

Outpatient Versus Inpatient Percutaneous Coronary Intervention in Patients With Left Main Disease (from the EXCEL Trial)



Prakriti Gaba, MD^a, Patrick W. Serruys, MD, PhD^{b,c}, Dimitri Karpaliotis, MD, PhD^{a,d}, Nicholas J. Lembo, MD^{a,d}, Adrian P. Banning, MD^e, Zixuan Zhang, MS^d, Marie-Claude Morice, MD^f, David E. Kandzari, MD^g, Anthony H. Gershlick, MD^h, Ori Ben-Yehuda, MD^{a,d}, Joseph F. Sabik, III, MDⁱ, Arie Pieter Kappetein, MD, PhD^j, and Gregg W. Stone, MD^{d,k,*}

Prior studies in patients with noncomplex coronary artery disease have demonstrated the safety of percutaneous coronary intervention (PCI) in the outpatient setting. We sought to examine the outcomes of outpatient PCI in patients with unprotected left main coronary artery disease (LMCAD). In the EXCEL trial, 1905 patients with LMCAD and site-assessed low or intermediate SYNTAX scores were randomized to PCI with everolimus-eluting stents versus coronary artery bypass grafting. The primary end point was major adverse cardiovascular events (MACE; the composite of death, stroke, or myocardial infarction). In this sub-analysis, outcomes at 30 days and 5 years were analyzed according to whether PCI was performed in the outpatient versus inpatient setting. Among 948 patients with LMCAD assigned to PCI, 935 patients underwent PCI as their first procedure, including 100 (10.7%) performed in the outpatient setting. Patients who underwent outpatient compared with inpatient PCI were less likely to have experienced recent myocardial infarction. Distal left main bifurcation disease involvement and SYNTAX scores were similar between the groups. Comparing outpatient to inpatient PCI, there were no significant differences in MACE at 30 days (4.0% vs 5.0% respectively, adjusted OR 0.52 95% CI 0.12 to 2.22; $p = 0.38$) or 5 years (20.6% vs 22.1% respectively, adjusted OR 0.72, 95% CI 0.40 to 1.29; $p = 0.27$). Similar results were observed in patients with distal left main bifurcation lesions. In conclusion, in the EXCEL trial, outpatient PCI of patients with LMCAD was not associated with an excess early or late hazard of MACE. These data suggest that outpatient PCI may be safely performed in select patients with LMCAD. © 2020 Elsevier Inc. All rights reserved. (Am J Cardiol 2021;143:21–28)

Percutaneous coronary intervention (PCI) is performed in >900,000 patients per year in the United States.¹ Given rising health care costs, recent policy initiatives have focused on curbing unnecessary spending on these common and expensive cardiovascular procedures.^{2,3} The Centers for Medicare and Medicaid Services has encouraged

physicians to perform PCI in the less-expensive outpatient setting rather than the more costly inpatient setting through initiatives such as the Recovery Audit Program and the 2-midnight rule.^{3–7} Although this shift toward outpatient PCI may reduce healthcare expenditures, whether performing PCI in the outpatient setting is safe in all patients is

^aNewYork-Presbyterian Hospital/Columbia University Irving Medical Center, New York, New York; ^bDepartment of Cardiology, National University of Ireland Galway (NUIG), Galway, Ireland; ^cDepartment of Cardiology, Imperial College of London, London, United Kingdom; ^dClinical Trials Center, Cardiovascular Research Foundation, New York, New York; ^eJohn Radcliffe Hospital, Oxford, United Kingdom; ^fHôpital Privé Jacques Cartier, Ramsay Générale de Santé, Massy, France; ^gPiedmont Heart Institute, Atlanta, Georgia; ^hUniversity Hospitals of Leicester NHS Trust, Leicester, United Kingdom; ⁱDepartment of Surgery, UH Cleveland Medical Center, Cleveland, Ohio; ^jThoraxcenter, Erasmus MC, Rotterdam, the Netherlands; and ^kThe Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, New York. Manuscript received October 29, 2020; revised manuscript received and accepted December 7, 2020.

DISCLOSURES: The EXCEL trial was sponsored by Abbott Vascular (Santa Clara, CA). Dr. Serruys: Consultant – Abbott, Biosensors, Medtronic, Micell Technologies, SINOMED, Philips/Volcano, Xeltis, HeartFlow. Dr. Karpaliotis: Honoraria – Abbott Vascular, Medtronic, Boston Scientific, Abiomed; options – Saranas, SoundBite, Traverse Vascular. Dr. Lembo: Advisory board – Abbott Vascular; speakers bureau – Abbott Vascular,

Boston Scientific, Medtronic, Abiomed. Dr. Banning: Institutional sponsorship for a fellowship from Boston Scientific and lecture fees from Boston Medtronic and Abbott Vascular. Partially funded by the NHS Oxford NIHR Biomedical Research Centre. Dr. Kandzari: Consulting honoraria – Medtronic, Biotronik, Cardiovascular Systems, Inc.; Institutional research/grant support – Medtronic, Biotronik, Boston Scientific, Orbus Neich, Teleflex. Dr. Sabik: Consultant – Medtronic. Advisory board – Medtronic Cardiac Surgery. Dr. Kappetein: Employee – Medtronic. Dr. Stone: Speaker or other honoraria from Cook, Terumo, QOOL Therapeutics and Orchestra Biomed; Consultant to Valfix, TherOx, Cardiomech, Vascular Dynamics, Robocath, HeartFlow, Gore, Ablative Solutions, Miracor, Neovasc, V-Wave, Abiomed, Ancora, MAIA Pharmaceuticals, Vectorious, Reva, Matrizyme; Equity/options from Ancora, Qool Therapeutics, Cagent, Applied Therapeutics, Biostar family of funds, SpectraWave, Orchestra Biomed, Aria, Cardiac Success, MedFocus family of funds, Valfix. Other authors: None.

See page 27 for disclosure information.

*Corresponding author: Tel: and fax: (646) 434-4134.

E-mail address: gregg.stone@mountsinai.org (G.W. Stone).

uncertain. Prior studies have demonstrated comparable rates of short-term and long-term mortality and major adverse cardiac events (MACE) in patients undergoing outpatient versus inpatient PCI.^{8–15} However, patients with high-risk features or complex coronary artery disease have traditionally been excluded from most of these studies. Only recently, 1 study by Taxiarchi et al¹⁶ noted similar rates of 30 day mortality in patients with left main coronary artery disease (LMCAD) that underwent same day hospital discharge compared with those that required overnight stays. The EXCEL (Evaluation of Xience Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial demonstrated that outcomes after PCI were noninferior to those after surgical coronary artery bypass grafting (CABG) in selected patients with unprotected LMCAD.¹⁶ In the present sub-study from the EXCEL trial, we examined both 30 day and 5 year outcomes in patients with LMCAD who underwent outpatient versus inpatient PCI.

Methods

The EXCEL trial was a prospective, unblinded, randomized, multicenter trial that compared PCI with XIENCE everolimus-eluting stents (Abbott Vascular, Santa Clara, California) and CABG in patients with LMCAD and site-assessed low or intermediate SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) scores. The design, rationale, and primary outcomes of the trial have been published previously.^{17,18} The decision to perform inpatient versus outpatient PCI was made by each participating operator for each enrolled patient according to local standard of care. The EXCEL trial was approved by the institutional review board or ethics committee at each participating center. Major end points were adjudicated by an independent clinical events committee at the Cardiovascular Research Foundation (New York, New York).

The primary end point was MACE, a composite of all-cause mortality, myocardial infarction (MI), or stroke at 3 years. Major powered secondary end points were the composite rate of all-cause mortality, MI, or stroke at 30 days and the composite of death, MI, stroke, or unplanned revascularization for ischemia at 3 years. Other secondary end points included stent thrombosis and bleeding according to TIMI (Thrombolysis in Myocardial Infarction) criteria. The present report includes all outcomes through 5 years after randomization.

For the present analysis patients undergoing outpatient versus inpatient PCI procedures were compared. The following patients were excluded: (1) Those assigned to CABG in whom PCI was performed; and (2) PCI-assigned patients treated either with CABG as their initial procedure without attempted PCI, medical therapy, or staged PCI in which the first procedure was not left main (LM) intervention.

Categorical variables are denoted by frequencies and percentages and were compared using the Chi-square or Fisher exact test. Continuous variables are reported as means \pm standard deviation and were compared with the Student's *t* test. Time-to-event outcomes were estimated by Kaplan-Meier rates and were compared by the log-rank test. The association between outpatient and inpatient PCI with outcomes at 30 days and 5 years were assessed using multivariable logistic regression rather than Cox proportional hazards regression given violation of the proportional hazards assumption during late follow-up.¹⁹ Given the modest number of 30-day primary end point events, covariates in the 30-day multivariable models were limited to recent MI (within 7 days), SYNTAX score, LM diameter stenosis, and the presence of a distal bifurcation lesion. At 5 years, the following covariates were included in the multivariable models: age, gender, body mass index, hyperlipidemia, hypertension, current, or recent (<1 month) cigarette use, prior cerebrovascular accident or transient ischemic attack, history of congestive heart failure, diabetes, recent MI (within 7 days),

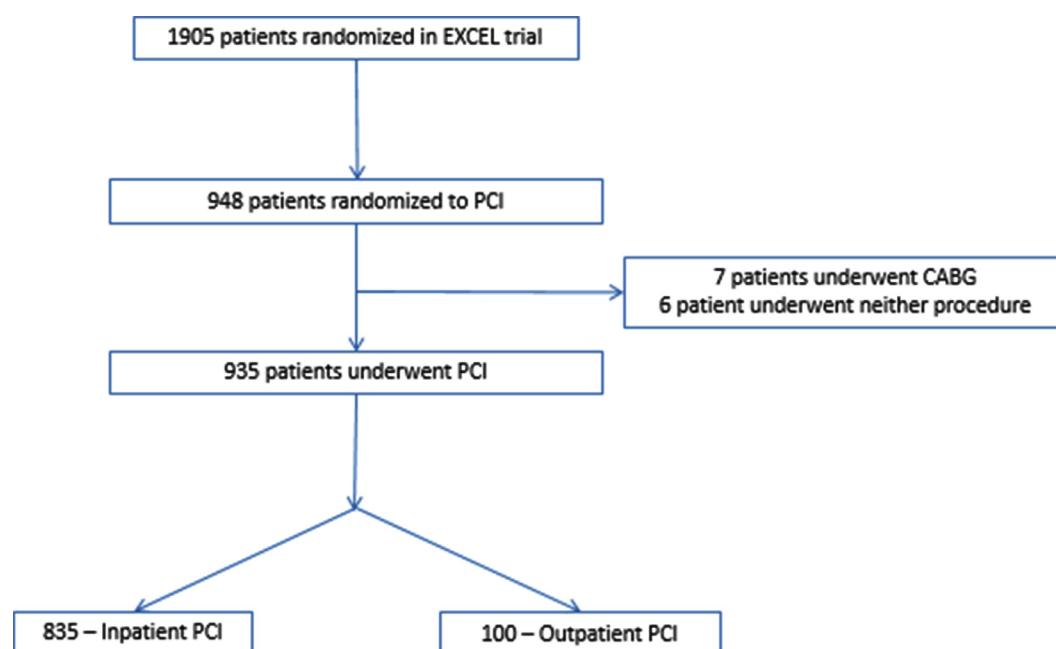


Figure 1. Patient selection flowchart. CABG = coronary artery bypass grafting; LM = left main; PCI = percutaneous coronary intervention.

SYNTAX score, LM diameter stenosis, and presence of a distal bifurcation lesion. All angiographic variables were determined by core laboratory assessment (Cardiovascular Research Foundation). Sensitivity analyses were performed in the high-risk subset of patients with distal LM bifurcation disease. All tests were 2-sided, and $p < 0.05$ was considered statistically significant. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

Results

Among the 1905 patients with LMCAD studied in EXCEL, 948 were assigned to PCI and 957 to CABG. Among the 948 PCI-assigned patients, PCI of the LM coronary artery was the first procedure in 935 (98.6%) patients, comprising

the study population. Among these 935 patients, PCI was performed in the outpatient setting in 100 (10.7%) and in the inpatient setting in 835 (89.3%) (Figure 1). Baseline characteristics are shown in Table 1. Compared with patients undergoing LM PCI in the inpatient setting, those undergoing outpatient PCI were less likely to have presented with unstable angina, non-ST-segment elevation myocardial infarction, or a recent MI within the 7 days, but were just as likely to have had a prior MI. Age, gender, and major co-morbidities were similar in both groups. The frequencies of assessing ECGs at discharge and CKMB levels at baseline and 22-26 hours after PCI were slightly lower in the outpatient group (Table 1). Patients undergoing inpatient and outpatient PCI also had similar core-laboratory assessed anatomic SYNTAX scores and involvement of the distal left main bifurcation or trifurcation,

Table 1
Baseline characteristics in patients undergoing outpatient versus inpatient percutaneous coronary intervention

Variable	Outpatient PCI (n=100)	Inpatient PCI (n=835)	p Value
Age (years)	67.8±8.9	65.8±9.6	0.07
Men	77/100 (77%)	635/835 (76%)	0.83
White	87/100 (87%)	747/810 (92%)	0.07
Diabetes mellitus	33/100 (33%)	249/835 (30%)	0.51
Insulin-treated	6/100 (6%)	65/835 (8%)	0.52
Hypertension, medically-treated	80/100 (80%)	614/835 (74%)	0.16
Hyperlipidemia, medically-treated	86/100 (86%)	575/834 (69%)	0.0004
Current smoker	22/100 (22%)	198/830 (24%)	0.68
Prior myocardial infarction	20/100 (20%)	145/822 (18%)	0.56
Prior PCI	23/99 (23%)	147/834 (18%)	0.17
Prior CABG	0/100 (0%)	0/835 (0%)	—
Congestive heart failure	9/100 (9%)	57/833 (7%)	0.43
Prior stroke or transient ischemic attack	5/100 (5%)	46/834 (6%)	0.83
Peripheral vascular disease	11/100 (11%)	85/832 (10%)	0.81
Chronic obstructive pulmonary disease	4/100 (4%)	60/834 (7%)	0.23
History of anemia	9/100 (9%)	90/831 (11%)	0.57
Clinical presentation			
Recent MI (within 7 days)	5/100 (5%)	135/831 (16%)	0.003
STEMI	1/100 (1%)	12/828 (1%)	1.00
NSTEMI	4/100 (4%)	119/828 (14%)	0.004
Unstable angina pectoris	12/100 (12%)	213/831 (26%)	0.003
Stable angina pectoris	68/100 (68%)	427/831 (51%)	0.002
Silent myocardial ischemia	15/100 (15%)	47/831 (6%)	0.0004
Body mass index (kg/m ²)	29.0±5.5	28.5±4.9	0.55
Renal insufficiency*	19/99 (19%)	141/823 (17.1%)	0.61
Thrombocytopenia†	5/44 (11%)	32/480 (7%)	0.22
ECG performed at baseline	96/100 (96%)	810/835 (97%)	0.26
ECG performed at discharge	85/100 (85%)	722/835 (87%)	0.47
Normal sinus rhythm on EKG			
At baseline	87/92 (95%)	673/710 (95%)	0.81
At discharge	77/83 (93%)	602/640 (94%)	0.64
CKMB assessed at baseline	91/100 (91%)	812/835 (97%)	0.006
CKMB assessed 10-14 hrs post-PCI	83/100 (83%)	743/835 (89%)	0.08
CKMB assessed 22-26 hrs post-PCI	82/100 (82%)	748/835 (90%)	0.02
CKMB level at baseline (u/L)	2.8±3.2	4.9±8.1	0.22
CKMB level 10-14 hrs post-PCI (u/L)	7.2±11.2	11.0±16.7	0.05
CKMB level 22-26 hrs post-PCI (u/L)	11.0±18.0	11.3±16.9	0.43
Left ventricular ejection fraction (%)	54.6±11.3	57.3±9.4	0.02

Values are n/N (%) or mean±standard deviation.

* Creatinine clearance ≤60 mL/min;

† platelet count <150,000. CABG=coronary artery bypass grafting; CKMB=creatinine kinase MB band; ECG=12-lead electrocardiogram; MI=myocardial infarction; NSTEMI=non-ST-segment elevation myocardial infarction; PCI=percutaneous coronary intervention; STEMI=ST-segment elevation myocardial infarction.

Table 2

Angiographic and procedural characteristics in patients undergoing outpatient versus inpatient percutaneous coronary intervention

	Outpatient PCI (n=100)	Inpatient PCI (n=835)	p Value
SYNTAX score (core laboratory)	25.7±8.9	27.1±8.7	0.13
Low (<23)	35/94 (37%)	256/811 (32%)	0.27
Intermediate (23-32)	38/94 (40%)	351/811 (43%)	0.60
High (>32)	21/94 (22%)	204/811 (25%)	0.55
Left main diameter stenosis (%)	61.8±12.3	64.5±12.4	0.04
Left main stenosis location:			
Ostial/midshaft lesion	53/95 (56%)	451/815 (55%)	0.96
Distal lesion (bifurcation or trifurcation)	69/95 (73%)	658/815 (81%)	0.06
Distal lesion only	42/95 (44%)	364/815 (45%)	0.87
Left main PCI performed	98/98 (100%)	808/808 (100%)	—
Number of PCIs per patient			
1	95/100 (95%)	755/827 (91%)	0.20
2	5/100 (5%)	71/827 (9%)	0.22
3	0/100 (0%)	1/827 (0.1%)	1.00
Number of coronary arteries treated			
1	54/100 (54%)	381/835 (46%)	0.21
2	33/100 (33%)	322/835 (39%)	0.28
3	11/100 (11%)	113/835 (14%)	0.48
4	2/100 (2%)	19/835 (2%)	1.00
Non-left main lesions treated per subject			
Left anterior descending	29/100 (29%)	237/835 (28%)	0.90
Proximal left anterior descending	1/100 (1%)	21/835 (3%)	0.50
Left circumflex	12/100 (12%)	143/835 (17%)	0.19
Right	20/100 (20%)	230/835 (28%)	0.11
Posterior descending	1/100 (1%)	17/835 (2%)	0.71
Total stent length (left main and non-left main) (mm)	45.5±33.4	49.6±36.0	0.22
Arterial access site			
Femoral	79/100 (79%)	606/835 (73%)	0.17
Radial	20/100 (20%)	228/835 (27%)	0.12
Brachial	1/100 (1%)	1/835 (0.1%)	0.20
Arterial closure device used	53/99 (54%)	439/835 (53%)	0.86
Intravascular ultrasound used	79/100 (79%)	643/835 (77%)	0.65
Fractional flow reserve used	18/100 (18%)	66/834 (8%)	0.0009
Contrast volume (mL)	230.2±106.8	264.8±128.6	0.02
Hemodynamic support during PCI	5/100 (5%)	47/835 (6%)	0.80

Values are n/N (%) or mean±standard deviation. PCI=percutaneous coronary intervention; SYNTAX=Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

although the LM diameter stenosis was slightly lower in the outpatient PCI group (Table 2).

The majority of patients had a single PCI performed and 1 or 2 vessels treated, similar in both groups (Table 2). Arterial access was most commonly obtained using a transfemoral approach in both groups. Fractional flow reserve was more frequently used in patients undergoing outpatient compared with inpatient PCI, and total contrast volume utilized was lower in patients undergoing outpatient PCI. Total stent length, intravascular ultrasound use, utilization of arterial closure devices, and requirement for hemodynamic support were similar between the 2 groups. There were modest differences in medication use between the groups at discharge and during follow-up (Table 3). Patients undergoing outpatient PCI were discharged in <24 hours in 86 (86.0%) of cases. The median [interquartile range (IQR)] length of stay after PCI was 1 (1, 1) days after outpatient PCI and 2 (1, 3) days after inpatient PCI ($p < 0.0001$).

Median [IQR] time to follow-up was 1825 days [1806, 1825] and 1825 days [1807, 1825] in the outpatient and

inpatient groups respectively ($p = 0.13$). At 30 days, patients who underwent outpatient compared with inpatient PCI experienced similar rates of the composite outcome of death, MI, or stroke (4.0% vs 5.0% respectively, adjusted odds ratio [OR] 0.52, 95% confidence interval [CI] 0.12 to 2.22, $p = 0.38$) (Table 4 and Figure 2, left panel). There were also no significant differences in the patients rates of death, MI or stroke, or the rates of unplanned ischemia-driven revascularization, stent thrombosis, or TIMI major and/or minor bleeding (Table 4). At 5 years, there was no significant difference in the composite outcome of death, MI, or stroke between patients undergoing outpatient versus inpatient PCI (20.6% vs 22.1% respectively, adjusted OR 0.72, 95% CI 0.40 to 1.29, $p = 0.27$) (Table 5 and Figure 2, right panel). Nor were there differences in the rates of all-cause mortality or other end points between the 2 groups (Table 5). These results were consistent in patients undergoing PCI of distal LM bifurcation lesions (Supplementary Tables 1 and 2).

Table 3

Medical therapy after outpatient versus inpatient percutaneous coronary intervention

Medications	Outpatient PCI (n=100)	Inpatient PCI (n=835)	p Value
At discharge			
Warfarin	3/100 (3%)	8/831 (1%)	0.10
NOAC	0/100 (0%)	1/831 (0.1%)	1.00
Aspirin	97/98 (99%)	825/830 (99%)	0.49
ADP antagonist	98/100 (98%)	816/831 (98%)	0.70
Statins	92/100 (92%)	806/831 (97%)	0.02
Beta-blockers	76/100 (76%)	699/831 (84%)	0.04
Calcium channel blockers	4/100 (4%)	51/831 (6%)	0.39
ACEI/ARBs	48/100 (48%)	480/831 (58%)	0.06
Nitrates	5/100 (5%)	24/831 (3%)	0.23
At 30 days			
Warfarin	3/100 (3%)	13/817 (2%)	0.40
NOAC	0/100 (0%)	0/817 (0%)	—
Aspirin	96/98 (98%)	814/824 (99%)	0.37
ADP antagonist	98/100 (98%)	813/825 (99%)	0.66
Statins	92/100 (92%)	802/825 (97%)	0.01
Beta-blockers	76/100 (76%)	702/823 (85%)	0.02
Calcium channel blockers	5/100 (5%)	60/817 (7%)	0.39
ACEI/ARBs	48/100 (48%)	493/818 (60%)	0.02
Nitrates	7/100 (7%)	40/817 (5%)	0.37
At 5 years			
Warfarin	5/78 (6%)	27/667 (4%)	0.37
NOAC	0/78 (0%)	7/666 (1%)	1.00
Aspirin	72/78 (92%)	640/688 (93%)	0.82
ADP antagonist	55/79 (70%)	422/689 (61%)	0.15
Statins	74/79 (94%)	671/685 (98%)	0.04
Beta-blockers	62/79 (79%)	600/684 (88%)	0.02
Calcium channel blockers	19/78 (24%)	117/669 (18%)	0.14
ACEI/ARBs	39/78 (50%)	468/681 (69%)	0.0009
Nitrates	14/78 (18%)	67/670 (10%)	0.03

Values are n/N (%). ACEI=angiotensin-converting enzyme inhibitor; ADP=adenosine diphosphate; ARB=angiotensin II receptor blocker; NOAC=non-vitamin K antagonist oral anticoagulants; PCI=percutaneous coronary intervention.

Discussion

The major findings from this substudy from the EXCEL trial are that among patients with LMCAD and site-assessed low or intermediate SYNTAX scores: (1) at 30 days there were no significant differences in death, MI, or stroke or

other adverse outcomes whether LM-PCI was performed in the outpatient or inpatient setting; (2) at 5 years there remained no significant differences in death, MI, or stroke, as well as other outcomes after performance of PCI in the outpatient or inpatient setting; and (3) the 30-day and 5-year primary and secondary end points between the 2 groups were also similar in patients undergoing PCI of distal LM bifurcation lesions. Given the high costs of inpatient PCI and the shift of many procedures to the outpatient setting, these findings are meaningful and timely.^{6,7,20}

Our findings are consistent with those from Taxiarchi et al¹⁶. No significant differences were noted in the primary composite end point of death, MI, or stroke after outpatient versus inpatient LM PCI at 30 days. We additionally extend these findings to the long term. No significant differences were noted in the primary composite end point of death, MI, or stroke after outpatient versus inpatient LM PCI at 5 years. Although recent MI and clinical presentation with unstable angina or non-ST-segment elevation myocardial infarction were more frequent in the inpatient cohort, other co-morbidities and angiographic complexity were similar between the 2 groups. Post-procedural clinical outcomes, both at 30 days and 5 years, were not significantly different between outpatient and inpatient PCI after adjustment for these and other baseline characteristics which slightly varied. Importantly, distal LM bifurcation involvement, which can be technically challenging to treat,^{21,22} was equally distributed between the groups (approximately 80% of patients) and was not a risk factor for adverse outcomes after outpatient LM-PCI.

The occurrence of secondary outcomes, including TIMI major or minor bleeding, was also similar between the 2 groups at 30 days and 5 years, and may be attributed to improvements in pharmacologic and after-procedural patient care. Despite the fact that femoral arterial access was more common than radial access in EXCEL, the shift away from bleeding-prone glycoprotein IIb and/or IIIa inhibitors have notably decreased after-procedural hemorrhagic complications.²³ Moreover, arterial closure devices, used in approximately half of patients in EXCEL, have been associated with lower after-procedural bleeding, hematoma formation, and ultimately hospital stay.²⁴ The contemporary transition to greater use of radial access would be likely to further decrease bleeding and vascular complications after outpatient LM PCI.²⁵

Table 4

Thirty-day risks of the primary and secondary outcomes after outpatient versus inpatient percutaneous coronary intervention

	Outpatient PCI (n=100)	Inpatient PCI (n=835)	Unadjusted OR (95% CI)	P _{unadjusted}	Adjusted OR (95% CI)	P _{adjusted}
Death, MI, or stroke	4% (4)	5% (42)	0.79 (0.28-2.24)	0.65	0.52 (0.12-2.22)	0.38
Death, MI, stroke, or unplanned IDR	4% (4)	5% (42)	0.79 (0.28-2.24)	0.65	0.52 (0.12-2.22)	0.38
All-cause death	0% (0)	1% (9)	—	—	—	—
Cardiac	0% (0)	1% (9)	—	—	—	—
Non-cardiac	0% (0)	0% (0)	—	—	—	—
MI	4% (4)	4% (33)	1.01 (0.35-2.92)	0.98	—	—
Stroke	0% (0)	0.7% (6)	—	—	—	—
Unplanned IDR	1% (1)	0.6% (5)	1.68 (0.19-14.50)	0.64	—	—
Stent thrombosis	0% (0)	0.7% (6)	—	—	—	—
TIMI major or minor bleeding	4% (4)	3% (28)	1.20 (0.41-3.50)	0.74	—	—

Values are Kaplan-Meier estimated event rates, % (n). IDR=ischemia-driven revascularization; MI=myocardial infarction; OR=odds ratio; PCI=percutaneous coronary intervention; TIMI=Thrombolysis in Myocardial Infarction.

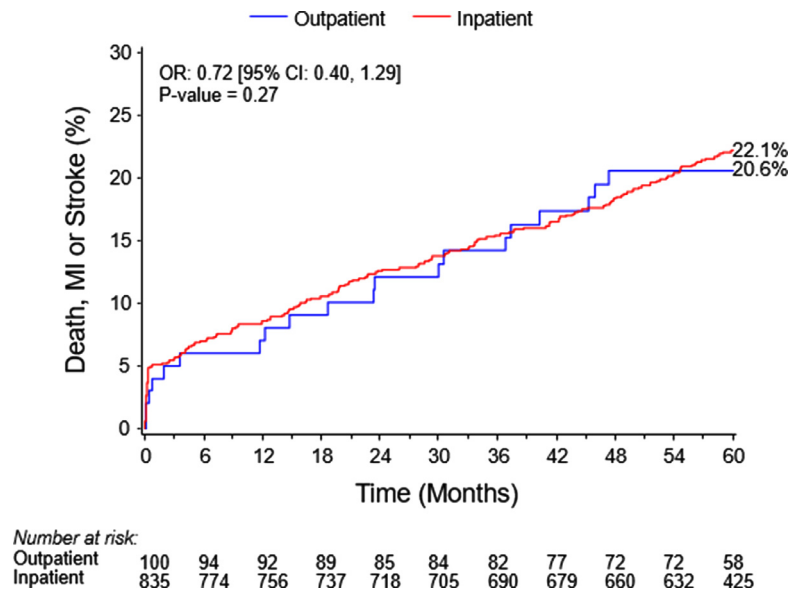


Figure 2. Kaplan-Meier survival curves for the composite outcome of death, myocardial infarction, or stroke in patients undergoing outpatient versus inpatient percutaneous coronary intervention at 5 years. CI = confidence interval; HR = hazard ratio; MI = myocardial infarction.

Table 5

Five-year risk of the primary and secondary outcomes after outpatient versus inpatient percutaneous coronary intervention

	Outpatient PCI (n = 100)	Inpatient PCI (n = 835)	Unadjusted OR (95% CI)	Punadjusted	Adjusted OR (95% CI)	Padjusted
Death, MI, or stroke	21% (20)	22% (181)	0.91 (0.54-1.54)	0.74	0.72 (0.40-1.29)	0.27
Death, MI, stroke, or unplanned IDR	31% (30)	32% (258)	0.97 (0.61-1.53)	0.90	0.83 (0.50-1.38)	0.47
All-cause death	13% (12)	13% (105)	0.96 (0.51-1.82)	0.91	0.78 (0.38-1.59)	0.50
Cardiac	5% (5)	7% (56)	0.74 (0.29-1.90)	0.53	—	—
Non-cardiac	8% (7)	6% (49)	1.23 (0.54-2.79)	0.63	—	—
MI	12% (11)	11% (84)	1.12 (0.58-2.19)	0.73	—	—
Stroke	1% (1)	3% (25)	0.33 (0.04-2.48)	0.28	—	—
Unplanned IDR	17% (16)	17% (134)	1.01 (0.57-1.79)	0.97	—	—
Stent thrombosis	1% (1)	2% (15)	0.56 (0.07-4.29)	0.58	—	—
TIMI major or minor bleeding	7% (7)	6% (46)	1.31 (0.57-3.00)	0.52	—	—

Values are Kaplan-Meier estimated event rates, % (n). IDR=ischemia-driven revascularization; MI=myocardial infarction; OR=odds ratio; PCI=percutaneous coronary intervention; TIMI=Thrombolysis in Myocardial Infarction.

It is important to emphasize that most patients in EXCEL underwent inpatient LM PCI. Thus, the favorable outcomes after outpatient LM PCI may be attributable to the selected nature of this cohort, that is, patients with visually-assessed low to intermediate SYNTAX scores and with co-morbidities as reflected in the characteristics of the patients enrolled. These outcomes also reflect the experience level of the operators in EXCEL, including their use of intracoronary imaging in most cases to guide LM intervention. Furthermore, fluoropolymer-coated everolimus-eluting stents, the primary stent type utilized in the EXCEL trial, have been associated with low rates of stent thrombosis, which may have contributed to the safety of outpatient LM PCI in our study; in this regard the low rates of stent thrombosis in both inpatient and outpatient groups at 5-year follow-up are notable.^{17,26,27} Strict adherence to dual antiplatelet therapy with aspirin and an adenosine diphosphate antagonist, which have been shown to decrease peri-procedural and 30-day stent thrombosis and MI, is another likely contributor to the similar outcomes observed in both

groups.²⁸ In addition, the high rates of LM stent implantation with intravascular ultrasound imaging guidance in EXCEL has previously been associated with lower in-hospital and long-term mortality and likely contributed to a low rate of peri-procedural complications in the outpatient group.^{29,30}

This study has some limitations. First, this study was a post hoc analysis and the performance of outpatient versus inpatient PCI was not randomized. Second, although multivariable analysis was used to account for discrepancies in baseline characteristics between the 2 studied patient groups, unmeasured confounders cannot be excluded, and the present results should be considered hypothesis generating. Third, a detailed assessment as to the experience level of each operator with LM-PCI is not available, although all investigators were qualified by the sponsor as routinely performing such interventions prior to study participation; whether less experienced operators than those participating in the EXCEL trial could have achieved these results is unknown. Finally, the results should not be extended to

patients not studied in EXCEL, including those with visually-assessed high SYNTAX score and those with heart failure and severely reduced left ventricular ejection fractions requiring mechanical circulatory support.

In conclusion, in the EXCEL trial, there were no significant differences with regards to MACE, mortality or other early or late adverse outcomes in selected patients with LMCAD who underwent outpatient compared with inpatient PCI. LM-PCI was also safe in patients with technically challenging disease, including distal LM bifurcation lesions. Given the nationwide imperative for implementing value-based care, the findings of this study are meaningful and suggest that outpatient PCI may be a reasonable alternative to inpatient PCI in patients with LMCAD and visually-assessed low to intermediate SYNTAX scores, when performed by experienced operators. Additional prospective studies are warranted to confirm these findings.

Credit Author Statement

Prakriti Gaba: Conceptualization, Writing - Original Draft; Patrick W. Serruys: Conceptualization; Dimitri Karpaliotis: Investigation; Nicholas J. Lembo: Investigation; Adrian P. Banning: Investigation; Zixuan Zhang: Formal analysis; Marie-Claude Morice: Investigation; David E. Kandzari: Investigation; Anthony H. Gershlick: Investigation; Ori Ben-Yehuda: Project administration; Joseph F. Sabik III: Conceptualization; Arie Pieter Kappetein: Conceptualization; Gregg W. Stone: Conceptualization, Writing - Review & Editing.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this study.

Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.amjcard.2020.12.039>.

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jimenez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER 3rd, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB. American Heart Association Statistics Committee. Stroke Statistics Subcommittee. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation* 2016;133:e38–360.
2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER 3rd, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. American Heart Association Statistics Committee. Stroke Statistics Subcommittee. Executive summary: heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation* 2014;129:399–410.
3. Kumbhani DJ, Marso SP. Inpatient or outpatient status for elective percutaneous coronary intervention: doctor, "You Gotta Let Me Know Should I Stay or Should I Go?". *Circ Cardiovasc Interv* 2016;9:e003699.
4. Blankenship JC, Marshall JJ. Reimbursement for coronary intervention. *Catheter Cardiovasc Interv* 2013;81:745–747.
5. Rinfret S, Kennedy WA, Lachaine J, Lemay A, Rodes-Cabau J, Cohen DJ, Costerousse O, Bertrand OF. Economic impact of same-day home discharge after uncomplicated transradial percutaneous coronary intervention and bolus-only abciximab regimen. *JACC Cardiovasc Interv* 2010;3:1011–1019.
6. Centers for Medicare & Medicaid Services. Recovery audit program fiscal year 2012: FY 2012 report to congress as required by section 1893(h) of the Social Security Act and section 6411(c) of the Affordable Care Act.
7. Centers for Medicare & Medicaid Services. CMS-1599-P: Medicare program: hospital inpatient prospective payment systems for acute care hospitals and the long term care hospital prospective payment system and proposed FY 2014 rates: quality reporting requirements for specific providers: hospital conditions of participation.
8. Bundhun PK, Soogund MZ, Huang WQ. Same day discharge versus overnight stay in the hospital following percutaneous coronary intervention in patients with stable coronary artery disease: a systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2017;12:e0169807.
9. Vora AN, Dai D, Gurm H, Amin AP, Messenger JC, Mahmud E, Mauri L, Wang TY, Roe MT, Curtis J, Patel MR, Dauerman HL, Peterson ED, Rao SV. Temporal trends in the risk profile of patients undergoing outpatient percutaneous coronary intervention: a report from the National Cardiovascular Data Registry's CathPCI Registry. *Circ Cardiovasc Interv* 2016;9:e003070.
10. Brayton KM, Patel VG, Stave C, de Lemos JA, Kumbhani DJ. Same-day discharge after percutaneous coronary intervention: a meta-analysis. *J Am Coll Cardiol* 2013;62:275–285.
11. Abdelal E, Rao SV, Gilchrist IC, Bernat I, Shroff A, Caputo R, Costerousse O, Pancholy SB, Bertrand OF. Same-day discharge compared with overnight hospitalization after uncomplicated percutaneous coronary intervention: a systematic review and meta-analysis. *JACC Cardiovasc Interv* 2013;6:99–112.
12. Bertrand OF, De Larochelliere R, Rodes-Cabau J, Proulx G, Gleeton O, Nguyen CM, Dery JP, Barbeau G, Noel B, Larose E, Poirier P, Roy L. Early Discharge After Transradial Stenting of Coronary Arteries Study I. A randomized study comparing same-day home discharge and abciximab bolus only to overnight hospitalization and abciximab bolus and infusion after transradial coronary stent implantation. *Circulation* 2006;114:2636–2643.
13. Heyde GS, Koch KT, de Winter RJ, Dijkgraaf MG, Klees MI, Dijkman LM, Piek JJ, Tijssen JG. Randomized trial comparing same-day discharge with overnight hospital stay after percutaneous coronary intervention: results of the Elective PCI in Outpatient Study (EPOS). *Circulation* 2007;115:2299–2306.
14. Rao SV, Kaltenbach LA, Weintraub WS, Roe MT, Brindis RG, Rumsfeld JS, Peterson ED. Prevalence and outcomes of same-day discharge after elective percutaneous coronary intervention among older patients. *JAMA* 2011;306:1461–1467.
15. Muthusamy P, Busman DK, Davis AT, Wohns DH. Assessment of clinical outcomes related to early discharge after elective percutaneous coronary intervention: COED PCI. *Catheter Cardiovasc Interv* 2013;81:6–13.
16. Taxiarchi P, Kontopantelis E, Kinnaird T, Curzen N, Banning A, Ludman P, Shoaib A, Rashid M, Martin GP, Mamas MA. Adoption of same day discharge following elective left main stem percutaneous coronary intervention. *Int J Cardiol* 2020.
17. Stone GW, Sabik JF, Serruys PW, Simonton CA, Genereux P, Puskas J, Kandzari DE, Morice MC, Lembo N, Brown WM 3rd, Taggart DP, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogats G, Mansour S, Noisieux N, Sabate M, Pomar J, Hickey M, Gershlick A, Buszman P, Bochenek A, Schampaeert E, Page P, Dressler O, Kosmidou I, Mehran R, Pocock SJ, Kappetein AP. Investigators EXCEL Trial. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. *N Engl J Med* 2016;375:2223–2235.

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jimenez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER 3rd, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB. American Heart Association Statistics Committee. Stroke Statistics Subcommittee. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation* 2016;133:e38–360.
2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER 3rd, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. American Heart Association Statistics Committee. Stroke Statistics Subcommittee. Executive summary:

18. Kappetein AP, Serruys PW, Sabik JF, Leon MB, Taggart DP, Morice MC, Gersh BJ, Pocock SJ, Cohen DJ, Wallentin L, Ben-Yehuda O, van Es GA, Simonton CA, Stone GW. Design and rationale for a randomised comparison of everolimus-eluting stents and coronary artery bypass graft surgery in selected patients with left main coronary artery disease: the EXCEL trial. *EuroIntervention* 2016;12:861–872.
19. Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice MC, Puskas J, Kandzari DE, Karpaliotis D, Brown WM 3rd, Lembo NJ, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogats G, Mansour S, Noiseux N, Sabate M, Pomar J, Hickey M, Gershlick A, Buszman PE, Bochenek A, Schampaert E, Page P, Modolo R, Gregson J, Simonton CA, Mehran R, Kosmidou I, Genereux P, Crowley A, Dressler O, Serruys PW. Investigators EXCEL Trial. Five-year outcomes after PCI or CABG for left main coronary disease. *N Engl J Med* 2019;381:1820–1830.
20. Amin AP, Pinto D, House JA, Rao SV, Spertus JA, Cohen MG, Pancholy S, Salisbury AC, Mamas MA, Frogge N, Singh J, Lasala J, Masoudi FA, Bradley SM, Wasfy JH, Maddox TM, Kulkarni H. Association of same-day discharge after elective percutaneous coronary intervention in the United States with costs and outcomes. *JAMA Cardiol* 2018;3:1041–1049.
21. Valgimigli M, Malagutti P, Rodriguez-Granillo GA, Garcia-Garcia HM, Polad J, Tsuchida K, Regar E, Van der Giessen WJ, de Jaegere P, De Feyter P, Serruys PW. Distal left main coronary disease is a major predictor of outcome in patients undergoing percutaneous intervention in the drug-eluting stent era: an integrated clinical and angiographic analysis based on the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) and Taxus-Stent Evaluated At Rotterdam Cardiology Hospital (T-SEARCH) registries. *J Am Coll Cardiol* 2006;47:1530–1537.
22. Kandzari DE, Gershlick AH, Serruys PW, Leon MB, Morice MC, Simonton CA, Lembo NJ, Banning AP, Merkely B, van Boven AJ, Ungi I, Kappetein AP, Sabik JF 3rd, Genereux P, Dressler O, Stone GW. Outcomes among patients undergoing distal left main percutaneous coronary intervention. *Circ Cardiovasc Interv* 2018;11:e007007.
23. Mehran R, Pocock S, Nikolsky E, Dangas GD, Clayton T, Claessen BE, Caixeta A, Feit F, Manoukian SV, White H, Bertrand M, Ohman EM, Parise H, Lansky AJ, Lincoff AM, Stone GW. Impact of bleeding on mortality after percutaneous coronary intervention results from a patient-level pooled analysis of the REPLACE-2 (randomized evaluation of PCI linking angiogram to reduced clinical events), ACUITY (acute catheterization and urgent intervention triage strategy), and HORIZONS-AMI (harmonizing outcomes with revascularization and stents in acute myocardial infarction) trials. *JACC Cardiovasc Interv* 2011;4:654–664.
24. Marso SP, Amin AP, House JA, Kennedy KF, Spertus JA, Rao SV, Cohen DJ, Messenger JC, Rumsfeld JS, National Cardiovascular Data R. Association between use of bleeding avoidance strategies and risk of periprocedural bleeding among patients undergoing percutaneous coronary intervention. *JAMA* 2010;303:2156–2164.
25. Valgimigli M, Gagnor A, Calabro P, Frigoli E, Leonardi S, Zaro T, Rubartelli P, Briguori C, Ando G, Repetto A, Limbruno U, Cortese B, Sganzerla P, Lupi A, Galli M, Colangelo S, Ierna S, Ausiello A, Presbitero P, Sardella G, Varbella F, Esposito G, Santarelli A, Tresoldi S, Nazzaro M, Zingarelli A, de Cesare N, Rigattieri S, Tosi P, Palmieri C, Brugaletta S, Rao SV, Heg D, Rothenbuhler M, Vranckx P, Juni P, Investigators MATRIX. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. *Lancet* 2015;385:2465–2476.
26. Palmerini T, Kirtane AJ, Serruys PW, Smits PC, Kedhi E, Kereiakes D, Sangiorgi D, Bacchi Reggiani L, Kaiser C, Kim HS, De Waha A, Ribichini F, Stone GW. Stent thrombosis with everolimus-eluting stents: meta-analysis of comparative randomized controlled trials. *Circ Cardiovasc Interv* 2012;5:357–364.
27. Palmerini T, Biondi-Zoccai G, Della Riva D, Mariani A, Sabate M, Smits PC, Kaiser C, D'Ascenzo F, Frati G, Mancone M, Genereux P, Stone GW. Clinical outcomes with bioabsorbable polymer- versus durable polymer-based drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *J Am Coll Cardiol* 2014;63:299–307.
28. Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, Mehran R, Mukherjee D, Newby LK, O'Gara PT, Sabatine MS, Smith PK, Smith SC Jr. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation* 2016;134:e123–e155.
29. Singh V, Badheka AO, Arora S, Panaich SS, Patel NJ, Patel N, Pant S, Thakkar B, Chothani A, Deshmukh A, Manvar S, Lahewala S, Patel J, Patel S, Jhamnani S, Bhinder J, Patel P, Savani GT, Patel A, Mohamad T, Gidwani UK, Brown M, Forrester JK, Cleman M, Schreiber T, Grines C. Comparison of in-hospital mortality, length of hospitalization, costs, and vascular complications of percutaneous coronary interventions guided by ultrasound versus angiography. *Am J Cardiol* 2015;115:1357–1366.
30. Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, Yun SC, Lee CW, Hong MK, Lee JH, Park SW, Investigators MAIN-COMPARE. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. *Circ Cardiovasc Interv* 2009;2:167–177.