

## Indication for Open Heart Surgery in Type 2 Diabetic Patients: Does It Actually Affect the Dosage of Postoperative Insulin Therapy?

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### ABSTRACT

**Background:** Despite the wide variety of pathologies mandating open heart surgeries, most of the available guidelines on perioperative glycemic control in cardiac surgery are based on coronary artery bypass graft surgery (CABG).

**Aim of study:** In this retrospective study, we aimed to compare the postoperative insulin doses in type-2 diabetic patients, regardless of whether the surgery was for ischemic heart disease (IHD) or another cardiac pathology, thereby facilitating future predictions and appropriate adjustments to insulin dosing.

**Methods:** We included 370 type-2 diabetes patients who had open heart surgery in Cairo, Ain-Shams and Fayoum University hospitals throughout the previous five years, beginning in January 2021. The perioperative glycemic status and the required postoperative insulin dosage were extensively monitored and studied after the patients were divided into two equal groups: The CABG group and the non-CABG group.

**Results:** Random blood sugar levels in the CABG group were significantly higher ( $165.7 \pm 86$  vs.  $139.5 \pm 75$  mg/dl), which demands significantly higher insulin doses ( $2.84 \pm 1.37$  vs.  $2.11 \pm 1.26$ , P value < 0.001) for strict glycemic control through the first 3 days in the post-operative intensive care unit (ICU). Additionally, the maximal insulin dose was significantly higher in the CABG group (26.4 IU vs. 8.26 IU, P value < 0.001).

**Conclusion:** Diabetic candidates for CABG are at higher risk for postoperative disturbed glucose levels and need for higher doses of insulin therapy.

**Keywords:** CABG, IHD, Glycemic state, Postoperative insulin.

### INTRODUCTION

Over 30-40% of patients undergoing open-heart surgeries are diabetic, with more than 2-5% of the patients accidentally discovered within the preoperative preparation period (<sup>1, 2</sup>). Perioperative hyperglycemia has been shown to increase the adverse outcomes of open-heart surgeries by three to four times, leading to complications such as sternal wound infections, intractable arrhythmias, and even death (<sup>3, 4</sup>). It is well-known that strict perioperative control of the glycemic state significantly lowers postoperative morbidity and mortality (<sup>5, 6</sup>).

Most of the commonly cited and widely distributed recommendations focus on managing the perioperative glycemic state in type 2 diabetic patients undergoing coronary artery bypass grafting (CABG) (<sup>7, 8</sup>). However, there is limited data available concerning the same issue in patients undergoing cardiac valve surgeries, adult congenital heart problems, and other non-CABG cardiac procedures. Given that diabetes and atherosclerosis share several common pathogenic pathways, they can mutually influence one another. For example, oxidative stress is often induced by the degenerative vascular changes linked to atherosclerosis, which serves as the primary pathological condition in coronary artery disease (<sup>9, 10</sup>).

This oxidative process involves the elevation of inflammatory cytokines such as monocyte chemoattractant protein-1 and interleukin-6, as well as high levels of oxidized low-density lipoprotein, all of which contribute to impaired insulin release from beta cells and aggravated insulin resistance (<sup>11, 12</sup>).

We argued that the pathology requiring heart surgery could significantly impact the glycemic state, thereby altering the care strategy. Furthermore, it may assist in predicting postoperative outcomes associated with diabetes-related comorbidities. Thus, in this study, we closely monitored the postoperative plasma glucose level and the maximal controlling dose of the infused insulin, aiming to predict the acquired insulin regimen following cardiac surgeries rather than CABG.

### PATIENTS AND METHODS

**Study design:** This study included 370 patients who underwent elective cardiac surgeries at Cairo, Ain-Shams, and Fayoum University Hospitals through the period between January 2021 and December 2024. Patients were divided into two groups based on the procedure done: Group A (CABG group; 185 patients) and group B (non-CABG group; 185 patients). Following surgery, data on random blood sugar, daily insulin need, peak insulin dose, intensive care unit (ICU) stay, hospital stay, sternal wound infection, and early mortality were gathered and analyzed.

#### Definitions:

- Diagnosis and the broad lines for management of type-2 diabetes mellitus in cardiac surgery patients depended upon recommendations published and revised by the American Diabetes Association Professional Practice Committee (<sup>7</sup>).
- Indications and recommendations for CABG and the other cardiac procedures were all decided following American College of

Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines<sup>(13, 14)</sup>.

- Prolonged mechanical ventilation (MV) (> 24 hours), prolonged ICU stay (> 3 days), prolonged hospital stays (> 14 days), and early postoperative mortality (within 30 days postoperatively) were defined regarding guidelines from the Society of Thoracic Surgeons (STS)<sup>(15)</sup>.

**Exclusion criteria:** Patients with total arterial grafting, concomitant aortic surgeries, patients with urgent/Emergency cardiac surgeries and cases with infective endocarditis.

#### Study endpoints:

- The study's **primary endpoints** were postoperative random blood sugar levels, daily insulin regimen and the maximum insulin dose.
- **Secondary endpoints** were prolonged MV time, prolonged ICU stay, prolonged hospital stay and sternal wound infection.

#### Perioperative systemic diabetic control protocol:

- **Pre-operative measures:** Even with the optimal antidiabetic medicine, patients who have unstable random blood sugar levels and glycated hemoglobin levels more than 7 gm/dl are at a higher risk of postoperative morbidity and death. Therefore, unless an urgent indication arises, we would prefer to postpone such individuals. To lessen the risk of diabetic ketoacidosis and lactic acidosis, we transitioned from oral hypoglycemic medications, mainly metformin and SGLT-2, to a weight-adjusted basal dose of insulin with 6-8 hourly injections after meals as needed.
- **Intra-operative measures:** Continuous intravenous insulin infusion is utilized to maintain the patient's glucose level between 140 and 180 mg/dL (7.8–10 mmol/L) during surgery, with hourly monitoring of random blood sugar to prevent hypoglycemia (A drop in glucose levels below 120 mg/dL) and to mitigate the risk of hypokalemia (A decrease in potassium levels below 3.5 mEq/L).
- **Postoperative measures:** In the postoperative ICU, we continued the insulin infusion therapy on the same

regimen, however once the patient is stable and eating, we shifted from IV insulin to a subcutaneous regimen, using either the basal-bolus strategy or a sliding scale based on the patient's status.

**Follow up after hospital discharge:** All patients were monitored in our clinics on a monthly basis for the first three months following discharge and then tri-monthly for the subsequent year. The follow-up procedure included wound care, a chest examination, a plain chest X-ray, electrocardiography, random blood sugar (RBS) testing, and, in some cases, monitoring of the HbA1c level.

**Sampling method:** With an alpha error of 5%, a 95% confidence level, and an 80% power sample, the Medcalc 19 program was used to determine the appropriate sample size population (370 patients) [Equations are provided by Brown *et al.*<sup>(16)</sup>].

**Ethical approval:** The Ethics Committee of the Fayoum Faculty of Medicine authorized this study [No: R 693]. After receiving all of the information, all participants signed their permissions. The Helsinki Declaration was followed throughout the course of the investigation.

#### Statistical analysis

SPSS version 22.0 was used to manage the data and conduct statistical analysis. Continuous data were reported as mean  $\pm$  SD or median with interquartile range, and categorical data as percentages. P values  $\leq$  0.05 indicate statistical significance. All statistical investigations were carried out with the aid of a skilled statisticians.

## RESULTS

A total of 370 patients (102 females) were separated into two groups: Group A (the CABG group; 185 patients) and Group B (Non-CABG group; 185 patients). Our sample's mean age was  $58.25 \pm 5.456$  years. There was no significant difference between the groups in terms of demographic and clinical baseline characteristics ( $p > 0.05$ ) (Table 1).

**Table (1):** Preoperative parameters

Preoperative parameter	Group A (185)	Group B (185)	P Value
Age (years)	$54.56 \pm 7.84$	$53.79 \pm 9.43$	P = 0.4025
Female sex (number %)	53 (28.65%)	49 (26.49%)	P = 0.6425
BMI (Kg/m <sup>2</sup> )	$27.8 \pm 6.5$	$28.20 \pm 5.42$	P = 0.5140
Smokers (number %)	97 (52.43%)	103 (55.68%)	P = 0.4154
FEV-1 (%)	$62.52 \pm 6.7$	$63.42 \pm 6.2$	P = 0.1807
LVEF (%)	$45.7 \pm 11.80$	$46.05 \pm 12.40$	P = 0.7811
NYHA class			
2	80 (43.24%)	85 (45.95%)	P = 0.6005
3	65 (35.14%)	70 (37.84%)	P = 0.5901
4	40 (21.62%)	30 (16.21%)	P = 0.1846
Preoperative insulin dependent patients	63 (34.05%)	71 (38.38%)	P = 0.3869
HBA1C	$6.8 \pm 0.9$	$6.8 \pm 0.7$	P = 1.0000

LVEF; Left Ventricular Ejection Fraction, NYHA class; New York Heart Association class, HBA1c; Glycated hemoglobin.

There were no statistically significant differences between the two groups regarding the operative time and the total bypass time. The CABG group demonstrated a significantly higher number of patients requiring high vasopressor support (Table 2).

**Table (2):** Postoperative parameters

Intra-operative parameter	Group A (185)	Group B (185)	P Value
Operative time (hours)	3.2 ± 0.97	3.1 ± 1.1	P = 0.3419
Bypass time (hours)	1.7 ± 0.5	1.6 ± 0.9	P = 0.1696
High vasopressor therapy <sup>17</sup>	35 (18.92%)	21 (11.35%)	P = 0.0425

- **Primary endpoints:** In terms of our key outcomes, the CABG group required significantly higher doses of the daily insulin regimen and the maximum dose to maintain the elevated random plasma glucose levels (P value < 0.05).
- **Secondary endpoints:** Taking into account the secondary outcomes, a notably greater proportion of patients in the CABG group had extensive sternal wound infections and needed lengthier stays in the intensive care unit with mechanical ventilatory support. These patients also needed longer hospital stays for the best blood glucose control and recuperation (P value < 0.05) (Table 3).

**Table (3):** Postoperative parameters

Post-operative parameter	Group A (185)	Group B (185)	P Value
<b>Primary Endpoints:</b>			
Random blood sugar (mmol/L)	165.7 ± 86	139.5 ± 75	P = 0.0019
Daily insulin regimen (IU)	2.84 ± 1.37	2.11 ± 1.26	P < 0.001
Maximal daily insulin dose (IU)	26.4	8.26	P < 0.001
<b>Secondary Endpoints:</b>			
Prolonged MV time (> 24 hours)	13 (7.02%)	3 (1.62%)	P = 0.0107
Prolonged ICU stay (> 3 days)	17 (9.19%)	6 (3.24%)	P = 0.0179
Deep Sternal wound infection	11 (5.41%)	2 (1.08%)	P = 0.0111
Prolonged Hospital stay (> 14 days)	19 (10.27%)	2 (1.08%)	P = 0.0001

MV; Mechanical Ventilation.

## DISCUSSION

By increasing insulin resistance through the concurrent release of stress hormones and inflammatory mediators, surgical intervention, whether cardiac or otherwise, is recognized as a significant risk factor for impaired glycemic control<sup>(17)</sup>.

Too many papers have been published discussing the differences in effects among patients undergoing open-heart surgery compared to other surgical procedures. These studies have suggested that the cardiac condition, along with the necessity for cardiopulmonary bypass, significantly contributes to elevated perioperative insulin resistance and an increased risk of postoperative diabetes-related complications<sup>(6, 18, 19)</sup>. Type 2 diabetes and atherosclerosis interact and can enhance each other by releasing monocytic chemokines, interleukin-6, and other pro-inflammatory substances that worsen insulin resistance and accelerate the formation of atherosclerotic plaques<sup>(20, 21)</sup>.

In contrast to other patients undergoing surgery for valvular disorders, which are usually brought on by rheumatic activity or senile degenerative issues and do not share the same pathophysiologic mechanisms as type 2 diabetes mellitus, diabetic patients undergoing CABG for atherosclerotic coronary artery disease will

theoretically be at a higher risk of experiencing dysglycemia after surgery<sup>(22)</sup>.

In this study, we explored whether specific surgical cardiac issues, particularly the CABG operation, which is currently the most commonly performed heart surgery worldwide<sup>(23, 24)</sup>, could influence the postoperative glycemic state and, consequently, the required insulin therapy.

In 2017, **Bardia et al.**<sup>(25)</sup> reported no statistically significant association between preoperative high HbA1c (> 6.5 mmol/dl) and postoperative disturbed glycemic level following isolated cardiac valvular surgery. This coincides well with our results that concluded far less significant effect of the non-CABG procedures on the postoperative glycemic control compared to the CABG group. In the same year, according to **Wang et al.**<sup>(26)</sup>, the only diabetes indicator capable of predicting long-term mortality after CABG on its own is HbA1c. This reinforces the notion that maintaining long-term glycemic control is more beneficial than making quick adjustments to glucose levels just before CABG.

In 2024, **Fukuda et al.**<sup>(27)</sup> found no significant difference regarding the demographic data comparing insulin needs in CABG and non-CABG procedures but reported significantly higher post operative glycemic

level, daily insulin dose and the peak insulin dose (24.6 U vs 9.7 U,  $P < 0.001$ ) during the post-operative care.

The same paper reported longer Ventilator support, ICU and in-hospital stays among the CABG-group patients. Moreover, their CABG patients reported higher incidence of postoperative diabetes-related complications. In contrary, In their report published in 2019, *Shoghli et al.* <sup>(28)</sup> claimed no statistically significant effect of valvular heart surgery in the diabetic patients on the postoperative insulin need, hospital stay and postoperative sternal wound complications.

In their meta-analysis studying the prevalence and interactions between diabetes and valvular heart diseases, *Lu et al.* <sup>(29)</sup> reported that patients with significant valvular heart disease (VHD) were significantly likely to have diabetes. It had a negative impact on the two-year prognosis for patients with MR, but it was linked to a decreased chance of severe left-sided regurgitant valvular disorders. More work should be done to improve our knowledge of concurrent VHD and diabetes and its consequences.

## CONCLUSION

Our study found that diabetic patients who underwent CABG needed a larger amount of postoperative insulin than those who had other cardiovascular procedures. Early aggressive insulin treatment should be initiated in patients with ischemic heart disease who require CABG.

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