

Original Research

A Preliminary Experience Report: Drug-Eluting Stents Versus Coronary Artery Bypass Surgery in Patients with a Single Lesion in the Proximal Left Anterior Descending Artery Suffering from Diabetes Mellitus and Chronic Stable Angina

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Introduction: Treatment of lesions located in the proximal segment of the left anterior descending artery (pLAD), either with coronary artery bypass grafting (CABG) or percutaneous coronary intervention, in patients with diabetes mellitus has been associated with an unfavourable outcome. The aim of the present study was to compare the long-term clinical outcome of drug-eluting stents (DES) vs. CABG with a left internal mammary artery (LIMA) graft in patients with a pLAD lesion who suffered from chronic stable angina and diabetes mellitus.

Methods: We studied 77 consecutive patients suffering from chronic stable angina, diabetes mellitus, and with an isolated pLAD lesion. Thirty-nine patients underwent DES implantation and 38 LIMA grafting. Primary endpoints were the occurrence of major adverse cardiac events, defined as death, myocardial infarction, and target vessel revascularisation. Secondary endpoints included the length of stay in hospital, in-hospital complications, and the recurrence of chest pain.

Results: More in-hospital complications were observed in the CABG group than in the DES group. The mean duration of hospitalisation after CABG was 7.76 ± 2.82 days vs. 1.17 ± 1.15 days after DES. The mean follow-up period was 19.7 ± 6.3 months for the DES group and 19.7 ± 7.4 months for the surgical group. The incidence of major adverse cardiac events was similar in the two groups. There were two re-interventions in the DES group and none in the surgical group. Recurrent angina occurred in 2 patients in the DES group and 3 patients in the CABG group.

Conclusions: The present study demonstrates that patients with diabetes mellitus, chronic stable angina, and single vessel disease in the pLAD have an excellent long-term outcome with both DES implantation and LIMA anastomosis. The surgical approach, however, was associated with more in-hospital complications and a longer hospitalisation.

Percutaneous coronary intervention (PCI) with stent implantation and coronary artery bypass grafting (CABG) with the use of the left internal mammary artery (LIMA) are equally ac-

ceptable options for the treatment of lesions located in the proximal segment of the left anterior descending artery (pLAD). However, both surgical and percutaneous coronary revascularisation procedures are

associated with a less favourable outcome in diabetic patients compared with non-diabetics.¹⁻³ This is mainly due to the increased perioperative mortality, more aggressive form of atherosclerotic disease, faster occlusion of the grafts and higher restenosis rates observed in patients with diabetes mellitus.¹⁻³

Previous studies comparing bare metal stent implantation and CABG in diabetic patients with multi-vessel coronary artery disease showed that patients treated with stenting had significantly worse event-free survival than those treated with CABG, due to the higher need for repeat revascularisation in the PCI group.⁴⁻⁵ Drug-eluting stents (DES) have significantly reduced both clinical and angiographic restenosis, leading to a remarkable decrease in revascularisation procedures.⁶⁻¹² These encouraging results have also been demonstrated in patients suffering from diabetes mellitus.^{13,14} However, the majority of the trials included patients with multi-vessel disease and chronic stable angina or acute coronary syndromes.

The aim of the present study was to compare the clinical outcome of PCI with DES versus bypass surgery with LIMA grafting in patients with chronic stable angina and diabetes mellitus who had an isolated pLAD stenosis.

Methods

Study population

In the study we included patients suffering from diabetes mellitus (type II non-insulin-dependent) and chronic stable angina, who had an isolated significant lesion (>75%) in the pLAD, between the ostium and the first diagonal branch. Patients with lesions in the first diagonal branch, total occlusion of the LAD, or multi-vessel coronary artery disease were excluded from our study. Patients with acute coronary syndromes, a myocardial infarction during the last month, or a low ejection fraction (EF <30%) were also excluded. All patients were treated either with PCI in the first author's centre (April 2004 until April 2006), or surgically in one of four different cardiovascular surgical departments (January 2001 until November 2005).

During the study period a total of 314 patients with diabetes mellitus underwent revascularisation, 191 by PCI with DES and 123 with CABG. Of these, 77 consecutive patients who satisfied the above criteria were finally analysed: 39 underwent PCI with DES implantation and 38 patients underwent CABG with LIMA grafting.

Written informed consent to the revascularisation procedure was obtained from each patient.

Angiographic analysis

Quantitative coronary angiography was performed using a computer-based TCS system (Mendron, Tel-Aviv, Israel). The projection used for angiographic analysis was the 'worst' view. Lesions were characterised according to the modified American College of Cardiology/American Heart Association classification. To specify the grade of stenosis as a percentage, we compared the critical portion of stenosis with the lumen of the normal vessel, proximal and distal to the stenosis area, as a reference. Restenosis was defined as stenosis of more than 50% of the luminal diameter. The angiographic analysis was performed during the baseline coronary angiography for both study groups.

Percutaneous coronary intervention

All patients scheduled for PCI received 100 mg of aspirin and 75 mg clopidogrel once a day for a minimum of 5 days before the intervention. PCI was performed by standard techniques and sirolimus-eluting stents (Cypher stent, Cordis Johnson & Johnson Medical Company, Waterloo Office Park), paclitaxel-eluting stents (Taxus, Boston Scientific Corp., Natick, Massachusetts, USA) or zotarolimus-eluting stents (Endeavor, Medtronic, Santa Rosa, CA, USA) were used. The type of DES used was left to the operator's discretion. During the intervention all patients received 70 units/kg bolus IV of heparin. Pre-dilatation of the target lesion and administration of platelet glycoprotein IIb/IIIa inhibitors for 24 hours after the intervention were also at the operator's discretion. By protocol in our department the target lesion is scheduled to be covered by a single DES. In cases where additional DES are required, then by protocol the same type of DES was implanted. Combined antiplatelet treatment was continued for at least 6 months after PCI.

Coronary artery bypass graft surgery

All patients referred for surgical revascularisation were treated only with LIMA grafting. The treatment after hospital discharge included aspirin in all patients, in addition to the remaining pharmacological treatment, which was left to the referring physician's discretion.

Follow up

As the follow-up period was longer in the surgical arm, the follow-up period of the PCI group was used for reference. Clinical follow up was performed in both groups of patients by telephone (n=55, 71.4%) or by visits to our department (n=22, 28.5%). The primary endpoint was the occurrence of any of the following major adverse cardiac events (MACE): cardiac and non-cardiac death, myocardial infarction, and target vessel revascularisation, either surgical or percutaneous. In case of MACE, the time interval between intervention and occurrence was recorded. Secondary endpoints included the length of hospital stay after the intervention, peri-procedural and in-hospital complications, and the recurrence of chest pain. For chest pain evaluation specific details were noted, including the time of reappearance; rest or effort pain; the characteristics of the pain, such as the frequency, the intensity, the duration, and the conditions under which the pain was relieved, the response to rest or to the sublingual administration of nitroglycerine.

Statistical analysis

Data for categorical variables are expressed as the number and the percentage of patients. For continuous variables, data are expressed as mean \pm SD and were compared with the unpaired Student's t-test. Fisher's exact test or a chi-square test was used for the comparison of categorical variables. Event rates were estimated by the Kaplan-Meier method and compared by means of the log-rank test. A p-value <0.05 was considered significant. SPSS software (version 11.0) was used for the analyses (SPSS, Chicago, IL, USA).

Results

The baseline demographic characteristics of the study population were similar in the two groups, as shown in Table 1. The baseline angiographic characteristics are given in Table 2. In the DES group the mean number of stents implanted was 1.13 ± 0.3 stents per patient. The mean stent length was 19.17 ± 3.22 mm and the mean stent diameter was 2.98 ± 0.25 mm.

Table 1. Demographic characteristics of patients undergoing percutaneous coronary intervention (PCI) with implantation of drug-eluting stents (DES) or coronary artery bypass grafting (CABG).

	DES group n=39	CABG group n=38	p
Age	59.43 \pm 13.11	61.28 \pm 9.67	0.48
Men	31 (79.48%)	29 (76.31%)	0.79
Hypertension	25 (64.10%)	23 (60.52%)	0.81
Smoking	16 (41.02%)	17 (44.73%)	0.99
Hypercholesterolaemia	18 (46.15%)	23 (60.53%)	0.26
Family history of CAD	16 (41.02%)	24 (63.15%)	0.06
Mean LVEF	48.3 \pm 6.8	48.6 \pm 7.8	0.89
Previous MI	9 (23.07%)	8 (21.05%)	0.99

CAD – coronary artery disease; LVEF – left ventricular ejection fraction; MI – myocardial infarction.

Table 2. Angiographic characteristics.

	DES group n=39	CABG group n=38	p
Lesion classification:			
A	8 (20.51%)	12 (31.57%)	0.30
B1	28 (71.79%)	23 (60.52%)	0.34
B2	3 (7.69%)	2 (5.26%)	0.99
C	0 (0%)	1 (2.63%)	0.49
Mean number of stents	1.13 \pm 0.3		
Mean stent length (mm)	19.17 \pm 3.22		
Mean stent diameter (mm)	2.98 \pm 0.25		
Mean inflation pressure (atm)	16.51 \pm 3.14		
Taxus stent	17 (43.59%)		
Cypher stent	14 (35.89%)		
Endeavor stent	8 (20.51%)		

Abbreviations as in Table 1.

The majority of patients (n=17, 43.59%) received paclitaxel-eluting stents. Sirolimus-eluting stents were used in 14 patients (35.89%) and zotarolimus-eluting stents were implanted in 8 patients (20.51%).

In-hospital outcome

There was no occurrence of MACE during the in-hospital stay in either group. However, more complications were observed in the surgical arm. Nine patients (23.68%) in the surgical cohort experienced postoperative complications versus 1 (2.56%) in the DES group ($p < 0.01$, Table 3). Specifically, 8 patients treated surgically had pleural effusion and one had a new onset of atrial fibrillation. In the PCI group, one patient had periprocedural ventricular fibrillation which was successfully cardioverted. The mean duration of hospitalisation after CABG was 7.76 ± 2.82 days versus 1.17 ± 1.15 days after PCI ($p < 0.0001$, Table 3).

Long-term follow up

The mean follow-up period was 19.7 ± 6.3 months for the DES group and 19.7 ± 7.4 months for the surgical group. Event-free survival was similar in the two groups: in the DES group 93% of patients were event-free versus 97% of the CABG group ($p = 0.20$, Table 4 and Figure 1). In the DES group there was one non-cardiac death due to cancer 8 months post-intervention. There was one myocardial infarction in the surgical group, two months post-operatively. There was no statistically significant difference regarding the target vessel revascularisation rate. There were 2 (5.12%) re-interventions in the DES group and none in the surgical group ($p = 0.49$). The two patients (5.12%) in the DES group required new a PCI due to restenosis at 5 months and

12 months. Recurrent angina occurred in 2 patients (5.12%) in the DES group, who were treated with a new PCI, and in 3 patients (7.89%) in the surgical group ($p = 0.67$), who were treated only medically since new angiography was not performed (Table 4).

Discussion

The in-hospital and the two-year clinical outcomes were similar for the two methods. However, the surgical approach was associated with more in-hospital complications and longer hospitalisation. The results of the present study demonstrate that patients with diabetes mellitus, chronic stable angina and single vessel disease in the pLAD can be treated safely and effectively either with DES implantation or surgically with LIMA.

Several reports of PCI with bare metal stents have demonstrated a higher incidence of target vessel revascularisation in patients with diabetes mellitus.¹⁵⁻²¹ Previous studies comparing angioplasty or bare metal stent implantation with surgical revascularisation showed that diabetics with multi-vessel coronary artery disease had a better outcome with CABG.²²⁻²⁸ More specifically, the Arterial Revascularization Therapy Study I (ARTS I) showed that, in the subgroup of diabetic patients, event-free survival was lower in the PCI arm compared with the surgical arm, as a result of the higher need for repeat revascularisation in the PCI group.^{4,5}

Large clinical trials have shown that DES have significantly reduced angiographic and clinical restenosis.^{6-10,29,30} Sub-analyses from the SIRIUS and TAXUS trials revealed that the first generation of DES significantly improved event-free survival compared with bare metal stents in patients with stenosis in the LAD. More specifically, in the sub-analysis of the

Table 3. In-hospital clinical outcomes.

	DES group n=39	CABG group n=38	p
Death	0 (0%)	0 (0%)	1.00
MI	0 (0%)	0 (0%)	1.00
Target vessel revascularisation:			
PCI	0 (0%)	0 (0%)	1.00
CABG	0 (0%)	0 (0%)	1.00
In-hospital complications	1 (2.56%)	9 (23.68%)	0.007
Length of hospital stay (days)	1.17 ± 1.15	7.76 ± 2.82	0.01

Abbreviations as in Table 1.

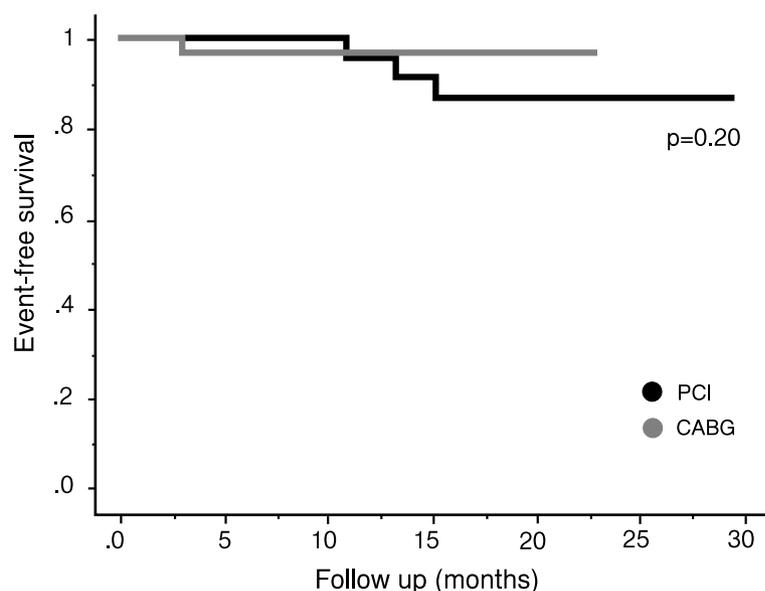


Figure 1. Freedom from major adverse cardiac events (MACE) after percutaneous coronary intervention (PCI) with implantation of a drug-eluting stent, and after coronary artery bypass grafting (CABG). The curves do not diverge and thus there is no statistical difference between the 2 groups ($p=0.20$).

Table 4. Endpoints during clinical follow up.

	DES group n=39	CABG group n=38	p
Death:			
Non-cardiac	1 (2.56%)	0 (0.0%)	0.99
Cardiac	1 (2.56%)	0 (0.0%)	0.99
Myocardial infarction	0 (0.0%)	0 (0.0%)	1.00
Target vessel revascularisation:			
PCI	2 (5.12%)	1 (2.63%)	0.49
CABG	2 (5.12%)	0 (0.0%)	0.49
MACE	0 (0.0%)	0 (0.0%)	1.00
Angina	3 (7.69%)	1 (2.63%)	0.61
	2 (5.12%)	3 (7.89%)	0.65

MACE – major adverse cardiac events. Other abbreviations as in Table 1.

TAXUS IV trial, which included 318 patients with diabetes mellitus, a 44% lower incidence of MACE was observed in the paclitaxel-eluting stent group compared to BMS, mainly due to a reduction of the target lesion revascularisation rate by 65%. Similarly, in the SIRIUS trial 279 patients with diabetes mellitus were analysed: MACE were reduced in diabetic patients from 25% with bare metal stents to 9.2% with sirolimus-eluting stents.^{13,14} In our study the incidence of MACE at 2-year follow-up was less than 10% in the PCI cohort.

There are a limited number of studies comparing surgical revascularisation with DES implantation in patients with diabetes. The ARTS II trial, which included a sub-group of diabetic patients with multi-vessel coronary artery disease, compared stenting with sirolimus-eluting stent implantation and CABG.⁵ The study showed that the need for repeat revascularisation in this particular population was in favour of the surgically

treated patients. Similarly, two recently reported studies including patients with diabetes mellitus and multi-vessel coronary artery disease demonstrated that the long-term outcome was better in the surgical arm compared with the PCI arm because of the higher revascularisation rate in the latter group.^{31,32} These findings were confirmed in the Argentine Randomized Study of Coronary Angioplasty versus Coronary Bypass Surgery in Multi Vessel Disease (ERACI) III trial.³³ Although in these studies the majority of patients had multi-vessel disease, the impact of DES on restenosis in patients with diabetes mellitus seems favourable, possibly as a result of the potent anti-inflammatory effect of the compounds delivered locally at the target lesion.³⁴ Furthermore, patients with acute coronary syndromes were also included.

There are limited data comparing surgical treatment with the use of DES in patients with isolated

pLAD lesions. Hong et al compared PCI with DES versus minimally invasive direct coronary bypass grafting (MIDCAB) in patients with pLAD stenosis.³⁵ The implantation of DES was associated with a similar rate of MACE compared with CABG during the follow-up period. In contrast, Herz et al compared the efficacy of DES implantation in the LAD with off-pump bypass grafting.^{36,37} During an 18-month follow-up period the clinical outcome was better in the surgical group. Similar results were reported by Moshkovitz et al in a total of 232 patients.³⁸ However, in these studies the majority of patients included had multi-vessel disease and they also included patients suffering from acute coronary syndromes.

Conclusions

In our study there was no significant difference in the outcomes between the two groups during the follow-up period. However, this was a non-randomised, retrospective study. Moreover, there is growing evidence that DES may develop late thrombosis related to delayed endothelialisation or discontinuation of antiplatelet treatment.^{39,40} Therefore, large, prospective trials with a long follow-up will be required in order to determine the optimal therapeutic approach in chronic stable angina patients with diabetes mellitus and a single pLAD lesion.

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