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Impact of Angiographic Complete Revascularization After Drug-Eluting Stent Implantation or Coronary Artery Bypass Graft Surgery for Multivessel Coronary Artery Disease

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Background**—**This study sought to evaluate the clinical impact of angiographic complete revascularization (CR) after drug-eluting stent implantation or coronary artery bypass graft surgery for multivessel coronary disease.

Methods and Results**—**A total of 1914 consecutive patients with multivessel coronary disease undergoing drug-eluting stent implantation (1400 patients) or coronary artery bypass graft surgery (514 patients) were enrolled. Angiographic CR was defined as revascularization in all diseased segments according to the Synergy Between PCI With Taxus and Cardiac Surgery classification. The outcomes of patients undergoing CR were compared with those undergoing incomplete revascularization (IR) after adjustments with the inverse-probability-of-treatment weighting method. Angiographic CR was performed in 917 patients (47.9%) including 573 percutaneous coronary intervention (40.9%) and 344 coronary artery bypass graft (66.9%) patients. CR patients were younger and had more extensive coronary disease than IR patients. Over 5 years, CR patients had comparable incidences of death (8.9% versus 8.9%; adjusted hazard ratio, 1.04; 95% confidence interval, 0.76 to 1.43; $P=0.81$), the composite of death, myocardial infarction, and stroke (12.1% versus 11.9%; adjusted hazard ratio, 1.04; 95% confidence interval, 0.79 to 1.36; $P=0.80$), and the composite of death, myocardial infarction, stroke, and repeat revascularization (22.4% versus 24.9%; adjusted hazard ratio, 0.91; 95% confidence interval, 0.75 to 1.10; $P=0.32$) compared with IR patients. However, 368 patients (19.2%) with multivessel IR had a greater tendency toward higher risk of death, myocardial infarction, stroke, or repeat revascularization (30.3% versus 22.1%; adjusted hazard ratio, 1.27; 95% confidence interval, 0.97 to 1.66; $P=0.079$) than those without multivessel IR.

Conclusions**—**Angiographic CR with drug-eluting stent implantation or coronary artery bypass grafting did not improve long-term clinical outcomes in patients with multivessel disease. This finding supports the strategy of ischemia-guided revascularization. **(*Circulation*. 2011;123:2373-2381.)**

Key Words: bypass surgery ■ coronary disease ■ revascularization ■ stent

In patients with multivessel coronary disease (MVD), complete revascularization (CR) strategy has been regarded as associated with better long-term clinical outcomes after percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).[1,2] Because of technical complexity, low ejection fraction, or safety concerns regarding the implantation of multiple drug-eluting stents (DES), however, diseased segments have often been incompletely revascularized in patients undergoing PCI.[2] Furthermore, even with CABG, the strategy of incomplete revascularization (IR) has occasionally been adopted to reduce operation-related complications, particularly when minimally invasive or off-pump surgery is attempted.[3]

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Clinical Perspective on p 2381

Although previous studies have demonstrated the clinical impact of CR after PCI or CABG, additional studies are needed to assess the outcomes of updated treatments, such as DES, left internal mammary artery (LIMA) grafting, off-pump surgery, and current medications. We therefore evaluated the long-term clinical impacts of angiographic CR, compared with IR, in patients receiving PCI with DES or CABG for MVD.

Methods

Patients

Patients with MVD in the Asan Medical Center Multivessel Registry who underwent DES implantation or CABG between January 2003 and December 2005 were included in this study.[4] Patients who underwent prior CABG or concomitant valvular or aortic surgery and those who had an acute myocardial infarction (MI) within 24 hours before revascularization or presented with cardiogenic shock were excluded. In addition, because of retrospective angiographic analysis, patients who did not have available angiograms captured at the index PCI or CABG were excluded. The institutional review board

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approved the use of clinical data for this study, and all patients provided written informed consent for enrollment in our registry. The authors had full access to and take full responsibility for the integrity of the data. All authors have read, and agree to, the manuscript as written.

Procedures

The selection of PCI or CABG was at each physician's discretion. Stents were implanted as described.[4,5] The choice of DES type and the use of intravascular ultrasound, glycoprotein IIb/IIIa inhibitor, or other devices to facilitate optimal stenting were at the operator's discretion. Each patient undergoing PCI was administered a loading dose of 200 mg aspirin and 300 mg clopidogrel before the procedure. After DES implantation, patients received standard dual antiplatelet therapy, consisting of 100 mg/d aspirin and 75 mg/d clopidogrel, for at least 6 months, with clopidogrel continued for longer periods in patients at high risk of ischemic complications. Coronary artery bypass grafting was performed with standard bypass techniques,[6] with the LIMA primarily attempted to be grafted to the left anterior descending artery. On- or off-pump surgery was performed at the operator's discretion.[7] The decision on whether to perform CR or IR was made by interventional cardiologists or cardiac surgeons. Percutaneous coronary intervention was preferred for patients at high surgical risk because of combined morbidity. However, CABG was considered the primary option for MVD in patients with severe angiographic complexity or low left ventricular function.[6]

Clinical End Points and Follow-Up

The primary outcome of interest was major adverse cardiovascular events (MACE), consisting of all-cause death, MI, and stroke, a marker of treatment safety. The secondary outcome of interest was major adverse cardiac and cerebrovascular events (MACCE), consisting of MACE plus repeat revascularization. A diagnosis of MI was defined as either complications at index admission (defined as new pathological Q waves after index treatment) or follow-up MI requiring subsequent hospitalization (defined as an emergency admission with a principal diagnosis of MI), as described.[8] Q-wave MI was defined as the documentation of a new pathological Q wave after index treatment. Repeat revascularization included target vessel revascularization, regardless of whether the procedure was clinically or angiographically driven, and non–target vessel revascularization. Stroke, as indicated by neurological deficits, was confirmed by a neurologist on the basis of imaging modalities. In the PCI group, stent thrombosis was defined according to the Academic Research Consortium classification.[9] All outcomes of interest were carefully verified and adjudicated by independent clinicians.

Clinical, angiographic, procedural or operative, and outcome data were prospectively recorded in the dedicated PCI and surgical databases by independent research personnel. Patients were clinically followed up at 1, 6, and 12 months and annually thereafter, via office visit or telephone contact. To ensure accurate assessment of clinical end points, additional information was obtained from visits or telephone contacts with living patients or family members and from medical records obtained from other hospitals, as necessary. To validate complete follow-up data on mortality, information about vital status was obtained through January 31, 2010, from the National Population Registry of the Korea National Statistical Office with the use of each patient's unique personal identification number.

Angiographic Analysis

Of the 3042 patients enrolled in the Asan Medical Center Multivessel Registry between 2003 and 2005, 1914 (62.9%) underwent retrospective angiographic analyses with the use of dedicated angiographic software (CASS-5, Pie-Medical, Netherlands) in the angiographic core laboratory of the CardioVascular Research Foundation, Seoul, Korea. Diseased segments and lesion characteristics were categorized according to the Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) classification (Figure 1).[10] Coronary artery bypass grafting patients were assessed by comparing the diagnostic angiographic analysis with the surgical procedure report.

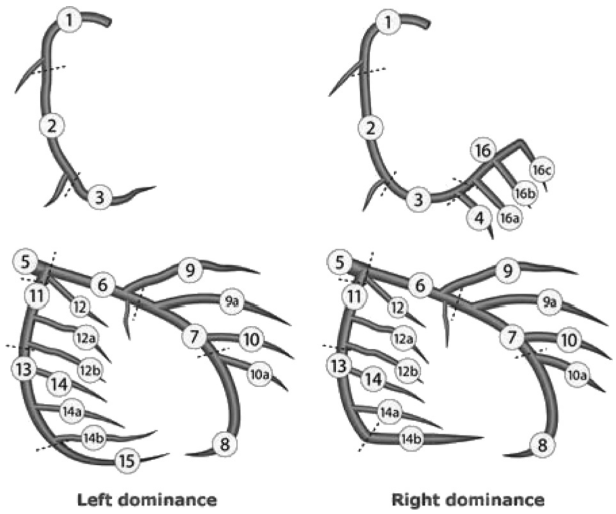

Figure 1. Definitions of coronary segments according to the Synergy Between PCI With Taxus and Cardiac Surgery classification. Images were captured from http://www.syntaxscore.com/.

Complete revascularization in PCI patients was assessed by comparing the diagnostic and postprocedural angiograms.

Complete revascularization was defined as any attempt to revascularize all diseased segments, with either PCI or CABG, during the index hospitalization or within 30 days after the index procedure, but before a new MI or urgent target lesion revascularization. To assess the impact of varying definitions of CR, we defined 4 types of CR. Angiographic CR-1, according to the SYNTAX classification, was defined as angioplasty or grafting in all diseased coronary segments (≥1.5 mm), consisting of the right coronary artery (segments 1, 2, and 3) and its main branches, including the posterior descending artery (segment 4 or 15) and the posterolateral branch (segment 16); the left anterior descending artery (segments 5, 6, 7, and 8) and its major diagonal branches (segment 9 or 10); and the left circumflex artery (segments 11 and 13) and its major obtuse marginal branches (segment 12 or 14).[11–13] Angiographic CR-2 was defined as revascularization in all diseased segments ≥2.5 mm in diameter. Patients not meeting these criteria were considered IR patients. We also applied a more practical definition of proximal CR, when the diseased proximal arteries (segments 1, 2, 3, 5, 6, 7, and 11) underwent angioplasty or received at least 1 graft.[11,13] In addition, we evaluated the impact of multivessel IR, in which ≥2 diseased vessels were incompletely revascularized. The left main artery (segment 5) was considered revascularized when the left anterior descending artery was bypassed in the CABG group or the left main artery was directly treated percutaneously in the PCI group.

Statistical Analysis

Differences in baseline clinical and angiographic characteristics and procedural findings were compared with the t test for continuous variables and the χ^2 or Fisher exact test for categorical variables, as appropriate. Survival curves were constructed with the Kaplan–Meier method and compared with the log-rank test. Patients were censored at 5 years (1800 days) or when the events occurred.

Differences between the CR and IR groups in risk-adjusted, long-term rates of study outcomes were assessed with multivariable Cox proportional hazards regression with important covariates that had a significant effect ($P<0.1$) on the clinical outcomes. Covariates considered in the Cox models were patient age, sex, body mass index, presence of hypertension, smoking, hypercholesterolemia, diabetes mellitus, and atrial fibrillation; prior history of MI, stroke, peripheral vascular disease, congestive heart failure, chronic renal failure, and PCI; and left ventricular ejection fraction. The proportional hazards assumption was confirmed by examination of log (−log [survival]) curves and by testing of partial (Schoenfeld) residuals,[14] and no relevant violations were found. Analyses were

Table 1. Baseline Patient Characteristics

Variable	PCI CR (n=573)	PCI IR (n=827)	PCI *P*	CABG CR (n=344)	CABG IR (n=170)	CABG *P*
Clinical characteristics						
Age, y	60.8±10.47	62.7±9.8	<0.001	61.6±8.7	62.2±8.0	0.50
Male sex	389 (67.9)	586 (70.9)	0.24	253 (73.5)	122 (71.8)	0.67
Left ventricular ejection fraction, %	59.5±8.2	58.3±8.8	0.009	57.0±10.7	55.5±11.4	0.14
Diabetes mellitus	172 (30.0)	271 (32.8)	0.28	151 (43.9)	66 (38.8)	0.27
Hypertension	312 (54.5)	486 (58.8)	0.11	211 (61.3)	108 (63.5)	0.63
Current smoker	175 (30.5)	238 (28.8)	0.48	72 (20.9)	34 (20.0)	0.81
Hyperlipidemia	153 (26.7)	189 (22.9)	0.10	164 (47.7)	87 (51.2)	0.46
Prior myocardial infarction	60 (10.5)	79 (9.6)	0.57	78 (22.7)	47 (27.6)	0.22
Previous coronary angioplasty	86 (15.0)	159 (19.2)	0.041	57 (16.6)	33 (19.4)	0.43
Previous congestive heart failure	7 (1.2)	13 (1.6)	0.59	15 (4.4)	5 (2.9)	0.43
Obstructive pulmonary disease	3 (0.5)	12 (1.5)	0.10	7 (2.0)	6 (3.5)	0.37
Cerebrovascular disease	25 (4.4)	50 (6.0)	0.17	44 (12.8)	28 (16.5)	0.26
Peripheral vascular disease	10 (1.7)	20 (2.4)	0.39	29 (8.4)	17 (10.0)	0.56
Renal failure	10 (1.7)	27 (3.3)	0.08	23 (6.7)	15 (8.8)	0.38
Atrial fibrillation	20 (3.5)	24 (2.9)	0.54	9 (2.6)	3 (1.8)	0.76
Clinical presentation			0.57			0.54
Stable angina	275 (48.0)	420 (50.8)		115 (33.4)	58 (34.1)	
Unstable angina	245 (42.8)	338 (40.9)		209 (60.8)	106 (62.4)	
Acute myocardial infarction	53 (9.2)	69 (8.3)		20 (5.8)	6 (3.5)	
Angiographic characteristics						
SYNTAX score	15.0±7.1	19.0±7.7	<0.001	29.5±10.5	30.8±10.7	0.20
Angiographic stenosis						
Left anterior descending artery	509 (88.8)	770 (93.1)	0.005	340 (98.8)	169 (99.4)	0.53
Left circumflex artery	294 (51.3)	627 (75.8)	<0.001	270 (78.5)	150 (88.2)	0.007
Right coronary artery	332 (57.9)	686 (83.0)	<0.001	290 (84.3)	164 (96.5)	<0.001
Left main artery	104 (18.2)	110 (13.3)	0.013	160 (46.5)	72 (42.4)	0.37
Three-vessel disease	124 (21.6)	446 (53.9)	<0.001	236 (68.6)	143 (84.1)	<0.001
Any chronic total occlusion	91 (15.9)	202 (24.4)	<0.001	157 (45.6)	79 (46.5)	0.86
Procedural characteristics						
CABG procedures						
No. of conduits	…	…	…	3.6±1.0	2.9±1.1	<0.001
No. of arterial conduits	…	…	…	1.0±0.1	1.0±0.1	0.58
Internal thoracic artery	…	…	…	266 (77.3)	128 (75.3)	0.61
Off-pump surgery	…	…	…	92 (26.7)	42 (24.7)	0.62
PCI procedures						
No. of total stents	2.5±1.3	2.2±1.2	<0.001	…	…	…
Length of total stents, mm	63.6±36.3	55.9±32.3	<0.001	…	…	…
Mean stent size, mm	3.2±0.3	3.1±0.3	0.063	…	…	…

PCI indicates percutaneous coronary intervention; CABG, coronary artery bypass grafting; CR, complete revascularization; IR, incomplete revascularization; and SYNTAX, Synergy Between PCI With Taxus and Cardiac Surgery.

performed separately in PCI patients. We also adjusted for differences in patient baseline characteristics by using weighted Cox proportional hazards regression models with inverse-probability-of-treatment weighting.[15,16] With the use of this method, weights for patients receiving IR were the inverse of (1−propensity score), and weights for patients receiving CR were the inverse of propensity score. Propensity scores were estimated, without regard to outcomes, with multiple logistic regression analysis. A full nonparsimonious model was developed that included treatment effect (CR or IR) and the aforementioned variables. Model discrimination was assessed with C statistics, and model calibration was assessed with Hosmer-Lemeshow statistics. For the PCI group, a separate propensity for CR versus IR was derived. All analyses were repeated with the varying definitions of CR. Interactions between factors associated with CR and treatment strategy were tested by incorporation of formal interaction terms in the multivariable Cox model. All reported *P* values are 2 sided, and *P* values <0.05 were considered statistically significant. No adjustment was performed for multiple testing in several subgroups. SAS software, version 9.1, and the R programming language were used for statistical analyses.

Results

Patient Characteristics

Of the 1914 included patients, 1400 (73.1%) underwent PCI with DES implantation, and 514 (26.9%) underwent CABG. Angiographic CR-1 was performed in 917 patients (47.9%), including 573 PCI (40.9%) and 344 CABG (66.9%) patients ($P<0.001$). Table 1 shows the baseline clinical, angiographic and procedural characteristics of CR and IR patients according to the definition of angiographic CR-1. In the PCI group, CR patients were younger and had larger left ventricular ejection fraction, less prior angioplasty, and less extensive coronary disease and were treated with more stents than IR patients. Likewise, in the CABG group, CR patients had less extensive coronary disease and received more vascular conduits.

Angiographic CR-2, which considered diseased segments ≥2.5 mm in diameter, was performed in 1127 patients (58.9%), including 721 PCI (64.0%) and 406 CABG (36.0%) patients ($P<0.001$). Proximal CR assessing the proximal arterial segments was possible in 1194 patients (62.4%), including 792 PCI (56.6%) and 402 CABG (78.2%) patients ($P<0.001$). When IR was subdivided according to the number of nonrevascularized vessels, we found that 1-, 2-, and 3-vessel IR occurred in 629 patients (32.9%) (483 PCI [34.5%] and 146 CABG [28.4%]), 304 patients (15.9%) (284 PCI [20.3%] and 20 CABG [3.9%]), and 64 patients (3.3%) (60 PCI [4.3%] and 4 CABG [0.8%]), respectively (<0.001). Thus, multivessel IR was observed in 24.6% of PCI patients and 4.7% of CABG patients ($P<0.001$).

Unadjusted and Adjusted Outcomes

Patients were followed for a median of 1800 days (interquartile range, 1609 to 1800 days). The incidences of 5-year mortality according to the definition of angiographic CR-1 are shown in Figure 2. Table 2 shows 5-year incidences of MACE and MACCE according to the varying definitions of CR. The incidences of MACE and MACCE in the CR and IR groups did not differ when we used the definitions of angiographic CR-1 (Figure 3), CR-2, and proximal CR. However, multivessel IR was associated with higher incidences of MACE and MACCE in both PCI and CABG patients (Figure 4 and Table 2). Definite (17 patients) or probable (18 patients) stent thrombosis occurred in 35 patients (2.5%) within 5 years after DES implantation.

Because of the small number of events in the CABG group, statistical adjustments were performed for all patients and for the PCI subgroup (Table 3). With 2 methods of adjustment, angiographic CR-1, CR-2, and proximal CR were not associated with the risks of MACE and MACCE. After multivariate Cox adjustment, however, multivessel IR was associated with MACCE in overall patients. However, statistical significance was lost after adjustment with the inverse-probability-of-treatment weighting method. We did not observe significant interactions between CR (CR versus IR) and treatment strategy (PCI versus CABG) for MACE and MACCE with any definition of CR. The 5-year adjusted risk of mortality was also not associated with CR strategy with the use of either the multivariate Cox model (hazard ratio, 1.02; 95% confidence interval, 0.75 to 1.39; $P=0.91$) or the inverse-probability-of-treatment weighting method (hazard ratio, 1.04; 95% confidence interval, 0.76 to 1.43; $P=0.81$).

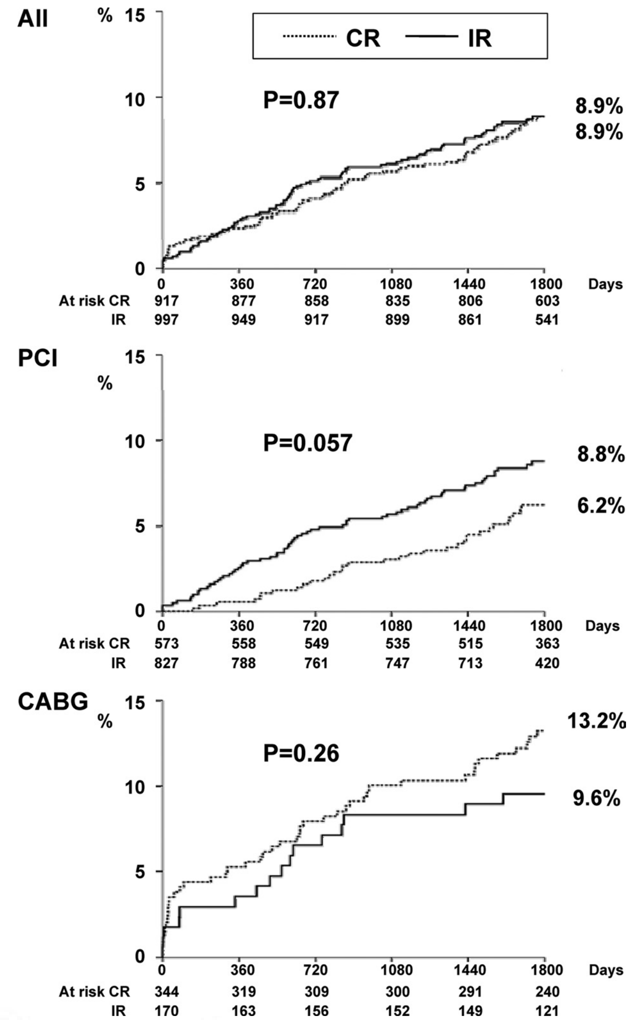

Figure 2. Unadjusted Kaplan–Meier mortality curves between complete revascularization (CR) and incomplete revascularization (IR) groups in all (**top**), percutaneous coronary intervention (PCI) (**middle**), and coronary artery bypass grafting (CABG) (**bottom**) patients.

Discussion

To assess the impact of angiographic CR on long-term clinical outcomes after revascularization for MVD, we performed detailed angiographic analyses based on varying definitions of CR.[1,11] These analyses showed that anatomic CR for all angiographic stenoses did not improve the long-term clinical outcomes after either PCI or CABG in patients with MVD. In patients with extensive coronary artery disease, however, multivessel IR may be associated with unfavorable long-term clinical outcomes.

Although PCI is often preferred because it is less invasive than CABG, PCI is less able to achieve CR in patients with multiple coronary lesions, especially in patients with decreased ventricular function.[17] A recent observational study in patients with MVD and impaired left ventricular function

Table 2. Estimated Kaplan–Meier Events Rates Over 5 Years

				MACE					MACCE				
Definitions	Patients	Strategy	Patient No.	No. of Patients With Events	1 y	3 y	5 y	*P*	No. of Patients With Events	1 y	3 y	5 y	*P*
Angiographic CR-1	All	IR	997	113	3.7	8.3	11.9	0.91	234	10.2	18.3	24.9	0.21
		CR	917	105	3.0	7.2	12.1		197	8.6	16.0	22.4	
	PCI	IR	827	91	3.5	7.7	11.7	0.11	204	10.7	18.9	26.3	0.35
		CR	573	50	0.7	4.3	9.4		132	9.0	16.9	24.0	
	CABG	IR	170	22	4.7	11.3	13.3	0.35	30	7.7	15.5	18.2	0.73
		CR	514	55	6.7	12.1	16.5		65	7.9	14.5	19.6	
Angiographic CR-2	All	IR	787	87	3.7	8.3	11.6	0.82	187	10.3	18.7	25.1	0.20
		CR	1127	131	3.1	7.4	12.3		244	8.8	16.2	22.7	
	PCI	IR	679	73	3.6	7.8	11.3	0.34	166	10.6	18.9	26.0	0.61
		CR	721	68	1.3	4.8	10.2		170	9.4	17.3	24.8	
	CABG	IR	108	14	4.6	11.3	13.3	0.53	21	8.4	17.0	20.1	0.74
		CR	406	63	6.4	12.0	16.0		74	7.7	14.2	18.9	
Proximal CR	All	IR	720	82	4.1	8.2	12.0	0.84	169	10.6	18.3	25.0	0.30
		CR	1194	136	3.0	7.5	12.0		262	8.7	16.6	22.9	
	PCI	IR	608	66	3.8	7.4	11.5	0.30	146	10.9	18.3	25.7	0.81
		CR	792	75	1.3	5.4	10.1		190	9.3	17.9	25.1	
	CABG	IR	112	16	5.4	12.7	14.6	0.86	23	9.0	18.2	21.3	0.48
		CR	402	61	6.3	11.6	15.7		72	7.5	13.9	18.5	
Multivessel IR	All	No	1546	168	2.9	7.1	11.5	0.102	326	8.6	16.0	22.1	0.001
		Yes	368	50	5.2	10.8	14.4		105	12.9	22.4	30.3	
	PCI	No	1056	99	1.6	5.1	10.1	0.094	240	9.0	16.7	24.0	0.034
		Yes	344	42	4.7	9.8	12.8		96	12.9	22.2	29.3	
	CABG	No	490	69	5.7	11.2	14.5	0.008	86	7.6	14.3	18.1	0.014
		Yes	24	8	12.5	25.0	33.6		9	12.5	25.0	38.3	

MACE indicates major adverse cardiovascular events; MACCE, major adverse cardiac and cerebrovascular events; CR, complete revascularization; IR, incomplete revascularization; PCI, percutaneous coronary intervention; and CABG, coronary artery bypass grafting.

found that PCI could not improve left ventricular function when CR could not be achieved.[18] Moreover, several other studies found that IR for MVD was associated with higher risks of long-term mortality or repeat revascularization after PCI with bare-metal stents[1,13,19,20] or DES.[2] Despite these findings, the impact of angiographic CR for MVD is still unclear, because only a few studies addressed this question after the widespread use of DES. Furthermore, because of advancements in procedural techniques and adjunctive medications, the incidence and clinical impact of CR require further evaluation.[21] Coronary artery bypass grafting has also shown advancements in perioperational management and the use of less invasive techniques and off-pump surgery; thus, the benefits of CR after CABG are also unclear.[22–24]

In our study, angiographic CR for MVD after either PCI or CABG was not associated with improvements in long-term clinical outcomes. Even for large segments, those ≥2.5 mm in diameter, or proximal arteries, anatomic CR did not reduce the risks of death, MI, stroke, and repeat revascularization. The reasons for the discrepancy between our results and those showing an association between CR and clinical outcomes, particularly after PCI, are not clear. Our lack of association may have been due to our use of definitions of CR based on detailed angiographic analyses in the core laboratory.[1,2,12,24] Therefore, unlike previous studies, in which angiographic CR was defined by the investigators, we avoided interobserver or interinstitutional differences in analyzing angiography results and defining CR. Second, the high rate of CR observed in our study may have influenced our results. For example, the rate of angiographic CR in our PCI group was 41%, higher than the rate of 31% observed in the New York PCI registry of patients with MVD, which showed that angiographic CR had a positive clinical impact in the DES era.[2] Alternatively, the higher CR rates we observed may have been due to their relatively lower angiographic and clinical risk; thus, the lower incidence of events in our study may have attenuated the impact of CR. Finally, our lack of association may be related to limitations in the angiographic evaluation of ischemia.[25,26] Of 1414 coronary lesions in the Fractional Flow Reserve Versus Angiography in Multivessel Evaluation (FAME) study, which compared outcomes of fractional flow reserve–guided and angiography-guided PCI, only 35% of the lesions with angiographic stenosis of 50% to 70% were functionally ischemic by fractional flow reserve.[26] Because 47% of lesions in the FAME study had angiographic stenosis of 50% to 70%, angiographic CR may have an inherent limitation in predicting clinical outcomes.

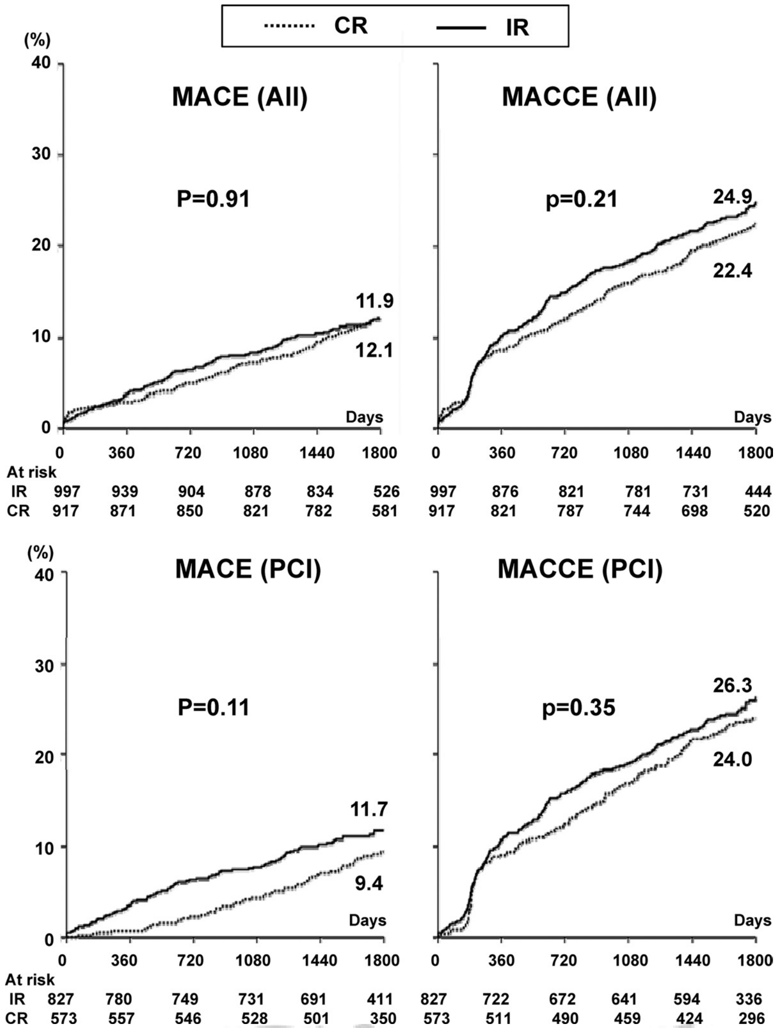

Figure 3. Unadjusted Kaplan–Meier event curves of major adverse cardiovascular events (MACE) and major adverse cardiac and cerebrovascular events (MACCE) between complete revascularization (CR) and incomplete revascularization (IR) groups in all (**top**) and percutaneous coronary intervention (PCI) (**bottom**) patients.

Our finding of a lack of association between CR and clinical prognosis after CABG was in good agreement with recent clinical studies. Since bypass grafting of the left anterior descending artery with the LIMA was routinely attempted, its strong benefit in maintaining long-term patency and subsequently relieving large ischemia of the left ventricle compensated the benefit of CR.[11,22,23] In the Coronary Artery Surgery Study (CASS) registry, in which only 16% of patients received an internal mammary artery conduit, CR improved survival compared with IR.[27] However, in recent studies in which LIMA conduits were utilized routinely, CR did not significantly improve long-term outcomes compared with IR.[11,23] In the Arterial Revascularization Therapies Study (ARTS), CR was associated with a better 18-month survival after PCI but not after CABG.[13] In our study, LIMA was used in 77% of the patients in the CR group and 75% of those in the IR group.

Despite the poor association between CR and patient prognosis, a large degree of myocardial ischemia had to be revascularized with either PCI or CABG. We observed a borderline significant association between multivessel IR and clinical prognosis. When multivessels were not revascularized, the risk of 5-year MACCE was significantly elevated in either PCI or CABG patients. A previous radionuclide study showed that revascularization for more than moderate ischemia (>10% of total myocardium) with the use of a myocardial perfusion scan improved survival.[28] Similarly, in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, which compared optimal medical therapy with prompt PCI for stable patients, patients with ischemia reduction after treatment, based on pretreatment and posttreatment thallium scans, tended to have lower risks of death and MI.[29] Thus, the association between CR and clinical outcomes in previous studies may be indirectly related to the extensive reduction of ischemia and not directly related to anatomic revascularization.[24,27]

Our study had several limitations. First, it was observational and nonrandomized in design. Therefore, despite rigorous statistical adjustments, there may be undetermined potential bias. Second, we did not prespecify or capture the conditions requiring CR during PCI or CABG. Therefore, although we repeated analyses with varying definitions of CR, our study did not assess the impact of detailed clinical features of patients on the decision-making process and its clinical outcomes. Furthermore, because of lack of information on serial enzymatic changes after CABG, the impact of periprocedural MI without Q wave could not be analyzed. Third, because of the use of different revascularization

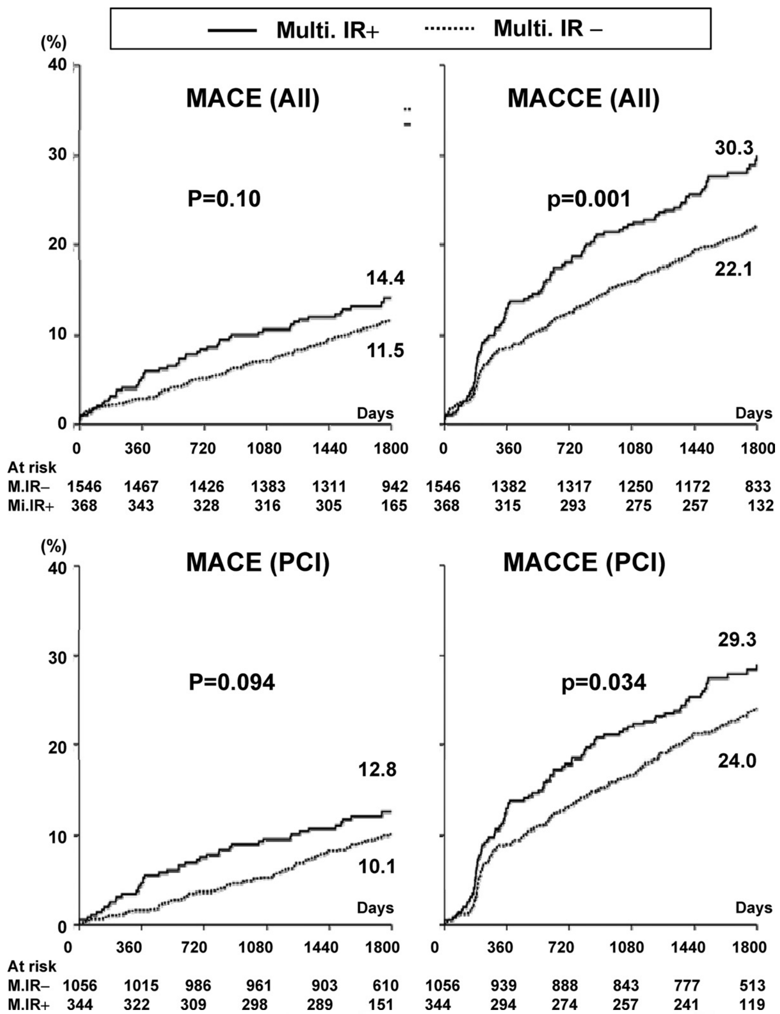

Figure 4. Unadjusted Kaplan–Meier event curves of major adverse cardiovascular events (MACE) and major adverse cardiac and cerebrovascular events (MACCE) in patients with and without multivessel (M) incomplete revascularization (IR) in all (**top**) and percutaneous coronary intervention (PCI) (**bottom**) patients.

Table 3. Adjusted Hazard Ratios of Adverse Outcomes

			Crude				Multivariate Adjustment				IPTW			
				95% CI				95% CI				95% CI		
Events	Treatment	Definitions	HR	LL	UL	*P*	HR	LL	UL	*P*	HR	LL	UL	*P*
MACE	All	Angiographic CR-1	0.99	0.76	1.29	0.91	1.04	0.80	1.36	0.75	1.04	0.79	1.36	0.80
		Angiographic CR-2	1.03	0.79	1.35	0.82	1.05	0.80	1.38	0.72	1.09	0.83	1.44	0.53
		Proximal CR	0.97	0.74	1.28	0.84	1.04	0.79	1.37	0.80	1.00	0.75	1.32	0.97
		Multivessel IR	1.27	0.92	1.74	0.14	1.26	0.92	1.74	0.15	0.97	0.66	1.43	0.89
	PCI	Angiographic CR-1	0.75	0.53	1.06	0.11	0.82	0.58	1.15	0.25	0.84	0.59	1.20	0.33
		Angiographic CR-2	0.85	0.61	1.18	0.34	0.90	0.65	1.25	0.53	0.95	0.68	1.33	0.77
		Proximal CR	0.84	0.60	1.17	0.30	0.90	0.65	1.25	0.53	0.95	0.67	1.34	0.76
		Multivessel IR	1.32	0.92	1.89	0.13	1.30	0.91	1.87	0.15	1.05	0.70	1.59	0.81
MACCE	All	Angiographic CR-1	0.89	0.73	1.07	0.21	0.90	0.75	1.09	0.29	0.91	0.75	1.10	0.32
		Angiographic CR-2	0.88	0.73	1.07	0.20	0.89	0.73	1.07	0.21	0.92	0.76	1.12	0.40
		Proximal CR	0.90	0.74	1.10	0.30	0.92	0.76	1.12	0.40	0.90	0.74	1.10	0.30
		Multivessel IR	1.42	1.14	1.77	0.002	1.44	1.16	1.79	0.001	1.27	0.97	1.66	0.079
	PCI	Angiographic CR-1	0.90	0.72	1.12	0.35	0.95	0.76	1.18	0.62	0.94	0.75	1.18	0.61
		Angiographic CR-2	0.95	0.76	1.17	0.61	0.99	0.80	1.22	0.90	1.00	0.81	1.25	0.99
		Proximal CR	0.97	0.79	1.21	0.81	1.01	0.82	1.26	0.90	1.04	0.83	1.30	0.73
		Multivessel IR	1.27	1.01	1.61	0.045	1.24	0.98	1.57	0.071	1.20	0.91	1.58	0.19

IPTW indicates inverse-probability-of-treatment weighting; HR, hazard ratio; CI, confidence interval; LL, lower limit; UL, upper limit; MACE, major adverse cardiovascular events; PCI, percutaneous coronary intervention; MACCE, major adverse cardiac and cerebrovascular events; CR, complete revascularization; and IR, incomplete revascularization.

techniques, the adjudication process of CR was not identical for the CABG and PCI groups. Because postoperational angiograms were not available for most patients in the CABG group, the definitions of CR may be more strictly applied to the PCI patients. In addition, because of the lack of information on postgrafting angiography, some patients who did not achieve successful revascularization might be considered the CR group. Fourth, because angiographic analysis was retrospectively performed for patients with available angiograms, selection bias may have occurred. Finally, because of our nonrandomized study design, the subgroup analysis of CABG or PCI may be underpowered to detect any significant clinical impact of CR.

In conclusion, we found that angiographic CR, when compared with IR, did not improve long-term clinical outcomes of PCI or CABG. The risks and benefits of revascularization treatment may be balanced by an ischemia-guided revascularization strategy.

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Disclosures

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CLINICAL PERSPECTIVE

Current guideline recommends complete revascularization (CR) with the use of percutaneous coronary intervention or coronary artery bypass grafting for stable patients with multivessel coronary disease because of its favorable long-term prognosis compared with the strategy of incomplete revascularization . However, in daily practice, CR is not always attempted because of hemodynamic instability, low ejection fraction, complex morphology, absence of objective ischemia, or preference for a minimally invasive procedure. In this regard, our study sought to investigate the benefit of CR with detailed angiographic analyses according to the Synergy Between PCI With Taxus and Cardiac Surgery classification for patients with multivessel disease undergoing percutaneous coronary intervention with drug-eluting stent or coronary artery bypass grafting. The major finding of our study was that CR, according to the varying definitions, did not improve clinical outcomes. Although the mechanism is not clear, the lack of association between CR and clinical prognosis may be closely related to the limitation of angiography to determine objective ischemia. In fact, recent clinical studies using fractional flow reserve, which is an invasive modality to determine objective ischemia in the tested epicardial coronary artery, demonstrated that the association between intermediate angiographic stenosis and functional ischemia is weak. Therefore, the strategy of angiographic CR might induce unnecessary procedures and subsequently fail to improve clinical outcome. Given this result and others with the use of invasive and noninvasive functional evaluation, an ischemia-guided procedure should be performed in treating patients with multivessel coronary disease.