

Six Months Clinical Follow up of Percutaneous Coronary Intervention in Diabetic and Non Diabetic Patients in Southern Iran

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Citation

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Abstract

Background:

Diabetes mellitus is a life threatening disease accompanied by several micro- and macrovascular complications, including coronary artery disease. Several modalities are available for interventional revascularization of coronary artery lesions, but their efficacy in diabetic patients has not been studied separately. We aimed to evaluate the effect of drug eluting stents in diabetic patients.

Methods:

Two hundred patients entered this study and were followed up for at least six months after their stenting. Clinical and angiographic outcome was compared in diabetic and non-diabetic patients.

Results:

Single vessel disease was the most common form in both groups, and LAD was the most common site of stenting. The majority of patients had a type C lesion. We observed no difference in the measured outcomes between the two arms of the study.

Conclusion:

Our findings suggest that DES can be used as an alternative for bypass surgery in diabetic patients with coronary artery diseases.

INTRODUCTION

Diabetes mellitus (DM) is a chronic and life threatening disease that is induced because of low production of insulin or insensitivity to this substance (1). It is a prevalent disorder and Canadian Community Health Survey (CCHS) had reported DM in 4.9% of Canadian population aged 12 years or more in 2005 (2).

Diabetes has a lot of complications; two main categories of these complications are macrovascular problems (e.g. stroke and heart disease) and micro vascular complications (e.g. blindness, renal failure and limb amputation) (2). Among macrovascular complications, cardiovascular diseases are associated with a large amount of mortality and morbidity (3). Both type I and II of DM are risk factors for coronary artery disease (4) but type I patients presents cardiovascular diseases in younger ages than type II (5).

Macrovascular complications lead to atherosclerosis in

coronary, cerebral and peripheral arteries which cause 80% mortality and 75% hospitalization in diabetic patients (3;6). In fact, diabetes alters the function of vascular endothelium, smooth muscle cells and platelets thus aggravating atherogenesis (7).

Coronary artery lesions are classified regarding their complexity into three major types, according to the classification by American College of Cardiology (ACC) and American Heart Association (AHA) (8). Type A lesions are less than 10 mm in length, concentric, non-angulated, and readily accessible and have a smooth contour, little or no calcification and no thrombus; these lesions are accompanied by a high success rate (>85%) of surgical treatment. Type B lesions are longer (10-20 mm), tubular, eccentric, moderately angulated (45-90 degrees) and with an irregular contour. They may be moderately to heavily calcified, may have bifurcations or may have some thrombus present, and their surgical treatment yields a lower success

rate (60-85%). Type C lesions are large and diffuse (>20 mm in length), extremely angulated (more than 90 degrees) and may arise side branches which are hard to protect. Extensive tortuosity of the proximal segment is common in these lesions and there is low success in their treatment (<60%). Several surgical techniques are available for treatment of the three groups of lesions.

Surgical revascularization and percutaneous coronary interventions (PCI) with coronary stents are extensively performed for diabetic patients in the recent decades, although the outcome of these procedures is unfavorable in diabetic patients (9; 10). Several previous studies have shown that angioplasty with drug eluting stents (DES) such as sirolimus eluting stents and paclitaxel eluting stents are more effective in comparison with bare metal stents and reduce the risk of restenosis and the need for repeating revascularization (9;11).

Because of high prevalence of restenosis in bare metal stents specifically in diabetic patients, we examined the impact of DES in reducing the chance of restenosis in a six months follow up of our patients after surgery.

MATERIALS AND METHODS

Between November 2004 and November 2006, we studied two hundred patients with coronary artery diseases (CAD), including 95 diabetic patients and 105 non-diabetic patients, who had undergone angiography and angioplasty with placement of DES. Patients were followed clinically for at least six months for any sign of possible coronary incidents.

All the patients had received at least 300-600 mg antiplatelet drug clopidogrel before angioplasty and stenting. After stenting, every patient was admitted in hospital for 24 hours, and emergently underwent angiography if they had chest pain or ECG changes such as ST-segment elevation or depression. Patients who didn't have chest pain and ECG changes were discharged with aspirin (80-325 mg/daily) and clopidogrel (75 mg/daily) for at least six months. Anti-ischemic drugs including beta-blockers, nitroglycerin, diltiazem, and statins were administered as well as anti-diabetics based on the patients requirements.

The first visit after angioplasty and stenting in which data was collected happened two weeks after the surgery and was followed by monthly visits. In the meantime, however, physicians were accessible to patients by phone, just in case something emergent would happen. This would ensure that

all relevant information was reported by the patients. Patients were further tested with cardiac scan and exercise test if they remained asymptomatic and showed no ECG changes during follow up. If they became symptomatic or showed ECG changes indicative of ischemia, coronary angiography was performed.

Cardiovascular accidents of our interest are listed in table 1. Table 2 lists conditions which were treated as an indication for angiography in asymptomatic patients. Patients were considered as candidates for repeated PCI or coronary artery bypass grafting (CABG) if a thrombosis was observed during angiography of stent location or new atherosclerotic lesions were seen in other vessels.

RESULTS

We had 200 patients including 95 in diabetic group and 105 in non-diabetic arm. Eighty-nine were female and 111 were male. Baseline characteristics of the participants are summarized in table 3. The majority of diabetic participants were females, while the majority of non-diabetic subjects were males. Hypertension and hyperlipoproteinemia were significantly more prevalent in the diabetic group, while smoking was less common in this group. Single vessel disease was the most prevalent in both groups (80% in diabetics and 71.4% in non-diabetics), followed by two-vessel disease (16.9% in diabetics and 25.7% in non-diabetics). Three-vessel disease was rare in both groups (approximately 2%).

Table 4 also describes the frequency of lesion types in each of the study groups. Although the more complex lesions (Type B2 and C) constitute a larger proportion of lesions in diabetic group, it does not reach statistical significance in terms of lesion type and characteristics ($p=0.209$). We used stents sized between 2.5-3.5 mm in diabetic group and 2.25-3.5 mm in non-diabetic group.

Table 5 summarizes the incidence of measured outcomes in the two groups. Target vessel failure is defined as occurrence of cardiac death, MI or revascularization due to ischemia. None of these outcome measures were different in the two groups.

Figure 1

Table 1 – Diagnostic measures for cardiovascular accidents

<ul style="list-style-type: none"> • Occurrence of symptoms during exercise test • Decrease in blood pressure during exercise test and/or systolic blood pressure below 120 mmHg • ST-segment depression equal or more than 2 mm and/or ST-segment depression in more than 5 lead and/or ST-segment depression persistent for 5 minutes after stopping the test • ST-segment elevation during exercise test • Chest pain starting in first steps of exercise test (i.e. low exercise work load) • Sustained ventricular tachycardia (VT), symptomatic ventricular arrhythmia and/or non-sustained polymorphic VT with successful resuscitation
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Figure 2

Table 2 – Indications for angiography in asymptomatic patients.

<ul style="list-style-type: none"> • Death because of coronary artery disease during six months after stenting • Symptoms of acute infarction defined as presence of one or more of these conditions: <ul style="list-style-type: none"> - ST-segment elevation - New Q-wave - 3-5 fold increase of serum creatine kinase MB (CKMB) level - Positive troponin-I test - New onset changes of ECG such as T-wave inversion in addition to a 3-5 fold increase of serum CKMB level • Symptoms of restenosis in operated vessels • Positive exercise test or positive result from cardiac scan with dipyridamole or thallium
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Figure 3

Table 3 – Baseline characteristics of the study population.

		Diabetic	Non-diabetic
Gender	Male	36	75
	Female	59	30
Mean age		57.12	55.46
Hypertension **		56	28
Hyperlipoproteinemia *		66	58
Smoker **		33	64
Target vessel	LAD	65	76
	RCA	15	23
	LCX	21	18
	Other	3	4

Abbreviations: LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery.

* p-value < 0.05
 ** p-value < 0.001

Figure 4

Table 4 – Lesion characteristics in both groups.

		Diabetic no (%)	Non-diabetic no (%)
Lesion type	A	1(2.5)	9(15.51)
	B1	7(17.5)	9(15.51)
	B2	11(27.5)	12(20.69)
	C	21(52.5)	28(48.29)

Figure 5

Table 5 – Incidence of cardiovascular events in the two arms of the study.

	Diabetic	Non-diabetic	P-value
Positive cardiac scan or exercise test	5	8	0.61
Restenosis in angiography	4	3	0.52
Acute or subacute MI	1	2	0.68
Late MI	2	1	0.45
CABG	3	2	0.50
Repeated PCI	1	0	0.27
Cardiac death	1	1	0.89
TVF	8	6	0.35

Abbreviations: MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary interventions; TVF, target vessel failure.

DISCUSSION

Several studies have evaluated the success rate of DES in management of coronary artery lesions, including TAXUS II, TAXUS IV, TAXUS VI and E-Sirius (12-15). Diabetic patients composed variable proportions of their study populations (11-31%). In comparison, 47.5% of our study population was diabetic patients. We observed a similar rate of cardiac death in our study.

Stone GW et al have shown that DES is accompanied with a lower risk of clinical and angiographic restenosis in nine month follow up (16). With subgroup analysis, they show that the risk of restenosis is lower in diabetic patients requiring oral medication or insulin therapy compared to the rest of diabetic patients. These findings are strongly supported by the evidence provided from TAXUS IV study (13). In another randomized controlled trial comparing sirolimus-eluting stents with standard (bare metal) stents, it was noted that none of the diabetic patients developed restenosis (17). In the same way restenosis occurred just as frequently in the two arms of our study. Clinically based, four out of 95 diabetic patients in comparison to 3 in 105 non-diabetics developed in stent restenosis (4.2% vs. 2.85 % P value = 0.52). In our study, restenosis was more common in diabetics than non diabetics, although it does not reach

statistical significance, probably due to low number of patients. Some studies suggest that increased rates of restenosis may result from an increased intimal proliferative response in diabetic patients, although the mechanisms are not clear (3). Other studies have observed that the relative reduction in the risk of restenosis with stents is independent of diabetes mellitus status (16). In RAVEL (RANdomized VELOCITY artery Lesion) study, the risk of restenosis after active stenting was 0% in 5-year follow up (18).

Stent thrombosis is well defined by the ARC committee (19). Iijima et al reported that stent thrombosis occurs more frequently in non-diabetic patients (9). They suggested that possible underlying mechanisms include increased intimal hyperplasia, higher coagulability, a higher inflammatory response, endothelial dysfunction, and co morbid conditions. In our study, 3 out of 105 non diabetics and 2 out of 95 diabetics had SCD and acute/ sub acute MI indicative of stent thrombosis.

One of the limitations of our study is the low number of patients with three-vessel coronary artery lesions. Further investigation should be targeted on the effectiveness of DES in this group of patients.

Drobinski and Le Feuvre stated in their 2005 article that the evidence body at that time was not strong enough to support the use of DES instead of surgical bypass of coronary arteries for diabetic patients with associated diseases. (20) Based on our observations, we conclude that PCI can be used as an alternative for CABG for diabetic patients with coronary artery problems. We believe the results of the ongoing FREEDOM trial can enlighten this situation. (21) This study, which is started in 2004 and is due in 2011, aims to compare 5-year mortality rates in diabetic individuals with multi vessel coronary artery disease who undergo either CABG or percutaneous coronary stenting.

We deem that preventive measures such as appropriate control of diabetes and maintaining an HbA_{1c} level of less than 7% should be applied to lower the complications of this disease. So we think that if in diabetic patients, single vessel disease is present, treated with a DES with the similar size of stent diameters such as ours and clopidogrel is used for at least 6 months, MACE is equal to non diabetics.

STUDY LIMITATIONS

Low number of patients is the most limitation in our study for interpretations and judgments.

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