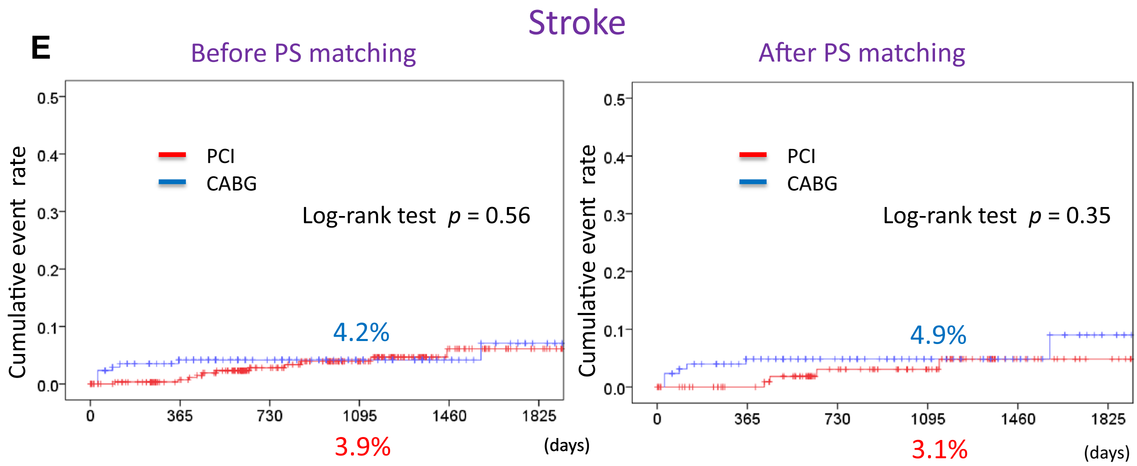


Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		2	2	2
N of patients at risk	128	109	58	12
CABG Group				
N of patients with at least 1 event		1	3	3
N of patients at risk	128	108	49	8

Fig. 2 (continued)

significant differences in the risk for all-cause mortality and cardiac death between the PCI and the CABG group. This finding was discrepant with the results of previous randomized trials. After propensity score matching, baseline characteristics of the PCI and CABG groups were much more comparable than those in the entire study

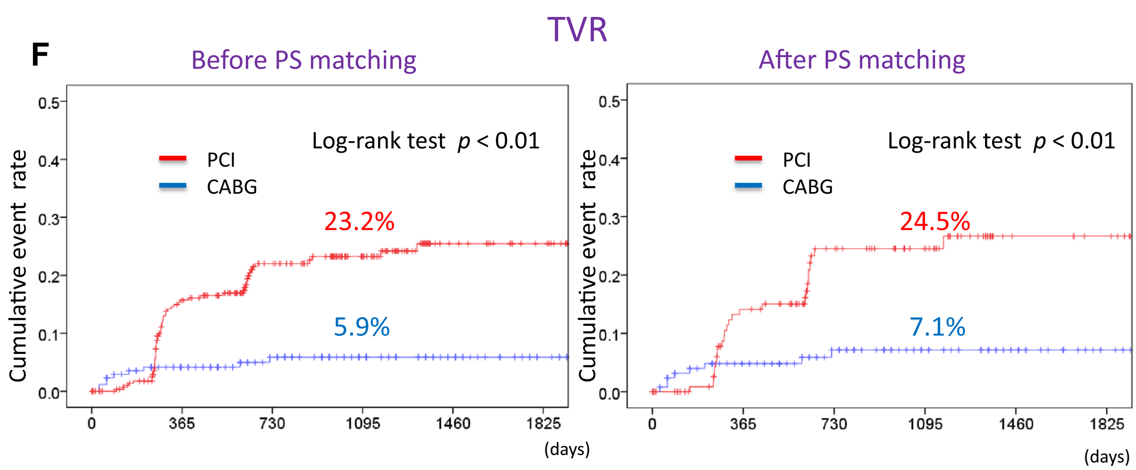
E



Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		2	9	11
N of patients at risk	298	256	135	35
CABG Group				
N of patients with at least 1 event		7	7	8
N of patients at risk	171	141	67	13

Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		0	3	4
N of patients at risk	128	111	59	12
CABG Group				
N of patients with at least 1 event		6	6	7
N of patients at risk	128	103	49	9

F



Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		42	57	59
N of patients at risk	298	216	93	26
CABG Group				
N of patients with at least 1 event		7	9	9
N of patients at risk	171	141	67	12

Interval	0	1 year	3 years	5 years
PCI Group				
N of patients with at least 1 event		16	25	26
N of patients at risk	128	95	43	10
CABG Group				
N of patients with at least 1 event		6	8	8
N of patients at risk	128	102	48	8

Fig. 2 (continued)

population and there was no significant differences in the 3-year cumulative incidence of incidence of cardiac death between the PCI and CABG groups (3.5% vs. 2.7%, $p = 0.72$). However, the adjusted HR of PCI relative to CABG in cardiac death might have showed a worse tendency of PCI relative to CABG in terms of cardiac death. Considering small study population and potential selection bias, we should interpret the conclusion carefully.

Table 3 Patient characteristics after propensity score matching

Variables	PCI ($n=128$)	CABG ($n=128$)	p value
Age, years	67.7 ± 11.9	68.2 ± 9.6	0.68
Age ≥ 80 years, n (%)	17 (13)	15 (12)	0.85
Men, n (%)	97 (76)	100 (78)	0.66
Hypertension, n (%)	106 (83)	108 (84)	0.74
DM, n (%)	83 (65)	71 (56)	0.13
IDDM, n (%)	22 (17)	28 (22)	0.34
Dyslipidemia, n (%)	93 (73)	97 (76)	0.57
Prior MI, n (%)	44 (34)	41 (32)	0.69
Prior stroke, n (%)	19 (15)	22 (17)	0.61
Peripheral arterial disease, n (%)	18 (14)	20 (16)	0.73
LMT involvement, n (%)	28 (9)	34 (27)	0.38
eGFR (ml/min/1.73 m^2)	57.7 ± 27.5	57.5 ± 27.7	0.94
eGFR < 30, n (%) *	18 (14)	24 (19)	0.40
Hemodialysis, n (%)	11 (9)	12 (9)	0.83
EuroSCORE			
Mean score	4.8 ± 3.1	4.9 ± 3.2	0.78
≥ 6, n (%)	45 (35)	49 (38)	0.60
LV dysfunction (EF < 40%), n (%)	20 (16)	23 (18)	0.62
Unstable angina pectoris	79 (27)	36 (21)	0.19
SYNTAX score			
Mean score	28.7 ± 9.8	28.3 ± 7.8	0.77
≥ 33, n (%)	50 (39)	38 (30)	0.11

Abbreviations are as in Table 1

Patients with three-vessel CAD were greatly associated with developed coronary atherosclerosis and showed a high SYNTAX score. Since treating three-vessel CAD requires a bigger number of stents and a much longer total length of implanted stents than usual, the risks of stent thrombosis and stent restenosis are high [11]. Restenosis and stent thrombosis are serious complications of PCI, which may lead to a poor prognosis [12]. Second-generation DES was developed by employing thinner stent struts and a variety of drugs and polymers to reduce vessel injury and improve endothelial healing problems [13]. Second-generation DES reduced the risks of clinically meaningful restenosis and definite stent thrombosis as compared with first-generation DES [5]. In our study, there was no incidence of stent thrombosis in the PCI group (Supplementary Table S2). There is a possibility that second-generation DES has contributed to reduce the risk of non-fatal MI and coronary revascularization.

No significant difference in the incidence of stroke was observed between the PCI and the CABG groups. One of the main reasons can be a high rate of off-pump surgery in the CABG group. Stroke is one of the most serious complications of conventional on-pump CABG, and off-pump CABG can reduce the complications associated with cardiopulmonary bypass surgery. A recent report showed that off-pump CABG was associated with a significantly lower rate of postoperative stroke than on-pump CABG, even in older and higher risk patients [14].

Previously Tsuneyoshi et al. reported CABG is superior to second-generation DES in three-vessel CAD and after propensity-matched analysis [15]. The incidence of all-cause death was significantly higher in the PCI group than CABG group and those of cardiac death was similar between two groups, which were discrepant with the results of previous randomized trials. The differences of the previous and our study are the patient numbers in the CABG group and the definition of non-fatal MI. To evaluate the outcomes in patients with "de novo" three-vessel coronary artery disease, we excluded patients who had performed coronary revascularization. We investigated the non-fatal MI events including periprocedural MI.

The risk of TVR was extremely higher in the PCI group than in the CABG group, particularly between the first and second year after the procedure. The majority of TVR in the PCI group was angiographically driven (78%), detected at frequently scheduled angiographic follow-up, whereas the majority of TVR in the CABG group was clinically driven (78%). Oculostenotic reflex, which means coronary revascularization for antiographic stenosis without evidence of ischemia, was reported as a negative aspect of routine follow-up CAG. A randomized trial evaluating the long-term clinical impact of routine follow-up coronary angiography after PCI showed no clinical benefits and an increasing number of any coronary revascularization within the first year. Target lesion revascularization within the first year after the index PCI was performed more frequently in angiographic follow-up group than in clinical follow-up group (7.0% vs. 1.7%; log-rank $p < 0.001$). [16] We should reconsider the scheduled angiography after coronary revascularization.

Study limitations

This study has four important limitations. First and most importantly, this was a single center, retrospective study with a relatively small number of patients. Further studies are needed to validate these results. Second, its observational study design with selection bias precluded definitive conclusions on the superiority of either PCI or CABG because of unmeasured confounders such as frailty; however, the lack of randomization is inevitable in daily clinical practice. Third, the practice patterns including indication of revascularization and medical therapy were different from those in the current clinical practice. Finally, we could not exclude the influence of scheduled angiography on the TLR rate in the PCI group within 3 years.

Conclusions

Compared with CABG, PCI with second-generation DES was not associated with the long-term risks of all-cause death, cardiac death, non-fatal MI, and stroke, but was associated with a higher risk of TVR in the treatment of three-vessel CAD.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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