Changing glucose control target and risk of surgical site infection in a Southeast Asian population

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Objective: Hyperglycemia is associated with surgical site infection and mortality in cardiac surgical patients. There is overriding evidence that glycemic control improves morbidity and mortality. However, the optimal glucose range in these patients remains controversial. Intensive glucose control can lead to mortality among critically ill adults because of episodic, moderate hypoglycemia. Therefore, we examined the effect of different glucose target control on the incidence of surgical site infection in our prospective cohort of diabetic and nondiabetic patients undergoing coronary artery bypass grafting.

Methods: Data from 1442 patients who underwent elective coronary artery bypass grafting at a tertiary heart center in Singapore from 2009 to 2011 were obtained. The first glucose level on arrival in the cardiothoracic intensive care unit was set at 4 to 8 mmol/L in 2009 and 2010 and 4 to 10 mmol/L in 2011. Glucose control was achieved with intravenous insulin infusion with a strict glucose monitoring protocol. Clinical covariates were analyzed, with surgical site infection as the primary outcome.

Results: The majority of patients presenting for coronary artery bypass grafting were male, Chinese, and diabetic. Diabetic patients had significantly higher glucose levels on arrival in the cardiothoracic intensive care unit. The change in target glucose control was independently associated with an increase in surgical site infection (odds ratio, 2.280; 95% confidence interval, 1.250-4.162; $P = .007$). Subgroup analysis revealed that unlike in nondiabetic patients, a less stringent target was independently associated with a significant increase in surgical site infection incidence from 2.2% to 6.9% for the diabetic patients (odds ratio, 3.131; 95% confidence interval, 1.431-6.851; $P = .004$).

Conclusions: A target blood glucose of less than 8 mmol/L was associated with a lower incidence of surgical site infection in diabetic patients presenting for elective coronary artery bypass grafting in the local Southeast Asian population. (J Thorac Cardiovasc Surg 2015;149:323-8)

See related commentary on pages 328-9.

Hyperglycemia is associated with adverse outcomes in cardiac surgical patients, including increased morbidity, such as surgical site infection (SSI), and mortality.[1,2] Patients with insulin resistance or diabetes mellitus (DM) who undergo coronary artery bypass grafting (CABG) may develop hyperglycemia.[3] Factors contributing to the increase in insulin resistance include increased levels of catecholamines, growth hormone, and cortisol as a stress response to surgery or from pharmacologic agents given perioperatively, such as inotropes and beta-blockers.

There is overriding evidence that glycemic control improves both morbidity, such as SSI, and mortality in patients undergoing CABG.[4-6] However, the optimal range for blood glucose in cardiac surgical patients remains an area of controversy, and it is unclear whether the target control is different between diabetic and nondiabetic patients. The general consensus remains that glucose levels greater than 200 mg/dL (>11.1 mmol/L) is detrimental, but the lower limit and the tightness of control is debatable. In the original study of tight glucose control by Van den Berghe and colleagues,[7,8] a glucose control between 81 and 108 mg/dL (4 and 6 mmol/L) was advocated, but in a recent multicenter trial (Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation [NICE-SUGAR]),[9] intensive glucose control actually led to increased mortality among critically ill adults, primarily because of episodes of moderate hypoglycemia. Therefore, we

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
CT-ICU = cardiothoracic intensive care unit
DM = diabetes mellitus
SSI = surgical site infection
NICE-SUGAR = Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation

embarked on this study to determine the incidence of SSI at both the sternotomy and the graft harvest sites in our population and to study the effect of the change in glucose target control from 75 to 150 mg/dL (4-8 mmol/L) to 75 to 180 mg/dL (4-10 mmol/L) on the incidence of SSI.

Given that the prevalence of DM in our local population who present for CABG is approximately 50%, which is higher than that of the Western population,[10-12] it is important for us to determine an optimal blood glucose range to reduce the incidence of SSI and subsequent mortality. Therefore, we also aimed to study the difference in target control between diabetic and nondiabetic patients in our local Asian population undergoing CABG.

PATIENTS AND METHODS

Patient Selection

After institutional review board approval, we prospectively followed up 1481 patients who underwent elective isolated CABG with open vein harvesting between January 1, 2009, and December 31, 2011, at a tertiary heart center in Singapore. Written informed consent was obtained from all patients. All patients, regardless of their DM status, were included in this study. However, 39 patients were excluded because there were incomplete data for analysis. Therefore, the total number of patients who met the inclusion and exclusion criteria was 1442.

Targets for Glucose Control in Insulin Protocol

Between 2009 and 2010, as part of a clinical improvement project, the target first glucose on arrival in the cardiothoracic intensive care unit (CT-ICU) was set at 4 to 8 mmol/L. The upper limit was increased to 10 mmol/L in 2011 on the basis of the suggested guidelines of the Society of Thoracic Surgeons Practice Guideline series: Blood Glucose Management During Adult Cardiac Surgery.[13] Blood glucose targets were maintained via intravenous insulin with a sliding scale. Hyperglycemia and hypoglycemia were defined as greater than 11.1 mmol/L and less than 4.0 mmol/L, respectively.

Postoperative Glucose Monitoring

All patients undergoing elective CABG during the study period had their blood glucose level monitored immediately on arrival to the CT-ICU. This level is a surrogate marker of the intraoperative glucose control. In the postoperative period in the CT-ICU, blood glucose was monitored every 2 to 4 hours, and more frequently if needed, up to the first 48 hours. All blood glucose levels were measured with standard point-of-care analyzers in the hospital. All glucose readings of a patient were measured from the same point-of-care machine.

Postoperative Surgical Site Infection

The primary outcome of this study was SSI. This includes both superficial (graft site) and deep (sternal) infection. An infection control nurse who was blinded to the study assessed the patients daily until the day of discharge for evidence of infection.

Surgical and Perfusion Management

All CABG procedures at our institution were performed with blood cardioplegia as the method of myocardial protection. The conditions and conduct of cardiopulmonary bypass remained constant throughout the study period.

Statistical Analysis

Population demographics, medical history, preoperative risk assessment, intraoperative variables, and postoperative outcomes were analyzed descriptively. Univariate analysis was performed using a Mann-Whitney U test for continuous variables and Fisher exact test for categorical variables. The factors from the univariate analysis with $P < .05$ were included in the multivariate logistic regression model for further analysis.

One-way analysis of variance with post hoc Bonferroni correction was done to calculate the statistical significance when comparing the diabetic and nondiabetic patients with and without SSI. All statistical analyses were performed using IBM SPSS version 21.0. (IBM, Armonk, NY).

RESULTS

Between 2009 and 2011, a total of 1481 patients underwent elective isolated CABG with open vein harvesting. Complete data were captured for 1442 of these patients, and they were subsequently analyzed.

Patient Demographics

There was no significant change in patient profile over the 3 years (Table 1).

Differences Between Diabetic and Nondiabetic Patients

There was a significantly larger proportion of female patients who were diabetic compared with the male patients. More Indians were diabetic, and this was consistent over the study period. Median preoperative serum glucose level was significantly higher in the diabetic population (8.2 mmol/L) than in the nondiabetic population (5.9 mmol/L). Likewise, glycosylated hemoglobin A1c among diabetic patients was significantly higher at 7.5% (25th-75th percentile: 6.7%-8.6%) than in nondiabetic patients, 5.8% (25th-75th percentile: 5.6%-6.1%) (Table 2).

The durations of both cardiac bypass and surgery were similar in the cohorts over the 3 years. Diabetic patients had significantly higher levels of the first glucose on arrival to the CT-ICU and up to 48 hours postoperatively in comparison with their nondiabetic counterparts ($P < .001$). The incidence of hyperglycemia within the first 48 hours on arrival to the ICU was significantly higher for the diabetic patients ($P < .001$) (Table 2).

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