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Outcomes After Left Main Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting According to Lesion Site

Results From the EXCEL Trial

Anthony H. Gershlick, MBBS,[a] David E. Kandzari, MD,[b] Amerjeet Banning, MD,[a] David P. Taggart, MD,[c] Marie-Claude Morice, MD,[d] Nicholas J. Lembo, MD,[b,e] W. Morris Brown III, MD,[b] Adrian P. Banning, MD,[c] Béla Merkely, MD, PhD, DSc,[f] Ferenc Horkay, MD,[f] Ad J. van Boven, MD, PhD,[g] Piet W. Boonstra, MD, PhD,[g] Ovidiu Dressler, MD,[h] Joseph F. Sabik III, MD,[i] Patrick W. Serruys, MD, PhD,[j] Arie Pieter Kappetein, MD, PhD,[k] Gregg W. Stone, MD[e,h]

ABSTRACT

OBJECTIVES The authors sought to determine the extent to which the site of the left main coronary artery (LM) lesion (distal bifurcation versus ostial/shaft) influences the outcomes of revascularization with percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG).

BACKGROUND Among 1,905 patients with LM disease and site-assessed SYNTAX scores of <32 randomized in the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial, revascularization with PCI and CABG resulted in similar rates of the composite primary endpoint of death, myocardial infarction (MI), or stroke at 3 years.

METHODS Outcomes from the randomized EXCEL trial were analyzed according to the presence of angiographic core laboratory–determined diameter stenosis ≥50% involving the distal LM bifurcation (n = 1,559; 84.2%) versus disease isolated to the LM ostium or shaft (n = 293; 15.8%).

RESULTS At 3 years, there were no significant differences between PCI and CABG for the primary composite endpoint of death, MI, or stroke for treatment of both distal LM bifurcation disease (15.6% vs. 14.9%, odds ratio [OR]: 1.08, 95% confidence interval [CI]: 0.81 to 1.42; p = 0.61) and isolated LM ostial/shaft disease (12.4% vs. 13.5%, OR: 0.90, 95% CI: 0.45 to 1.81; p = 0.77) ($p_{interaction}$ = 0.65). However, at 3 years, ischemia-driven revascularization occurred more frequently after PCI than CABG in patients with LM distal bifurcation disease (13.0% vs. 7.2%, OR: 2.00, 95% CI: 1.41 to 2.85; p = 0.0001), but were not significantly different in patients with disease only at the LM ostium or shaft (9.7% vs. 8.4%, OR: 1.18, 95% CI: 0.52 to 2.69; p = 0.68) ($p_{interaction}$ = 0.25).

CONCLUSIONS In the EXCEL trial, PCI and CABG resulted in comparable rates of death, MI, or stroke at 3 years for treatment of LM disease, including those with distal LM bifurcation disease. Repeat revascularization rates during follow-up after PCI compared with CABG were greater for lesions in the distal LM bifurcation but were similar for disease isolated to the LM ostium or shaft. (J Am Coll Cardiol Intv 2018;11:1224–33) © 2018 by the American College of Cardiology Foundation.

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Effective revascularization of patients with stenosis of the left main (LM) coronary artery reduces mortality compared with medical therapy (1). Coronary artery bypass grafting (CABG) has historically been regarded as the gold standard therapy for patients presenting with LM coronary artery disease (LMCAD), although this practice is based on data from nonrandomized studies (2–10) or underpowered randomized trials using first-generation drug-eluting stents (11–14). The recently completed EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) and the NOBLE (Nordic-Baltic-British Left Main Revascularization Study) randomized trials (15,16) have provided data comparing percutaneous coronary intervention (PCI) using contemporary drug-eluting stents with CABG for LMCAD. The larger of these trials, the EXCEL trial, reported similar 3-year outcomes for the composite primary endpoint of death, myocardial infarction (MI), or stroke with PCI using fluoropolymer-based cobalt chromium everolimus-eluting stents (CoCr-EES) compared with CABG. Thirty-day major events were less common after PCI, although long-term ischemia-driven revascularization rates were lower after CABG.

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Whether outcomes after revascularization of patients with LMCAD vary according to the pattern of atherosclerosis in the LM stem, specifically whether the disease involves the distal LM bifurcation or is limited to the LM ostium or shaft, has not been reported from randomized trials. A multicenter registry study reported that patients with ostial or mid-shaft LMCAD had a favorable prognosis after PCI with first-generation drug-eluting stents (17). A propensity-adjusted analysis from the DELTA (Drug-Eluting Stent for Left Main Coronary Artery Disease) registry indicated that distal bifurcation disease had worse outcomes than ostial or shaft disease after PCI (18). Neither study compared these PCI outcomes to a control arm of patients undergoing CABG. Nonetheless, PCI guidelines and appropriateness criteria recommendations for revascularization vary according to coronary artery disease complexity, including distal LM bifurcation involvement (19,20). We thus examined the outcomes of PCI versus CABG according to LM lesion location in a prespecified analysis from the EXCEL trial to determine the extent to which this parameter should influence revascularization decisions in patients with LMCAD.

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CI = confidence interval

CoCr-EES = cobalt chromium everolimus-eluting stent(s)

LM = left main coronary artery

LMCAD = left main coronary artery disease

MI = myocardial infarction

OR = odds ratio

PCI = percutaneous coronary intervention

QCA = quantitative coronary angiography

TVR = target vessel revascularization

METHODS

PROTOCOL AND PATIENT SELECTION. The design of the EXCEL trial has been previously reported (21). In brief, the EXCEL trial was an international, open-label, multicenter trial in which 1,905 patients with LMCAD and low or intermediate SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) scores (≤32) eligible for both PCI and CABG as assessed by a local heart team were randomized to treatment with CoCr-EES (XIENCE, Abbott Vascular, Santa Clara, California) or CABG. The primary endpoint was the composite rate of death, MI, or stroke at a median follow-up of 3 years. Major secondary endpoints included death, MI,

From the [a]University Hospitals of Leicester, University of Leicester, Leicester Biomedical Research Centre, Leicester, United Kingdom; [b]Piedmont Heart Institute, Atlanta, Georgia; [c]Department of Cardiac Surgery, John Radcliffe Hospital, Oxford, United Kingdom; [d]Ramsay Générale deSanté, Hopital Privé Jacques Cartier, Massy, France; [e]Center for Interventional Vascular Therapy, Division of Cardiology, NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, New York; [f]Heart and Vascular Center, Semmelweis University, Budapest, Hungary; [g]Medisch Centrum Leeuwarden, Leeuwarden, the Netherlands; [h]Clinical Trials Center, Cardiovascular Research Foundation, New York, New York; [i]Department of Surgery, University Hospitals Cleveland Medical Center, Cleveland, Ohio; [j]International Centre for Circulatory Health, National Heart and Lung Institute, Imperial College, London, United Kingdom; and the [k]Erasmus Medical Centre, Rotterdam, the Netherlands. Dr. Gershlick has received lecture fees and travel support from Abbott Vascular. Dr. Kandzari has received consulting fees from Medtronic, Boston Scientific, and Micell; and grant support from Medtronic, Abbott Vascular, Boston Scientific, Biotronik, and Medinol. Dr. Lembo has received fees for lectures and for serving on advisory boards from Abbott Vascular, Boston Scientific, and Medtronic. Prof. A.P. Banning is partially funded by The NIHR Oxford Biomedical Research Centre; and has received lecture fees from Abbott Vascular, and Boston Scientific; and institutional research funding from Boston Scientific. Dr. Merkely has received lecture fees and institutional grant support from Abbott. Dr. Sabik has received fees for serving on advisory boards from Medtronic; and is a consultant for Medtronic, Edwards Lifesciences, and Sorin. Dr. Serruys has receiving consulting fees from Abbott, Biosensors, Medtronic, Micell Technologies, QualiMed, SINOMED, St. Jude Medical, Stentys, Svelte Medical Systems, Philips/Volcano, and Xeltis. Dr. Kappetein is an employee of Medtronic. Dr. Stone's employer, Columbia University, receives royalties for sale of the MitraClip. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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TABLE 1 Baseline Clinical Characteristics

	Lesion Location		
	Ostial/Shaft Only (n = 293)	Distal Bifurcation (n = 1,559)	p Value
Age, yrs	64.8 ± 10.4	66.1 ± 9.4	0.11
Male	208 (71.0)	1208 (77.5)	0.02
Diabetes	97 (33.1)	447/1,558 (28.7)	0.13
Insulin treated	32 (10.9)	112/1,558 (7.2)	0.03
Hypertension	223 (76.1)	1,148/1,558 (73.7)	0.38
Hyperlipidemia	204 (69.6)	1,100/1,555 (70.7)	0.70
Current smoker	78/292 (26.7)	328/1,546 (21.2)	0.04
Prior myocardial infarction	37/289 (12.8)	281/1,547 (18.2)	0.03
Prior percutaneous coronary intervention	44 (15.0)	273/1,556 (17.5)	0.29
Prior stroke or transient ischemic attack	17 (5.8)	97/1,557 (6.2)	0.78
Presentation with acute coronary syndrome	114/292 (39.0)	613/1,552 (39.5)	0.88
Left ventricular ejection fraction, %	57.2 ± 9.3	57.1 ± 9.3	0.90
Chronic kidney disease*	49/285 (17.2)	248/1,532 (16.2)	0.67

Values are mean ± SD, n (%), or n/N (%). *Estimated glomerular filtration rate <60 ml/min.

TABLE 2 Baseline Angiographic and Procedural Characteristics

	Lesion Location		
	Ostial/Shaft Only (n = 293)	Distal Bifurcation (n = 1,559)	p Value
Ostial or shaft diameter stenosis ≥50%	293 (100.0)	730/1,534 (47.6)	<0.0001
Ostial diameter stenosis ≥50%	268 (91.5)	402/1,534 (26.2)	<0.0001
Shaft diameter stenosis ≥50%	107 (36.5)	652/1,534 (42.5)	0.057
Distal left main bifurcation	0 (0.0)	1,559 (100.0)	–
Distal left main trifurcation	0 (0.0)	642 (41.2)	–
Left main diameter stenosis, %	65.9 ± 10.8	64.4 ± 12.1	0.03
Number of non-left main diseased vessels			
0	70 (23.9)	259/1,559 (16.6)	0.003
1	96 (32.8)	483/1,559 (31.0)	0.55
2	86 (29.4)	522/1,559 (33.5)	0.17
3	41 (14.0)	295/1,559 (18.9)	0.04
SYNTAX score	19.8 ± 7.5	27.9 ± 9.0	<0.0001
Vessels stented or bypassed			
Left anterior descending	186 (63.5)	1,200 (77.0)	<0.0001
Left circumflex	150 (51.2)	1,002 (64.3)	<0.0001
Right coronary artery	86 (29.4)	514 (33.0)	0.22
>1 Stent used in left main*	24/133 (18.0)	342/781 (43.8)	0.0006
≥1 Arterial conduits†	146/146 (100.0)	732/743 (98.5)	0.23
≥2 Arterial conduits†	31/146 (21.2)	247/743 (33.2)	0.004
≥1 Venous conduits†	114/146 (78.1)	555/740 (75.0)	0.43
≥2 Venous conduits†	43/146 (29.5)	269/740 (36.4)	0.11

Values are n (%), n/N (%), or mean ± SD. *Percutaneous coronary intervention group only. †Coronary artery bypass grafting group only. Angiographic data are core laboratory assessed.

or stroke at 30 days, and the composite of death, MI, stroke, or ischemia-driven revascularization at 3 years. These endpoints were adjudicated by an independent clinical events committee after review of original source documents. The endpoint definitions have been previously described (21). At the time of the present analysis, 3-year follow-up is complete for all randomized EXCEL trial patients.

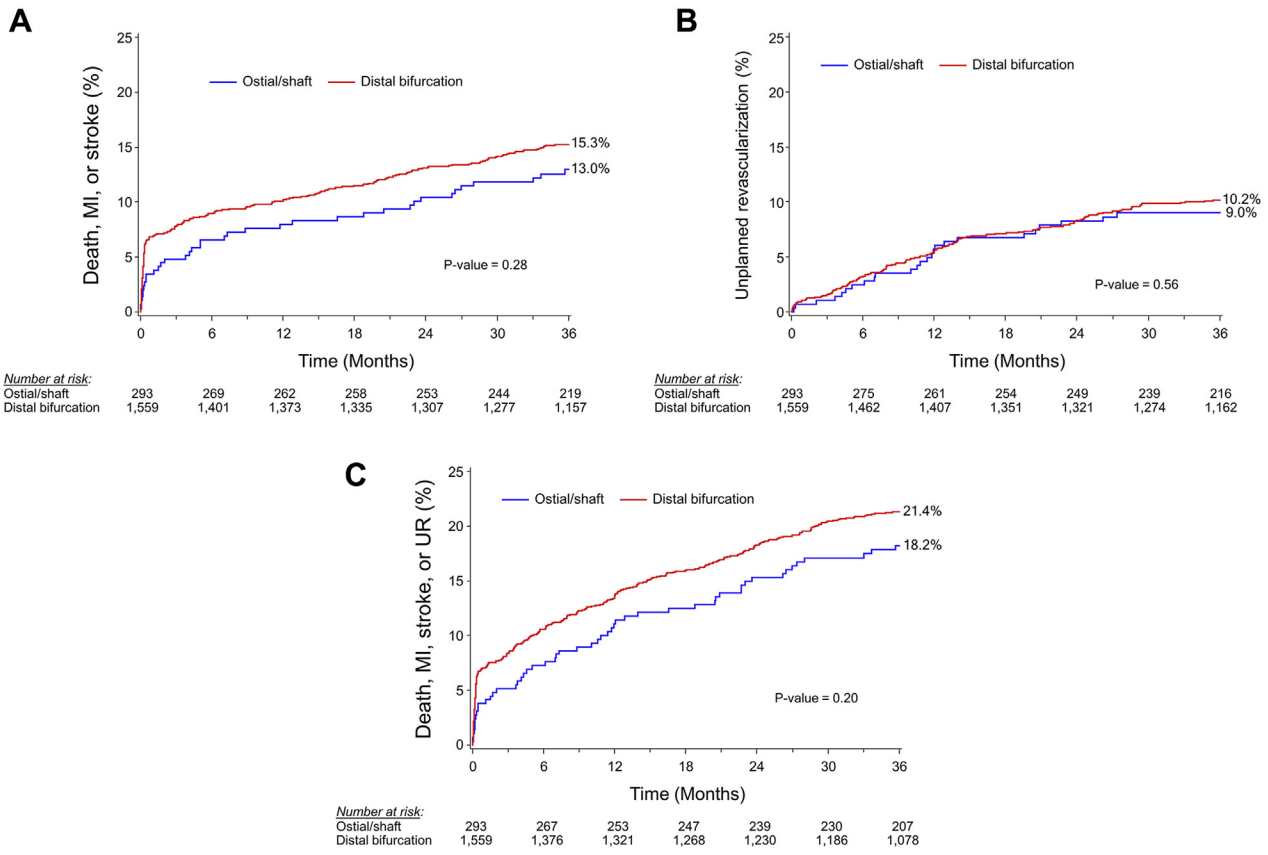
Baseline angiograms were analyzed at an independent angiographic core laboratory (Cardiovascular Research Foundation, New York, New York). For the present study, patients were included if the baseline angiographic film was available for analysis and demonstrated a LM diameter stenosis ≥50% by quantitative coronary angiography (QCA). Patients were then grouped into: 1) those with distal LM bifurcation involvement (QCA diameter stenosis ≥50%), including patients with or without disease of the LM ostium or shaft; or 2) those with isolated disease (QCA diameter stenosis ≥50%) of the LM ostium or shaft.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD and were compared between groups using Student's *t*-test or Wilcoxon rank sum test for non-normally distributed data. Categorical variables were summarized as counts and percentages, and were compared between groups using the chi-square or Fisher exact test. We estimated rates of adverse events using time-to-first event Kaplan-Meier methodology and tested differences between groups using the log-rank test. We performed univariable and multivariable logistic regression, and reported odds ratios (ORs) and 95% confidence intervals (CIs). Interaction testing was performed to determine whether the relative risks between the 2 subgroups were different. All statistical tests were 2-sided, with $p < 0.05$ considered statistically significant. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

PATIENTS AND BASELINE CHARACTERISTICS. Among the 1,905 patients randomized in the EXCEL trial, QCA was not available in 27 patients (1.4%); and by QCA, the LM diameter stenosis was <50% in 26 patients (1.4%). Thus, 1,852 patients met criteria for inclusion in the present study, including 1,559 patients (84.2%) who had angiographic core laboratory-confirmed distal LM bifurcation involvement and 293 patients (15.8%) who had isolated disease of the LM ostium or shaft. Baseline clinical and QCA characteristics and selected procedural data in the 2 groups are shown in Tables 1 and 2. Compared with patients with isolated disease of the LM ostium or shaft, those with

FIGURE 1 3-Year Outcomes According to LM Disease Location Pooled Across Randomization Assignment



(A) The primary composite endpoint of death, myocardial infarction (MI) or stroke; **(B)** unplanned revascularization (UR) for ischemia; **(C)** the composite endpoint of death, MI, stroke, or UR for ischemia. For each endpoint, the 3-year event rates were slightly higher if the distal left main (LM) bifurcation was diseased, although these differences did not reach statistical significance. CI = confidence interval; HR = hazard ratio.

distal bifurcation disease were less likely to have insulin-treated diabetes, but were more likely to be male, nonsmokers, have prior MI, have a higher SYNTAX score with more 3-vessel disease, and be treated with a 2-stent bifurcation technique or multiple arterial grafts.

Among the 1,559 patients with distal LM bifurcation disease, 789 (50.6%) were randomized to PCI and 770 (49.4%) to CABG. Among the 293 patients with isolated disease of the LM ostium or shaft, 141 (48.1%) were randomized to PCI and 152 (51.7%) to CABG. Baseline clinical and core laboratory–assessed angiographic characteristics and selected procedural data in the PCI versus CABG groups according to the location of LM disease appear in Online Tables 1 and 2. The baseline characteristics of the randomized groups were well balanced, except that in the ostial/shaft group, PCI-assigned patients had slightly more hypertension than CABG-assigned patients, whereas in the distal bifurcation group, PCI-assigned patients were more likely to be smokers and had a slightly higher SYNTAX score than CABG-assigned patients.

CLINICAL OUTCOMES. The median (interquartile range) duration of follow-up in both groups was 3.0 (3.0 to 3.0) years. Three-year follow-up data were not available in 17 of 293 patients (5.8%) in the ostial/shaft group and in 78 of 1,559 patients (5.0%) in the distal bifurcation group who were either lost to follow-up or withdrew ($p = 0.67$). In the entire study cohort (pooled across randomization), 3-year event rates were nonsignificantly higher in patients with distal LM bifurcation disease compared with those with isolated ostial/shaft disease (**Figure 1**). The 3-year outcomes according to LM disease location and treatment appear in **Table 3 and Figures 2 and 3**. At 30 days, the rates of the composite primary endpoint of death, MI, or stroke, and of the composite endpoint of death, MI, stroke, or unplanned revascularization

TABLE 3 Outcomes in Patients Randomized to PCI Versus CABG

	Lesion Location								
	Ostial/Shaft Only				Distal Bifurcation				
	PCI (n = 141)	CABG (n = 152)	OR (95% CI)	p Value	PCI (n = 789)	CABG (n = 770)	OR (95% CI)	p Value	$p_{interaction}$
30-day event rates									
Death, myocardial infarction, or stroke	0.7 (1)	6.0 (9)	0.11 (0.01–0.91)	0.01	5.6 (44)	8.1 (62)	0.67 (0.45–1.01)	0.055	0.10
Death	0.0 (0)	0.7 (1)	–	0.33	1.1 (9)	1.2 (9)	0.98 (0.39–2.47)	0.95	0.91
Myocardial infarction	0.7 (1)	4.0 (6)	0.17 (0.02–1.46)	0.07	4.4 (35)	6.4 (49)	0.68 (0.44–1.07)	0.10	0.22
Stroke	0.0 (0)	2.0 (3)	–	0.09	0.8 (6)	1.2 (9)	0.65 (0.23–1.83)	0.40	0.90
Ischemia-driven revascularization	0.0 (0)	1.3 (2)	–	0.17	0.8 (6)	1.3 (10)	0.58 (0.21–1.61)	0.29	0.91
Death, myocardial infarction, stroke, or ischemia-driven revascularization	0.7 (1)	6.7 (10)	0.10 (0.01–0.82)	0.008	5.6 (44)	8.6 (66)	0.63 (0.42–0.94)	0.02	0.09
3-yr event rates									
Death, myocardial infarction, or stroke	12.4 (17)	13.5 (20)	0.90 (0.45–1.81)	0.67	15.6 (122)	14.9 (112)	1.07 (0.81–1.42)	0.80	0.65
Death	8.8 (12)	6.1 (9)	1.48 (0.60–3.62)	0.42	7.8 (61)	5.9 (44)	1.38 (0.93–2.06)	0.15	0.89
Myocardial infarction	3.7 (5)	6.8 (10)	0.52 (0.17–1.57)	0.23	8.7 (67)	8.4 (63)	1.04 (0.73–1.49)	0.91	0.24
Stroke	2.3 (3)	4.1 (6)	0.53 (0.15–1.79)	0.35	2.4 (18)	2.9 (21)	0.74 (0.41–1.34)	0.53	0.62
Ischemia-driven revascularization	9.7 (13)	8.5 (12)	1.18 (0.52–2.69)	0.72	13.2 (100)	7.2 (52)	2.00 (1.41–2.85)	0.0002	0.25
Death, myocardial infarction, stroke, or ischemia-driven revascularization	18.2 (25)	18.3 (27)	1.00 (0.55–1.82)	0.85	23.6 (184)	19.0 (143)	1.34 (1.05–1.72)	0.058	0.37

Values are % (n), unless otherwise indicated. Data are Kaplan-Meier estimated event rates.
CABG = coronary artery bypass grafting; CI = confidence interval; HR = hazard ratio; OR = odds ratio; PCI = percutaneous coronary intervention.

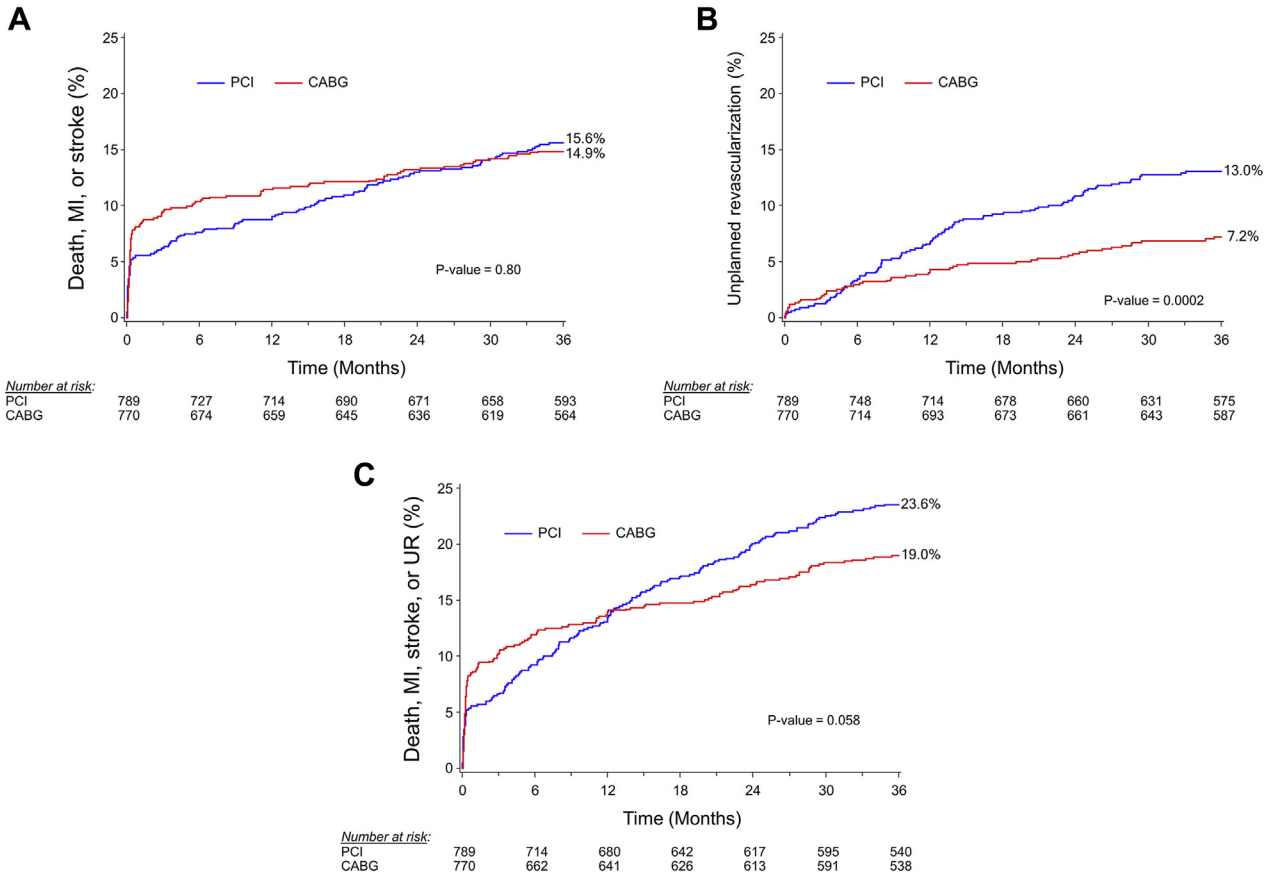
were lower with PCI compared with CABG in patients with ostial/shaft disease. In patients with distal bifurcation disease these rates were numerically lower with PCI, but the differences were not statistically significant. At 3 years, the rate of the primary composite endpoint of death, MI, or stroke was not significantly different between PCI and CABG, either in the distal bifurcation group or the isolated ostial/shaft group ($p_{interaction} = 0.65$). Similarly, there were no significant differences between PCI and CABG in the 3-year rates of the composite endpoint of death, MI, stroke, or ischemia-driven revascularization in either group according to LM disease location ($p_{interaction} = 0.37$). Ischemia-driven revascularization at 3 years, however, was more frequent after PCI than CABG among patients with LM distal bifurcation disease (13.0% vs. 7.2%; OR: 2.00; 95% CI: 1.41 to 2.85; p = 0.0001) (**Figure 2B**), but not in patients with LM disease isolated to the ostium or shaft (9.7% vs. 8.4%; OR: 1.18; 95% CI: 0.52 to 2.69; p = 0.68) ($p_{interaction} = 0.25$). The relative rates of ischemia-driven revascularization with PCI versus CABG in the LM distal bifurcation and isolated LM ostial/shaft groups were not influenced by the extent of non-LMCAD (Online Table 3).

Detailed data on the ischemia-driven revascularization events occurring within 3 years after randomization are shown in **Table 4**. PCI was the most frequent repeat revascularization procedure irrespective of whether the original intervention was PCI or CABG. In patients with distal bifurcation disease, target vessel revascularization (TVR) was more common after PCI compared with CABG. Conversely, TVR rates after PCI were lower in the ostial/shaft group, and similar after PCI and CABG. Non-TVR rates were also higher after PCI compared with CABG in the distal bifurcation group, but not in the ostial/shaft group. Finally, as shown in **Table 5**, the 3-year primary and major secondary composite event rates in the ostial/shaft group were similar after PCI and CABG irrespective of the baseline angiographic core laboratory-derived SYNTAX score. The primary endpoint rate was also similar after PCI and CABG across SYNTAX score tertiles in those with distal bifurcation disease. The major secondary composite event rate was significantly greater in the PCI group in patients with SYNTAX scores >32, but not in those with anatomically less complex disease.

DISCUSSION

The major findings of this pre-specified substudy from the randomized EXCEL trial that compared the

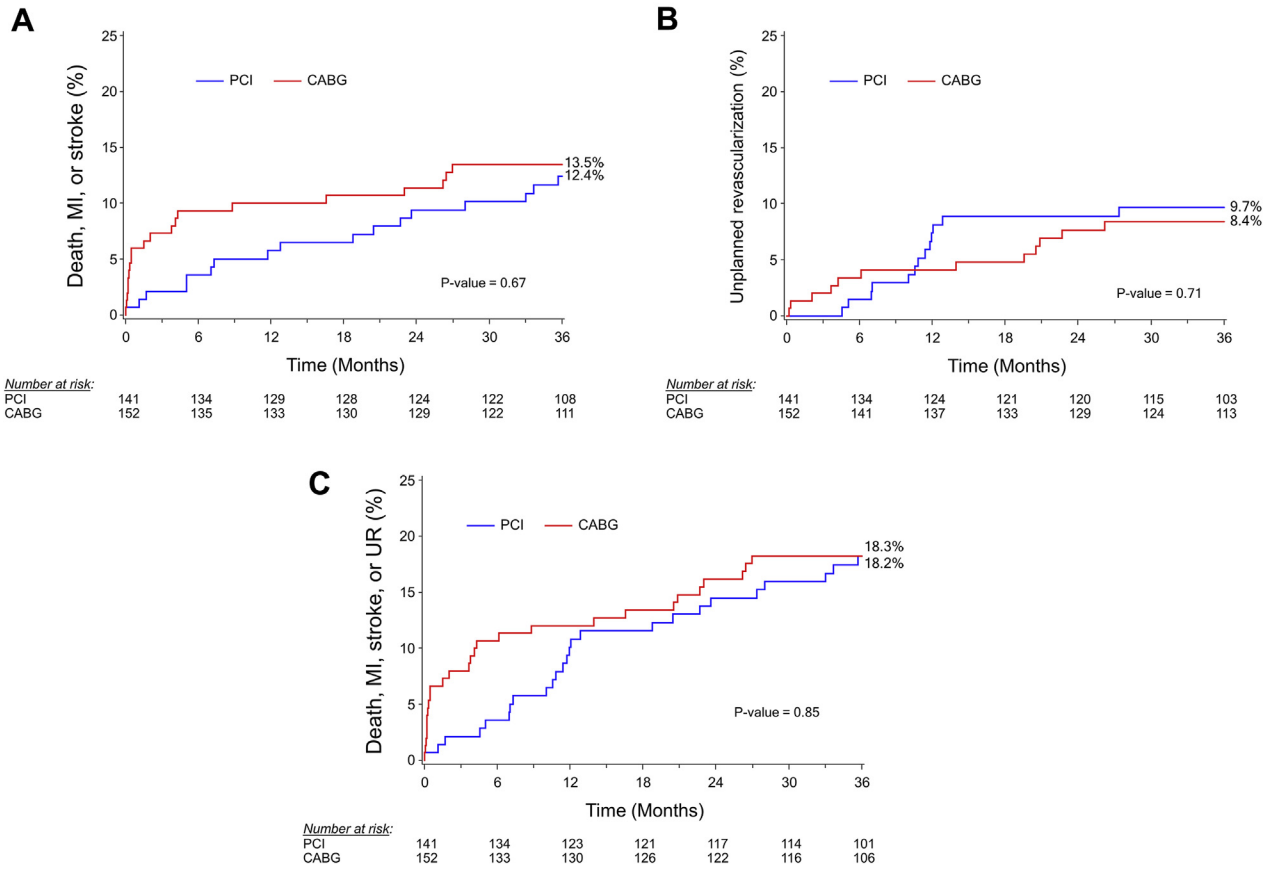
FIGURE 2 3-Year Outcomes in Patients With Distal LM Bifurcation Disease Randomized to PCI Versus CABG



(A) The primary composite endpoint of death, myocardial infarction (MI) or stroke; **(B)** unplanned revascularization (UR) for ischemia; **(C)** the composite endpoint of death, MI, stroke, or UR for ischemia. There were no significant differences in the composite endpoint measures between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), although UR was required more frequently after PCI. Abbreviations as in Figure 1.

outcomes of LM revascularization (PCI vs. CABG) according to the site of LM disease are as follows: 1) in the trial as a whole, despite a significantly higher SYNTAX score in patients with distal LM bifurcation involvement, the 3-year rates of adverse cardiovascular events were not significantly higher after revascularization in such patients compared to those with isolated LM ostial/shaft disease; 2) at 30 days, the composite rate of death, MI, or stroke, and the composite rate of death, MI, stroke, or unplanned revascularization were lower in patients randomized to PCI versus CABG, especially in those with ostial/shaft disease; 3) at 3 years, there were no significant differences in the composite rate of death, MI, or stroke (the primary study endpoint), nor in the composite rate of death, MI, stroke, or unplanned revascularization with PCI compared with CABG, either in patients with distal LM bifurcation involvement or with isolated LM ostial/shaft disease; 4) the 3-year rates of ischemia-driven unplanned revascularization were significantly higher after PCI compared with CABG in patients with distal LM bifurcation disease but were not increased in those with isolated LM ostial/shaft disease; 5) most repeat revascularizations were PCI procedures, and TVR and non-TVR rates during 3-year follow-up were increased after initial treatment with PCI compared to CABG in the distal bifurcation group, but not in those with isolated ostial/shaft disease; and 6) the 3-year rates of the primary endpoint of death, MI, or stroke were similar after PCI and CABG irrespective of LM lesion location and SYNTAX score, whereas the 3-year secondary composite endpoint of death, MI, stroke, or ischemia-driven revascularization was significantly increased only in patients with distal bifurcation disease and SYNTAX scores >32.

FIGURE 3 3-Year Outcomes in Patients With LM Disease Isolated to the Ostium or Shaft Randomized to PCI Versus CABG



(A) The primary composite endpoint of death, myocardial infarction (MI), or stroke; **(B)** unplanned revascularization (UR) for ischemia; **(C)** the composite endpoint of death, MI, stroke, or UR for ischemia. There were no significant differences in in any of these event rates in patients treated with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Abbreviations as in Figure 1.

The main EXCEL trial report (16) demonstrated no difference in the primary composite endpoint of death, MI, or stroke at 3 years when patients with LMCAD and low or intermediate SYNTAX scores were treated with PCI with CoCr-EES compared with CABG. In this initial analysis, outcomes were not differentiated according to site of the LM lesion. In contrast to nonbifurcation LM disease, PCI of distal LM bifurcation disease is procedurally more complex and has been associated with increased cardiovascular event rates (17,18,22–25), particularly when a 2-stent technique is required to treat disease affecting both the left anterior descending and left circumflex coronary arteries. However, interventional techniques and stents have substantially improved over the last decade, thus warranting re-examination as to whether the presence of distal LM bifurcation disease still adversely affects LM PCI outcomes in the contemporary revascularization era. To the best of our knowledge, the present analysis from the EXCEL trial represents the first robust randomized comparison of PCI versus CABG outcomes according to the site of LM stem disease in the contemporary era.

The most important finding from the present study is that the 3-year composite rate of major adverse cardiovascular events, namely death, MI, or stroke, was comparable with PCI and CABG regardless of whether the distal bifurcation was versus was not involved, with ORs of 1.08 and 0.91, respectively. The negative interaction effect for this comparison indicates that the relative treatment effects of PCI versus CABG were independent of the presence of distal LM bifurcation disease for major cardiovascular events at 3 years.

TABLE 4 Detailed Analysis of all Ischemia-Driven Revascularization Occurring Within 3-Years After Randomization

	Lesion Location							
	Ostial/Shaft Only				Distal Bifurcation			
	PCI (n = 141)	CABG (n = 152)	OR (95% CI)	p Value	PCI (n = 789)	CABG (n = 770)	OR (95% CI)	p Value
Revascularization, any	9.7 (13)	8.5 (12)	1.18 (0.52–2.69)	0.72	13.2 (100)	7.2 (52)	2.01 (1.42–2.84)	0.0002
PCI	7.5 (10)	7.8 (11)	0.98 (0.40–2.38)	0.93	11.0 (83)	6.4 (46)	1.86 (1.28–2.69)	0.002
CABG	3.0 (4)	0.7 (1)	4.41 (0.49–39.93)	0.16	3.3 (25)	0.8 (6)	4.17 (1.63–9.71)	0.001
Revascularization type								
TVR	9.0 (12)	7.0 (10)	1.32 (0.55–3.16)	0.56	11.4 (86)	6.9 (50)	1.75 (1.22–2.51)	0.004
TLR	7.5 (10)	6.3 (9)	1.21 (0.48–3.08)	0.70	9.8 (74)	6.6 (48)	1.52 (1.05–2.22)	0.03
Non-TLR	2.3 (3)	0.7 (1)	3.28 (0.34–31.92)	0.29	3.4 (26)	0.6 (4)	5.42 (2.08–14.15)	<0.0001
Non TVR	2.3 (3)	2.1 (3)	1.45 (0.32–6.60)	0.94	2.4 (18)	0.6 (4)	4.73 (1.60–13.95)	0.004

Values are % (n), unless otherwise indicated. Data are Kaplan-Meier estimated event rates.
Abbreviations as in Table 3.

The favorable outcome in terms of major cardiovascular events in the EXCEL trial with PCI for treatment of distal LM bifurcation disease is particularly notable given that the mean SYNTAX score in the distal LM bifurcation group was 28 (compared with 20 in patients with isolated LM ostial/shaft disease), and that 41% of the PCI-assigned distal bifurcation group had trifurcation disease. These results are consistent with findings from the principal EXCEL report that the relative rates of the primary outcome measure were similar with PCI and CABG in patients with angiographic core laboratory–determined low, intermediate, and high SYNTAX scores (16). However, patients with visually assessed SYNTAX scores ≥33 were excluded from the EXCEL trial (per protocol); as such, the present results cannot be generalized to patients with distal LM bifurcation disease and very extensive non-LMCAD. Similarly, consistent with contemporary practice, only 44% of PCI-assigned patients with distal LM bifurcation disease required 2 stents. In this regard, Palmerini et al. (22) previously reported that adverse events after LM PCI occurred more frequently in the LM distal versus non-distal disease location only when a planned 2-stent technique was required. Larger studies are thus warranted to determine whether the present results apply to patients with highly complex distal LM bifurcation and trifurcation disease. A detailed analysis from the EXCEL trial regarding PCI outcomes according to provisional versus planned 2-stent treatment (and the specific approach) is underway.

In the entire EXCEL trial population, despite comparable 3-year rates of death, MI, or stroke with PCI and CABG, ischemia-driven revascularization during long-term follow-up was required more frequently in patients randomized to PCI. In the current analysis.

TABLE 5 3-Year Composite Adverse Events According to Left Main Disease Location, SYNTAX Score, and Randomized Treatment

	Lesion Location					
	Ostial/Shaft Only			Distal Bifurcation		
	PCI (n = 141)	CABG (n = 152)	p Value	PCI (n = 789)	CABG (n = 770)	p Value
Death, myocardial infarction, or stroke						
SYNTAX score <22	9.3 (8/87)	11.1 (11/105)	0.67	10.2 (20/199)	14.0 (34/250)	0.19
SYNTAX score 22–32	21.0 (8/41)	17.2 (6/35)	0.81	17.2 (59/346)	16.5 (49/306)	0.86
SYNTAX score >32	0.0 (0/7)	30.0 (3/10)	0.13	16.8 (37/222)	13.4 (27/207)	0.38
Death, myocardial infarction, stroke, or ischemia-driven revascularization						
SYNTAX score <22	16.3 (14/87)	17.1 (17/105)	0.83	15.9 (31/199)	19.8 (48/250)	0.21
SYNTAX score 22–32	23.6 (9/41)	20.2 (7/35)	0.84	26.5 (91/346)	21.2 (63/306)	0.16
SYNTAX score >32	14.3 (1/7)	30.0 (3/10)	0.41	25.5 (56/222)	14.4 (29/207)	0.008

Values are % (n/N). Data are Kaplan-Meier estimated event rates.
Abbreviations as in Table 3.

we observed that repeat revascularization for ischemia within 3 years was required significantly more frequently after PCI only when distal LM bifurcation disease was present (OR: 2.00; 95% CI: 1.41 to 2.85). Unplanned revascularization rates not significantly different between PCI and CABG when the LM disease was limited to the ostium or shaft (OR: 1.19; 95% CI: 0.52 to 2.69). Previously reported studies have also demonstrated that distal LM bifurcation lesion location is an important predictor of TLR after PCI (25). Although in the present study the interaction effect for this comparison was negative, interaction testing is inherently underpowered, and given the mechanistic plausibility of this finding and consistency with prior reports, we believe it is likely to be true.

Thus, whereas improved stent technology (CoCr-EES as used in the EXCEL trial) and operator technique results in comparable 3-year prognosis (death, MI, or stroke) with PCI compared with CABG in patients with operator-assessed low and intermediate SYNTAX scores regardless of LM lesion location, late revascularization rates (mostly repeat PCI) are still somewhat higher after PCI treatment of distal LM bifurcation disease compared with CABG, but not of LM ostial/shaft disease. The heart team, in concert with the patient, must determine whether this excess revascularization risk after initial PCI of distal LM stem disease is offset by the early advantages of the less invasive PCI procedure, as evidenced by a lower composite rate of death, MI, or stroke at 30 days, and fewer periprocedural major adverse events as previously reported (16). Finally, in patients with disease isolated to the LM ostium or shaft, PCI resulted in lower adverse event rates at 30 days and comparable outcomes at 3 years, both for the primary endpoint as well as unplanned revascularization. As such, PCI may be considered the preferred revascularization modality in patients with LMCAD limited to the LM ostium and shaft.

STUDY LIMITATIONS. The present study was prespecified in the EXCEL trial protocol, but as an analysis of subgroups, has reduced power. Specifically, the number of patients with isolated LM ostial/shaft disease was modest. Randomization was not stratified according to lesion location within the LM stem, and some differences in baseline characteristics between the randomized groups were present. The results should therefore be considered hypothesis generating. A detailed analysis of how the distal bifurcation stenting strategy may have affected outcomes is being performed and may be of particular interest to determine whether a specific approach might reduce the long-term rates of repeat revascularization after PCI. Finally, follow-up is only complete through 3 years. Longer-term follow-up (currently planned to 5 years) in the present and other studies is required to determine whether differences between PCI and CABG emerge over time as a function of LM disease complexity.

CONCLUSIONS

In the present analysis from the EXCEL trial, treatment of patients with LM disease involving the distal LM bifurcation with PCI using CoCr-EES compared with CABG resulted in fewer adverse events at 30 days and a comparable composite 3-year rate of death, MI, or stroke at 3 years, but necessitated more frequent repeat revascularization procedures during late follow-up. In patients with LM disease isolated to the ostium or shaft, PCI compared with CABG resulted in fewer adverse events at 30 days and comparable rates of death, MI, stroke, and unplanned revascularization at 3 years.

ADDRESS FOR CORRESPONDENCE: Dr. Anthony H. Gershlick, University Hospitals of Leicester, University of Leicester, Leicester Biomedical Research Centre, Groby Road, Leicester LE3 9QP, United Kingdom. E-mail: agershlick@aol.com.

PERSPECTIVES

WHAT IS KNOWN? Recent trials suggest no difference in hard endpoint outcomes between PCI and CABG in the treatment of LMCAD. Other registry data suggest worse outcomes for distal LM stem bifurcation disease compared with ostial/shaft disease.

WHAT IS NEW? These data for the first time compare 2 randomized revascularization options applied to the ostium/shaft or distal bifurcation LMCAD. They confirm that there is no difference, even for distal LM stem disease, in terms of hard endpoints. They also tell us that repeat revascularization was significantly more common with distal LMCAD initially treated with PCI, but that repeat revascularization was similar for ostial/shaft disease.

WHAT IS NEXT? An understanding of which patients with distal LMCAD (anatomy, stent choice, conduit used) do better with CABG and who can be treated with PCI is needed.

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KEY WORDS EXCEL, left main stem, lesion site, substudy

APPENDIX For supplemental tables, please see the online version of this paper.