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Original Article

Effect of Continuous Intravenous Insulin Infusion on Early Outcome after Off-Pump Coronary Artery Bypass Grafting in Diabetic Patients

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ABSTRACT

Background: Perioperative hyperglycemia is common among diabetic patients undergoing coronary artery bypass grafting (CABG) and may contribute to postoperative complications. Continuous intravenous insulin infusion is widely used to achieve controlled glycemia, but its effect on early outcomes after off-pump CABG (OPCABG) remains uncertain. **Objective:** To evaluate the effect of continuous intravenous insulin infusion on early postoperative outcomes in diabetic patients undergoing OPCABG. **Methods & Materials:** This prospective observational comparative study was conducted at the National Institute of Cardiovascular Diseases (NICVD), Dhaka, from July 2018 to June 2019. Sixty-four diabetic patients undergoing elective OPCABG were purposively selected and divided equally into a continuous intravenous insulin infusion group (Group A, n=32) and a subcutaneous insulin group (Group B, n=32). Postoperative blood glucose, troponin I, arrhythmia, wound infection, inotropic support, ICU stay, hospital stay, and in-hospital mortality were compared. **Results:** Mean postoperative blood glucose was significantly higher in Group A than Group B on the operative day (184.91±28.40 vs. 163.70±8.32 mg/dL, p<0.001), 1st POD (176.90±25.30 vs. 161.20±19.80, p=0.007), 2nd POD (170.30±17.50 vs. 158.90±14.40, p=0.005), and 3rd POD (168.30±12.20 vs. 157.70±17.60, p=0.007). Troponin I, inotropic support, arrhythmia, wound infection, ICU stay, and hospital stay were also significantly higher in Group A. Mortality did not differ significantly. **Conclusion:** Continuous intravenous insulin infusion was not associated with improved early postoperative outcomes in this study.

Keywords: *Continuous insulin infusion; Diabetes mellitus; OPCABG; Glycemic control; Postoperative outcomes*

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INTRODUCTION

Coronary artery disease (CAD) is a major cause of morbidity and mortality worldwide and is primarily caused by atherosclerotic narrowing of the coronary arteries, resulting in myocardial ischemia and ischemic heart disease [1]. The burden of CAD is also substantial in Bangladesh, although nationally representative epidemiological data remain limited. Available studies have reported considerable variation in CAD prevalence between rural and urban populations, with a particularly high burden among urban working professionals [2,3]. Coronary artery bypass grafting (CABG) remains an established revascularization strategy for patients with significant multivessel or complex coronary artery disease.

Diabetes mellitus (DM) is one of the most important comorbidities influencing the clinical course of patients undergoing CABG. The prevalence of diabetes among patients undergoing CABG is considerably higher than that in the general population, making perioperative glycemic management an important component of cardiac surgical care [4]. The increasing prevalence of diabetes in Bangladesh further emphasizes the importance of effective strategies for managing hyperglycemia in patients undergoing cardiac surgery [5]. Compared with non-diabetic patients, diabetic patients undergoing CABG frequently have more extensive and diffuse coronary artery disease and a higher prevalence of hypertension, renal dysfunction and other cardiovascular comorbidities. Consequently, they are at increased risk of postoperative complications, including myocardial dysfunction, infection, renal impairment, neurological complications and prolonged intensive care unit (ICU) and hospital stay [6-10].

Hyperglycemia during the perioperative period is particularly important in diabetic patients undergoing CABG. Surgical stress stimulates counter-regulatory hormones and promotes increased hepatic glucose production, insulin resistance and lipolysis. Consequently, elevated circulating free fatty acids may increase myocardial metabolic stress and adversely affect myocardial contractility and electrical stability [11]. In addition, hyperglycemia promotes oxidative stress, endothelial dysfunction and inflammation through several mechanisms, including formation of advanced glycation end products, activation of protein kinase C and alterations in the polyol pathway [12-14]. These processes may contribute to impaired vascular function, thrombosis, inflammation and postoperative cardiovascular complications [15,16].

Insulin has metabolic as well as anti-

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inflammatory and endothelial-protective effects. It facilitates myocardial glucose uptake, suppresses free fatty acid release and promotes more efficient myocardial energy utilization. Furthermore, insulin may attenuate inflammatory responses and improve endothelial and platelet function through modulation of nitric oxide-dependent pathways [17-20]. Therefore, appropriate perioperative insulin therapy may provide benefits beyond simple reduction of blood glucose concentration.

Off-pump coronary artery bypass grafting (OPCABG) avoids cardiopulmonary bypass and may reduce some of the inflammatory and metabolic disturbances associated with conventional CABG. However, diabetic patients undergoing OPCABG remain vulnerable to perioperative hyperglycemia and its associated complications. Evidence suggests that both sustained hyperglycemia and acute fluctuations in blood glucose can increase oxidative stress and endothelial injury [21-23]. Thus, maintaining relatively stable and appropriate glycemic control may be particularly important for improving early postoperative outcomes.

Intravenous insulin can be administered intermittently or as a continuous infusion. Continuous intravenous insulin infusion allows more precise and flexible adjustment of insulin requirements during the rapidly changing metabolic conditions of the perioperative period. However, excessive glycemic control may increase the risk of hypoglycemia, which can cause serious neurological and systemic consequences. Therefore, continuous insulin infusion requires close and frequent monitoring of blood glucose levels, particularly during the postoperative ICU period when patients may be sedated and unable to report symptoms of hypoglycemia [24.25].

Several protocols have therefore been developed to achieve controlled perioperative glycemia while minimizing hypoglycemia. The Portland protocol, developed at St. Vincent Medical Center, has been used extensively for continuous intravenous insulin therapy in diabetic patients undergoing open-heart surgery and emphasizes protocol-based insulin administration with regular glucose monitoring [26]. Evidence suggests that effective perioperative glycemic control may reduce postoperative morbidity, wound complications and ICU or hospital stay and may contribute to improved early outcomes following CABG [12,27,28].

Despite the recognized importance of perioperative glycemic management, evidence regarding the effect of continuous intravenous insulin infusion specifically on early outcomes following OPCABG in diabetic patients remains clinically relevant, particularly in resource-limited settings. Therefore, the present study was undertaken to evaluate the effect of continuous intravenous insulin infusion on early postoperative outcomes after off-pump coronary artery bypass grafting in diabetic patients.

OBJECTIVE

The main objective was to evaluate the effect of continuous intravenous insulin infusion on early postoperative outcomes in diabetic patients undergoing off-pump coronary artery bypass grafting (OPCABG).

METHODS & MATERIALS

This prospective observational study was conducted in the Department of Cardiac Surgery at the National Institute of Cardiovascular Diseases (NICVD), Sher-e-Bangla Nagar, Dhaka, Bangladesh, over a period of one year from July 2018 to June 2019.

A total of 64 diabetic patients undergoing elective off-pump coronary artery bypass grafting (OPCABG) were included in the study. Patients were selected purposively after detailed history taking, clinical examination, and relevant investigations according to predefined inclusion and exclusion criteria. Ethical approval was obtained from the Institutional Ethical Review Committee of NICVD, and written informed consent was obtained from all participants before enrollment. Patients with preoperative arrhythmia, associated valvular heart disease, previous or redo CABG, left ventricular ejection fraction (LVEF) ≤35%, significant hepatic or renal dysfunction, chronic obstructive pulmonary disease (COPD), or preoperative cerebrovascular disease including stroke were excluded from the study.

The enrolled patients were divided into two groups according to the method used for perioperative glycemic control, with 32 patients in each group. Group A (CII group) consisted of diabetic patients undergoing OPCABG whose perioperative blood glucose was controlled using continuous intravenous insulin infusion according to the Portland protocol. Group B (SQI group) consisted of diabetic patients undergoing OPCABG whose blood glucose was controlled using sliding-scale subcutaneous short-acting insulin injection. All patients underwent routine preoperative assessment before surgery. Bedside blood glucose was measured using an Accu-Chek glucose analyzer, while laboratory investigations, including serum glucose and other relevant biochemical parameters, were performed using a Beckman Coulter AU480 analyzer.

In Group A, continuous intravenous insulin infusion was initiated in the operating theatre after induction of anesthesia and was continued postoperatively in the intensive care unit according to the Portland protocol. Blood glucose was monitored at intervals specified by the protocol, and the insulin infusion rate was adjusted according to the measured glucose concentration. The target blood glucose level was maintained between 150 and 200 mg/dL. Continuous intravenous insulin infusion was continued until 7:00 AM of the 3rd postoperative day (POD). Patients who had not yet established adequate enteral nutrition continued to receive intravenous insulin even after transfer from the ICU when clinically indicated. Once adequate enteral nutrition was tolerated, preoperative glycemic-control medication was resumed according to the clinical condition of the patient.

In Group B, blood glucose was controlled using sliding-scale subcutaneous short-acting insulin. Subcutaneous insulin was administered at four-hour intervals throughout the hospital course according to the predefined sliding scale, to maintain blood glucose below 200 mg/dL. For comparative assessment of postoperative glycemic control, the average daily blood glucose level was calculated from all blood glucose measurements obtained from the day of surgery through the 2nd POD.

Postoperative monitoring was performed in all patients according to standard cardiac surgical practice. Blood glucose levels were measured serially according to the respective insulin protocol. The average blood glucose level up to the 2nd POD was calculated and compared between the two groups. Patients were monitored continuously by ECG in the ICU until 7:00 AM of the 3rd POD for detection of significant postoperative arrhythmias. Twelve-lead ECG was performed daily up to the 3rd POD and again at hospital discharge. Additional ECG examinations were performed when clinically indicated, particularly in patients with new-onset or persistent atrial fibrillation. Serum troponin I was measured at 7:00 AM on the 3rd POD to assess postoperative myocardial injury. Patients were also evaluated for postoperative wound infection throughout their hospital stay, and any in-hospital mortality was recorded.

Serum potassium levels were maintained between 4.0 and 5.5 mmol/L throughout the postoperative period. Intravenous potassium supplementation was administered according to the standardized ICU protocol, while oral potassium supplementation was given after the patient tolerated enteral nutrition. Any clinically significant postoperative complications were appropriately managed according to standard institutional protocols.

The principal early postoperative outcomes assessed in the study were postoperative blood glucose control, average blood glucose level up to the 2nd POD, significant cardiac arrhythmia, serum troponin I level on the 3rd POD, postoperative wound infection, and in-hospital mortality. The outcomes of patients receiving continuous intravenous insulin infusion were compared with those receiving subcutaneous insulin therapy to evaluate the effect of continuous intravenous insulin infusion on early

outcomes following OPCABG in diabetic patients.

Statistical Analysis: All collected data were checked, verified, coded, and entered into Statistical Package for Social Sciences (SPSS) version 24.0 for analysis. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage. Intergroup comparisons of continuous variables were performed using the independent-samples Student's t-test, while categorical variables were compared using the Chi-square test or Fisher's exact test where appropriate. A p-value <0.05 was considered statistically significant. The results were presented in appropriate tabular and graphical forms.

RESULT

Table I shows the baseline demographic and clinical characteristics of the study participants. The mean age was 56.53 ± 5.01 years in Group A and 58.50 ± 6.80 years in Group B. Males predominated in both groups (75.0% vs. 87.5%). The mean BMI, preoperative blood glucose, ejection fraction, and preoperative troponin I were also comparable between the groups, with no statistically significant differences (p>0.05).

Table I
Baseline demographic and clinical characteristics of the study participants.

Variable		Group A n=32 (%)	Group B n=32 (%)	p-value
Age group	41–50 years	9 (28.1)	6 (18.8)	0.192
	51–60 years	13 (40.6)	15 (46.9)	
	61–70 years	10 (31.3)	11 (34.4)	
Age (years), mean ± SD		56.53 ± 5.01	58.50 ± 6.80	
Gender	Male	24 (75.0)	28 (87.5)	0.2
	Female	8 (25.0)	4 (12.5)	
BMI (kg/m²), mean ± SD		25.47 ± 4.41	24.04 ± 3.48	0.17
Preoperative blood glucose (mg/dL), mean ± SD		178.15 ± 14.60	172.23 ± 13.14	0.093
Ejection fraction (%), mean ± SD		57.50 ± 1.36	58.11 ± 1.30	0.081
Preoperative troponin I, mean ± SD		0.89 ± 0.21	0.78 ± 0.17	0.406

Student's t-test and Chi-square test.

Table II demonstrates the preoperative diabetes treatment and operative characteristics of the study participants. Preoperative diabetes treatment was comparable between the two groups (p=0.428). In Group A, 14 (43.8%) patients were receiving insulin, 15 (46.9%) were receiving oral hypoglycemic agents, and 3 (9.4%) were managed with dietary control. In Group B, these proportions were 10 (31.3%), 16 (50.0%), and 6 (18.8%), respectively. The mean duration of surgery was significantly longer in Group A than in Group B (4.23 ± 0.47 vs. 3.91 ± 0.65 hours, p=0.027). However, the mean number of grafts was similar between the groups (2.81 ± 0.39 vs. 2.75 ± 0.42, p=0.761).

Table II
Comparison of preoperative diabetes treatment and operative characteristics between the two groups.

Variable	Group A N (%)	Group B N (%)	p-value
Preoperative diabetes treatment			
Insulin	14 (43.8)	10 (31.3)	0.428
Oral hypoglycemic agents	15 (46.9)	16 (50.0)	
Diet control	3 (9.4)	6 (18.8)	
Duration of surgery (hours), mean ± SD	4.23 ± 0.47	3.91 ± 0.65	0.027*
Number of grafts, mean ± SD	2.81 ± 0.39	2.75 ± 0.42	0.761

Student's t-test and Chi-square test.

Table III shows the effect of continuous intravenous insulin infusion on postoperative glycemic control. Mean blood glucose levels were significantly higher in Group A than in Group B on the day of surgery and on the 1st, 2nd, and 3rd postoperative days (p<0.05). The 3-day average blood glucose level was also significantly higher in Group A than in Group B (171.80 ± 21.39 vs. 159.30 ± 16.38 mg/dL, p=0.011).

Table III
Effect of continuous intravenous insulin infusion on postoperative glycemic control.

Postoperative period	Group A (n=32), Mean ± SD (mg/dL)	Group B (n=32), Mean ± SD (mg/dL)	p-value
Day of operation	184.91 ± 28.40	163.70 ± 8.32	<0.001*
1st postoperative day	176.90 ± 25.30	161.20 ± 19.80	0.007*
2nd postoperative day	170.30 ± 17.50	158.90 ± 14.40	0.005*
3rd postoperative day	168.30 ± 12.20	157.70 ± 17.60	0.007*
3-day average blood glucose	171.80 ± 21.39	159.30 ± 16.38	0.011*

Student's t-test.

Table IV shows the comparison of postoperative myocardial injury and inotropic support between the two groups. The mean postoperative troponin I level was significantly higher in Group A than in Group B (6.52 ± 1.68 vs. 4.32 ± 1.34, p<0.001). Similarly, the duration of postoperative inotropic support was significantly longer in Group A (55.62 ± 11.60 vs. 45.14 ± 10.19 hours, p=0.001).

Table IV
Effect of continuous intravenous insulin infusion on postoperative myocardial injury and cardiac support.

Outcome	Group A (n=32), Mean ± SD	Group B (n=32), Mean ± SD	p-value
Postoperative troponin I	6.52 ± 1.68	4.32 ± 1.34	<0.001*
Duration of postoperative inotropic support (hours)	55.62 ± 11.60	45.14 ± 10.19	0.001*

Student's t-test.

Table V shows the postoperative complications among the study participants. Postoperative arrhythmia occurred significantly more frequently in Group A than in Group B (18.8% vs. 3.1%, p=0.040). Similarly, wound infection was significantly more common in Group A (15.6% vs. 0%, p=0.021). Although in-hospital mortality was observed only in Group A (3.1% vs. 0%), the difference was not statistically significant (p=0.317).

Table V
Effect of continuous intravenous insulin infusion on postoperative complications.

Postoperative complication	Group A N (%)	Group B N (%)	p-value
Postoperative arrhythmia	6 (18.8)	1 (3.1)	0.040*
Wound infection	5 (15.6)	0 (0.0)	0.021*
In-hospital mortality	1 (3.1)	0 (0.0)	0.317

Chi-square test.

Table VI shows the comparison of ICU and postoperative hospital stay between the two groups. The mean ICU stay was significantly longer in Group A than in Group B (68.45 ± 11.25 vs. 47.84 ± 7.60 hours, p<0.001). Likewise, the mean postoperative hospital stay was significantly longer in Group A than in Group B (25.33 ± 3.56 vs. 14.35 ± 2.16 days, p<0.001).

Table VI
Effect of continuous intravenous insulin infusion on ICU and postoperative hospital stay.

Outcome	Group A (n=32), Mean ± SD	Group B (n=32), Mean ± SD	p-value
ICU stay (hours)	68.45 ± 11.25	47.84 ± 7.60	<0.001*
Postoperative hospital stay (days)	25.33 ± 3.56	14.35 ± 2.16	<0.001*

Student's t-test.

DISCUSSION

The present study evaluated the effect of continuous intravenous insulin infusion on early postoperative outcomes among diabetic patients undergoing OPCABG. Contrary to the expected beneficial effect of continuous insulin therapy, patients in the continuous insulin infusion group had significantly higher postoperative blood glucose levels, higher postoperative troponin I levels, longer inotropic support, higher rates of postoperative arrhythmia and wound infection, and longer ICU and hospital stays than those receiving subcutaneous insulin. These findings differ from several previous studies reporting improved glycemic control and postoperative outcomes with continuous intravenous insulin therapy.

In the present study, postoperative glycemic control was significantly different between the two groups. The mean blood glucose level remained higher in the continuous insulin group from the day of surgery through the third postoperative day, and the 3-day average glucose was also significantly higher. This finding is contrary to the randomized study by Markovitz et al. (2002), in which continuous insulin infusion achieved satisfactory postoperative glucose control in 64.7% of patients compared with only 28.6% receiving intermittent insulin injections [29]. The authors concluded that continuous insulin infusion provided better and faster postoperative glycemic control after CABG.

Similarly, Furnary et al. (2003) reported significantly lower postoperative glucose concentrations among diabetic patients treated with continuous intravenous insulin compared with subcutaneous insulin (177 ± 30 vs. 213 ± 41 mg/dL) [30]. Their large cohort also demonstrated lower mortality with continuous insulin infusion. In another large analysis, Furnary et al. (2004) reported that increasing perioperative glucose levels were associated with increased mortality, deep sternal wound infection, and length of hospital stay, whereas continuous insulin infusion was associated with substantial reductions in mortality and wound infection [26].

The higher postoperative troponin I level observed in Group A in the present study suggests greater biochemical evidence of myocardial injury. This finding contrasts with the proposed cardioprotective effects of insulin described in previous literature. The Portland Diabetic Project suggested that improved glycometabolic control with continuous insulin may enhance myocardial glucose utilization and favorably influence myocardial energy metabolism [26,30]. However, these findings were derived predominantly from observational data and therefore may not establish a direct causal relationship between insulin infusion and myocardial protection.

The present study also demonstrated a significantly higher incidence of postoperative arrhythmia in the continuous insulin group. This is again inconsistent with the findings of Furnary et al., who observed reductions in postoperative cardiac complications, including new-onset atrial fibrillation, following implementation of continuous insulin therapy [26,30]. The difference between the present findings and previous reports may be related to differences in patient characteristics, perioperative management, insulin protocols, glucose targets, and the use of OPCABG rather than conventional CABG.

Wound infection was significantly more frequent in the continuous insulin group in the present study (15.6% vs. 0%). This finding differs markedly from previous evidence. Zerr et al. (1997) demonstrated that improved perioperative glucose control reduced the risk of postoperative wound infection in diabetic patients undergoing cardiac surgery [31]. The Portland experience similarly reported a substantial reduction in deep sternal wound infection following implementation of continuous intravenous insulin therapy [26,30]. Furthermore, a propensity-matched study of diabetic patients undergoing CABG with bilateral internal mammary artery grafts found significantly fewer deep sternal wound infections with continuous insulin infusion than with sliding-scale insulin therapy [32].

The longer duration of inotropic support observed in Group A is also inconsistent with the proposed cardiovascular benefits of continuous insulin therapy. The Portland Diabetic Project reported improved cardiac outcomes with continuous insulin treatment, including reductions in cardiac-related mortality [26,30]. Nevertheless, postoperative inotropic requirement is influenced by several factors, including myocardial ischemia, ventricular function, operative duration, hemodynamic instability, and anesthetic management. Therefore, the difference observed in the present study should not necessarily be attributed solely to the insulin regimen.

In the present study, ICU and postoperative hospital stays were significantly longer in Group A. This finding contrasts with previous observational evidence. Nyenwe et al. (2011) reported that continuous intravenous insulin was associated with a shorter postoperative hospital stay among diabetic patients undergoing CABG, although complication rates were similar between continuous infusion and subcutaneous insulin groups [33]. The Portland Diabetic Project also reported an association between improved glycemic control with continuous insulin therapy and reduced length of hospital stay [26,30].

One possible explanation for the discrepancy is that the present study was conducted in a relatively small population of only 64 patients, with 32 patients in each group. Moreover, the study was prospective observational rather than randomized. Importantly, the duration of surgery was significantly longer in Group A than in Group B, which could have contributed to postoperative myocardial injury, hemodynamic instability, prolonged inotropic support, and longer ICU and hospital stays. Other potentially important confounding variables may also have influenced the outcomes.

Another important consideration is the glucose target used in the present study. Group A was managed according to the Portland protocol with a target of 150–200 mg/dL, whereas contemporary approaches increasingly favor avoidance of both severe hyperglycemia and excessive glucose lowering. The optimal perioperative glucose target remains controversial. The GLUCO-CABG randomized trial found no significant advantage of intensive glucose control targeting 100–140 mg/dL compared with a more conservative target of 141–180 mg/dL for reducing major postoperative complications [34]. This suggests that excessively aggressive glycemic control may not necessarily translate into better clinical outcomes.

A review by Umpierrez and Korytkowski (2016) emphasized that perioperative hyperglycemia is common in cardiac surgery and is associated with adverse outcomes, while the optimal glucose target remains uncertain [35]. Therefore, the objective of perioperative insulin therapy should be appropriate and stable glycemic control while avoiding both severe hyperglycemia and hypoglycemia, rather than simply administering insulin continuously.

Overall, the findings of the present study differ from much of the previous literature, which generally supports continuous intravenous insulin infusion for achieving better glycemic control and reducing postoperative complications after CABG. The discrepancy may be explained by the small sample size, observational study design, differences in patient characteristics and surgical techniques, differences in glucose targets and insulin protocols, and possible confounding by the significantly longer operative duration in the continuous insulin group. Therefore, the present findings should be interpreted cautiously and confirmed by larger randomized studies, particularly among diabetic patients undergoing OPCABG.

LIMITATIONS

This study had several limitations. First, the sample size was relatively small, with only 64 patients, which may have limited the statistical power and generalizability of the findings. Second, the study had a prospective observational design rather than a randomized controlled design, and purposive sampling may have introduced selection bias. Third, the duration of surgery was significantly longer in the continuous insulin infusion group, which may have acted as a confounding factor for postoperative complications and recovery. Fourth, the study was conducted at a single tertiary cardiac center, limiting the generalizability of the findings to other settings. Finally, only early postoperative outcomes were assessed, and long-term outcomes were not evaluated.

CONCLUSION

Continuous intravenous insulin infusion did not demonstrate better early postoperative outcomes than subcutaneous insulin therapy in diabetic patients undergoing OPCABG in this study. The continuous insulin group had significantly higher postoperative blood glucose and troponin I levels, greater postoperative arrhythmia and wound infection rates, longer inotropic support, and prolonged ICU and hospital stays. However, these findings should be interpreted cautiously because of the small sample size, observational study design, and significant difference in operative duration between the groups. Larger, well-designed randomized controlled studies are needed to determine the optimal perioperative insulin strategy for diabetic patients undergoing OPCABG.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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