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# Perioperative Glycemic Control and its Outcome in Patients following Open Heart Surgery

## Abstract

**Background:** Diabetes is not uncommon in patients requiring cardiac surgery. These patients have a higher incidence of morbidity and mortality. Subsequently, diabetes represents a major medico-economic problem in both developed and developing countries. This study was designed to observe the association between glycemic control and outcome of patients after open heart surgery in adult population. **Materials and Methods:** Data was collected retrospectively in all patients who underwent open cardiac surgery (coronary artery bypass grafting, valve, or bypass grafting with valve surgery) and survived 72 hours postoperatively and had diabetes. The study was conducted from January 2015 to December 2016. **Results:** Of the 129 patients included in the study, male dominated 101 (78.3%). Most frequent surgery was coronary artery bypass grafting (CABG) 123 (95.3%), CABG plus aortic valve replacement 4 (3.1%), and CABG plus mitral valve replacement 2 (1.6%). Considering diabetes, only 3 (2.3%) were on diet control, 112 (86.8%) on oral hypoglycemic agents (OHA), whereas 9 (7%) had control on both insulin and OHA. Only 5 (3.9%) had type I diabetes. The mean fasting blood sugar (FBS) was 154.58 g/dl, and the mean duration of diabetic mellitus was observed 12.32 years. Microvascular and macrovascular complications were 26/129 (20.16%) and 17/129 (13.17%), respectively. Total 75 (58.1%) patients did not require insulin and 54 (41.9%) were treated with insulin intraoperatively to keep the blood glucose level less than 200 g/dl. Cardiac arrhythmias were frequent in the insulin group ( $P < 0.05$ ), which was also associated with increased stay in the cardiac intensive care unit. **Conclusion:** Inadequate glycemic control during open cardiac surgery can possibly lead to increased perioperative morbidity and mortality and with decreased long-term survival and recurrent ischemic events. Therefore, aiming for blood glucose levels around 140 mg/dl appears reasonable. Further studies are required to define specific glucose ranges for a clearer definition of recommended blood glucose goals in postoperative cardiac patients for the best outcomes in patients with diabetes mellitus.

**Keywords:** *Insulin, open heart surgery, perioperative glycemic control, postoperative outcome*

## Introduction

It is estimated that approximately 30–40% of patients for coronary artery bypass graft surgery (CABG) have diabetes mellitus or impaired glucose tolerance.<sup>[1,2]</sup> These patients present higher incidence of morbidity and mortality and increased length of hospital stay.<sup>[3,4]</sup>

Adequate glycemic control in perioperative period is essential for improving the outcome in surgical patients, especially those undergoing CABG.<sup>[5]</sup> However, the uncertainty still remains in the appropriate level of perioperative glycemic control needed to achieve the best possible outcome. Some researchers advocate tight glycemic

control (blood glucose 80–110 mg/dl) to improve outcome and decreased wound infections.<sup>[6,7]</sup> Whereas others reported no improvement in morbidity and mortality with the tight control and even suggest possibilities of some adverse effects in such patients.<sup>[8]</sup>

As a consequence of these conflicting data and some recent research,<sup>[9]</sup> the Institute for Healthcare Improvement and Society of thoracic surgeons guidelines<sup>[10-12]</sup> recommend keeping blood glucose levels to less than 180 mg/dl both intraoperatively and during the ICU stay.

The objective of this study was to observe the association between perioperative glycemic control and the outcome of patients following open heart surgery.

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## Materials and Methods

This was a retrospective cohort study and was exempted by the Ethical Review Committee of Aga Khan University for informed consent. Patients having diabetes who were admitted for open heart surgery in the last 2 years from January 2015 to December 2016 with survival for at least 72 h were enrolled in this study.

Patients with diabetes mellitus either on diet control, insulin dependent or noninsulin dependent before open heart surgery (CABG, valves replacement and bypass grafting with valve surgery) were included in the study. Patients with nondiabetic, poor glycemic control, having emergency surgery, having surgery with off-pump bypass, age less than 18 years, on dialysis, and having a history of cerebral vascular accident/transient ischemic attack (CVA/TIA) within the last six months were excluded from the study.

For all patients included in the study, medical record (MR) numbers were obtained, files were retrieved from medical records, and data were collected on a predesigned data collecting form by one of the investigators.

All statistical analyses was performed using Statistical Packages for Social Science version 19 (SPSS Inc., Chicago, IL, USA). Mean and standard deviation were computed for quantitative observation and analyzed by independent sample *t*-test whereas proportion and percentage were computed for complication according to the level of blood glucose and analyzed by Chi-square test.  $P \leq 0.05$  was considered significant.

## Results

A total of 129 patients were observed in the study over the period of 2 years. Demographic features, surgical variables, and disease measures for all 129 patients are outlined in Table 1. There were 101 (78.3%) males and 28 (21.7%) females. Most frequent surgery was CABG alone 123 (95.3%), CABG plus aortic valve replacement (AVR) 4 (3.1%), and CABG plus mitral valve replacement (MVR) 2 (1.6%). The control of diabetes mellitus (on diet control, insulin alone, or combination of insulin with oral hypoglycemic agents [OHA]) was also observed. Only 3 (2.3%) had diet control diabetes, 112 (86.8%) had diabetes control with oral hypoglycemic agents (OHA), 9 (7%) had diabetes control through insulin with OHA, and 5 (3.9%) had controlled it with insulin alone. The mean fasting blood sugar (FBS) was  $154.58 \pm 55.56$  g/dl and the mean duration of diabetic mellitus was  $12.32 \pm 5.49$  years. Recurrent hypoglycemia was observed only in one female patient preoperatively who had diet control diabetes. No intra and postoperative complications were found in that patient.

Further, prior history of both macro and microvascular complications related to DM were also observed. Microvascular complications were detected in

26/129 (20.16%) and macrovascular complications were detected in 17/129 (13.17%). Microvascular complications were categorized as retinopathy, neuropathy, and nephropathy, whereas macrovascular complications were categorized as prior myocardial infarction (MI), prior congestive heart failure (CHF), and peripheral vascular disease (PVD) [Table 2].

Assessments were done related to the methods to control diabetes during the intraoperative phase and blood glucose levels, both intra and postoperatively [Table 3]. It was found that 75 (58.1%) patients did not require

**Table 1: Demographic, surgery and diabetic measure of the patients [n=129]**

Variables	Point estimates
Age (years)	61.2±8.71 [35-85]
Weight (kg)	72.99±6.81 [55-89]
Height (cm)	166.29±5.51 [152-178]
BMI (km/m <sup>2</sup> )	26.39±2.10 [22.03-33.76]
Gender *	
Male	101 (78.3%)
Female	28 (21.7%)
Surgery*	
CABG	123 (95.3%)
CABG + AVR	4 (3.1%)
CABG + MVR	2 (1.6%)
Diabetes control*	
Insulin + OHA	9 (7%)
Insulin	5 (3.9%)
Oral hypoglycemic agents	112 (86.8%)
Diet	3 (2.3%)
Fasting blood sugar (FBS)	154.58±55.56 [80-418]
Duration of diabetic mellitus	12.32±5.49 Years [0.5-25]
Recurrent Hypoglycemia*	1 (0.8%)

Results are presented as mean±SD, [min-max] and \*n (%)

**Table 2: History of diabetic mellitus complication (n=129)**

Complications	Frequency	Percentage
Microvascular Complication	26/129	20.16%
Retinopathy	5	19.2%
Neuropathy	7	26.9%
Nephropathy	4	15.4%
Retinopathy + Neuropathy	2	7.7%
Retinopathy + Nephropathy	3	11.5%
Neuropathy + Nephropathy	2	7.7%
Retinopathy + Neuropathy + Nephropathy	3	11.5%
Macrovascular Complication	17/129	13.17%
Prior MI	9	52.9%
Prior CHF	2	11.8%
PVD	4	23.5%
Prior MI + CHF + PVD	2	11.8%

Percentages of sub-complications were computed by micro and macro individually

insulin intraoperatively, and 54 (41.9%) patients were managed by bolus insulin during the intraoperative phase; the frequency of bolus dose was also monitored. The average dose of insulin was 13.1 IU. In patients who received insulin intra-operatively, average blood glucose level was 243.6 g/dl. The threshold to use insulin bolus was blood sugar more than 180 g/dl. In addition, 102 patients needed insulin boluses on day one, 91 on day two, and 81 on day three after the surgery.

Patients were followed postoperatively despite patients' glucose managed with or without insulin and monitored for any postoperative complication. Cardiac arrhythmias, renal failure, ventilator support >24 hours, and length of stay >3 were statistically significant among patients having insulin for targeted glycemic control (<200 g/dl) in cardiac intensive care unit (CICU) [Table 4].

**Table 3: Intraoperative control on DM (n=129)**

Variables	Point estimates
Intraoperative	
No insulin	75 (58.1%)
Bolus Insulin	54 (41.9%)
Frequency use of insulin	
1	20 (15.5%)
2	23 (17.8%)
3	10 (7.8%)
4	01 (0.8%)
Average dose of insulin (IV) (n=54)	13.140±8.01 [4-36]
Level of Blood Glucose (>180 gm/dl)	
Intraoperative (n=54)	243.69±43.91 [189-448]
Postoperative	
Day 1 (n=102, 79.1%)	234.62±47.40[184-452]
Day 2 (n=91, 70.5%)	231.14±45.56[181-414]
Day 3 (n=81, 62.8%)	232.26±43.92[181-383.5]

Results are presented as mean±SD, [min-max] and \*n (%)

**Table 4: Intraoperative control of blood sugar and postoperative complication in CICU (n=129)**

Complication	Intraoperative Treatment		P
	No Insulin (n=75)	Insulin (n=54)	
Renal failure	20 (26.7%)	25 (46.3%)	0.021
Cardiac arrhythmias	5 (6.7%)	12 (22.2%)	0.01*
Myocardial infarction	0	0	NA
Deep sternal infection	2 (2.7%)	0 (0%)	0.509
Multisystem failure	2 (2.7%)	1 (1.9%)	0.762
ventilator support >24 hours	5 (6.7%)	12 (22.2%)	0.016
Length of stay >3 days	8 (10.7%)	17 (31.5%)	0.003*
Early mortality (CICU or within 30 days)	0	0	NA
Length prolonged Mechanical ventilation	5 (6.7%)	7 (13%)	0.225

Results are presented as n (%) and mean±SD, [min-max]. Complication in CICU was observed in 61 (47.3%) patients

## Discussion

Perioperative blood glucose control and administration of insulin during open heart surgery in diabetic patients is expected to have beneficial effects on patients' outcome. Administration of insulin will increase glucose uptake by myocytes, promoting glycogenesis, and reducing free fatty acids, while protecting heart against ischemia provided by cardiopulmonary bypass.<sup>[13]</sup> Furthermore, hyperglycemia has a pro-inflammatory effect that may contribute to postoperative capillary leak syndrome, platelet dysfunction, and altered immune response that could be avoided by blood glucose control.<sup>[14]</sup>

By revision of studies conducted on the effect of tight glycemic control of diabetic patients on patients' outcome after CABG surgery, there was no fixed blood glucose range taken as a single reference in these studies. The definition of tight glycemic control was different and the method by which one can achieve it was also varied. To date, it remains unclear how tight the glycemic control should be. For safety, in our study, the recommendations of American Association of Clinical Endocrinologists and American Diabetes Association (ADA/AACE) were followed to define tight glycemic control to be between 110 and 149 mg/dl and moderate glycemic control to be between 150 and 180 mg/dl.<sup>[12]</sup>

In 2009, normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial made much change in concept of tight glycemic control as they found that intensive glucose control (81–108 mg/dl) actually increased 90-day mortality with more episodes of hypoglycemia recommending more liberal control of blood glucose level.<sup>[15]</sup>

Numerous studies have now shown that patients with acute coronary syndromes (ACS) who present with hyperglycemia are at a higher risk of death and in-hospital complications.<sup>[16-18]</sup> Capes and co-workers<sup>[19]</sup> in meta-analysis of 15 studies showed that the risk of in-hospital death in nondiabetic patients with ACS and the admission glucose >110mg/dl was 3.9 times greater than in patients who were normoglycemic.

Desai *et al.*<sup>[20]</sup> found in a study on isolated CABG patients that liberal blood glucose control between 121 and 180 mg/dl have better outcome in relation to blood glucose control and target range needed and similar outcome to tight glycemic control regarding morbidity and mortality.

Girish *et al.*<sup>[21]</sup> also supported in their review that it is sensible to maintain blood sugar level between a safe intermediate range of 140–180 mg/dl or better still <150 mg/dl keeping in view the potentially dangerous consequences of hypoglycemia and hyperglycemia.

The relationship between tight glycemic control and decreased surgical wound infection was addressed first



in 1991 when the American College of Cardiology and American Heart Association noted increased incidence of wound infection in diabetic patients.<sup>[22]</sup>

A cohort study by Estrada *et al.*<sup>[23]</sup> of 1574 patients who had undergone coronary artery bypass grafting assessed for 30 days for mortality, infection rates (sternum, harvest site, sepsis, pneumonia, urinary tract), and the utilization of resources found no statistical significant relationship between surgical site infection and blood glucose level between diabetic and nondiabetic groups.

Arrhythmias following cardiac surgery are common affecting up to 20–30% of patients.<sup>[24]</sup> The mechanisms by which atrial fibrillation can occur after cardiac surgery is unclear, but certain theories such as cooling of atrium, increased sympathetic activity, and withdrawal of preoperative B-blockers are acknowledged on animal and human trials.<sup>[25,26]</sup> All the previous factors could contribute to change in refractory period in the atrium predisposing to atrial fibrillation.<sup>[27]</sup> In our study, a significant reduction in arrhythmias was found in group which was not on insulin. This is a unique finding in this study but other studies also support tight glycemic with better arrhythmias control in this regard.<sup>[6,28]</sup>

Length of CICU stay was also relatively high in patients who received insulin to manage glycemic control intraoperatively compared with those who did not receive insulin for glycemic control. These findings were also contradictory to other studies which showed a significant reduction in the amount of time spent on ventilation for patients who had tight glycemic control. However, there was also significant heterogeneity in the data.<sup>[6,29]</sup> On the contrary, another study stated that hypoglycemia with thorough insulin therapy is independently associated with increased risk for respiratory complications and prolonged hospital and intensive care unit length of stay after cardiac surgery.<sup>[30]</sup>

Based on recent information, the new Society of Thoracic Surgeons guidelines and the American Association of Clinical Endocrinologists and American Diabetes Association (AAACE/ADA) consensus statement seem appropriate and allay the concern for hypoglycemia with the new recommended range of <180 and 140–180 mg/dL.<sup>[31]</sup> More studies analyzing blood glucose target ranges are required to further recommend an intensive blood glucose goal range of 80–110 mg/dL, especially in the cardiac surgery population. Even throughout the Van Den Berghe trials<sup>[32,33]</sup> the average blood sugar of patients in the intensive control arm was approximately 140 mg/dL. Thus, aiming for blood glucose levels around 140 mg/dl appears reasonable. Mortality and morbidity benefits are seen with overall control of hyperglycemia; however, the exact range is still not clearly defined, as previously thought. Additional comparisons of specific glucose ranges would allow for a clearer definition of recommended blood glucose goals

in postoperative cardiac patients, resulting in the best outcomes and least incidence of hypoglycemia. Therefore, more studies are recommended with greater sample size and longer follow-up duration to confirm the results with CAD being included in macrovascular complication, as that was one of the limitation of this study.

## Conclusion

Hypo or hyperglycemia during open cardiac surgery can possibly lead to increased perioperative morbidity and mortality and can be associated with decreased long-term survival and recurring ischemic events. Therefore, aiming for blood glucose levels around 140 mg/dl appears reasonable; however, the exact range is still not clearly defined. Further studies are required to define specific glucose ranges for a clearer definition of recommended blood glucose goals in postoperative cardiac patients for the best outcomes in patients with diabetes mellitus.

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## Conflicts of interest

There are no conflicts of interest.

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