Journal of the American College of Cardiology
© 2008 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 51, No. 5, 2008
ISSN 0735-1097/08/$34.00
doi:10.1016/j.jacc.2007.09.054

Acute and Late Outcomes of Unprotected Left Main Stenting in Comparison With Surgical Revascularization

Pawel E. Buszman, MD, FACC,*‡ Stefan R. Kiesz, MD, FACC,†‡ Andrzej Bochenek, MD,* Ewa Peszek-Przybyla, MD,§ Iwona Szkrobka, MD,§ Marcin Debinski, MD,§ Bozena Bialkowska, MD,§ Dariusz Dudek, MD,‖ Agata Gruszka, MD,§ Aleksander Zurakowski, MD,§ Krzysztof Milewski, MD,§ Miroslaw Wilczynski, MD,§ Lukasz Rzeszutko, MD,‖ Piotr Buszman,* Jan Szymszal, PhD,¶ Jack L. Martin, MD, FACC,# Michal Tendera, MD, FACC*

Katowice, Ustron, and Krakow, Poland; San Antonio, Texas; and Philadelphia, Pennsylvania

Objectives The purpose of this study was to compare the early and late results of percutaneous and surgical revascularization of left main coronary artery stenosis.

Background Unprotected left main coronary artery (ULMCA) stenting is being investigated as an alternative to bypass surgery.

Methods We randomly assigned 105 patients with ULMCA stenosis to percutaneous coronary intervention (PCI; 52 patients) or coronary artery bypass grafting (CABG; 53 patients). The primary end point was the change in left ventricular ejection fraction (LVEF) 12 months after the intervention. Secondary end points included 30-day major adverse events (MAE), major adverse cardiac and cerebrovascular events (MACCE), length of hospitalization, target vessel failure (TVF), angina severity and exercise tolerance after 1 year, and total and MACCE-free survival.

Results A significant increase in LVEF at the 12-month follow-up was noted only in the PCI group (3.3 ± 6.7% after PCI vs. 0.5 ± 0.8% after CABG; $p = 0.047$). Patients performed equally well on stress tests, and angina status improved similarly in the 2 groups. PCI was associated with a lower 30-day risk of MAE ($p < 0.006$) and MACCE ($p = 0.03$) and shorter hospitalizations ($p = 0.0007$). Total and MACCE-free 1-year survival was comparable. Left main TVF was similar in the 2 groups. During the 28.0 ± 9.9-month follow-up, there were 3 deaths in the PCI group and 7 deaths in the CABG group ($p = 0.08$).

Conclusions Patients with ULMCA disease treated with PCI had favorable early outcomes in comparison with the CABG group. At 1 year, LVEF had improved significantly only in the PCI group. After more than 2 years, MACCE-free survival was similar in both groups with a trend toward improved survival after PCI. (Study of Unprotected Left Main Stenting Versus Bypass Surgery [LE MANS study]; NCT00375063). (J Am Coll Cardiol 2008;51:538–45) © 2008 by the American College of Cardiology Foundation

For more than 2 decades after the advent of coronary angioplasty, left main percutaneous coronary intervention (PCI) was not considered to be a viable alternative to coronary artery bypass grafting (CABG). The unpredictable occurrence of abrupt closure or restenosis put patients undergoing unprotected left main coronary artery (ULMCA) angioplasty at risk of severe perioperative complications and late sudden death. The advent of coronary stents dramatically lowered the incidence of abrupt vessel closure, and the application of drug-eluting stents (DES) decreased the risk of ULMCA in-stent restenosis (1–4). Additionally, the restoration of native, antegrade flow through the left main coronary artery (LMCA) may have an advantage over conventional bypass surgery (5).

Several investigators have reported the safety and feasibility of unprotected left main stenting with bare-metal stents (BMS) (6–11). Promising long-term results have been reported with both BMS and DES in a limited series of publications (1–4,12,13). In our nonrandomized registry, we observed improvements in left ventricular function following PCI for ULMCA disease (14). Thus far, there

From the *Medical University of Silesia, Katowice, Poland; †San Antonio Endovascular and Heart Institute, University of Texas Health Science Center at San Antonio, San Antonio, Texas; ‡American Heart of Poland, Ustron, Poland; §Upper-Silesian Heart Centre, Katowice, Poland; ‖Jagiellonian University, Krakow, Poland; ¶Silesian School of Engineering, Katowice, Poland; and #Bryn Mawr and Thomas Jefferson University, Philadelphia, Pennsylvania. This study was sponsored by the Polish Ministry of Science and Informatics (grant 4P05B00819).

Manuscript received March 21, 2007; revised manuscript received September 10, 2007, accepted September 17, 2007.

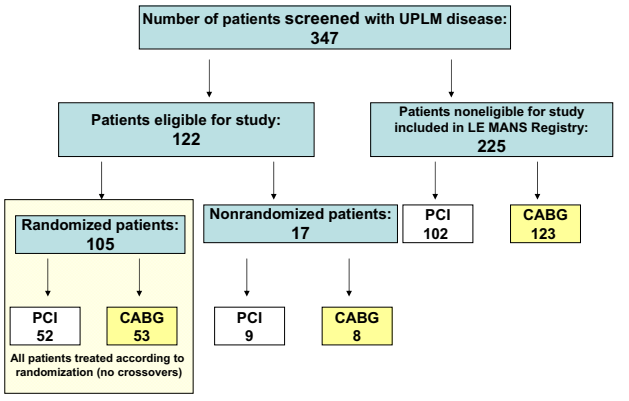

Figure 1 **Experimental Design of the Study**

Three hundred and forty-seven patients with unprotected left main (UPLM) disease were screened. Patients who were eligible for the study and signed informed consent (105 patients) were randomized to both treatment arms. Seventeen patients were not randomized due to their refusal. Patients not eligible for the study were included in the LE MANS registry. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

has not been a prospective randomized trial comparing the short- and long-term results of unprotected left main stenting with CABG. Additionally, it is not clear whether the method of revascularization affects left ventricular (LV) function in patients with left main stenosis.

Therefore, the purpose of the present study was to compare acute and late clinical end points, functional status, and LV function at 1 year following stent-supported PCI or CABG for ULMCA disease in a prospective randomized trial.

Materials and Methods

We enrolled 105 patients with >50% narrowing of ULMCA, with or without multivessel coronary artery disease suitable for equal revascularization both with PCI and CABG. All patients had to be symptomatic with documented myocardial ischemia. Exclusion criteria included acute myocardial infarction, total occlusion of left main, comorbid conditions, or coronary anatomic considerations that increased the surgical risk to a Euroscore of 8 or more, stroke or transient ischemic attack within 3 months, renal dysfunction, or contraindication to antiplatelet therapy.

Three hundred forty-seven consecutive patients with more than 50% left main stenosis were screened between 2001 and 2004. Based on a joint decision by the lead interventional and surgical investigators, 122 patients were suitable for both procedures; 105 gave consent and were randomized to either PCI (n = 52) or CABG (n = 53) (Fig. 1). Both groups were comparable with regard to basic clinical and angiographic data (Table 1). All randomized patients underwent their assigned therapy (no crossovers).

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CABG = coronary artery bypass grafting
DES = drug-eluting stent(s)
LVEF = left ventricular ejection fraction
MACCE = major adverse cardiac and cerebrovascular events
MAE = major adverse events
PCI = percutaneous coronary intervention
TVF = target vessel failure
TVR = target vessel revascularization
ULMCA = unprotected left main coronary artery

The LV function was evaluated by 2-dimensional echocardiography before and 12 months after the index procedure. Treadmill stress tests were performed at 1, 3, 6, and 12 months after the procedure. Patients in the PCI group underwent a follow-up angiography within 4 to 6 months. Major adverse cardiac and cerebrovascular events (MACCE) and other major adverse events (MAE) were recorded during the entire follow-up period up to 5 years.

Percutaneous revascularization. Direct stenting of the left main was a preferred strategy except for cases with critical luminal narrowing, for which predilatation was performed with small balloons (2.0 to 2.5 mm). For distal left main stenosis, stenting across the bifurcation toward the left anterior descending was performed first, and then provisional stenting of the circumflex artery with T-stenting or "culotte" technique was preferred. The crush stent technique was avoided. Post-dilation with kissing balloon angioplasty was always used to finish the distal left main stenting procedure. Drug-eluting stents were used for the left main with a reference diameter of <3.8 mm, and BMS were implanted if the left main reference diameter was 3.8 mm or greater. Based on these criteria, the left main was treated with DES in 35% of PCI patients. Stent length and diameter were selected on the basis of online quantitative coronary angiography (balloon to artery ratio 1:1.1) and post-dilated at high pressure (at least 16 atmospheres). A control intravascular ultrasound was recommended to assess the final results.

Intra-aortic balloon contrapulsation and percutaneous cardiopulmonary support were used only in the subgroup of patients with complex stenotic lesions in coronary vessels supplying more than 50% of the viable myocardium coexisting with significantly depressed LV function (left ventricular ejection fraction [LVEF] <25%). Therapy with acetylsalicylic acid and a thienopyridine (clopidogrel or ticlopidine) was initiated at least 2 days before the procedure. Intravenous glycoprotein IIb/IIIa blockers were used at the operator's discretion only in procedures performed in patients with complex coronary lesions and unstable angina. Unfractionated heparin was used in standard doses. Angiographic success was defined as left main residual stenosis <30%, minimal lumen diameter at least 3 mm, Thrombolysis In Myocardial Infarction flow grade 3, and no dissection. Clinical success included angiographic success and no death or myocardial infarction in-hospital outcome.

JACC Vol. 51, No. 5, 2008
February 5, 2008:538–45

Table 1 Baseline Characteristics of the Study Groups

Variables	PCI (n = 52)	CABG (n = 53)	p Value
Age (yrs)	60.6 ± 10.5	61.3 ± 8.4	0.69
Male (%)	60	73	0.13
CCS class	3.1 ± 1.0	2.8 ± 1.0	0.17
LVEF (%)	53.5 ± 10.7	53.7 ± 6.7	0.86
LVEF <50% (%)	21	17	0.58
DM (%)	19	17	0.80
Hypertension (%)	75	70	0.78
Hypercholesterolemia (%)	65	60	0.78
Previous myocardial infarction			
STEMI (%)	25	21	0.60
NSTEMI (%)	11	11	0.97
Euroscore	3.3 ± 2.3	3.5 ± 2.3	0.65
Distal LM disease (%)	56	60	0.63
No. of diseased vessels	1.7 ± 0.93	2.08 ± 0.83	0.33
1-vessel disease (%)	13	6	0.17
2-vessel disease (%)	27	19	0.32
3-vessel disease (%)	60	75	0.08
Syntax score	25.2 ± 8.7	24.7 ± 6.8	0.75
QCA baseline			
Proximal reference diameter (mm)	3.6 ± 0.9	3.8 ± 1.1	0.38
Distal reference diameter (mm)	3.4 ± 0.9	3.7 ± 1.0	0.47
Minimal lumen diameter (mm)	1.4 ± 0.6	1.5 ± 0.5	0.46
Percent diameter stenosis (%)	60 ± 12	60 ± 13	0.91
DES/arterial graft to LAD (%)	35	81	—
Dilated arteries/no. of grafts	2.3 ± 0.8	2.9 ± 0.8	0.006
Complete revascularization (%)	79	89	0.17
Hospitalization (days)	6.8 ± 3.7	12.04 ± 9.6	0.0007

Values are mean ± SD or %.

CABG = coronary artery bypass grafting; CCS = Canadian Cardiovascular Society; DES = drug-eluting stent; DM = diabetes mellitus; LAD = left anterior descending; LIMA = left internal mammary artery; LM = left main; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; QCA = quantitative coronary angiography; STEMI = ST-segment elevation myocardial infarction; NSTEMI = non–ST-segment elevation myocardial infarction.

Surgical revascularization. Operations were performed using standard anesthetic techniques. All but 1 operation were performed through a median sternotomy, with standard cardiopulmonary bypass and moderate systemic hypothermia. One patient underwent off-pump CABG. Left internal mammary artery grafts were used in 72% of CABG patients, and radial artery grafts were used in 9%.

Pharmacologic treatment after revascularization. All patients stayed on double antiplatelet treatment for at least 12 months. Other pharmacological treatments (e.g., statins, angiotensin-converting enzyme inhibitors, beta-blockers) were recommended based on current practice and were left to the discretion of a supervising physician.

Primary end point. The change in LVEF assessed by 2-dimensional echocardiography 12 months after the index intervention was the primary end point of this study.

Secondary end points. Secondary end points included 30-day and 1-year MAE and MACCE, length of hospitalization, exercise tolerance measured with an electrocardiographic treadmill stress test along with angina severity according to the Canadian Cardiovascular Society classification after 1 year, total survival and freedom from MACCE, and target vessel failure (TVF) and revascularization (TVR).

The MAE were defined as all-cause mortality, acute myocardial infarction (defined as an increase in creatine phosphokinase (CPK)-MB to higher than 3 times the upper limit of normal after PCI and 5 times after CABG), repeat revascularization, acute heart failure (e.g., pulmonary edema, cardiogenic shock), or low output syndrome requiring intravenous inotropic agents and/or intra-aortic balloon pump support, post-procedural complications leading to reintervention, stroke, arrhythmia (ventricular fibrillation, ventricular tachycardia, or atrial fibrillation), major bleeding requiring additional blood transfusion, and infections compromising post-procedural rehabilitation. Any cardiac mortality, acute myocardial infarction, stroke, repeat intervention, and/or acute/subacute in-stent thrombosis were considered MACCE. Target vessel failure was defined as any MACCE related to insufficient flow through the LMCA, and TVR as any repeat intervention (PCI or CABG) caused by a narrowing of the LMCA. The incidence of stent thrombosis was evaluated in accordance with the Academic Research Consortium Definitions of Stent Thrombosis (15).

All clinical outcomes were analyzed by the Clinical Event Committee. Echocardiographic and stress test recordings were read centrally by a group of independent investigators unaware of treatment assignment. Left ventricular ejection fraction was assessed according to the recommendations of the American Society of Echocardiography, based on the Simpson method of LV volume measurement and second harmonic imaging (Sonos 7500, Phillips Medical Systems, Andover, Massachusetts) (16). Reproducibility for 2-dimensional echocardiography recordings and measurements of LVEF calculated as a coefficient of variance ranged between 3.6% and 4.0%.

The treadmill stress test was performed using the Cornell protocol (17) and evaluated according to ACC/AHA guidelines (18).

The 12-lead electrocardiography and CPK/CPK-MB levels were checked every 12 h during the first 3 days after the procedure and then subsequently in cases of myocardial ischemia (prolonged chest pain and/or electrocardiographic changes).

Safety and ethics. The study protocol and written informed consent were approved by the Ethics Committee at the Medical University of Silesia. Percutaneous coronary intervention procedures were carried out by experienced interventional cardiology teams in high-volume centers (2,500 to 4,700 PCI procedures per year) with cardiac surgery backups on site. Surgery was carried out by experienced cardiac surgery teams (performing 2,000 to 3,000 CABG procedures per year with mortality rates of 2% to 3%).

Statistical analysis. All analyses were performed according to the intention-to-treat principle. The data with parametric distribution were expressed as means ± standard deviations, whereas nonparametric data were expressed as absolute numbers ± percentage. Moreover, 95% confidence intervals (CIs) and relative risk (RR) for results of the primary end point and selected secondary end points were calculated.

The parametric variables between the groups were compared using the unpaired Student *t* test. The 2-way analysis of variance (ANOVA) and Newman-Keuls tests were used for comparison of the parametric data between and within the 2 groups at different time points if the Shapiro-Wilk test showed normal distribution of variables and the Levene test showed homogeneity of variances. For parametric data not fulfilling the above criteria, the Wilcoxon test was used to compare the variables within the group at different time points and the Mann-Whitney *U* test to compare variables between the groups at the same time points. The ANOVA Friedman test was used to compare rank variables of different time points and the Mann-Whitney *U* test to compare variables between the groups at the same time points.

The chi-square test or Fisher exact test was used for comparison of nonparametric variables. Survival curves were drawn using Kaplan-Meier analysis. The F-Cox test was used for comparison of the survival curves between the treatment arms.

The number of patients in both treatment groups was established based on prior observations (14) that differences in LVEF of more than 5% from the base value would be significant and detected with $p \leq 0.05$ and rejected with the power of the test >90%. The calculations were performed for the paired *t*, ANOVA, and Wilcoxon tests to make sure that irrespective of the distribution of the observed values, the study would obtain the relevant power of the test for its primary end point. Additionally, a delta between the 12-month and basic values of LVEF was calculated to support the significance of the observed changes above 3-point scores between the groups with a power of unpaired *t* test >85%.

Results

Early outcome. Angiographic success was obtained in all PCI patients, and in-hospital clinical success was observed in 98% of the patients in the PCI group and in 92% in the CABG group ($p = 0.4$). The patients assigned to CABG waited longer for the index procedure: 14.0 ± 27.1 days (median 4 days) prior to CABG versus 4.4 ± 14.2 days (median 2 days) prior to PCI. There were no events during this period.

Between the index procedure and 30 days later, there were no deaths in the PCI group and 2 deaths in the CABG group ($p = 0.16$). PCI was associated with a significantly lower risk of MAE (8% vs. 28%; 95% CI 0.64 to 0.94; RR 0.78; $p = 0.006$) and MACCE (2% vs. 13%; 95% CI 0.79 to 0.99, RR 0.88; $p = 0.03$) and shorter hospitalizations (6.8 ± 3.7 days vs. 12.0 ± 9.6 days; $p = 0.0007$) (Table 2). A significant reduction of angina severity (Canadian Cardiovascular Society classification) after 1 month was observed in both groups (ANOVA Friedman test: $p < 0.001$).

Late outcome. The LVEF values at baseline and after 12 months are presented in Figure 2. The absolute change in LVEF (calculated as a delta) was significantly greater after PCI than after CABG (3.3 ± 6.7%; 95% CI 1.3 to 5.3 vs. 0.5 ± 0.8%; 95% CI 1.4 to 2.5; $p = 0.047$). One year after

Table 2 Detailed List of MAE in CABG and PCI Group During the First Year After the Procedure

	CABG (n = 53)			PCI (n = 52)		
	0 to 30 Days	1 to 12 Months	0 to 12 Months	0 to 30 Days	1 to 12 Months	0 to 12 Months
Death	2	2	4	0	1	1
Nonfatal myocardial infarction	2	1	3	1	0	1
Unstable angina	0	3	3	1	7	8
Major bleeding	3	0	3	0	0	0
Stroke	2	0	2	0	0	0
Acute heart failure	3	1	4	2	1	3
Repeat revascularization	0	5	5*	1	14	15*
PCI LM	0	2	2	0	5	5
Other vessel PCI	0	3	3	1	8	9
CABG	0	0	0	0	1	1
Renal insufficiency	1	0	1	0	0	0
Other (infection, post-cardiotomy syndrome, sternal refixation)	7	1	8	0	0	0
Severe arrhythmia (VF, VT, AF)	3	2	5	1	2	3
Any MACCE	7†	6	13	1†	15	16
Any MAE	15‡	9	24	4‡	16	20

*p = 0.01. †p = 0.03. ‡p = 0.006.

AF = atrial fibrillation; MACCE = major adverse cardiac and cerebrovascular events; MAE = major adverse events; VF = ventricular fibrillation; VT = ventricular tachycardia; other abbreviations as in Table 1.

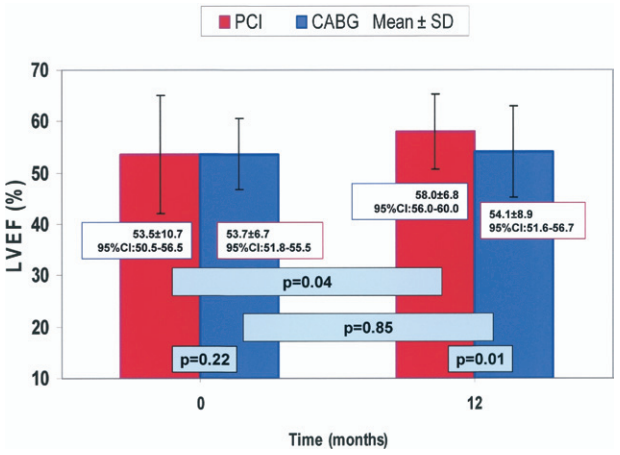

Figure 2 **LVEF in PCI and CABG Groups at Baseline and After 12 Months**

There was no significant difference in LVEF between the groups at baseline (p = 0.22). After 1 year, LVEF improved significantly in the PCI group (p = 0.04) but did not in the CABG group (p = 0.85). There was a significant difference in LVEF between the groups after 12 months (p = 0.01). CI = confidence interval; LVEF = left ventricular ejection fraction; SD = standard deviation; other abbreviations as in Figure 1.

revascularization, LVEF was also significantly better in the PCI group (Mann-Whitney *U* test: p = 0.01).

Post-procedure reduction of angina severity was maintained through 12 months of observation in both groups (Fig. 3). Patients after PCI had more angina after 6 months (Mann-Whitney *U* test: p = 0.01) but had similar angina status to CABG patients after 12 months (p = 0.11).

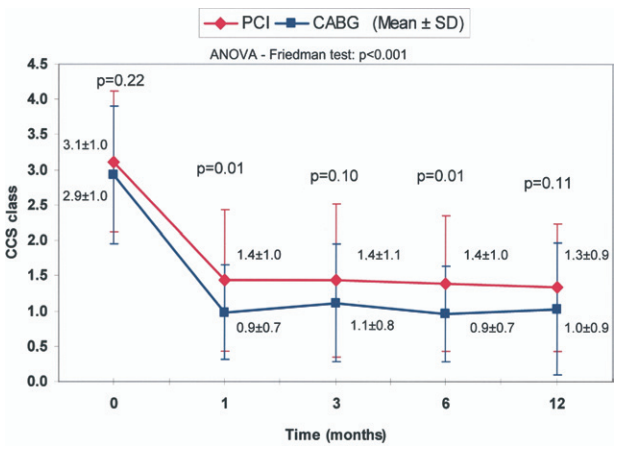

Figure 3 **CCS Functional Class at Baseline and Follow-Up**

At the same time points, angina status based on Canadian Cardiovascular Society (CCS) classification was maintained through 12 months of observation. Patients after PCI had more angina after 1 month and after 6 months (Mann-Whitney *U* test: p = 0.01) but had similar rates of angina as CABG patients after 12 months (p = 0.11). ANOVA = analysis of variance; other abbreviations as in Figures 1 and 2.

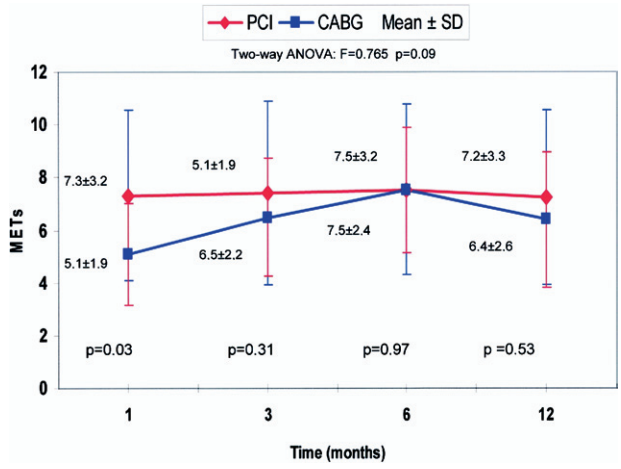

Figure 4 **Results of Treadmill Stress Tests After PCI and CABG**

Patients after PCI and CABG performed equally well on treadmill stress tests with an exception of the first month post-procedure, when patients after PCI performed better (Fig. 4).

Actuarial 1-year survival was comparable in both groups: 98.1% for PCI and 92.5% for CABG (p = 0.37). During 28 ± 9.9 months of follow up, there were 3 deaths in the PCI group (1 death during the first year) and 7 deaths in the CABG group (4 deaths during the first year, including in-hospital events). According to Kaplan-Meier analysis, there was a trend toward better long-term survival after PCI (F-Cox test: p = 0.08) (Fig. 5). The risk of MACCE and MAE in 12 months of observation was comparable in both groups (RR 1.09, 95% CI 0.85 to 1.38 and RR 0.89, 95% CI 0.64 to 1.23 for MACCE and MAE, respectively). The MACCE-free 1-year survival was nonsignificantly lower in the PCI group compared with the CABG group (71.2% vs. 75.5%, respectively; p = 0.29), and the difference was mainly related to repeat revascularization (RR 1.27, 95% CI 1.05 to 1.54; p = 0.01) (Table 2). Similarly, long-term MACCE-free survival did not differ significantly between the groups (53.9% vs. 56.6%, respectively; F-Cox test: p = 0.47) (Fig. 6).

The TVF was similar after CABG and PCI (9.4% vs. 9.6%; p = 0.97). Left main in-stent restenosis occurred in 5 patients (9.6%), including 1 restenosis in the DES subgroup (5.5%) and 4 in the BMS subgroup (11.7%). Four patients were successfully treated with repeat PCI; in 1 patient after repeat PCI, a second restenosis occurred and CABG was performed (TVR, 9.6%).

Acute, subacute, and late stent thrombosis did not occur in the PCI group.

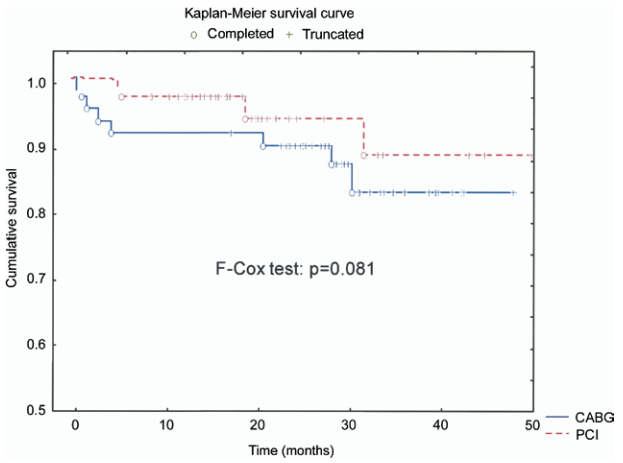

Figure 5 **Survival After PCI and CABG**

According to Kaplan-Meier analysis, there was a trend toward better long-term survival after PCI (F-Cox test: p = 0.081). Abbreviations as in Figure 1.

Discussion

The Left Main Stenting trial is the first prospective randomized study comparing the outcome of PCI versus CABG in patients with ULMCA disease.

Our study showed that there was a lower risk of 30-day events (MACCE and MAE) after PCI compared with CABG. After 12 months, LVEF improved significantly only in the PCI group. Both groups demonstrated similar improvement in angina and good long-term functional capacity on exercise stress testing. During the 28 ± 9.9 months of follow up, MACCE-free survival was comparable in the PCI and CABG groups, but there was a trend toward lower risk of death in the PCI group.

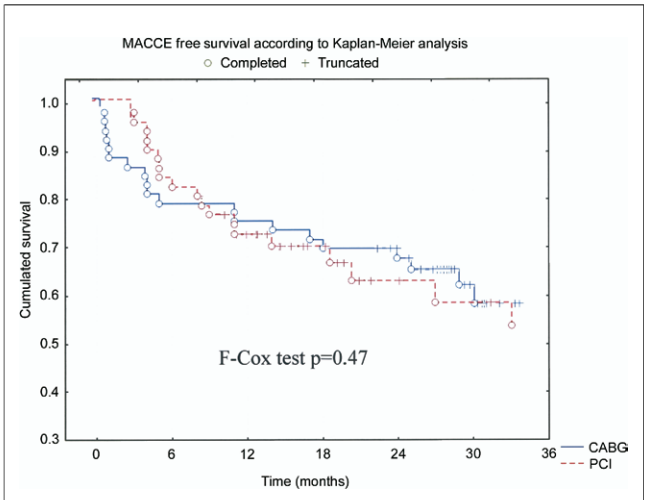

Figure 6 **MACCE-Free Survival After PCI and CABG**

Long-term MACCE-free survival did not differ significantly between the groups (53.9% vs. 56.6%, respectively; F-Cox test: p = 0.47). MACCE = major adverse cardiac and cerebrovascular events; other abbreviations as in Figure 1.

Improvement in LVEF with stenting but not after CABG may be explained by restoration of physiologic antegrade flow in the LMCA and major vessels, lack of perioperative reperfusion injury, and low incidence of myocardial infarction. The notion of the importance of physiologic antegrade flow is supported by the observations of Schmuziger and Christenson (5) after surgical restoration of physiologic perfusion of the LMCA by ostial patch angioplasty. Our prospective registry of ULMCA stenting also showed significant improvement of systolic LV function after percutaneous reconstruction of the left main lumen (14). Previous surgical registries reported a high incidence of perioperative myocardial infarction in patients with left main disease undergoing bypass surgery (19,20), whereas left main stenting has been associated with a low risk of in-hospital death or myocardial infarction (1–4,21). This potentially could also influence LV function in our study. Despite that, ULMCA stenosis remains one of the main indications for CABG because the randomized studies conducted in the 1970s and 1980, demonstrated an advantage of CABG over conservative treatment with a 65% relative reduction in mortality (21–26). Most recent studies evaluating surgical treatment for this cohort of patients reported an in-hospital mortality rate from 1.7% to 7.0% (19–21,27), which corresponds well with our findings of an in-hospital mortality rate of 3.8%. One-year survival of CABG patients in the present study was 92.5%, which is also comparable to prior reports that showed 1-year survival of 86% to 94% (21,22,26,28). On the other hand, a low risk of 30-day and 1-year mortality (0% to 4%) after elective DES implantation in ULMCA was recorded for large groups of patients in nonrandomized studies (21,27). This was confirmed in our study, for which there was a trend toward better survival after PCI in 3- to 4-year follow-ups despite selective use of DES only for small left main reference diameters (F-Cox test: p = 0.08).

Recently published nonrandomized studies comparing DES implantation and CABG confirmed that treatment of ULMCA disease with PCI resulted in fewer early cardiac MAE and a lower or similar rate of late cardiovascular events (21,27). In our randomized study, we confirmed a lower rate of 30-day MAE and MACCE in the PCI group, as well as a similar rate of TVR and late MACCE during 3 to 4 years of follow-up. This is the first study that recorded all MAE (e.g., arrhythmia, heart and renal failure, excessive bleeding) to compare results of percutaneous and surgical myocardial revascularization. Based on the current literature, those factors have a negative influence on patients' post-procedural progress and are routinely used to compare different surgical techniques of revascularization (29,30). We believe that the treatment of periprocedural atrial fibrillation or infections needs time and resource-consuming therapy, not less than repeat angioplasty for restenotic lesions.

According to the new definition of in-stent thrombosis (15), there was no such late incidence in the PCI group. We connect this favorable outcome to selective use of DES and our technique of left main stenting (the provisional stenting of a side branch and no crashed stents). The strategy of selective use of DES was chosen because at the start of the trial, DES with diameters of more than 3.5 mm were not available. Furthermore, our prior experience demonstrated that when the left main reference diameter is greater than 3.8 mm, the use of large-diameter BMS with high radial strength results in very limited recoil and large minimal luminal diameter after the procedure (14). Nonetheless, the total left main restenosis rate was only 9.6%. There was 1 case of restenosis in a patient with DES (5.5%) and 4 cases of restenosis with BMS (11.7%) with a total TVR of 9.6%. In comparison, the TVR after ULMCA stenting in RESEARCH/T-SEARCH registries was 6% and 23%, respectively, after DES and BMS implantation (4,31).

The innovative strategy of this study is also related to a rigid follow-up and routine control angiography, as well as treatment of in-stent ULMCA restenosis with repeat PCI. In all 5 cases with renarrowing of the left main, successful percutaneous intervention was accomplished, resulting in good long-term results. Only 1 patient during the long-term observation underwent surgical revascularization. Similar good outcomes after repeat PCI for left main in-stent restenosis have been confirmed by other authors (32).

Study limitations. The main limitation of our study is the relatively small number of randomized patients. This is related to the fact that surgical revascularization is presently considered the treatment of choice for patients with severe narrowing of ULMCA, and all current guidelines limit indications for left main stenting only to patients with protected left main stenosis or patients with high surgical risk (33). Therefore, based on prior experience, a prespecified number of patients had to be randomized to show the advantage of left main stenting for improvement of LV function (14). Because of the size of this study, it must be considered hypothesis generating rather than offering a definitive answer. Our results must be confirmed in a larger randomized trial.

Conclusions

Based on the results of our study, we conclude that patients with ULMCA disease treated with stent-supported PCI have favorable early outcomes in comparison with CABG. At 1 year, LVEF improved only in the PCI group. Both procedures resulted in similar angina relief at 1 year and equal risk of left main TVF. Freedom from MACCE was comparable after more than 2 years of follow-up, and there was a trend for better survival in the PCI group. These findings support the need for larger randomized trials with clinical primary end points.

Reprint requests and correspondence: Dr. Pawel E. Buszman, Katowice 40-635, Ziolowa 45/47, Poland. E-mail: pbuszman@ka.onet.pl.

REFERENCES

1. Chieffo A, Colombo A. Treatment of unprotected left main coronary artery disease with drug-eluting stents: is it time for a randomized trial? Nat Clin Pract Cardiovasc Med 2005;2:396–400.
2. Chieffo A, Stankovic G, Bonizzoni E, et al. Early and mid-term results of drug-eluting stent implantation in unprotected left main. Circulation 2005;111:791–5.
3. Park SJ, Kim YH, Lee BK, et al. Sirolimus-eluting stent implantation for unprotected left main coronary artery stenosis: comparison with bare metal stent implantation. J Am Coll Cardiol 2005;45:351–6.
4. Valgimigli M, van Mieghem CA, Ong AT, et al. Short- and long-term clinical outcome after drug-eluting stent implantation for the percutaneous treatment of left main coronary artery disease: insights from the Rapamycin-Eluting and Taxus Stent Evaluated At Rotterdam Cardiology Hospital registries (RESEARCH and T-SEARCH). Circulation 2005;111:1383–9.
5. Schmuziger M, Christenson JT. Surgical patch ostiumplasty of the left main coronary artery. Thorac Cardiovasc Surg 1996;44:27–30.
6. Silvestri M, Barragan P, Sainsous J, et al. Unprotected left main coronary artery stenting: immediate and medium-term outcomes of 140 elective procedures. J Am Coll Cardiol 2000;35:1543–50.
7. Park SJ, Lee CW, Kim YH, et al. Technical feasibility, safety, and clinical outcome of stenting of unprotected left main coronary artery bifurcation narrowing. Am J Cardiol 2002;90:374–8.
8. Park SJ, Hong MK, Lee CW, et al. Elective stenting of unprotected left main coronary artery stenosis: effect of debulking before stenting and intravascular ultrasound guidance. J Am Coll Cardiol 2001;38:1054–60.
9. Park SJ, Park SW, Hong MK, et al.. Stenting of unprotected left main coronary artery stenoses: immediate and late outcomes. J Am Coll Cardiol 1998;31:37–42.
10. Park SJ, Park SW, Hong MK, et al. Long-term (three-year) outcomes after stenting of unprotected left main coronary artery stenosis in patients with normal left ventricular function. Am J Cardiol 2003;91:12–6.
11. Black A, Cortina R, Bossi I, Choussat R, Fajadet J, Marco J. Unprotected left main coronary artery stenting: correlates of midterm survival and impact of patient selection. J Am Coll Cardiol 2001;37:832–8.
12. Tan WA, Tamai H, Park SJ, et al. Long-term clinical outcomes after unprotected left main trunk percutaneous revascularization in 279 patients. Circulation 2001;104:1609–14.
13. Takagi T, Stankovic G, Finci L, et al. Results and long-term predictors of adverse clinical events after elective percutaneous interventions on unprotected left main coronary artery. Circulation 2002;106:698–702.
14. Peszek-Przybyła E, Buszman P, Białkowska B, et al. Stent implantation for unprotected left main coronary artery disease. The long-term outcome of 62 patients. Kardiol Pol 2006;64:1–6.
15. Serruys PW, Daemen J. A nuisance in both bare-metal and drug eluting stents. Circulation 2007;115:1433–9.
16. Gottdiener JS, Bednarz J, Devereux R, et al. American Society of Echocardiography recommendations for use of echocardiography in clinical trials. J Am Soc Echocardiogr 2004;17:1086–119.
17. Braunwald E. Exercise stress testing. In: Braunwald E, editor. Heart Disease: A Textbook of Cardiovascular Medicine. Philadelphia, PA: WB Saunders Company, 1992:163–4.
18. Gibbons RJ, Balady GJ, Beasley JW, et al. ACC/AHA guidelines for exercise testing. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). J Am Coll Cardiol 1997;30:260–311.
19. Ellis SG, Hill CM, Lytle BW. Spectrum of surgical risk for left main coronary stenoses: benchmark for potentially competing percutaneous therapies. Am Heart J 1998;135:335–8.
20. Society of Cardiothoracic Surgery in Great Britain and Ireland: National Adult Cardiac Surgical Database. Available at: http://

www.ctsnet.org/file/SCT2000pages116-121LMS.pdf. Accessed November 30, 2007.
21. Chieffo A, Morici N, Maisano F, et al. Percutaneous treatment with drug-eluting stent implantation versus bypass surgery for unprotected left main stenosis: a single-center experience. Circulation 2006;113:2542–7.
22. Caracciolo EA, Davis KB, Sopko G, et al. Comparison of surgical and medical group survival in patients with left main coronary artery disease. Long-term CASS experience. Circulation 1993;91:2325–43.
23. Detre KM, Peduzzi P, Takaro T, Hultgren HN, Murphy ML, Kroncke G. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. The Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. N Engl J Med 1984;311:1333–9.
24. Chaitman BR, Fisher LD, Bourassa MG, et al. Effect of coronary bypass surgery on survival patterns in subsets of patients with left main coronary artery disease. Report of the Collaborative Study in Coronary Artery Surgery (CASS). Am J Cardiol 1981;48:765–77.
25. Takaro T, Hultgren HN, Lipton MJ, Detre KM. The VA cooperative randomized study of surgery for coronary arterial occlusive disease. II. Subgroup with significant left main lesions. Circulation 1976;54:107–17.
26. Varnauskas E. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med 1988;319:332–7.
27. Lee MS, Kapoor N, Jamal F, et al. Comparison of coronary artery bypass surgery with percutaneous coronary intervention with drug-eluting stents for unprotected left main coronary artery disease. J Am Coll Cardiol 2006;47:864–70.
28. Dzavik V, Ghali WA, Norris C, et al. Long-term survival in 11,661 patients with multivessel coronary artery disease in the era of stenting: a report from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) investigators. Am Heart J 2001;142:119–26.
29. Villarea R, Hariharan R, Liu B, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol 2004;43:742–8.
30. Légaré JF, Buth KJ, King S, et al. Coronary bypass surgery performed off pump does not result in lower in-hospital morbidity than coronary artery bypass grafting performed on pump. Circulation 2004;109:887–92.
31. Valgimigli M, Malagutti P, Rodriguez Granillo GA, et al. Single-vessel versus bifurcation stenting for the treatment of distal left main coronary artery disease in the drug-eluting stenting era. Clinical and angiographic insights into the Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital (T-SEARCH) registries. Am Heart J 2006;152:896–902.
32. Kereiakes DJ, Faxon DP. Left main coronary revascularization at the crossroads. Circulation 2006;113:2480–4.
33. Silber S, Albertsson P, Aviles FF, et al. Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Eur Heart J 2005;26:804–47.

APPENDIX

Echocardiography and quantitative coronary angiography core laboratories were located in the Upper-Silesian Heart Center in Katowice, Poland. The Central Ethics Committee for all participating centers was located at the Upper-Silesian Heart Center in Katowice, Poland. For primary studies, the approval of only 1 independent review board, appropriate for a coordinating institution, is required and acknowledged for multicenter studies in Poland.

Seven patients were included in the study at Jagiellonian University, Krakow, Poland; 58 patients at the Medical University of Silesia in Katowice, Poland; and 40 patients in the First and Second Departments of Invasive Cardiology, American Heart of Poland, Ustron, Poland.