

# The Impact of Diabetes on Early and Midterm Outcome of Patients Undergoing Coronary Artery Bypass Grafting Surgery

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**Background:** Diabetic patients constitute about 25% of patients undergoing coronary artery bypass graft surgery (CABG). The impact of diabetes on the results of this operation, especially in Asian patients is not well understood. The present study aims to evaluate the effect of this important risk factor on the early and midterm outcome following CABG.

**Methods:** This study was performed in Shahid Madani Heart Hospital, Tabriz, Iran from April 1998 to April 2003. Considering our inclusion and exclusion criteria, 1269 patients available for follow up were enrolled and evaluated for their early (30 days) and midterm mortality.

**Results:** Diabetic patients constituted 332 (26.2%) of our patients. Female gender, hypertension, hyperlipidemia and peripheral arterial disease (PAD) were more prevalent in diabetics. Early mortality was not significantly different between two groups (6.6% in diabetics vs. 5% in non-diabetics,  $P=0.300$ ) and this was true for early cardiac death (6.3% in diabetics vs. 4.7% in nondiabetics,  $P=0.200$ ). However, in midterm follow up of  $4.1 \pm 1.6$  years, diabetic patients had significantly higher mortality (18.7% in diabetics vs. 11.2% in non-diabetics,  $P<0.001$ ). Also total mortality was significantly higher in diabetics (25.3% in diabetics vs. 16.2% in non-diabetics,  $P<0.001$ ). In univariate regression analyses diabetes was an independent risk factor for midterm mortality.

**Conclusion:** Diabetes may not be an independent risk factor for early death following CABG. However, it is an important predictor of midterm mortality.

**Keywords:** Coronary Artery Bypass, Diabetes Mellitus, Outcome

## Introduction

The incidence of diabetes is increasing markedly and the World Health Organization estimates that by 2025, about 5.4% of the world population (300 million people) will be diabetic.<sup>1</sup> It is a well-known risk factor for coronary artery disease and cardiovascular death.<sup>2</sup> The reported prevalence of diabetes among patients undergoing coronary artery bypass surgery (CABG) has been estimated to be 12-38%.<sup>3-5</sup> Coronary artery disease is more extensive, diffuse and distal with a rapidly progressive nature in diabetic compared with non-diabetic patients.<sup>6-8</sup>

Traditionally it has been accepted that patients with diabetes have poorer outcome than non-dia-

betics following CABG.<sup>9</sup> There is less controversy about the role of diabetes in increasing long-term mortality of patients undergoing CABG.<sup>3,9-12</sup> However, there are conflicting data about the early and midterm result of CABG in diabetic patients.<sup>9-15</sup> Considering the effect of ethnicity on atherosclerosis and coronary heart disease, and the fact that it should be regarded as a risk factor when assessing potential risks associated with any surgical or medical intervention,<sup>14,16,17</sup> we decided to evaluate the early and midterm survival of diabetic patients undergoing CABG in our hospital.

## Patients and Methods

Among 2151 patients undergoing CABG in Shahid Madani heart center from April 1998 to April 2003, a total of 1269 cases were eligible for follow up in this retrospective study. Hypertension was defined as blood pressure of  $\geq 140/90$ mmHg recorded at least two times or current antihypertensive therapy. Diabetes was defined as fasting plasma glucose

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of >126mg per 100ml for at least two measurements or current antidiabetic therapy according to the World Health Organization criteria. Hyperlipidemia was described as total cholesterol of >200mg per 100ml or a history of elevated serum total cholesterol during the previous 6 months resulting in lipid lowering agent prescription. Current smokers or those who had stopped smoking during previous 3 years were considered smokers. Peripheral arterial disease was applied to a history of intermittent claudication or lower extremity revascularization or the presence of peripheral occlusive disease during the performance of an abdominal aortography procedure. Patients with a history of ischemic stroke were classified as a separate group in the analyses. Patients with history of previous CABG, percutaneous coronary intervention, significant valvular heart disease needing intervention, those with emergency CABG and patients suffering from early post operation myocardial infarction (MI) in first 24 hours following CABG or those dying during surgery were excluded from the study as well as patients who had undergone off pump CABG because of their low number. The study included demographic data, risk factors, angiographic data, history of MI, heart failure, chronic obstructive lung disease which may affect early post operative course and cerebrovascular events (CVA). Early mortality was considered as death during first month after CABG and midterm mortality referred to death after first month with a mean follow up period of about  $4.1 \pm$

1.6 years. Death was either cardiac or noncardiac. Cardiac death was any mortality related to heart disease or sudden death and non-cardiac death was due to other causes.

### Statistical analysis

Statistical analysis was performed using SPSS for windows v.11.5 package (SPSS Inc; Chicago, IL). Comparing of continuous variables between the two study groups was done by 'independent samples t-test'. Stepwise logistic regression analysis was used to evaluate the possible role of variables which may affect the mortality rate. Categorical variables were analyzed by Chi-square or Fisher's exact tests as appropriate. A p value of  $\leq 0.05$  was considered significant.

### Results

Among 1269 patients with perfect profile and available for midterm follow up, 332 (26.2%) were diabetic and the remaining 937 (73.8%) were non-diabetics. Table 1 shows demographic and basic characteristics of these patients. Female gender, hypertension, hyperlipidemia and peripheral arterial disease were more prevalent among diabetics. There was a nonsignificant trend to higher rate of chronic renal failure in diabetics. Smoking was more prevalent in nondiabetic patients, but there was no significant difference in the prevalence of prior MI, stroke, chronic obstructive pulmonary disease (COPD) and atrial fibrillation between two

**Table 1.** Basic characteristics of patients with and without diabetes.

Characteristic	All patients (n=1269)	Diabetes (n=332)	Non-Diabetes (n=937)	P value
Age	56.8±9.2	58.6±8.4	56.2±9.8	0.010
Females	306(24.1%)	109(32.8%)	197(21%)	<0.001
Hypertension	609 (47%)	187 (56.3%)	422 (43.8%)	<0.001
Hyperlipidemia	649 (51.1%)	221 (66.6%)	428 (44.4%)	<0.001
Smoking	518 (39.9%)	109 (36.1%)	409 (42.4%)	<0.001
CRF	33 (2.5%)	12 (3.6%)	21 (2.17%)	0.226
Prior MI	540 (41.6%)	138 (41.6%)	402 (41.7%)	0.700
Prior stroke	2 (0.16%)	0 (0%)	2 (2.1%)	0.999
History of AF	15 (1.2%)	2 (0.6%)	13 (1.4%)	0.400
History of COPD	17 (1.3%)	1 (0.3%)	16 (1.7%)	0.060
PAD	45 (3.5%)	21 (6.3%)	24 (2.6%)	0.003
Ejection fraction	43±9.7	42±10.7	44±9.3	0.010
1-2 VD	310 (24.4%)	94(28.3%)	216 (23%)	0.060
3VD or LM stenosis	959 (75.6%)	238 (71.7%)	721 (77%)	
Use of LIMA	1187 (93.5%)	310 (93.4%)	877 (93.6%)	0.900

CRF: Chronic renal failure; MI: Myocardial infarction; AF: Atrial fibrillation; COPD: chronic obstructive pulmonary disease; PAD: peripheral arterial disease; 1-2VD, 1-2 vessel disease; 3VD: 3 vessel disease; LM: left main coronary artery; LIMA: left internal mammary artery.

**Table 2.** Early and midterm mortalities in patients with and without diabetes

	All patients (n=1269)	Diabetes (n=332)	Non-Diabetes (n=937)	P value
<b>Overall death</b>	236 (18.5%)	84 (25.3%)	152 (16.2%)	<0.001
<b>Early mortality</b>	69 (5.4%)	22 (6.6%)	47 (5.0%)	0.300
<b>Early Cardiac death</b>	65 (5.1%)	21 (6.3%)	44 (4.7%)	0.200
<b>Midterm mortality</b>	167 (13.2%)	62 (18.7%)	105 (11.2%)	<0.001
<b>Midterm Cardiac death*</b>	89/132 (67.4%)	35 /49 (71.4%)	54/83 (65.1%)	0.006

\* Data regarding midterm cardiac death were available for 132 patients; 49 in diabetic group and 83 without diabetes.

groups of diabetics and non-diabetics. Also mean left ventricular ejection fraction (EF) was mildly lower in diabetic patients. In more than 93% of all patients, left internal mammary artery was used as a graft regardless of the group (Table 1)

Overall survival after surgery and during follow up period was significantly lower in diabetics. During the first month after CABG and 24h after operation, 69 patients (5.4%) died. Cardiac mortality was the major cause of death in this period and constituted 94% of deaths or 65 (5.1%) patients (Table 2). There was no significant difference in this early mortality rate among those with and without diabetes. Excluding first post-operative month and during midterm follow up of  $4.1 \pm 1.6$  years, 167 deaths was reported which significantly was higher in diabetics. Midterm survival during this time was 88.8% in nondiabetics and 81.3% in diabetics ( $P=0.001$ ). Data regarding cardiac death in midterm follow up were available for 132 patients. Cardiac deaths constituted 35 (71.4%) in diabetic and 54(65.1%) in non- diabetic groups ( $P=0.006$ ). In stepwise logistic regression analysis, diabetes was not an independent predictor of early cardiac mortality; however, it was an independent predictor of midterm cardiac death.

## Discussion

The prevalence of diabetes is rising owing to an increasingly aged and obese population.<sup>18</sup> Arteriosclerosis is responsible for 80% of deaths in patients with DM.<sup>13</sup> The adverse impact of DM on the outcome of coronary artery disease patients is related to its atherosclerotic, pro-inflammatory, and pro-thrombotic effects.<sup>2</sup> However, the majority of such studies were carried out in western countries and limited information was available for the Asian population. In addition, the prevalence of DM in Asian CABG patients was consistently higher than that in Caucasians.<sup>14</sup>

There are conflicting data about the effect of diabetes on in-hospital mortality and morbidity following CABG.<sup>9-15</sup> According to our study and to several other reports,<sup>3,9,11,14,15</sup> one month mortality in patients with diabetes was not significantly different from those without diabetes. On the other hand,

in one of the largest studies from North America, Carson et al. showed significantly higher 30 day mortality and in-hospital morbidity among diabetic patients.<sup>13</sup> Another study by Thourani et al showed similar results.<sup>12</sup> Some of this increased risk may be related to higher non-cardiac risk profile of diabetic patients presenting with high prevalence of hypertension, chronic renal failure and peripheral arterial disease, especially cerebrovascular disorders, in this subgroup of patients.<sup>13,14,19,20</sup> However, in these studies diabetic patients also had poor cardiac status including higher prevalence of left ventricular hypertrophy, lower left ventricular ejection fraction and higher rate of multivessel and left main coronary artery disease. Leavitt et al, found that long term survival of diabetic patients undergoing CABG in the absence of renal failure or peripheral artery disease( PAD) was not significantly different from nondiabetics.<sup>20</sup> Also, Yamamoto et al, found that using left internal mammary artery graft results in similar survival rate between diabetic and non diabetic patients.<sup>15</sup> We think that different baseline characteristics of patients enrolled in these studies may be an important factor affecting short term results. Enrolling patients with diffuse distal coronary artery disease and poor run off could increase post-operative infarction and mortality, while excluding this group of patients will result in better short term outcome. As described above there is less controversy about poor long term outcome of CABG in diabetic patients. Different pattern of coronary artery involvement in diabetic patients including diffuse<sup>21</sup> and more distal<sup>6-8</sup> distribution of atherosclerosis is an important factor affecting the rate of subsequent ischemic events and recurrent angina or infarction. Schwartz et al. showed that grafted vessels in diabetic patient were smaller than non-diabetics with more diffuse involvement.<sup>22</sup> Also, Mosseri et al, showed that angiographically normal coronary arteries of diabetic patients are narrower than normal subjects.<sup>23</sup> Diabetic patients undergoing CABG also have higher in-hospital morbidity. Hyperglycemia has some adverse consequences. Uncontrolled hyperglycemia may be associated with dehydration and electrolyte disturbances.<sup>13</sup> Impaired function of polymorphonuclear leukocytes

is the other adverse effect of hyperglycemia which leads to higher rate of post-operative infections and impaired wound healing.<sup>24</sup> Zerr et al, showed that lowering mean blood glucose level to less than 200 mg/dL in the immediate post-operative period results in a reduced incidence of deep wound infection in diabetic patients.<sup>25</sup> It has been shown that using a continuous insulin infusion protocol in peri-operative period to control blood glucose results in lower rate of in-hospital mortality and morbidity.<sup>26,27</sup>

Diabetic patients in our study had higher prevalence of hypertension, hyperlipidemia and PAD with female predominance and slightly lower ejection fraction.

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