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Incidence, Characteristics, Predictors, and Outcomes of Repeat Revascularization After Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting

The SYNTAX Trial at 5 Years

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ABSTRACT

OBJECTIVES The study sought to determine the incidence, predictors, characteristics, and outcomes of repeat revascularization during 5-year follow-up of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) trial.

BACKGROUND Limited in-depth long-term data on repeat revascularization are available from randomized trials comparing percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

METHODS Incidence and timing of repeat revascularization and its relation to the long-term composite safety endpoint of death, stroke, and myocardial infarction were analyzed in the SYNTAX trial ($n = 1,800$) using Kaplan-Meier analysis.

RESULTS At 5 years, repeat revascularization occurred more often after initial PCI than after initial CABG (25.9% vs. 13.7%, respectively; $p < 0.001$), and more often consisted of multiple repeat revascularizations (9.0% vs. 2.8%, respectively; $p = 0.022$). Significantly more repeat PCI procedures were performed on de novo lesions in patients after initial PCI than initial CABG (33.3% vs. 13.4%, respectively; $p < 0.001$). At 5-year follow-up, patients who underwent repeat revascularization versus patients not undergoing repeat revascularization had significantly higher rates of the composite safety endpoint of death, stroke, and myocardial infarction after initial PCI (33.8% vs. 16.6%, respectively; $p < 0.001$), and a trend was found after initial CABG (22.4% vs. 15.8%, respectively; $p = 0.07$). After multivariate adjustment, repeat revascularization was an independent predictor of the composite safety endpoint after both initial PCI (hazard ratio [HR]: 2.2; 95% confidence interval [CI]: 1.6 to 3.0; $p < 0.001$) and initial CABG (HR: 1.8; 95% CI: 1.2 to 2.9; $p = 0.011$).

CONCLUSIONS Repeat revascularization rates are significantly higher after initial PCI than after initial CABG for complex coronary disease. Repeat revascularization is an independent predictor of death, stroke, and myocardial infarction for myocardial revascularization. (J Am Coll Cardiol Intv 2016;9:2493–507) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CI = confidence interval

DES = drug-eluting stent(s)

HR = hazard ratio

MI = myocardial infarction

NTVR = nontarget vessel revascularization

PCI = percutaneous coronary intervention

TLR = target lesion revascularization

TVR = target vessel revascularization

Repeat revascularization is a controversial endpoint in clinical trials comparing percutaneous coronary intervention (PCI) with coronary artery bypass grafting (CABG). It is often criticized because of its subjective and biased nature, as the underlying incentive to perform repeat revascularization may be different after PCI than CABG.

However, repeat revascularization as an outcome can be of great importance (1,2). Although it is usually considered an adverse outcome or failure of the initial treatment, repeat revascularization is an efficient therapy associated with a reduction in morbidity and mortality (3,4). Although its incidence is highly time dependent, the need for repeat revascularization also varies greatly depending on the studied population (5,6).

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Few data beyond early follow-up of repeat revascularization exist and therefore it remains largely unclear which patients are at risk for repeat revascularization, what current practice regarding repeat revascularization does entail, and what is the actual impact of repeat revascularization on short-term and long-term clinical outcomes. Particularly, despite the completion of numerous trials comparing PCI with CABG, very limited in-depth long-term follow-up data on practice of repeat revascularization in randomized trials is available (1,7). Therefore, this study aims to provide insights from a randomized trial comparing PCI with CABG into the predictors, characteristics, and short-term and 5-year outcomes of repeat revascularization in the SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) trial.

METHODS

STUDY DESIGN. The SYNTAX trial is a randomized, prospective, multicenter trial on the basis of an all-comers design that included patients with complex coronary artery disease as defined by the presence of unprotected left main or 3-vessel disease. Patients (n = 1,800) were randomized on a 1:1 basis by the Heart Team consensus to undergo either CABG or PCI with TAXUS Express paclitaxel-eluting stents (Boston Scientific, Marlborough, Massachusetts). If considered unsuitable for randomization, patients were entered in to 1 of 2 parallel nested registries (PCI registry, n = 193; CABG registry, n = 1,077) (8). This study only included comparisons between the randomized cohorts of patients. Indications for repeat revascularization were not specified in the original trial protocol and were on the basis of local practice at each participating site.

DEFINITIONS. The primary endpoint of the SYNTAX trial was a composite of major adverse cardiac or cerebrovascular events that includes all-cause death, myocardial infarction (MI), stroke, and repeat revascularization. Because the primary interest of this analysis is to investigate repeat revascularization and clinical outcomes during follow-up, the individual endpoints of repeat revascularization (all, repeat PCI, and repeat CABG) and all-cause mortality were evaluated, as well as the composite safety endpoint of all-cause death, MI, and stroke. Definitions of these individual components have been previously reported (9). An independent Clinical Events Committee, including cardiologists, cardiac surgeons, and a neurologist, reviewed all primary clinical endpoints. In addition, revascularization was divided into target vessel revascularization (TVR), target vessel target lesion revascularization (TLR), revascularization of a de novo lesion in a target vessel (remote TVR), revascularization of a de novo lesion in a nontarget vessel (NTVR), de novo lesion revascularization (in both target and nontarget vessel), and, for patients who had previously undergone CABG, revascularization of a bypass graft.

During the Heart Team meeting when patients were assessed for randomization, both the interventional cardiologist and surgeon documented which vessels with a ≥1.5 mm diameter and a 50% stenosis needed revascularization. Incomplete revascularization was assessed by correlating this pre-operative statement to the actual revascularization.

Throughout the manuscript, initial PCI and initial CABG will refer to the procedures to which patients were randomized at the start of the SYNTAX trial. Repeat PCI and repeat CABG will refer to repeat revascularizations, irrespective of what was the initial procedure.

As initial therapy after randomization, a staged revascularization procedure was allowed if performed within 72 h after the first procedure and during the same hospital stay or within 14 days in patients with renal insufficiency or post-procedural contrast-induced nephropathy. All staged procedures have been adjudicated by the Clinical Events Committee as such.

To determine procedural adverse events of repeat revascularization, the following events were counted when occurring during 30 days after repeat

revascularization: death, stroke, subsequent repeat revascularization(s) and MI, and the corresponding composite endpoint. To evaluate the effect of successful repeat revascularization, an additional analysis was performed by not taking into account MI events occurring on the same day as the repeat revascularization. Furthermore, a comparative analysis between groups of initial PCI and initial CABG was performed of elective and urgent repeat revascularizations.

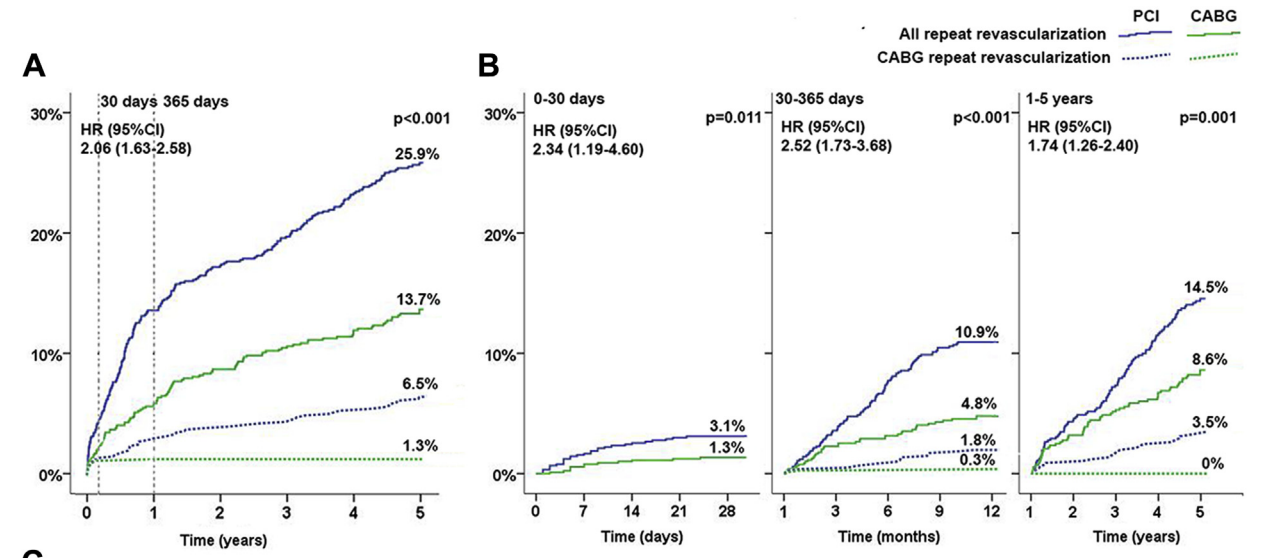
Indications leading to repeat revascularization included stable angina, unstable angina, MI, silent ischemia (established by stress testing), and other reasons including both periprocedural complications (bleeding, graft failure or stent thrombosis, and technique-related adverse events) and evidence of progression of disease (not classified as angina).

STATISTICAL METHODS. Continuous variables are given as mean ± SD and compared using the Student *t* test. Discrete variables are expressed as counts and percentages, and comparisons between groups were done with the chi-square or Fisher exact test, when appropriate. For comparisons across subgroups, the Kruskal-Wallis test, the Wilcoxon rank sum test using pairwise comparisons, and the chi-square test for comparing proportions (of categorical variables) between >2 groups have been used. Bonferroni method was used to adjust p values for multiple comparisons. Five-year clinical outcomes were estimated using the Kaplan-Meier method, with comparisons made using the log-rank test (overall or pairwise as appropriate). To account for the informative censoring in the presence of multiple endpoints, competing risks survival analysis was performed by means of nonparametric methods using the cumulative incidence competing risk method (10–12). Landmark analyses were used to describe the occurrence of repeat revascularization in time: early (within 30 days), intermediate (between 30 days and 1 year), or late (through 1 to 5 years). After careful selection of baseline characteristics and periprocedural variables on the basis of clinical judgment (Online Appendix), univariable assessment and multiple testing to ensure stability, a multivariable model has been fitted. Multivariable predictors of repeat revascularization after initial PCI and initial CABG were determined using Backward Wald stepwise selection with a significance level of <0.10 for entry and exit in a Cox proportional hazards model. Correlations between variables were explored with the Pearson correlation coefficient and highly correlated variables were not included in the multivariable model. To evaluate the impact of repeat revascularization on clinical outcomes, a comparison was made between patients with no repeat revascularization versus events that occurred after repeat revascularization in patients who did undergo repeat revascularization. Multivariable Cox proportional hazard analyses were used to determine whether repeat revascularization was an independent predictor of the composite safety endpoint of all-cause death, stroke, and MI (Model 1), while adjusting for baseline characteristics and periprocedural variables (Online Appendix). A second model was fitted to relate the type of repeat revascularization (repeat PCI revascularization and repeat CABG revascularization) with the composite safety endpoint, using a stepwise 2-block model (Model 2). A third model was fitted to relate target lesion revascularization (restenosis surrogate) and de novo lesion revascularization (marker of disease progression) with the composite safety endpoint, using a stepwise 2-block model (Model 3). The proportionality of hazards assumption was checked using the global proportionality of hazards test on the basis of Schoenfeld residuals. There was no departure from the proportionality of hazards assumption in the groups of patients with initial CABG (predictors of repeat revascularization: chi-square = 9.11, df = 10, p = 0.52; predictors of composite safety endpoint: chi-square = 5.35, df = 9, p = 0.80) and initial PCI (predictors of repeat revascularization: chi-square = 13.66, df = 9, p = 0.14; predictors of composite safety endpoint: chi-square = 6.34, df = 8, p = 0.61). A 2-sided p value of 0.05 was considered to be statistically significant for all tests. All analyses were conducted using SPSS 21.0 (SPSS Inc., Chicago, Illinois) and SAS V.9.3 software (SAS Institute, Cary, North Carolina).

RESULTS

INCIDENCE, TIMING, AND TYPE OF REPEAT REVASCULARIZATION. During 5-year follow-up, 459 repeat revascularization events were registered; 86.2% consisting of repeat PCI and 14.8% of repeat CABG revascularization. Rates of repeat revascularization at 5 years after initial CABG and initial PCI were 13.7% and 25.9%, respectively (p < 0.001). At all time points during follow-up, repeat revascularization rates were significantly higher after initial PCI than after initial CABG (**Figure 1**). After initial CABG treatment, almost all repeat CABG procedures were performed within 30 days, with other repeat revascularizations thereafter consisting almost exclusively of repeat PCI. Conversely, after initial PCI treatment, the relative number of subsequent CABG procedures in relation to repeat PCI revascularization remained stable over the length of follow-up.

FIGURE 1 Incidence of Repeat Revascularization



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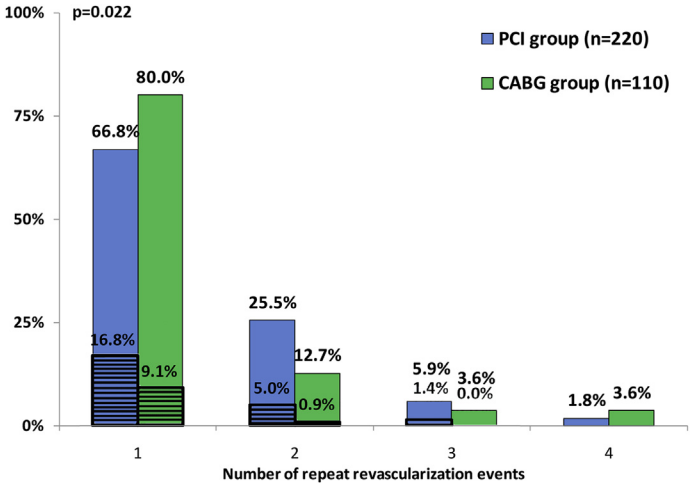
	5-year			0-30 days			31-365 days			1-5 years		
	PCI group	CABG group	p-value	PCI group	CABG group	p-value	PCI group	CABG group	p-value	PCI group	CABG group	p-value
All repeat revascularization	25.9%	13.7%	<0.001	3.1%	1.3%	0.011	10.9%	4.8%	<0.001	14.5%	8.6%	0.001
PCI repeat revascularization	21.5%	12.9%	<0.001	2.5%	0.5%	0.001	9.1%	4.1%	<0.001	11.6%	8.6%	0.062
CABG repeat revascularization	6.5%	1.3%	<0.001	1.0%	0.9%	0.94	1.8%	0.3%	0.003	3.5%	0%	<0.001

(A) All-time and **(B)** landmark Kaplan-Meier estimates of repeat revascularization with separation of events **(C)**. **Solid lines** indicate any repeat revascularizations whereas **dotted lines** indicate repeat CABG procedures after initial PCI **(blue lines)** or CABG **(green lines)**. The p values are by log-rank. CABG = coronary artery bypass grafting; CI = confidence interval; HR = hazard ratio; PCI = percutaneous coronary intervention.

FIGURE 2 Number and Type of Repeat Revascularizations



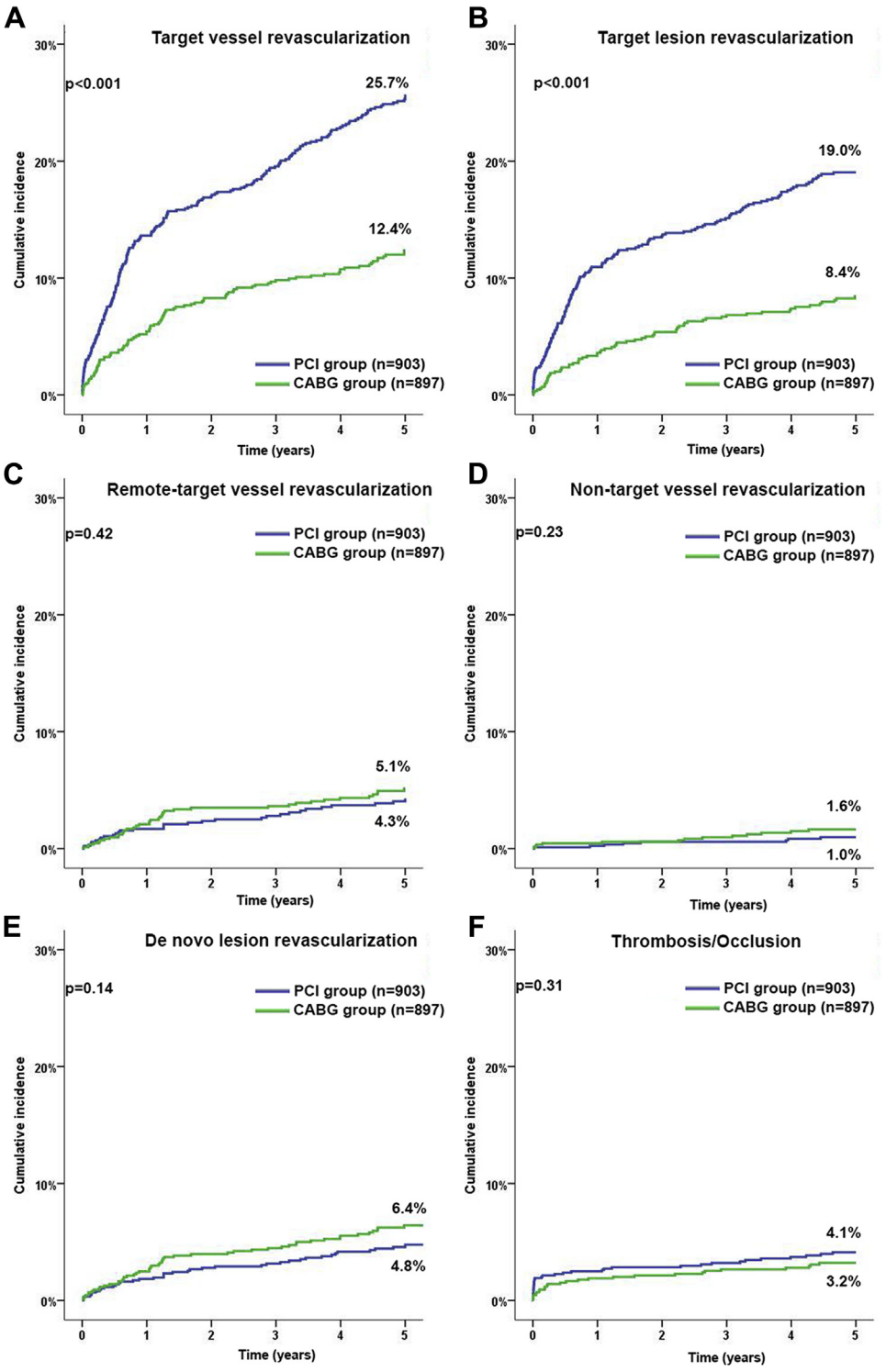
Proportion of patients requiring repeat revascularization after PCI **(blue)** and CABG **(green)**. Of the entire 1,800 patients, more patients after initial PCI than after initial CABG required multiple repeat revascularizations (9.0% vs. 2.8%, respectively; p = 0.022). Hashed rectangles represent repeat CABG revascularizations. Abbreviations as in Figure 1.

Patients after initial PCI more often required multiple repeat revascularizations (9.0% vs. 2.8%, respectively; p = 0.022) (Figure 2).

Kaplan-Meier analysis revealed a higher 5-year cumulative incidence of TVR, mainly driven by TLR (19.0% after initial PCI vs. 8.4% after initial CABG; p < 0.001), but no difference between groups in remote-TVR or NTVR (Figure 3). There were no differences in revascularization for de novo lesions between initial PCI and initial CABG (4.8% vs. 6.4%, respectively; p = 0.14). The 5-year cumulative incidence of stent thrombosis or graft occlusion was similar after initial PCI and initial CABG (5.5% and 4.0%, respectively; p = 0.13), as well as the rate of stent thrombosis or graft occlusion leading to repeat revascularization (4.1% and 3.2%, respectively; p = 0.31).

In a competing risks analysis, the cumulative incidence of repeat revascularization was 19.7% after initial PCI and 11.6% after initial CABG (Online Appendix). After initial PCI, death and MI as a first event occurred at a rate of 8.1% and 8.2%, respectively. After initial CABG, death and MI occurred as a first event at a rate of 9.2% and 3.7%, respectively.

FIGURE 3 **Repeat Revascularization During 5-Year Follow-Up**



Cumulative incidence of **(A)** target vessel revascularization, **(B)** target lesion revascularization, **(C)** remote target vessel revascularization, **(D)** nontarget vessel revascularization, **(E)** de novo lesion revascularization, and **(F)** thrombosis or occlusion leading to repeat revascularization. Abbreviations as in Figure 1.

Although considered as a single index procedure and not as repeat revascularization, 13.6% patients in the initial PCI group underwent a planned staged revascularization, resulting in a higher number of actual procedures for some patients in the initial PCI group.

REASONS FOR REPEAT REVASCULARIZATION. Symptomatic angina pectoris was the primary indication for repeat PCI and its occurrence was largely similar among patients randomized to initial PCI versus initial CABG (Table 1).

The percentage of repeat PCI procedures that were TVR were the majority of all repeat PCI procedures after both initial PCI and initial CABG (89.6% and 83.0%, respectively; p = 0.125), and about one-half of repeat PCIs in both initial PCI and initial CABG groups were performed as TLR procedures (55.7% vs. 51.5%, respectively; p = 1.00). Significantly more repeat PCIs were performed on de novo lesions in patients randomized to initial PCI versus those randomized to initial CABG (33.3% vs. 13.4%, respectively; p < 0.001). About 18% of repeat PCIs in patients initially treated with CABG were performed in bypass grafts.

After initial PCI treatment, 54 patients underwent repeat CABG, of which 88.9% had symptoms of angina. In about 70% the indication for repeat CABG was stable or unstable angina, whereas in only 5.6% this was because of acute MI. At the time of repeat CABG during follow-up, 64.8% of patients initially treated with PCI required reintervention in 3 vessels (vs. 12.5% after initial CABG; p = 0.021), whereas patients initially treated with CABG predominantly required reintervention in 1 vessel at the time of repeat CABG (62.5% vs. 18.5% after initial PCI; p = 0.048). Target vessel repeat revascularization by repeat CABG was similar in both groups (PCI: 85.9%, CABG: 83.3%; p = 1.00), whereas TLR was higher in patients initially treated with PCI. In the initial CABG group, few repeat CABG procedures were preceded by symptoms of angina or acute MI, but 4 events (50%) were as a result of acute complications within days of the initial CABG procedure (hemorrhage or acute graft failure) (Table 1).

TABLE 1 Characteristics of Repeat Revascularizations at the Time of Repeat Revascularization

	Repeat CABG Revascularization				All Repeat PCI Revascularizations			
	PCI Group (n = 54 Procedures)	CABG Group (n = 8 Procedures)	p Value		PCI Group (n = 259 Procedures)	CABG Group (n = 133 Procedures)	p Value	
			Unadjusted	Adjusted*			Unadjusted	Adjusted*
Angina symptoms								
Yes	88.9 (48/54)	37.5 (3/8)	0.003	0.009	74.1 (192/259)	76.7 (102/133)	0.58	1.00
No	5.6 (3/54)	37.5 (3/8)	0.024	0.072	16.2 (42/259)	17.3 (23/133)	0.79	1.00
Silent ischemia	5.6 (3/54)	25.0 (2/8)	0.12	0.36	9.3 (24/259)	6.0 (8/133)	0.33	0.99
Indication leading to revascularization								
Stable angina	42.6 (23/54)	12.5 (1/8)	0.14	0.70	35.5 (92/259)	40.6 (54/133)	0.33	0.413
Unstable angina	27.8 (15/54)	25.0 (2/8)	1.00	1.00	25.1 (65/259)	21.8 (29/133)	0.47	0.47
Acute MI	5.6 (3/54)	0 (0/8)	1.00	1.00	16.2 (42/259)	9.8 (13/133)	0.08	0.20
Silent ischemia	5.6 (3/54)	12.5 (1/8)	0.43	1.00	10.0 (26/259)	6.8 (9/133)	0.28	0.413
Other	18.5 (10/54)	50.0 (4/8)	0.07	0.35	13.1 (34/259)	21.8 (28/133)	0.042	0.20
Vessel type†								
Target vessel	85.9 (122/142)	83.3 (10/12)	0.68	1.00	89.6 (336/375)	83.0 (161/194)	0.025	0.125
Bypass graft	0 (0/142)	75.0 (9/12)	<0.001	<0.001	0.5 (2/375)	18.0 (35/194)	<0.001	<0.001
Target lesion	64.1 (91/142)	8.3 (1/12)	<0.001	<0.001	55.7 (209/375)	51.5 (100/194)	0.34	1.00
De novo lesion	21.8 (31/142)	0 (0/12)	0.13	0.65	33.3 (125/375)	13.4 (26/194)	<0.001	<0.001
Nontarget vessel‡								
De novo lesion	14.1 (20/142)	8.3 (1/12)	1.00	1.00	10.4 (39/375)	14.9 (29/194)	0.11	0.55
Number of vessels revascularized								
1	18.5 (10/54)	62.5 (5/8)	0.016	0.048	45.9 (84/183)	53.9 (55/102)	0.22	0.66
2	16.7 (9/54)	25.0 (2/8)	0.62	1.00	30.1 (55/183)	24.5 (25/102)	0.34	1.00
3	64.8 (35/54)	12.5 (1/8)	0.007	0.021	24.0 (44/183)	21.6 (22/102)	0.66	1.00

Values are % (n/N). *Bonferroni correction method for multiple comparisons. †Considered on a vessel basis and not a patient basis for repeat coronary artery bypass grafting (CABG) (percutaneous coronary intervention [PCI]: 142 vessels revascularized during 54 events in 54 patients, CABG: 12 vessels revascularized during 8 events in 8 patients) and all repeat PCIs (PCI: 375 vessels revascularized during 259 events in 183 patients, CABG 194 vessels revascularized during 133 events in 102 patients). ‡All de novo lesions.

MI = myocardial infarction.

BASELINE AND PROCEDURAL CHARACTERISTICS BY REPEAT REVASCULARIZATION. In the initial PCI group, patients that required repeat revascularization, compared with those who did not, had a significantly higher rate of diabetes, particularly medically treated diabetes (34.1% vs. 22.8%, respectively; $p < 0.001$), and had more complex disease as described by the SYNTAX score (26.6 ± 10.3 vs. 24.7 ± 11.6, respectively; $p = 0.023$) at the time of randomization (Table 2). They had more stents implanted but had a higher rate of incomplete revascularization (53.6% vs. 39.9% among patients not requiring repeat revascularization; $p < 0.001$).

In the initial CABG group, patients requiring repeat revascularization were younger, more often underwent an emergent index procedure, and had a lower mean logistic European System for Cardiac Operative Risk Evaluation score (3.0 ± 2.8 vs. 4.0 ± 4.6, respectively; $p = 0.001$) at the time of randomization (Table 2). The complexity of disease was comparable between patients requiring repeat revascularization and those who did not, as was the rate of incomplete revascularization (36.1% vs. 43.3%, respectively; $p = 0.24$). The number of grafts was similar, but patients who underwent repeat revascularization more frequently underwent complete arterial revascularization, particularly with the use of a radial artery.

PREDICTORS OF REPEAT REVASCULARIZATION. Tables with univariable analyses are provided in the Online Appendix.

In the final multivariable model to predict repeat revascularization in the initial PCI group, medically treated diabetes was a strong independent predictor of repeat revascularization (hazard ratio [HR]: 1.59; 95% confidence interval [CI]: 1.20 to 2.12; $p = 0.001$) (Table 3). The complexity of coronary disease as described by the SYNTAX score failed to be a predictor, but instead the number of overlapping stents (HR: 1.34; 95% CI: 1.09 to 1.64; $p = 0.005$) and incomplete initial revascularization (HR: 1.54; 95% CI: 1.17 to 2.02; $p = 0.002$) were found to be independent predictors of repeat revascularization. Repeat revascularization was also related to lack of antiplatelet therapy as medication at discharge.

In the initial CABG group, enrollment in the United States (HR: 1.75; 95% CI: 1.09 to 2.81; $p = 0.020$) and off-pump CABG (HR: 1.51; 95% CI: 0.94 to 2.44; $p = 0.091$) were predictors of repeat revascularization (Table 3). The presence of a left coronary artery lesion was found protective for repeat revascularization (HR: 0.55; 95% CI: 0.32 to 0.94; $p = 0.028$). Use of statins but lack of acetylsalicylic acid at discharge appears to be inversely related to repeat revascularization.

PROCEDURAL EVENTS FOLLOWING REPEAT REVASCULARIZATION. Thirty-day adverse event rates following any repeat revascularization were higher after initial PCI than after initial CABG; the composite endpoint of death, subsequent repeat revascularization, and MI occurred in 22.7% and 11.8%, respectively ($p = 0.017$) (Table 4). No strokes were registered in the interval of 30-days following any repeat revascularization. MI events occurring on the same day as repeat revascularization were excluded to assess the impact of successful repeat revascularization on the 30-day adverse event rates. Under these circumstances the difference between initial PCI and initial CABG lost statistical significance (13.6% vs. 9.1%, respectively; $p = 0.23$). Differences between initial PCI and initial CABG groups were consistent among all repeat revascularization and PCI repeat revascularization.

Although 30-day adverse event rates occurring after elective repeat revascularization were almost identical between groups, there was a trend toward a higher rate of the composite endpoint after urgent repeat revascularization in the PCI group (35.8% vs. 22.2% in the CABG group; $p = 0.096$), mainly driven by the MI rate (26.0% vs. 6.7% in the CABG group; $p = 0.006$).

OUTCOMES AT 5-YEAR FOLLOW-UP. After initial PCI, the composite safety endpoint of all-cause death, stroke and MI was significantly higher among patients that underwent repeat revascularization as compared to those who did not (27.9% vs. 16.6%, respectively; $p < 0.001$) (Figure 4). After initial CABG there was no difference in the composite safety endpoint (14.9% vs. 15.8%, respectively; $p = 0.62$).

Among patients that underwent repeat revascularization, patients that underwent initial PCI versus initial CABG had significantly higher rates of the composite of death, MI, or subsequent repeat revascularization (57.4% vs. 38.4%, respectively; $p = 0.003$), which was primarily driven by significantly higher rates of subsequent repeat revascularization (43.4% vs. 25.3%, respectively; $p = 0.012$) and MI (19.2% vs. 4.8%, respectively; $p = 0.001$). There was no significant difference in mortality in patients who underwent repeat revascularization after initial PCI versus initial CABG (20.2% vs. 13.9%, respectively; $p = 0.095$) (Figure 5A). When considering only patients that underwent repeat PCI

TABLE 2 Baseline and Procedural Characteristics

	PCI Group (n = 903)			CABG Group (n = 897)		
	Repeat Revascularization Group (n = 220)	No Repeat Revascularization Group (n = 683)	p Value	Repeat Revascularization Group (n = 110)	No-Repeat Revascularization Group (n = 787)	p Value
Clinical characteristics						
Age, yrs	64.8 ± 9.2	65.4 ± 9.8	0.45	63.4 ± 9.0	65.2 ± 9.9	0.07
Female	24.5 (54)	23.3 (159)	0.70	18.2 (20)	21. (169)	0.43
Non-White	5.0 (11)	2.3 (16)	0.044	8.2 (9)	3.9 (31)	0.08
Enrolled in the United States	14.1 (31)	13.5 (92)	0.82	22.7 (25)	12.3 (97)	0.003
Risk factors						
Family history of CAD	24.5 (52)	26.9 (174)	0.51	29.7 (30)	27.2 (205)	0.60
Hypertension	75.2 (164)	73.6 (499)	0.63	76.9 (83)	77.0 (603)	0.97
Hyperlipidemia	81.6 (177)	77.8 (528)	0.23	80.0 (88)	76.8 (598)	0.45
Medically treated DM	34.1 (75)	22.8 (156)	0.001	25.5 (28)	24.5 (193)	0.83
Insulin	15.9 (35)	7.9 (54)	0.001	13.6 (15)	9.9 (78)	0.23
Noninsulin	20.9 (46)	17.6 (120)	0.27	16.4 (18)	18.4 (145)	0.60
Current smoker	15.9 (35)	19.3 (132)	0.26	20.9 (23)	22.2 (173)	0.76
Previous MI	33.2 (72)	31.5 (213)	0.65	24.5 (27)	35.1 (273)	0.028
Previous CHF	4.6 (10)	3.8 (26)	0.63	7.3 (8)	5.1 (770)	0.34
Unstable angina	31.4 (69)	28.3 (193)	0.38	33.6 (37)	27.2 (214)	0.16
Peripheral artery disease	9.5 (21)	8.9 (61)	0.78	12.7 (14)	10.3 (81)	0.44
Carotid artery disease	10.0 (22)	7.5 (51)	0.23	4.5 (5)	8.9 (70)	0.12
Previous TIA/CVA	6.8 (15)	7.9 (54)	0.59	8.2 (9)	9.3 (72)	0.72
COPD	9.1 (20)	7.5 (51)	0.44	8.2 (9)	9.4 (74)	0.68
Renal impairment	0.5 (1)	1.3 (9)	0.47	0.9 (1)	1.9 (15)	0.71
BMI, kg/m^2	28.4 ± 4.8	28.0 ± 4.8	0.39	27.9 ± 4.8	27.9 ± 4.5	0.92
Logistic EuroSCORE	3.5 ± 3.3	3.9 ± 4.9	0.34	3.0 ± 2.8	4.0 ± 4.6	0.001
LVEF <50%	17.8 (38)	20.1 (134)	0.48	14.5 (16)	20.4 (159)	0.15
Coronary complexity						
3VD	59.1 (131)	60.9 (416)	0.63	55.5 (61)	62.0 (487)	0.19
Left main	40.9 (90)	39.1 (267)	0.63	44.5 (49)	38.0 (229)	0.19
LCA	89.5 (197)	89.3 (610)	0.92	84.5 (93)	89.6 (704)	0.12
LCxA	89.5 (197)	84.2 (575)	0.05	84.5 (93)	83.6 (657)	0.80
RCA	86.8 (191)	80.5 (550)	0.034	78.2 (86)	81.6 (641)	0.40
No. of lesions	4.5 ± 1.7	4.3 ± 1.8	0.06	4.3 ± 1.9	4.4 ± 1.8	0.65
SYNTAX Score	26.6 ± 10.3	24.7 ± 10.6	0.023	24.5 ± 9.7	24.7 ± 10.0	0.84

Continued on the next page

procedures, not only subsequent repeat revascularization and MI, but also 5-year mortality was higher in patients after initial PCI (20.6% vs. 11.5% after initial CABG; p = 0.021) (Figure 5B). Conversely, the composite safety endpoint was similar after initial PCI and initial CABG in patients not undergoing any repeat revascularization (HR: 0.96; 95% CI: 0.74 to 1.24; p = 0.73).

Outcome of MI may be masked by the fact that repeat revascularization is sometimes performed because of an MI, whereas MI can also occur periprocedurally as a result of repeat revascularization. Rates of an MI before repeat revascularization were similar after initial PCI and initial CABG (1.7% vs. 1.2%, respectively; p = 0.42), as well as rates of MI without any repeat revascularization (3.4% vs. 2.4%, respectively; p = 0.19). Rates of repeat revascularization without any MI during 5-year follow-up were significantly higher after initial PCI than after initial CABG (19.2% vs. 11.9%, respectively; p < 0.001). In the initial PCI group as compared to the initial CABG group, an MI occurred significantly more often on the same day as repeat revascularization (3.3% vs. 0.4%, respectively; p < 0.001). An MI also occurred significantly more often after repeat revascularization in the initial PCI versus initial CABG group (1.0% vs. 0.1%, respectively; p = 0.022).

THE INDEPENDENT IMPACT OF REPEAT REVASCULARIZATION. After performing multivariable analyses (Online Appendix), adjustment for baseline and periprocedural characteristics identified repeat revascularization as an independent predictor of the

TABLE 2 Continued

	PCI Group (n = 903)			CABG Group (n = 897)		
	Repeat Revascularization Group (n = 220)	No Repeat Revascularization Group (n = 683)	p Value	Repeat Revascularization Group (n = 110)	No-Repeat Revascularization Group (n = 787)	p Value
Procedural characteristics						
Total stents	5.1 ± 2.4	4.5 ± 2.2	0.001			
Total stent length	91.7 ± 51	84.7 ± 47	0.07			
Total overlapping stents	0.7 ± 0.7	0.6 ± 0.6	0.015			
Staged procedure	17.7 (39)	12.6 (86)	0.06			
On pump				75.5 (83)	80.2 (631)	0.25
Off pump				20.6 (22)	14.2 (106)	0.09
Arterial conduits				1.5 ± 0.7	1.4 ± 0.6	0.048
Venous conduits				1.2 ± 1.0	1.4 ± 0.9	0.07
Distal anastomoses				3.1 ± 0.9	3.2 ± 0.9	0.28
Grafts per patient				2.7 ± 0.7	2.8 ± 0.7	0.76
LIMA				98.1 (105)	96.7 (722)	0.56
Radial artery				20.6 (22)	13.1 (98)	0.038
BIMA				32.7 (35)	26.9 (201)	0.21
Second arterial graft				43.0 (46)	34.3 (256)	0.08
Complete arterial				28.0 (30)	17.4 (130)	0.008
Incomplete revascularization	53.6 (118)	39.9 (270)	<0.001	36.1 (274)	43.3 (388)	0.24
Revascularization priority*†						
Elective	92.3 (203)	94.7 (640)	0.57	90.9 (100)	92.5 (703)	1.00
Urgent	5.5 (12)	3.7 (25)	0.78	1.8 (2)	4.1 (31)	1.00
Emergent	2.3 (5)	1.6 (11)	1.00	7.3 (8)	3.4 (26)	0.18
Medication at discharge						
ASA	94.1 (207)	97.0 (656)	0.0044	97.3 (107)	87.2 (663)	0.002
Thienopyridine	93.6 (206)	87.8 (661)	0.003	25.5 (28)	18.7 (142)	0.09
Statins	84.5 (186)	87.4 (591)	0.27	70.9 (78)	75.0 (570)	0.36

Values are mean ± SD or % (n). *Elective: scheduled in advance as it does not involve a medical emergency; urgent: can wait until the patient is stable; emergent: no choice but immediate intervention. †Bonferroni correction method for multiple comparisons.

3VD = 3-vessel disease; ASA = acetylsalicylic acid; BIMA = bilateral mammary artery; BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular event(s); DM = diabetes mellitus; EuroSCORE = European System for Cardiac Operative Risk Evaluation; IABP = intra-aortic balloon pump; LCA = left coronary artery; LCxA = left circumflex artery; LIMA = left internal mammary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PAD = peripheral artery disease; RCA = right coronary artery; SYNTAX = Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery; TIA = transient ischemic attack; other abbreviations as in Table 1.

TABLE 3 Independent Predictors of Repeat Revascularization

	HR	95% CI	p Value
PCI group (n = 903)			
Medically treated DM	1.59	1.20–2.12	0.001
Number of overlapping stents	1.34	1.09–1.64	0.005
Incomplete revascularization	1.54	1.17–2.02	0.002
No ASA at discharge	2.18	1.23–3.85	0.008
No thienopyridine at discharge	6.03	3.36–10.8	<0.001
CABG group (n = 897)			
United States vs. Europe	1.75	1.09–2.81	0.020
Left coronary artery lesion	0.55	0.32–0.94	0.028
Off pump	1.51	0.94–2.44	0.091
No ASA at discharge	0.25	0.08–0.80	0.019
Statins at discharge	0.64	0.42–0.97	0.036

ASA = acetylsalicylic acid; CI = confidence interval; HR = hazard ratio; other abbreviations as in Tables 1 and 2.

composite safety endpoint in the initial PCI group (HR: 1.65; 95% CI: 1.20 to 2.27; p = 0.002) (Table 5), for both repeat PCI (HR: 1.67; 95% CI: 1.20 to 2.32; p = 0.002) and repeat CABG (HR: 1.72; 95% CI: 1.02 to 2.88; p = 0.041). Target lesion revascularization was also identified as an independent predictor of the composite safety endpoint (HR: 1.69; 95% CI: 1.20 to 2.38; p = 0.003), but not de novo lesion revascularization (HR: 1.49; 95% CI: 0.80 to 2.79; p = 0.21).

In the initial CABG group, repeat revascularization was not a predictor of the composite safety endpoint (HR: 0.92; 95% CI: 0.54 to 1.75; p = 0.92). However, although repeat PCI after initial CABG was not a predictor (HR: 0.69; 95% CI: 0.34 to 1.37; p = 0.28), repeat CABG was associated with the composite safety endpoint (HR: 3.32; 95% CI: 1.21 to 9.11; p = 0.020). Neither TLR nor de novo lesion revascularization were found to be independent predictors of the

TABLE 4 Periprocedural Mortality and Morbidity

	Type of Repeat Revascularization						Urgency of Repeat Revascularizations					
	All Repeat Revascularizations			PCI Repeat Revascularizations			Elective*			Urgent†		
	PCI Group (n = 220)	CABG Group (n = 110)	p Value	PCI Group (n = 183)	CABG Group (n = 102)	p Value	PCI Group (n = 97)	CABG Group (n = 65)	p Value	PCI Group (n = 123)	CABG Group (n = 45)	p Value
Events <30 days of repeat revascularization												
Composite endpoint‡	22.7%	11.8%	0.017	24.0%	11.8%	0.012	6.2%	4.6%	0.74	35.8%	22.2%	0.096
Subsequent repeat revascularization	10.0%	7.3%	0.42	12.0%	7.8%	0.27	4.1%	4.6%	1.00	13.8%	8.9%	0.39
Myocardial infarction	15.0%	3.6%	0.002	16.4%	3.9%	0.002	1.0%	1.5%	1.00	26.0%	6.7%	0.006
Death	7.3%	1.8%	0.040	6.6%	1.0%	0.031	1.0%	0%	1.00	12.2%	4.4%	0.25
Events <30 days of repeat revascularization, excluding myocardial infarction on the same day												
Composite endpoint‡	13.6%	9.1%	0.23	14.2%	8.8%	0.18	6.2%	4.6%	0.74	19.5%	15.6%	0.59
Subsequent repeat revascularization	8.6%	7.3%	0.67	10.4%	7.8%	0.48	5.2%	4.6%	1.00	11.4%	11.1%	0.96
Myocardial infarction	0.9%	0%	0.55	1.1%	0%	0.54	0%	0%	1.00	1.6%	0%	1.00
Death	5.5%	1.8%	0.15	4.4%	1.0%	0.16	1.0%	0%	1.00	8.9%	4.4%	0.52

*Elective repeat revascularization consists of procedures performed for stable angina pectoris or silent myocardial ischemia. †Urgent repeat revascularization consists of procedures performed for unstable angina pectoris or acute myocardial infarction. ‡Each patient may have had more than 1 event in each category.

Abbreviations as in Table 1.

composite safety endpoint (HR: 1.06; 95% CI: 0.50 to 2.22; p = 0.89; and HR: 0.67; 95% CI: 0.27 to 1.67; p = 0.39, respectively).

Considering not only events occurring after repeat revascularization but also before repeat revascularization, the results were similar (Online Appendix).

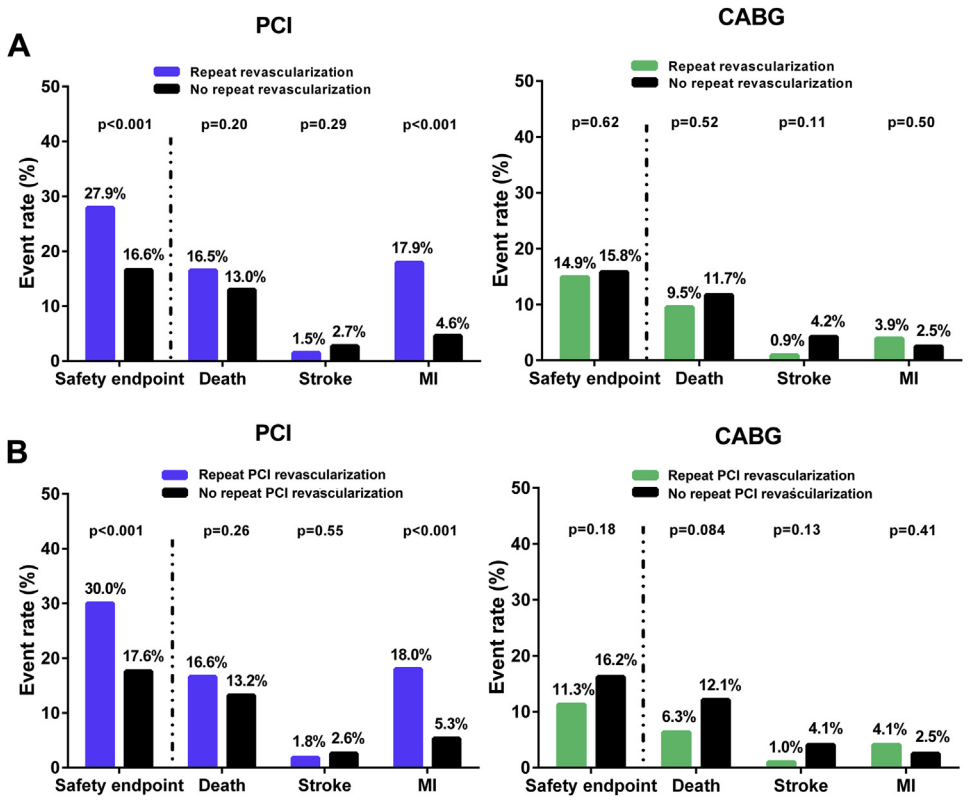
DISCUSSION

The present study is the first in-depth analysis of repeat revascularization from any randomized trial comparing CABG with PCI, whose findings are essential in understanding the underlying mechanisms of clinical differences between CABG and PCI, and provide insights into potential improvements in both surgical and interventional treatment. The main findings are that: 1) repeat revascularization rates were significantly higher after PCI compared with CABG at early, intermediate, and long-term intervals, and more often consisted of multiple repeat revascularizations during follow-up; 2) in agreement with available guidelines, repeat revascularizations were most frequently performed by means of PCI after both initial PCI and initial CABG (13,14); 3) the consequences of repeat revascularization were apparent in the short term and comparable between PCI and CABG, whereas long-term rates of all-cause death, stroke, and MI were significantly higher after repeat revascularization after initial PCI but not initial CABG; and 4) long-term outcomes were comparable among patients not requiring repeat revascularization after either initial PCI or initial CABG.

Data from large PCI trials have demonstrated incremental technical advances over time, with the latest generation of drug-eluting stents (DES) achieving the lowest rates of restenosis, stent thrombosis, and recurrent MI that may all account for repeat revascularization (15). In ARTS-I (Arterial Revascularization Therapies Study), use of bare-metal stents in the PCI group led to a repeat revascularization rate of 30.3%, whereas use of DES in the ARTS-II and SYNTAX trial was associated with lower repeat revascularization rates (20.3% and 25.9%, respectively) (7,16). The current study was performed with first-generation DES and showed that repeat revascularization rates were still about twice as high after PCI than after CABG during 5-year follow-up. It has been suggested that outcomes would have been different had a second-generation DES been used (17). However, the recent results from the BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease) trial showed that even with the use of second-generation everolimus-eluting stents for multivessel disease, CABG results were significantly better than PCI at 5-year follow-up due to a reduction in repeat revascularization as well as spontaneous MI (18).

In the current study, repeat revascularization after initial PCI consisted mainly of TVR and less for de novo lesions. It appears that both progression of disease and stent restenosis or thrombosis are more prominent after initial PCI than after initial CABG treatment. By placing anastomoses distal to potential

FIGURE 4 Clinical Outcomes After PCI and CABG With or Without Repeat Revascularization During Follow-Up

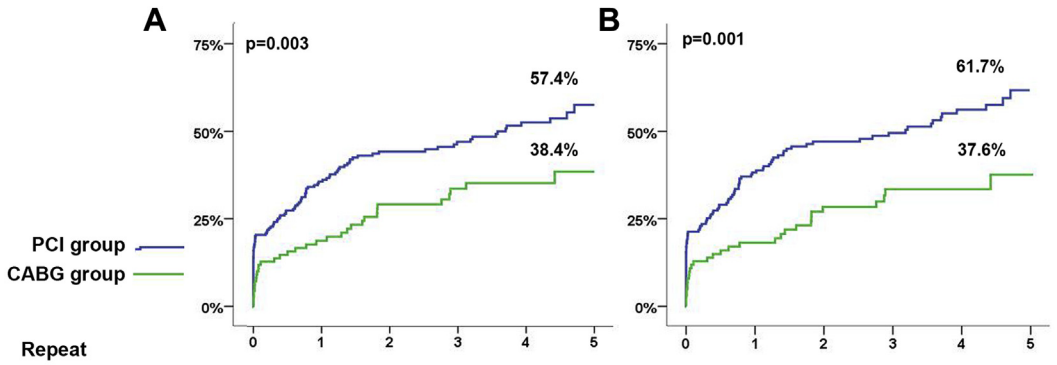


Rates of the composite safety endpoint of all-cause death, stroke, and myocardial infarction are compared between patients who required **(A)** any repeat revascularization or **(B)** only repeat PCI revascularization and those who did not require repeat revascularization. Safety endpoint was the composite endpoint of all-cause death, stroke, and myocardial infarction (MI). Abbreviations as in Figure 1.

future lesions, CABG may have a protective effect from repeat revascularization, although it does not prevent future lesions (19). The introduction of next-generation DES is encouraging with reduced rates of stent thrombosis and TVR that may potentially mitigate the differences between PCI and CABG (20,21), but their use will not eliminate later revascularization for de novo lesions. Assessment of long-term results and trials comparing these stents with CABG are required to assess whether reductions in TLR are sufficient to provide noninferior outcomes to CABG (22).

According to our data, reductions in repeat revascularization are translated into improved outcomes in clinical endpoints, particularly MI. In the short-term, repeat revascularization was associated with increased periprocedural mortality and morbidity, which is more prominent after initial PCI than initial CABG treatment, likely to be the result of more acute presentation. Therefore, as repeat revascularization can also be a life-saving procedure in the setting of an acute MI, it is important to mention that by excluding events occurring at the same day of repeat revascularization (the majority consisting of MI), the difference between initial PCI and CABG was no longer statistically significant, referring only to the intrinsic risk of the procedure. In the long-term, repeat revascularization was associated with increased rates of the composite safety endpoint, even after adjustment for baseline and procedural characteristics. Comparing PCI and CABG in the context of comparable rates of all-cause death and competing risks with repeat revascularization that are overestimated by Kaplan-Meier methods (23), patients undergoing initial PCI were more likely to return for repeat revascularization than those who underwent initial CABG, possibly particularly the result of preceding MI. As no difference was noted between initial PCI and initial CABG among patients who did not undergo repeat revascularization, the importance of

FIGURE 5 Kaplan-Meier Estimates of the Composite Safety Endpoint After Repeat Revascularization



Repeat revascularization type	All repeat revascularization			PCI repeat revascularization		
Index procedure	PCI group (n=220)	CABG group (n=110)	p-value	PCI group (n=183)	CABG group (n=102)	p-value
Composite endpoint	57.4%	38.4%	0.003	61.7%	37.6%	0.001
2nd+ Revascularization	43.4%	25.3%	0.012	50.9%	27.1%	0.002
Myocardial infarction	19.2%	4.8%	0.001	18.6%	5.3%	0.001
Death	20.2%	13.9%	0.095	20.6%	11.5%	0.021

Kaplan-Meier estimates after the **(A)** first revascularization and **(B)** first PCI repeat revascularization during follow-up after initial PCI **(blue line)** or CABG **(green line)**. Comparisons between index procedure in patients with **(A)** any repeat revascularization reveal a hazard ratio of 0.46 (95% confidence interval: 0.26 to 0.82; p = 0.008). The p values in figures are by log-rank test. Abbreviations as in Figure 1.

identifying patients at risk for revascularization must be underlined.

In our analyses we were unable to identify a set of baseline clinical variables that could identify patients in whom initial PCI offers similar results as initial CABG in terms of repeat revascularization and long-term clinical outcomes as a result of these interventions. However, we were able to identify patients at highest risk for repeat revascularization for whom specific treatment for appropriate risk-reduction would apply. The complexity of disease was not a predictor, unlike findings of other studies (24,25). Nevertheless, incomplete revascularization and the number of overlapping stents that are highly correlated to the SYNTAX score (26), were independent predictors of repeat revascularization (4). These findings underline the need for routine use of fractional flow reserve that has been shown to reduce the number of stents used during PCI with subsequent reductions in adverse events (27). Furthermore, in alignment with randomized trials evaluating post-PCI antiplatelet therapy and current guidelines, we found that nonuse of acetylsalicylic acid or thienopyridine predicted repeat revascularization (28,29), and medical therapy was also a predictor of worse long-term outcomes (30). Paradoxically, patients requiring repeat revascularization after initial CABG had less presence of comorbidities and qualified as lower risk at the time of the initial procedure (3). Off-pump CABG and enrollment in the United States versus Europe were independent predictors of repeat revascularization, most probably due to a more proactive approach for repeat revascularization in case of symptoms recurrence after initial CABG (31). Whether incomplete revascularization is an important factor when performing CABG, remains a matter of debate (32,33). Some data suggest that incomplete revascularization has a particular impact on the repeat revascularization rate (34), but incomplete revascularization after CABG failed to be an independent predictor in the current analysis. Similar to the findings in the PCI group, secondary prevention measures remain critical in reducing adverse events, including repeat revascularization (35). Not included in multivariable models, but an area in which CABG outcomes can be improved, is early post-operative complications (36). Many repeat CABG revascularizations were the result of early complications (hemorrhage or acute graft failure) after initial CABG, for which intraoperative graft flow measurements may prove beneficial, although no consensus has been reached over their use (35-37).

TABLE 5 Predictors of the Composite Safety Endpoint of All-Cause Death, Stroke, and MI

	Model 1*			Model 2†			Model 3‡		
	HR	95% CI	p Value	HR	95% CI	p Value	HR	95% CI	p Value
PCI group (n = 903)									
Age (yrs)	1.03	1.02–1.05	<0.001	1.03	1.02–1.05	<0.001	1.03	1.02–1.05	<0.001
Previous MI	1.62	1.19–2.20	0.002	1.65	1.22–2.25	0.001	1.64	1.21–2.23	0.002
PAD	2.03	1.35–3.07	0.001	2.05	1.36–3.09	0.001	2.03	1.34–3.08	0.001
Staged procedure	1.83	1.26–2.59	0.002	1.80	1.24–2.61	0.002	1.82	1.25–2.64	0.002
No ASA	2.47	1.43–4.24	0.001	2.45	1.42–4.21	0.001	2.55	1.49–4.37	0.001
No thienopyridine	3.79	2.12–6.77	<0.001	3.63	2.01–6.57	<0.001	3.92	2.20–6.99	<0.001
Statins	0.61	0.41–0.90	0.013	0.60	0.41–0.89	0.012	0.61	0.41–0.91	0.015
All repeat revascularization*	**1.65**	**1.20–2.27**	**0.002**		Not included			Not included	
PCI repeat revascularization†		Not included		**1.67**	**1.20–2.32**	**0.002**		Not included	
CABG repeat revascularization†		Not included		**1.72**	**1.02–2.88**	**0.041**		Not included	
Target lesion revascularization		Not included			Not included		**1.69**	**1.20–2.38**	**0.003**
De novo lesion revascularization		Not included			Not included		**1.49**	**0.80–2.79**	**0.21**
CABG group (n = 897)									
Age (yrs)	1.07	1.04–1.09	<0.001	1.07	1.04–1.09	<0.001	1.07	1.04–1.09	<0.001
COPD	1.88	1.27–3.29	0.013	1.87	1.17–3.05	0.014	1.82	1.11–2.99	0.017
PAD	2.54	1.34–3.08	<0.001	2.58	1.27–3.06	<0.001	2.51	1.65–3.81	<0.001
Renal impairment	2.63	1.17–6.16	0.023	2.47	1.38–3.16	0.034	2.56	1.12–5.87	0.028
SYNTAX score	1.02	1.00–1.04	0.078	1.02	1.00–1.04	0.10	1.02	1.00–1.03	0.07
No ASA	2.31	1.41–3.30	<0.001	2.29	1.34–3.09	<0.001	2.32	1.52–3.55	<0.001
Statins	0.48	0.36–0.72	<0.001	0.48	0.34–0.69	<0.001	0.47	0.33–0.68	<0.001
All repeat revascularization*	**0.92**	**0.54–1.75**	**0.92**		Not included			Not included	
PCI repeat revascularization†		Not included		**0.69**	**0.34–1.37**	**0.28**		Not included	
CABG repeat revascularization†		Not included		**3.32**	**1.21–9.11**	**0.020**		Not included	
Target lesion revascularization		Not included			Not included		**1.06**	**0.50–2.22**	**0.89**
De novo lesion revascularization		Not included			Not included		**0.67**	**0.27–1.67**	**0.39**

*Repeat revascularization (PCI or CABG) is included as separate variable in Model 1. †PCI repeat revascularization and CABG repeat revascularization are included as separate variables in Model 2. ‡Target lesion revascularization and de novo lesion revascularization are included as separate variables in Model 3. **Bold** values indicate variables of repeat revascularization.

PAD = peripheral artery disease; other abbreviations as in Tables 1, 2, and 3.

STUDY LIMITATIONS. The present study is a post hoc analysis of the SYNTAX trial and the results should therefore be interpreted within the limits of both statistical power and clinical relevance. The SYNTAX trial did not primarily intend to investigate the practice of repeat revascularization, although repeat revascularization was registered as a component of the primary endpoint under supervision of the independent Clinical Events Committee and was a standalone secondary endpoint. Angiography was not routinely performed and there are no available data on the use of fractional flow reserve or functional testing in the assessment of lesions.

CONCLUSIONS

Repeat revascularization is not a benign event as patients requiring repeat revascularization are at increased risk of both periprocedural and long-term events. Predictors of patients at risk for repeat revascularization highlight the need for adequate medical treatment as secondary prevention. Although procedural risk of repeat revascularization is similar after initial PCI and CABG procedure, long-term results show higher rates of clinically meaningful endpoints after repeat revascularization in the PCI group, which drove the differences favoring CABG over PCI in the more complex patients in the SYNTAX trial overall. However, comparison of long-term results of patients who did not undergo repeat revascularization revealed similar outcomes between PCI and CABG, suggesting that both careful patient selection and improvements in both PCI and CABG technology, techniques, and adjunctive therapies will have a favorable impact in the future.

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PERSPECTIVES

WHAT IS NEW? Repeat revascularization is a biased clinical outcome from randomized trials comparing PCI with CABG with limited in-depth long-term follow-up data available. This study therefore aimed to analyze the incidence, characteristics, and predictors of repeat revascularization as well as its long-term impact on hard clinical events during 5-year follow-up of the SYNTAX trial.

WHAT IS KNOWN? Repeat revascularization occurred more often after PCI than after CABG, and more often consisted of multiple repeat revascularizations. Significantly more repeat PCI procedures were performed on de novo lesions in patients after initial PCI than initial CABG. Repeat revascularization was an independent predictor of the composite safety endpoint of death, MI, and stroke after both treatment types for complex coronary artery disease.

WHAT IS NEXT? Careful selection of patients, use of novel interventional devices and functional assessment, together with aggressive medical therapy, should be the main approach in reducing the rate of repeat revascularization and the negative impact it has on clinical outcomes.

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APPENDIX For expanded Methods and Results sections as well as supplemental tables and figures, please see the online version of this article.