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Randomized Comparison of Percutaneous Coronary Intervention With Sirolimus-Eluting Stents Versus Coronary Artery Bypass Grafting in Unprotected Left Main Stem Stenosis

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Objectives The purpose of this randomized study was to compare sirolimus-eluting stenting with coronary artery bypass grafting (CABG) for patients with unprotected left main (ULM) coronary artery disease.

Background CABG is considered the standard of care for treatment of ULM. Improvements in percutaneous coronary intervention (PCI) with use of drug-eluting stents might lead to similar results. The effectiveness of drug-eluting stenting versus surgery has not been established in a randomized trial.

Methods In this prospective, multicenter, randomized trial, 201 patients with ULM disease were randomly assigned to undergo sirolimus-eluting stenting (n = 100) or CABG using predominantly arterial grafts (n = 101). The primary clinical end point was noninferiority in freedom from major adverse cardiac events, such as cardiac death, myocardial infarction, and the need for target vessel revascularization within 12 months.

Results The combined primary end point was reached in 13.9% of patients after surgery, as opposed to 19.0% after PCI (p = 0.19 for noninferiority). The combined rates for death and myocardial infarction were comparable (surgery, 7.9% vs. stenting, 5.0%; noninferiority p < 0.001), but stenting was inferior to surgery for repeat revascularization (5.9% vs. 14.0%; noninferiority p = 0.35). Perioperative complications including 2 strokes were higher after surgery (4% vs. 30%; p < 0.001). Freedom from angina was similar between groups (p = 0.33).

Conclusions In patients with ULM stenosis, PCI with sirolimus-eluting stents is inferior to CABG at 12-month follow-up with respect to freedom from major adverse cardiac events, which is mainly influenced by repeated revascularization, whereas for hard end points, PCI results are favorable. A longer follow-up is warranted. (Percutaneous Coronary Intervention [PCI] With Drug-Eluting Stents [DES] Versus Coronary Artery Bypass Graft [CABG] for Patients With Significant Left Main Stenosis; NCT00176397) (J Am Coll Cardiol 2011;57:538–45) © 2011 by the American College of Cardiology Foundation

Significant stenosis of the unprotected left main stem (ULM) has a worse prognosis than any other form of coronary artery disease (1). Coronary artery bypass grafting (CABG) is considered the standard of care for ULM as surgery provides a survival benefit in comparison to medical therapy (1–4).

See page 546

Concern about procedural risk, unpredictable occurrence of abrupt closure, restenosis, and long-term results led to guideline recommendations that percutaneous coronary intervention (PCI) be restricted to poor surgical candidates or bypass-protected ULM (5,6).

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The advent of coronary stents along with the evolution of dual antiplatelet therapy dramatically lowered the incidence of abrupt vessel closure, and the application of drug-eluting stents further decreased the risk of in-stent restenosis (7). Therefore, PCI is increasingly used to treat ULM lesions (8).

Limited evidence, mainly from registries (9,10), subanalyses of the Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) trial (11), and 1 small randomized trial (12), led to the recent updated recommendation that PCI may be considered an alternative to surgery in patients with anatomic low-risk conditions and clinical high risk of adverse events with surgery (13).

The current multicenter, randomized study was conducted to assess whether sirolimus-eluting stenting is noninferior in comparison to CABG using predominantly arterial grafts among patients with ULM stenoses at 12-month follow-up.

Methods

Patients age 18 to 80 years with stenosis (≥50%) of the ULM with or without additional multivessel coronary artery disease were included in this multicenter study. Patients had to be symptomatic or have documented myocardial ischemia.

Exclusion criteria were myocardial infarction <48 h requiring immediate intervention, additional valvular heart disease requiring surgery, previous surgical treatment for coronary artery or valvular disease, severe peripheral arterial disease, significant carotid stenosis requiring treatment, renal dysfunction requiring dialysis, any disease with limited life expectancy, overt congestive heart failure, and contraindication to antiplatelet therapy. Angiographic exclusion criteria were total occlusions, extreme left-dominant coronary artery perfusion, and distal lesion length >30 mm in a single lesion.

A consensus on patient eligibility had to be obtained from both a cardiac surgeon and cardiologist (E.B.) prior to randomization. Patients not eligible were also analyzed for clinical events at 12-month follow-up in a prospective registry.

The SYNTAX score and the logistic European system for cardiac operative risk evaluation (EuroSCORE) were computed for risk analysis by a cardiologist blinded to procedural data and clinical outcome (14,15).

The study was approved by the local ethics committee of the participating centers. Written informed consent was obtained from all patients. Balanced randomization was performed by a computerized randomization program at an independent institution. Stratification was performed according to centers.

PCI. PCI was performed using the femoral approach in all patients. Sirolimus-eluting stents were used in all except 2 patients, who required a stent diameter >4 mm and therefore received paclitaxel-eluting stents. Direct stenting of the ULM was the preferred strategy except for cases with critical luminal narrowing, for which pre-dilation was performed. Lesions in the ostium or body of the ULM usually received a single stent. On the basis of anatomic findings, distal ULM stenoses were treated by several techniques (16). Post-dilation with kissing balloon angioplasty was always used to finish the distal stenting procedure. Additional stenting of lesions distal to the ULM was performed according to standard clinical practice with the aim of complete revascularization. There was no recommendation to use intravascular ultrasound routinely.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
IQR = interquartile range
PCI = percutaneous coronary intervention
ULM = unprotected left main

Antiplatelet therapy was started the day before PCI with aspirin (at least 100 mg orally, followed by 100 mg or more per day indefinitely post-procedure) and clopidogrel (600 mg orally, followed by 75 mg/day for at least 12 months). Additional glycoprotein IIb/IIIa inhibitor use was left to the discretion of the operator.

CABG. Standard CABG surgery was performed under general anesthesia using a conventional sternotomy approach. Complete revascularization using arterial grafts was recommended. Off-pump techniques were used at the discretion of the surgeon. Antiplatelet therapy consisted of aspirin 100 mg per day preoperatively and was continued indefinitely post-operatively.

Other pharmacological treatments such as statins, angiotensin-converting enzyme inhibitors, and beta-blockers were recommended based on current practice in both treatment groups.

For both groups, complete revascularization was defined as bypass grafting or PCI of all lesions with >50% stenosis in vessels with a diameter of ≥2.0 mm.

Follow-up. All patients were closely monitored for at least 24 h post-procedure. Creatine kinase and MB activity was measured immediately after the procedure and 8, 16, and 24 h later. A 12-lead electrocardiogram was obtained immediately post-procedure and at 24 h.

Post-hospital follow-up included a 6-month outpatient visit with a clinical examination and a symptom-limited exercise stress test. The 12-month follow-up included a symptom-limited exercise stress test and coronary angiography. Restenosis was defined as >50% diameter stenosis by visual assessment. In case of recurrence of angina and/or a positive stress test, repeat revascularization was performed for restenosis. A final clinical follow-up by structured telephone interview was performed in November 2009, ensuring a longer follow-up.

End points and definitions. The primary composite end point was defined as freedom from major adverse cardiovascular events, which included death from any cause, myocardial infarction, and the need for repeat revascularization within 12 months.

Secondary end points included each individual component of the composite end point. The clinical angina status

was assessed according to the Canadian Cardiovascular Society classification. In addition, periprocedural adverse events were documented.

Myocardial infarction was defined as an increase in creatine kinase-MB activity >3 times the upper limit of normal after PCI and >5 times after CABG (17). In addition, standard electrocardiographic criteria were applied. The incidence of stent thrombosis was evaluated in accordance with the Academic Research Consortium definitions (17). Repeat revascularization was defined as any revascularization by CABG or PCI within 12 months, and was subdivided into target lesion revascularization of the ULM and distally located lesions or those of the right coronary artery.

Recorded periprocedural events were: 1) low cardiac output syndrome requiring intravenous inotropic agents and/or intra-aortic balloon counterpulsation; 2) congestive heart failure requiring hospital readmission; 3) cerebrovascular events (stroke, coma, transient ischemic attack, or prolonged ischemic neurological deficit); 4) pericardial tamponade; 5) arrhythmia (ventricular fibrillation, ventricular tachycardia, or new atrial fibrillation) requiring treatment; 6) major bleeding requiring additional blood transfusion; 7) resternotomy for bleeding; 8) renal insufficiency requiring dialysis; 9) major infections compromising post-procedural rehabilitation; 10) vascular access site complications requiring surgical intervention; and 11) sternum instability or infection requiring additional treatment.

All clinical outcomes were adjudicated by a clinical event committee consisting of a cardiothoracic surgeon and a cardiologist blinded to treatment allocation.

Statistical analysis. The objective was to determine whether PCI with sirolimus-eluting stents was not inferior to the currently accepted standard of CABG surgery. It was assumed that 15% of the patients treated by surgery and 12.5% treated by PCI would reach the combined primary end point at 12 months. A sample size of 100 from surgery and 100 from stenting achieved 80% power at a 5% significance level using a 1-sided equivalence test at the maximum allowable difference of 10% between the groups. This difference has been used previously and is very similar to the 9% rate for the left main subgroup in the SYNTAX trial (11,18).

All analyses were conducted according to the intention-to-treat principle. Patients lost to follow-up were included until the last contact. One-sided significance tests of noninferiority and exact 95% confidence intervals were computed for the differences in event rates between the randomized groups using procedures implemented in StatXact (Cytel Inc., Cytel Studio 8.0, Cambridge, Massachusetts) (19).

Despite not being powered for the analysis of individual end points of the combined end point, noninferiority margins were analyzed to allow hypothesis generation.

Data for categorical variables are expressed as number and percentage of patients. Most continuous variables had nonnormal distribution and are therefore presented as medians together with interquartile range (IQR). Continuous values were compared by unpaired Student *t* tests after testing for normal distribution, or Wilcoxon rank sum test when appropriate. Fisher exact test or chi-square tests were used for categorical variables. For long-term clinical end points, the Kaplan-Meier method was applied and differences assessed by the log-rank test. All statistical tests were performed with SPSS software, version 17.0 (SPSS Inc., Chicago, Illinois). A 2-tailed p value <0.05 was considered statistically significant. By protocol, there were no interim analyses.

Results

From July 2003 to February 2009, a total of 430 patients with ULM disease at 4 tertiary care centers were screened for inclusion into the trial. Of these, 201 patients met the inclusion criteria and were randomly assigned to PCI (n = 100) or CABG (n = 101). The remaining 229 patients entered the prospective registry (Fig. 1). Reasons for noninclusion in the randomized trial are listed in Figure 1.

Comparison of pre-procedural variables for the 2 randomized groups showed no significant differences (Table 1). The average interval between randomization and treatment was 1.0 days (IQR: 1.0 to 3.0 days) for patients assigned to PCI and 4.0 days (IQR: 2.0 to 7.0 days) for surgery ($p < 0.001$).

Procedural outcomes. All patients received the assigned treatment. However, 3 patients randomized to PCI had to be converted to CABG, without any subsequent complications. In 2 of these, the high-grade stenosis of ULM bifurcation could be crossed with a wire that extended only into the left circumflex artery; however, the left anterior descending coronary artery could not be wired. Another patient had a subtotal mid-left anterior descending artery stenosis that could not be recanalized; because complete revascularization was mandatory by trial protocol, conversion to CABG was indicated. A median of 2.0 (IQR: 1.0 to 4.0) sirolimus-eluting stents were implanted using a median implantation pressure of 16.0 atms (IQR: 14.0 to 18.0 atms). The median total stent length was 36.0 mm (IQR: 18.0 to 59.0 mm) (Table 2).

CABG was successfully performed in all patients randomized to surgery, with a median of 2.0 (IQR: 2.0 to 3.0) grafts and a total of 254 distal anastomoses. Nearly one-half of the patients (46%) were operated on using an off-pump ("beating heart") technique. In all patients, the left internal mammary artery was used to bypass the left anterior descending coronary artery, except for 1 who had a nonpatent left internal mammary artery. Additionally, 37 patients received radial arterial and 55 right internal mammary artery grafts. Altogether, 35 patients (35%) received 1 or more saphenous vein graft distal anastomoses. Total arterial revascularization was achieved in 66 patients (65%) (Table 2). The rates of complete revascularization were 98% in the PCI and 97% in the CABG groups.

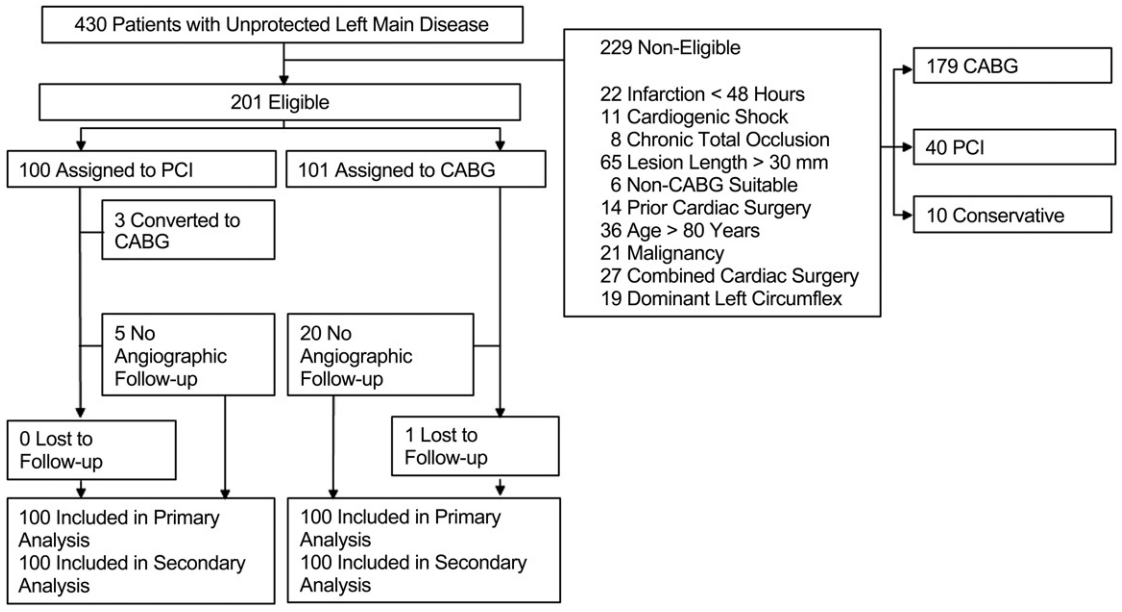

Figure 1 **Trial Profile Showing the Number of Screened, Randomized, and Registry Patients**

The reasons for noninclusion in the randomized trial are shown for registry patients. Additionally, the number of patients at follow-up for primary and secondary end point analysis in the randomized trial is shown. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

Periprocedural adverse events were rare after PCI, with 1 episode of acute renal failure (1%) and 3 episodes of atrial fibrillation (3%) in comparison to CABG (2 strokes [2%]; 1 critical illness neuropathy and persistent incomplete tetraplegia [1%]; 19 new atrial fibrillation/flutter episodes requiring treatment [19%]; 2 resternotomy for bleeding with additional blood transfusion [2%]; 1 renal insufficiency requiring dialysis [1%]; and 5 major infections compromis-

Table 1 **Patient Characteristics**

Variable	PCI (n = 100)	CABG (n = 101)	p Value
Age, yrs	66 (62–73)	69 (63–73)	0.24
Men	72 (72)	78 (77)	0.49
Body mass index, kg/m^2	27.2 (24.6–31.5)	27.0 (24.9–30.1)	0.31
Cardiovascular risk factors			
Current smoking	35 (35)	28 (28)	0.34
Hypertension	82 (82)	83 (82)	0.88
Hypercholesterolemia	68 (68)	65 (64)	0.89
Diabetes mellitus	40 (40)	33 (33)	0.35
Previous myocardial infarction	19 (19)	14 (14)	0.43
Q-wave infarction	17 (17)	10 (10)	
Non–Q-wave infarction	2 (2)	4 (4)	
Previous stroke	3 (3)	6 (6)	0.51
Baseline creatinine, μmol/l*	86.0 (76.5–100.0)	86.0 (75.0–97.0)	0.52
Left ventricular ejection fraction, %	65.0 (55.0–70.0)	65.0 (55.0–68.0)	0.88
Logistic EuroSCORE	2.4 (1.5–3.7)	2.6 (1.7–4.9)	0.08
Discharge medication			
Aspirin	100 (100)	101 (100)	0.99
Clopidogrel	100 (100)	32 (32)	<0.001
Beta-blocker	99 (99)	96 (95)	0.22
ACE inhibitor/AT-1 antagonist	98 (98)	93 (92)	0.11
Statins	97 (97)	95 (94)	0.51

Values are given as median (IQR) or n (%). *To convert μmol/l to mg/dl, multiply serum creatinine values by 0.0113.

ACE = angiotensin-converting enzyme; AT-1 = angiotensin receptor type 1; CABG = coronary artery bypass grafting; IQR = interquartile range; PCI = percutaneous coronary intervention.

JACC Vol. 57, No. 5, 2011
February 1, 2011:538–45

Table 2 Angiographic Characteristics

Variable	PCI (n = 100)	CABG (n = 101)	p Value
Lesion type			0.72
Ostial	20 (20)	23 (23)	
Trunk	6 (6)	8 (8)	
Distal	74 (74)	70 (69)	
Isolated left main	28 (28)	29 (29)	0.49
Left main + 1-vessel disease	35 (35)	27 (27)	
Left main + 2-vessel disease	26 (26)	28 (28)	
Left main + 3-vessel disease	11 (11)	17 (17)	
PCI technique for distal left main			
T-stenting	40 (40)	—	
Provisional T-stenting	30 (30)	—	
Crush-stenting	3 (3)	—	
V-stenting	1 (1)	—	
CABG, conduits per patient			
Left internal mammary artery	—	100 (99)	
Right internal mammary artery	—	55 (54)	
Radial artery	—	37 (37)	
Venous graft	—	35 (35)	
SYNTAX score (15)	24.0 (19.0–29.0)	23.0 (14.8–28.0)	0.09

Values are given as n (%) or median (IQR).
SYNTAX = Synergy Between PCI With Taxus and Cardiac Surgery; other abbreviations as in Table 1.

ing post-procedural rehabilitation [5%]). In total, 4 PCI patients (4%) had a periprocedural event in comparison to 30 CABG patients (30%) ($p < 0.001$).

The median total hospital days in the stenting group were 3.0 days (IQR: 2.0 to 4.0 days) and 13.0 days (IQR: 11.0 to 14.0 days) in the surgery group ($p < 0.001$), and the median hospital stay after revascularization was 1.0 days (IQR: 1.0 to 1.5 days) versus 8.0 days (IQR: 7.0 to 9.0 days) ($p < 0.001$).

Angiographic follow-up. Angiographic follow-up was not completed in 5 PCI (5%) and 20 CABG (20%) patients ($p < 0.001$) (Fig. 1). A significant target lesion restenosis occurred in 9 PCI patients (9%). Restenoses of the target lesion were usually focal, and all occurred in patients with distal ULM disease. Furthermore, 5 de novo stenoses in the PCI group were treated interventionally. There were no stent thromboses in the PCI group. After CABG, 25 anastomoses (n = 10 left internal mammary artery, n = 7 right internal mammary artery, n = 5 radial artery, n = 3 venous grafts) in 21 patients (21%) were totally occluded or had relevant stenosis of >50%. Most of these were asymptomatic. A new relevant stenosis in a native coronary was detected in 2 patients (2%).

Follow-up. At 12-month follow-up, the combined clinical end point was reached in 19.0% of patients after PCI and in 13.9% after CABG (Table 3). The difference in the event rates was 5.1% and did not satisfy the statistical criteria for noninferiority (upper bound >10.0%, p = 0.19 for noninferiority). Individual components of the combined end point revealed mixed results. Whereas noninferiority was confirmed for the difference in death and myocardial infarction, noninferiority was not established for the difference in repeat revascularization (Table 3). A total of 10 (10.0%) target lesion and 4 (4.0%) de novo artery stenosis revascu-

Table 3 Major Adverse Cardiac Events at 12-Month Follow-Up (in Descending Order of Severity) According to Intention-to-Treat Analysis

	PCI (n = 100)	CABG (n = 101)	95% CI for Differences	p Value Noninferiority
Death	2 (2.0)	5 (5.0)	−9.4 to 2.7	<0.001
Myocardial infarction	3 (3.0)	3 (3.0)	−5.8 to 5.9	0.002
<30 days	3 (3.0)	3 (3.0)	−5.8 to 5.9	0.002
Day 30 to 12 months	—	—	−3.7 to 3.7	<0.001
Myocardial infarction + death	5 (5.0)	8 (7.9)	−10.6 to 4.4	<0.001
Repeat revascularization	14 (14.0)	6 (5.9)	−0.3 to 17.1	0.35
<30 days	1 (1.0)	2 (2.0)	−6.1 to 3.7	<0.001
Day 30 to 12 months	13 (13.0)	4 (4.0)	−1.3 to 17.6	0.45
Any major adverse cardiac event	19 (19.0)	14 (13.9)	−5.3 to 15.7	0.19

Values are given as n (%).
CI = confidence interval; other abbreviations as in Table 1.

larizations occurred in the PCI group, compared with 6 (5.9%) repeat revascularizations after CABG. The majority of revascularizations were treated by PCI (83.0%). Of note, the incidence of major adverse cardiac events in ostial/shaft lesions was 1.0% versus 18.0% in distal left main lesions for the PCI group and 5.0% versus 8.9% for CABG patients. Combined rates of death, infarction, and stroke were 5.0% in the PCI versus 8.9% in the CABG group.

At longer follow-up of 36.5 months (IQR: 24.4 to 60.9 months), the results were similar for the combined clinical end point (Fig. 2A) and for the differences in death and myocardial infarction (Fig. 2B), as well as for repeat revascularization (Fig. 2C).

Noneligible patients in the registry had higher major adverse cardiac event rates at 12-month follow-up (PCI 27.5%, CABG 17.8%, conservative therapy 43.0%). Mortality at 1 year was 12.5% after PCI, 12.8% after CABG, and 33.1% after conservative therapy; the repeat revascularization rate was 20.9% after PCI and 4.5% after CABG. Only 1 myocardial infarction occurred post-procedure, in a patient who underwent CABG surgery.

Clinical symptoms and physical work capacity. Following PCI, the median angina class improved from 3.0 (IQR: 2.0 to 4.0) to 0.0 (IQR: 0.0 to 1.0; $p < 0.001$ vs. baseline) with 71.1% of patients being angina free. After CABG, the angina classification improved from 2.0 (IQR: 2.0 to 4.0) to 0.0 (IQR: 0.0 to 1.0; $p < 0.001$ vs. baseline; $p = 0.67$ vs. PCI), and 66.3% of patients were free from angina ($p = 0.33$ vs. PCI).

Discussion

This multicenter trial failed to show that sirolimus-eluting stenting is noninferior to CABG using predominantly arterial grafts at mid-term follow-up for patients with ULM disease. This was mainly caused by the higher rate of repeat revascularization, whereas for the end points death and myocardial infarction, the noninferiority criterion would have been reached. However, fewer periprocedural adverse events occurred in the PCI group, possibly due to its less invasive approach. In addition, the relief of symptoms during follow-up was similar between both reperfusion regimens.

Comparison with other studies. Recently published registries comparing drug-eluting stenting and CABG confirmed that treatment of ULM disease with PCI results in lower or similar rates of cardiovascular events at mid- to long-term follow-up (9,10,20,21). In a relatively small randomized study that did not use drug-eluting stents and arterial bypass grafts consistently, there was an improvement in left ventricular function in the PCI group, with fewer clinical adverse events (12). An important adverse prognostic factor in interventional treatment is location in the distal part of the ULM, as this requires more complex interventional techniques (22). Recently, the randomized SYNTAX trial of drug-eluting stenting versus CABG for ULM

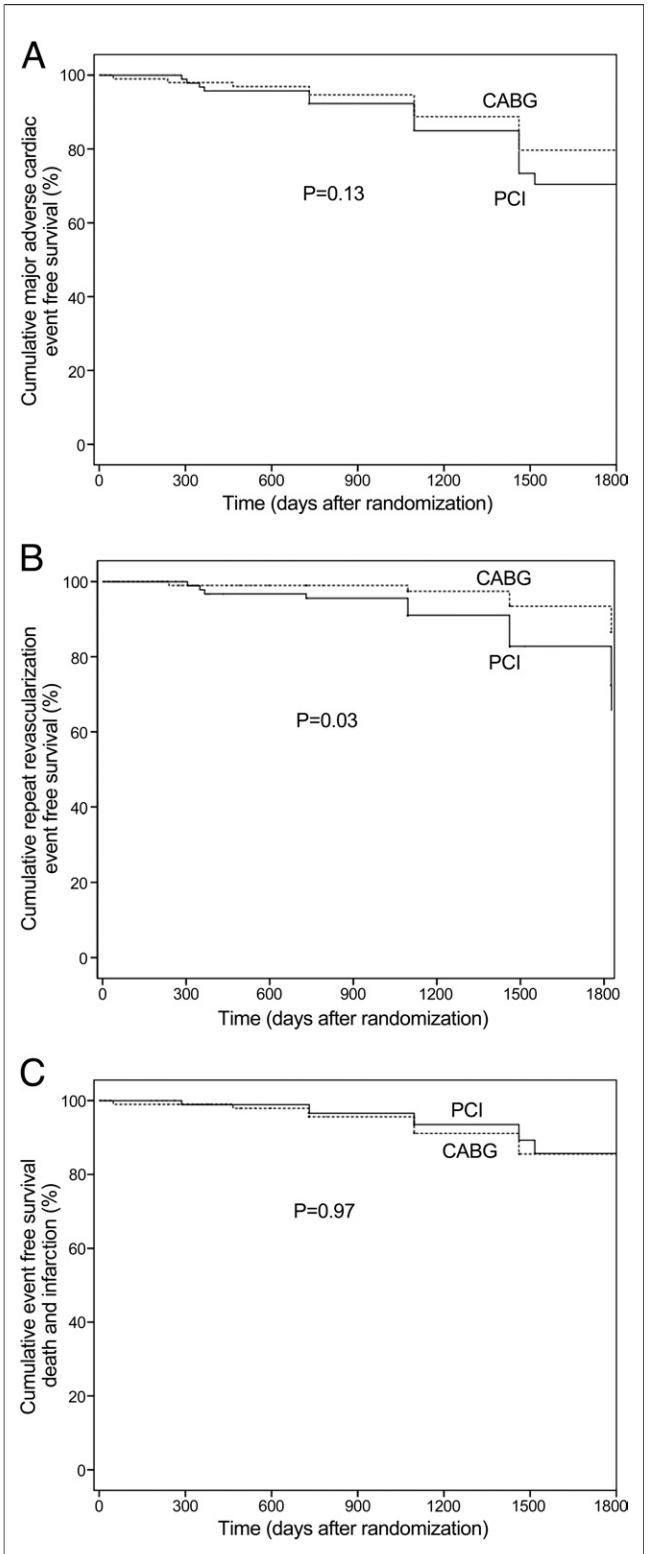

Figure 2 Kaplan-Meier Curves at Long-Term Follow-Up for the Primary End Point and Its Components

(A) Kaplan-Meier curve for the primary combined clinical end point. **(B)** Kaplan-Meier curve for acute myocardial infarction and death. **(C)** Kaplan-Meier curve for repeat revascularization. The log-rank test was used for the comparison between sirolimus-eluting stenting and CABG. Abbreviations as in Figure 1.

stenosis and triple-vessel disease reported similar major adverse cardiac and cerebrovascular event rates (13.7% CABG vs. 15.8% PCI; p = 0.44) at 12-month follow-up for the ULM disease subgroup (11). Repeat revascularization rates for ULM patients were similar to the current trial, with 11.8% after PCI in comparison to 6.5% after CABG (11). Cerebrovascular events were included in the primary end point in the SYNTAX trial. However, adding cerebrovascular events to the current trial would also have led to failure in meeting the criteria of noninferiority (p = 0.11 for noninferiority). Similar to the SYNTAX trial, patients not eligible for the current study were entered into a prospective registry. In the current trial, the percentage of noneligible patients was similar to the SYNTAX trial (56% vs. 58%) due to the pre-defined exclusion criteria. In contrast to the SYNTAX trial, noneligible registry patients undergoing PCI or surgery had worse clinical outcome at 12 months, which reflects the increased comorbidities and complexity of disease.

In addition to the components of the primary end point, we assessed adverse periprocedural events. These occurred significantly more often after the more invasive CABG approach. These adverse events might have prognostic impact and are therefore used to compare different surgical revascularization techniques (23,24).

Restenosis. The issue of restenosis after stenting has been partially addressed by the use of drug-eluting stents. However, as also shown in this trial, increased repeat revascularization after PCI remains an ongoing problem and was the main factor for noninferiority failure when compared with CABG. All restenoses were observed in patients with distal ULM disease, similar to results from other registries and randomized clinical trials. Such studies have revealed a target vessel revascularization rate ranging from 2% to 38%, depending on the percentage of patients with distal ULM disease (7,9,10,20–22,25). In contrast, the rate of repeat revascularization after CABG is usually in the range of 2% to 6%, similar to the current trial (9–11,20,21). At first glance, the high rate of occluded grafts and the much lower revascularization rate might be difficult to interpret. However, many previous CABG trials have shown similar rates of patients with occluded bypass grafts who do not have any symptoms and where no ischemia can be detected (26). Since there was no routine repeat coronary angiography in the SYNTAX trial, the rate of occluded bypass grafts cannot be estimated (11). It is worthwhile mentioning the 65% rate of total arterial revascularization achieved in CABG patients in the current study, a proportion that is significantly higher than that was observed in other recent clinical trials (12). The increased arterial revascularization rate may lead to improved patient outcomes during longer follow-up.

Stent thrombosis is a potentially important limitation of drug-eluting stents with impaired endothelialization and healing (27). This is particularly important if several drug-eluting stents are used with overlapping of the struts, resulting in increased drug dosages with subsequent impaired re-endothelialization (28). Whereas stent restenosis is usually associated with a relatively benign clinical outcome, stent thrombosis is associated with an increased risk of myocardial infarction of up to 70% and an increased risk of mortality of up to 45% (29,30). These findings necessitate prolonged dual antiplatelet medication with aspirin and clopidogrel for at least 12 months after drug-eluting stent implantation (31). In the current trial, no stent thrombosis was observed.

Mortality and infarction. The mortality and recurrent infarction rate in the CABG group was similar to the rate observed in previous trials, with in-hospital mortality rates of approximately 1% to 5% and long-term mortality rates of 5% to 15% (32–34). In contrast, early periprocedural mortality was 0 in the current PCI group.

Study limitations. The modest sample size and the lack of longer-term follow-up are limitations of the current study. The benefits of CABG compared with medical therapy emerged beyond 1 year in previous trials when perioperative mortality and morbidity in the CABG group become offset by mortality from coronary artery disease in the medical group (1–4). Hence, the apparent lack of difference of mortality and reinfarction at 1 year is not completely reassuring and does not contradict previously observed longer-term benefits of CABG. However, large observational studies have not shown any major difference at longer-term follow-up between CABG and PCI with respect to mortality and myocardial infarction (10,35). In addition, the longer follow-up of 36.5 months in the current study did not show a difference in comparison to the 12-month data. Another caveat is that the results were obtained only at highly experienced tertiary centers, which might preclude generalization, and also that stroke was not included in the combined clinical end point.

Conclusions

PCI with sirolimus-eluting stents is inferior to CABG at 12-month follow-up with respect to freedom from major adverse cardiac events in patients with ULM stenosis. Inferiority is mainly driven by the higher repeat revascularization rate, whereas death and myocardial infarction rates seem to be noninferior in PCI patients at lower perioperative morbidity. In highly experienced centers, the decision-making process on how to treat ULM disease should therefore be based on an interdisciplinary approach taking into account the individual success, periprocedural risk, potential restenosis, and graft occlusion rate based on the morphology of the underlying lesion and patient comorbidities.

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