

Revascularization of the Left Anterior Descending Artery with Drug-Eluting Stents: Comparison with Arterial Off-Pump Surgery

Itzhak Herz,¹ Raphael Mohr,² Yaron Moshkovitz,³ Yanai Ben-Gal,² Sharon Z Adam,² Roni Braunstein,² Gideon Uretzky, MD²

Departments of ¹Cardiology and ²Thoracic and Cardiovascular Surgery, The Tel Aviv Sourasky Medical Center and The Sackler Faculty of Medicine, Tel Aviv University, and ³The Catheterization Laboratories, Assouta Medical Center, Israel

ABSTRACT

Background: This study compared early results of left anterior descending artery (LAD) stenting using drug-eluting stents (Cypher) with off-pump bilateral internal thoracic arterial (BITA) grafting.

Methods: From June 2002 to June 2003, 200 consecutive patients underwent myocardial revascularization of the LAD territory, 100 by Cypher and 100 by BITA. The 2 groups were similar; however, left main disease and triple-vessel disease (20% and 75% versus 2% and 28%), age >70 (36% versus 17%) and intraaortic balloon pump (7% versus 0%) were more prevalent in the BITA group, and prior percutaneous coronary angioplasty to the LAD was more prevalent in the Cypher group (28% versus 16%).

Results: The number of coronary vessels treated per patient in the BITA group was higher (2.7 versus 1.45, $P < .01$). Thirty-day mortality was 1% in the BITA group and 0% in the Cypher group. Mean follow-up was 12 months. There was 1 late death in each group. Angina returned in 32% of the Cypher group and in 1% of the BITA group. There were 9 reinterventions in the Cypher group: 7 coronary angioplasties (including 2 to the LAD) and 2 surgical interventions. There was neither recurrent angina nor reintervention in the surgical group.

Conclusions: Despite a higher risk profile of patients treated with BITA, their clinical outcome is better. A longer and more complete angiographic follow-up is required to determine the role of drug-eluting stents in LAD revascularization.

INTRODUCTION

Significant stenosis of the left anterior descending artery (LAD), particularly when the proximal segment of the vessel is involved, is associated with adverse cardiac prognosis [Klein

1986, Hannan 1999]. Surgical revascularization of the LAD with the left internal thoracic artery (ITA) is still the only proven method of improving survival in patients with multivessel coronary artery disease and LAD stenosis [Buxton 1998, Lytle 2002]. Long-term survival and freedom from myocardial infarction (MI), recurrent angina, percutaneous interventions (PCI), and repeat operations may further be reduced by the use of bilateral ITA (BITA) [Kouchoukos 1990, Sofer 1999].

A proximal lesion in the LAD is a challenging area for PCI because of the concern for injury to the left main artery or occlusion of major side branches [Kimura 1996]. Therefore coronary artery bypass grafting (CABG) is often considered and sometimes performed as a therapeutic option for the treatment of this lesion, even in patients with single-vessel disease involving the LAD.

Several reports of nonrandomized studies comparing percutaneous coronary angioplasty (PTCA) and CABG have shown a trend to improved survival with CABG in patients with multiple vessel disease and proximal LAD stenosis [Jones 1996, Hannan 1999, Smith 2001]. Revascularization for isolated LAD disease using PTCA stent or left ITA to LAD resulted in a similar occurrence of adverse events and mortality and similar actuarial 2-year survival. However, repeat procedures were required less often after left ITA to the LAD (30%, 24%, for PTCA and stents respectively, vs. 5% for left ITA to the LAD, ($P < .001$) [O'Keefe 1999].

In a later report with more liberal use of stents for the proximal LAD, the only advantage of left ITA to the LAD was the lower rate of reinterventions during the 42-month follow-up period [Rodriguez 2003].

Significant reduction of restenosis and reintervention was recently reported with the introduction of drug-eluting stents (DES) [Moses 2003]. Most patients with proximal LAD stenosis referred for CABG in our center undergo off-pump coronary artery bypass (OPCAB) surgery. In many of these patients we use skeletonized BITA. We therefore decided to compare our initial clinical results with DES to the LAD to those of BITA grafting using OPCAB.

MATERIALS AND METHODS

Between June 2002 and June 2003, 100 consecutive patients underwent OPCAB with BITA. These patients were compared to 100 of 130 patients who underwent PCI with

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Address correspondence and reprint requests to: Itzhak Herz, MD, Department of Cardiology, The Tel Aviv Sourasky Medical Center, 6 Weizmann Street, Tel Aviv 64239, Israel; 972-3-6973207; fax: 972-3-6974808 (e-mail: isach@tasmc.health.gov.il).

LAD revascularization by means of Sirolimus drug-eluting stents (Cypher) and consented to participate in the follow-up study. Preoperative characteristics of patients in both groups are depicted in Table 1.

In the PCi group, stent implantation was performed after balloon angioplasty dilatation. All patients received aspirin (325 mg daily) before and after the procedure, and clopidogrel (a loading dose of 300 mg the day before the procedure and 75 mg daily for 3 months thereafter). During the procedure all patients were treated intravenously with heparin. Platelet glycoprotein IIb/IIIa inhibitors (abciximab) were used in only 8 patients in the PCi group. In most patients, only 1 Cypher was used for the LAD. However, more than 1 stent was used if required (long lesion, dissection, bifurcation, etc). DES, bare-stents, or PTCA were used for non-LAD lesions. Acute MI (within the previous 48 hours), poor ejection fraction (<25%), left main disease, calcification or thrombus within the LAD, long lesions (>30 mm), and bifurcation lesions were major criteria for exclusion of patients from the group treated with stents to the LAD. On the other hand, patients with diabetes or ostial LAD lesions were not excluded.

In the BITA group, all internal thoracic arteries were dissected as skeletonized vessels. In order to achieve left-sided (LAD + circumflex) arterial revascularization, we used the right ITA as an in situ or a composite T-graft.

Right system (PDA) revascularization was performed in 31 patients with saphenous vein grafts, in 4 patients with the distal end of the right ITA, and in 2 patients with the radial artery.

To decrease the risk of spasm of the arterial grafts, we treated all BITA patients with a high-dose intravenous infu-

Table 2. Number of Vessels Treated (Grafts or Stents)*

No. of Vessels Treated	BITA (n = 100)	Cypher (n = 100)	P
1	0	69	.000
2	44	20	.0027
3 or more	56	11	.000

*BITA indicates bilateral internal thoracic artery.

sion of isosorbide dinitrate (Isoket, 4-20 mg/h) during the first 24 to 48 postoperative hours [Gurevitch 1997]. Systolic blood pressure was maintained above 100 to 120 mm Hg. From the second postoperative day, all radial artery patients were treated postoperatively with calcium-channel blocker (diltiazem 90-180 mg/day orally).

Statistical Analysis

Data are expressed as mean $\pm$ SD or proportions, as appropriate. The χ^2 test and Fisher exact test were used to compare discrete variables. Multivariable regression analysis was used to evaluate risk factors for early return of angina and reintervention.

RESULTS

Results in the 2 groups were similar. However, left main disease, triple-vessel disease, and the use of intraaortic balloon pump were more prevalent in the BITA group. More patients in the BITA group were older than 70, and more patients in the Cypher group underwent prior PTCA to the LAD (Table 1).

The average number of coronary vessels treated in the BITA group was higher (2.7 versus 1.45 in the BITA and Cypher groups, respectively, $P < .01$). However, more patients in the Cypher group received only 1 stent, and more in the BITA group had revascularization of 3 vessels (Table 2). Thirty-day mortality was 1% in the BITA group and 0% in the Cypher group. Mean follow-up was 12 months. There was 1 late death in each group. Angina returned in 32 patients (32%) of the Cypher group compared to 1 patient (1%) in the BITA group ($P < .001$). There were 9 reinterventions in the Cypher group: 7 coronary angioplasties (including 2 to the LAD) and 2 surgical interventions. There were no reinterventions in the surgical group ($P < .001$, Cypher versus BITA).

In order to determine whether the difference between groups in recurrent angina and reinterventions was affected by the difference in preoperative characteristics or the number of vessels treated, we performed multivariable analysis with patient groups (PCi or BITA) as an independent variable. We first included the variables to be controlled, the number of vessels treated, prior intra-aortic balloon pump, left-main and triple-vessel disease, and prior PTCA to the LAD, and then the occurrence of recurrent angina or reintervention.

The regression model showed that after controlling for the above risk factors, the only independent predictor for recurrent angina was treatment with PCi (Cypher group, $P = .000$). Similarly, treatment with PCi was also the only significant predictor for reintervention ($P = .002$).

Table 1. Patient Characteristics*

	BITA (n = 100)	Cypher (n = 100)	P
Age >70 y	36	17	.002
Female	15	16	
Diabetes	28	30	
Hypertension	58	56	
Chronic obstructive pulmonary disease	3	5	
Chronic renal failure	5	3	
Peripheral vascular disease	18	10	
Old myocardial infarct	46	34	
Ejection fraction < 35%	5	2	
Acute myocardial infarct (7 days)	8	5	
Prior intraaortic balloon pump	7	0	.023
Prior PTCA	33	37	
Prior LAD PTCA	16	28	.04
Emergency	10	2	
Redo operation	2	2	
Congestive heart failure	7	1	.03
Left main	20	2	.0005
1-Vessel disease	0	36	.000
2-Vessel disease	25	35	
3-Vessel disease	75	28	.000

*BITA indicates bilateral internal thoracic artery; PTCA, percutaneous coronary angioplasty; LAD, left anterior descending artery.

DISCUSSION

This study compares early and midterm results of Cypher to the LAD to those of OPCAB with BITA, including left or right ITA to the LAD.

After 12 months of follow-up, which is long enough for the development of in-stent restenosis [13], survival was similar. However, a significant portion of the Cypher group (32%) experienced early return of angina, and 9% required reintervention. The incidence rates of recurrent angina and reintervention were significantly higher than those of the BITA group, and multivariable analysis showed that the only independent predictor of recurrent angina and reintervention was the revascularization technique used (ie, the use of PCI).

The surgical group of 100 consecutive BITA patients was selected from a larger group of 256 patients who underwent OPCAB performed during the study period. We decided to include only BITA patients, because vein graft failure is a major cause of recurrent angina, late MI, and the need for reinterventions [Weintraub 1994]. Revascularization with BITA was proved to be better than operations with single ITA with regard to survival and reduced rate of late adverse cardiovascular events [Taggart 2001]. The zero recurrence of angina and reintervention in this report is probably related to the excellent reported patency rate of the ITA grafts [Calafiore 2001].

Despite the above unfavorable observations in the PCI group, our study does not contradict previous reports suggesting a decreased restenosis rate with DES [Sousa 2001, Morice 2002, Moses 2003]. Only 2 of the 9 reinterventions were performed in the LAD territory (after Cypher implantation), 1 in a patient who was treated with 2 Cyphers to the LAD for in-stent restenosis, and the other in a patient who developed subacute thrombosis after Cypher implantation.

Reintervention in nontreated vessels, together with the fact that more patients in the Cypher group underwent revascularization of only 1 vessel and more in the BITA group had revascularization of 3 vessels, suggest that a major cause of recurrent angina and reintervention in the Cypher group was incomplete revascularization rather than early failure of the DES.

In conclusion, despite the higher risk profile of patients with BITA, their clinical outcome was better. Early results of Cypher to the LAD are encouraging, with an acceptable reintervention rate in the LAD territory. Larger and more complete angiographic follow-up is required to determine the role of DES in LAD revascularization.

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