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Elevated Pre-Operative Hba1c Affects Outcome of Coronary Artery Bypass Grafting

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Abstract

Aims: The objective of the study was to identify the impact of elevated haemoglobin A1c (HbA1c) and related co-morbidities on morbidity and mortality of patients undergoing coronary artery bypass grafting. *Settings and Design:* This was a prospective study in which 126 patients that underwent isolated, elective, off pump CABG from October 2010 to October 2012. *Methods and Material:* 126 patients undergoing coronary artery bypass grafting (CABG) were enrolled and preoperative HbA1c levels were obtained. The Portland protocol for insulin was used to achieve tight glucose control. The multivariate risk factors for morbidity and mortality were analyzed. *Statistical analysis used:* Statistical analysis was performed with the SPSS software package (version 16.0, SPSS Inc, Chicago, IL). The normality of the continuous variables was tested by using Kolmogorov-Smirmov Z test. Tests used were unpaired t-test for continuous variables and chi square test for dichotomous / categorical variables. A p value less than .05 was taken as significant. *Results:* In-hospital mortality was significantly higher for patients with HbA1c e" 7% and also the incidences of post-operative morbidities were significantly increased. These patients had more blood loss and received more blood products and had prolonged ventilatory time and spent more time in the hospital *Conclusions:* HbA1c may be a more accurate predictor of outcomes than merely a diagnosis of diabetes and is associated with adverse events after coronary artery bypass grafting.

Keywords: Glycosylated Haemoglobin; Coronary Artery Bypass Grafting ; Off-Pump; Diabetes.

Key Messages: *HbA1c is a powerful predictor of in-hospital death and morbidity.*

Introduction

Diabetes mellitus (DM) is a risk factor for coronary artery disease and its presence portends a worse outcome in patients undergoing coronary artery bypass grafting (CABG). The Joint Commission on Biochemical Nomenclature has proposed the term 'glycated haemoglobin'[1] which includes haemoglobin A1c (HbA1c) and other haemoglobins.

The American Diabetes Association has recommended the use of the blood HbA1c level as a method of assessing long-term glycemic control in diabetic patients [2]. HbA1c, also known as glycosylated haemoglobin, indicates a patient's blood glucose control during the previous 3 to 4 months. The American Diabetes Association (ADA) indicates HbA1c testing as an acceptable diagnostic test for diagnosing dysglycemia.The American Diabetes Association currently recommends that patients with HbA1c levels less than 7% is associated with a lower risk of diabetes-associated complication [3]. The relationship between preoperative plasma HbA1c levels and intra-operative insulin sensitivity is unknown, recent evidence suggests a prognostic value of HbA1c regarding outcomes after major surgical interventions [4]. At least 3 postoperative days of tight glycemic control with intravenous insulin infusion minimizes adverse outcomes such as renal failure, infections, length of stay and death in diabetic patients undergoing cardiac operations[5].

The American Heart Association guidelines indicate that it is paramount to achieve strict control of diabetic status, as well as other strategies for secondary prevention [6] . Along with glycemic control (HbA1c less than 7%), other general guidelines of particular importance include the following: dietary modifications (to lower total caloric, saturated fat, and cholesterol intake, maintain appropriate intake of nutrients and fiber), exercise, cessation of smoking, weight reduction, control of hyperlipidemia with statins (low density lipoprotein [LDL] cholesterol less than 100 mg/dL], control of blood pressure (less than 130/80), use of angiotensin converting enzyme inhibitors, and beta blockers.

Subjects and Methods

This was a prospective study in which 126 patients who underwent isolated, elective, off pump CABG from October 2010 to October 2012. During this period of study, the preoperative HbA1c levels were collected in patients scheduled for cardiac surgery. The primary aim of this study was to evaluate the effect of elevated HbA1c on morbidity and mortality following CABG surgery and to assess associated risk factors. We managed every single patient with the Portland protocol regardless of a diagnosis of diabetes. The blood glucose level was used as a continuous variable in the multivariable analysis.

Patients were divided into two groups: Group A- Hb A1C e" 7% and Group B- Hb A1C < 7%. Exclusion criteria for the study was On-pump CABG and CABG with additional surgical procedures.

Comparison between group A and group B was done in terms of patient characteristics, pre and post operative laboratory investigations, pre and post operative co-morbid conditions, ventilatory requirement, inotrope requirement, hospital stay, postoperative bleeding, wound infection, transfusion requirement and mortality. Statistical analysis was performed with the SPSS software package (version 16.0, SPSS Inc, Chicago, IL). The normality of the continuous variables was tested by using Kolmogorov-Smirmov Z test. Tests used were unpaired t-test for continuous variables and chi square test for dichotomous/categorical variables. A p value less than .05 was taken as significant.

Preoperative Definitions

Definitions for preoperative variables were according to the Society of Thoracic Surgeons National Database

Postoperative Definitions

Definitions for postoperative outcomes were also according to the Society of Thoracic Surgeons National Database. Cerebrovascular Accident (CVA) indicates whether a patient had a central neurologic deficit persisting more than 72 hours (permanent stroke), transient ischemic attack, deficit resolving within 24 hours, or deficit lasting more than 24 hours but less than 72 hours (reversible ischemic neurologic deficit); sternal wound infection may be superficial or deep(involving muscle, bone, or mediastinum requiring operative intervention); postoperative atrial arrhythmia was defined as the occurrence of new atrial arrhythmia in the absence of preoperative persistent or paroxysmal atrial arrhythmias. Need of inotropic agents was defined as an infusion of greater than 5mg / kg/ min dobutamine or any dose of epinephrine or norepinephrine for more than 12 hours**.**

Results

A total of 126 patients were analyzed in this analysis. Of the 126 patients enrolled 44 patients formed the group A (HbA1ce"7) and the rest 82 formed group B (HbA1c<7) group.

Patient Demographics and Risk Factors

Table 1 shows demographics. The two groups were found to be evenly matched with respect to established risk factors for HbA1c. There was no statistical difference between the two groups with respect to preoperative laboratory investigations.

Operative Data

Most patients in this study had multivessel coronary disease, more than 99% of patients received arterial grafting with the left internal thoracic artery grafting. Figure 1 depicts operative data from the whole cohort and compares both groups**.** In the group HbA1c e" 7%, the percentage of triple vessel was more commonly affected as compared to other group and coronary vessels was more diffusely affected. So, more grafts were required to revascularise the heart in patients with HbA1c e" 7%.

Clinical Outcome (morbidity and mortality)

Mediastinal drainage was found to be significantly higher (385.86 ± 38.299 vs. 128.46 ± 6.489, p< 0.01) in group A compared to group B and more blood was required to transfuse to group A. There was statistical difference between the two groups in transfusion of blood. In group A, 26 patients had transfusion of blood while in group B only 2 patients had blood transfusion (Table 3). Similarly inotropic and ventilatory support was significantly less in the group B. Prolonged hospital stay was also more frequent in patients with HbA1c e" 7% (hospital stays 12.24 ± 1.278 vs. 5.89 ± 0.112, p< 0.01) (Table 2). The incidence of adverse events was significantly higher for the patients with uncontrolled diabetes (HbA1c e" 7% group), including renal dysfunction (P< 0.01), wound infection (P< 0.01), and arrhythmias (p< 0.01). Although there was a trend toward more mortality in patients with HbA1ce"7% (18.2%) compared with those with HbA1c<7% (1.2%), which is statistically significant. In-hospital mortality was significantly higher for patients with HbA1c e" 7% (Figure 2). In patients with HbA1c less than 7%, there was only one death due to cardiac factor. Of the 7 deaths in patients with HbA1c of 7% or more, 5 were cardiac related. One patient died of complications of stroke, and one patient died of profuse bleeding.

Discussion

In patients with HbA1ce"7, there was a statistically significant increase in ventilator time, duration of inotropes, mediastinal drainage, blood transfusion, renal dysfunction, arrhythmias, wound infection, hospital stay and mortality. Coronary artery disease tended to be more extensive, involving multiple vessels in group A (single vessel-6.8%, double vessel-6.8% and triple vessel-86.4%) as compared to group B (single-12.2%, double vessel-41.5% and triple vessel-46.3%) which significantly affect the prognosis (p=0. 001). Marchiex et al. [7] also showed that patients with HbA1c e" 7 had increased prevalence of diffuse coronary artery disease and triple vessel disease. The mediastinal drainage was a significant increase in patients with HbA1c e" 7 (mean-385.86 ml) as compared to group B (mean-128.46 ml) which lead to increase units of blood transfusion (26 patients in group A as compared to 2 patients in group B) which significantly affect the morbidity and mortality. Sato et al. [8] showed that patients with elevated HbA1c also received more blood products (packed red blood cells, p=0.046). Similarly Halkos et al. [9] also showed the same results (p=0. 72).

In patients with HbA1c e" 7, the ventilator time (Group A mean=12. 43 hrs. and group B mean= 5.23 hrs.) and duration of inotropes (group A mean=14.68 hrs. and group B mean= 2.29 hrs.) was significantly increased which show that the outcome of CABG is affected. Sato et al. [8] showed that patients with elevated HbA1c had increased ventilator time (group A mean-9.3 hrs. and group B mean 8.7 hrs.). Lu and colleague [10] and Marchiex et al. [7] (p=0. 07) reported diabetes as an independent risk factor for prolonged ventilation.

In the postoperative period, conditions which were significantly affected were wound infection (group A=22.7% and group B=2.4%, p= <0.0001), renal dysfunction (group A=29.5% and group B=0%, p=<0.0001) and arrhythmias (group A=36.4% and group B=2.4%, p=<0.0001) While cerebrovascular accident (CVA) and recurrent myocardial infarction (MI) were not affected. This finding differs from reports by Szabo and colleagues [11] who found the incidence of stroke to be significantly increased in diabetic patients. Previous studies have reported an association between diabetes and sternal wound infections [10-12]. Trick and colleagues [12] found that diabetic patients with a preoperative blood glucose level of 200 mg/dL had a significantly higher chance of developing deep sternal wound infections. Lu and colleagues [10] identified insulin-dependent diabetes as an independent risk factor for developing deep sternal wound infections. Kubal et al.[13] Show that insulin-dependent diabetes was associated with more acute renal failure (adjusted odds ratio [OR] 4.15, p = 0.002), deep sternal wound infection (adjusted OR 2.96, p = 0.039), and prolonged postoperative stay (adjusted OR 1.60, p = 0.017). Angiopathy, neuropathy, and hyperglycaemia associated with DM are identified as the main reasons for predisposition to infections [14]. The mortality (case=18. 2% and control=1. 2%, p=<0.0001) was increased in patients with elevated HbA1c. Halkos et al. [9] reported that patients with HbA1c levels of 7% or more was associated with a significant increase in in-hospital mortality (1.4%), renal failure (p=.028), CVA and infection (p=.007) compared with patients with HbA1c levels less than 7%. Calafiore and colleagues [15] showed that diabetes was an independent risk factor for early cardiac death only and not for all-cause mortality. Rajakaruna and associates [16] found in a risk-adjusted analysis that diabetic patients (mortality-2.2%) had mortality outcomes comparable to those of nondiabetic patients (mortality-1%). Kubal and co-workers [13] showed that insulin-dependent diabetic patients had an increased risk of postoperative morbidity, but that just the history of diabetes was not associated with increased mortality. Thourani and associates[17], reporting 2,278 diabetic patients, observed an operative mortality of 3.9%. Carson and colleagues [18] compared diabetic patients with nondiabetic patients and found that patients with diabetes had a 23% to 37% increase in 30-day mortality and in-hospital morbidity compared with patients without diabetes. Furnary and colleagues[19] reported dramatic reductions in mortality and DSWI among diabetic patients (compared to nondiabetic patients) managed with a continuous insulin infusion. According to Marchiex et al.[7] the operative mortality was comparable in both groups; postoperative acute renal failure, sepsis, and infection were more frequently encountered in the diabetic population which lead to longer lengths of hospital stay. HbA1c is also an independent predictor of postoperative adverse events that is not entirely due to intra and postoperative glucose control.

Table 1: Comparison of Demographics and Risk Factor

Risk factor	Group A (HbA1c≥7%)			Group B (HbA1c<7%)			P-value
	N	%	Mean ± SEM	N	%	Mean ± SEM	
Pre-operative							
Mean Age			55.23±1.457			54.80±0.871	0.792
Male/Female	36/8			74/8			0.176
Body Mass Index			22.743±0.387			23.450±0.313	0.172
Diabetes Mellitus	40	90.9%		13	15.9%		<0.01
Hypertension	22	50.0%		40	48.8%		0.896
Hb%			12.111±0.157			11.634±0.122	0.021
RBS			139.55±1.880			135.20±1.366	0.063
Serum Urea			25.33±0.882			27.48±0.737	0.075
Serum Creatinine			0.718±0.024			0.761±0.015	0.125
Post-operative							
Hb%			9.34±0.146			10.87±0.119	<0.01
RBS			163.39±7.152			127.45±3.066	<0.01
Serum Urea			48.48±2.047			32.80±0.844	<0.01
Serum Creatinine			1.669±0.048			0.957±0.016	<0.01

SEM- Standard Error of Mean

Table 2: Comparison of ICU Parameters

	Group A (HbA1c≥7%) Mean ± SEM	Group B (HbA1c<7%) Mean ± SEM	P value
Mediastinal Drainage (ml)	385.86±38.299	128.46±6.489	<0.01
Inotropic Support (hrs.)	14.68±4.938	2.29±0.167	<0.01
Ventilator time (hrs.)	12.43±3.918	5.23±0.097	<0.01
Hospital stay(days)	12.24±1.278	5.89±0.112	<0.01

SEM- Standard Error of Mean

Table 3: Comparison of Blood Transfusion

Blood Transfused (Units)	Group A	Group B	p value
1 unit PRBC	13(29.5%)	2(2.4%)	<0.01
2 units PRBC	9(20.5%)	0(0%)	
3 units PRBC	1(2.3%)	0(0%)	
4 units PRBC	1(2.3%)	0(0%)	
5 units PRBC	1(2.3%)	0(0%)	
6 units PRBC	1(2.3%)	0(0%)	

Fig. 1: Percentage of Diseased and Grafted Vessel

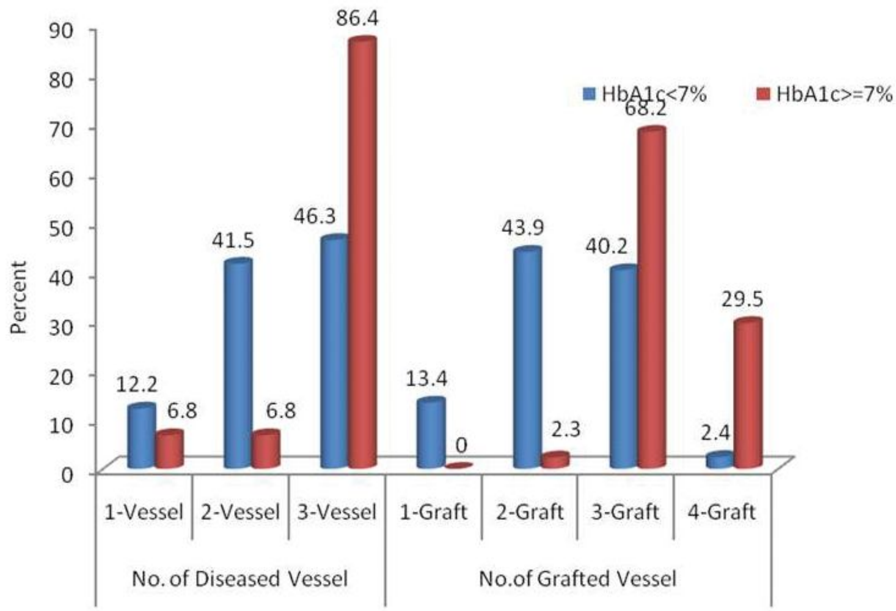
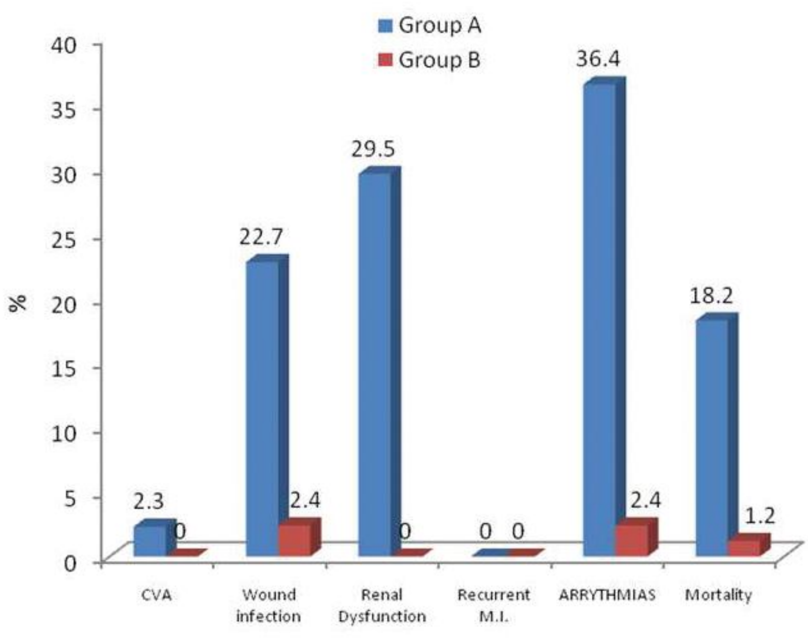


Fig. 2: Post-Operative Morbidities and Mortality



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