Strict versus liberal target range for perioperative glucose in patients undergoing coronary artery bypass grafting: A prospective randomized controlled trial

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Objective: The purpose of this study was to test the hypothesis that a liberal blood glucose strategy (121–180 mg/dL) is not inferior to a strict blood glucose strategy (90–120 mg/dL) for outcomes in patients after first-time isolated coronary artery bypass grafting and is superior for glucose control and target blood glucose management.

Methods: A total of 189 patients undergoing coronary artery bypass grafting were investigated in this prospective randomized study to compare 2 glucose control strategies on patient perioperative outcomes. Three methods of analyses (intention to treat, completer, and per protocol) were conducted. Observed power was robust (>80%) for significant results.

Results: The groups were similar on preoperative hemoglobin A_{1c} and number of diabetic patients. The liberal group was found to be noninferior to the strict group for perioperative complications and superior on glucose control and target range management. The liberal group had significantly fewer patients with hypoglycemic events (<60 mg/dL; $P < .001$), but severe hypoglycemic events (<40 mg/dL) were rare and no group differences were found ($P = .23$). These results were found with all 3 methods of analysis except for blood glucose variability, maximum blood glucose, and perioperative atrial fibrillation.

Conclusions: This study demonstrated that maintenance of blood glucose in a liberal range after coronary artery bypass grafting led to similar outcomes compared with a strict target range and was superior in glucose control and target range management. On the basis of the results of this study, a target blood glucose range of 121 to 180 mg/dL is recommended for patients after coronary artery bypass grafting as advocated by the Society of Thoracic Surgeons. (J Thorac Cardiovasc Surg 2012;143:318-25)

In recent years, data have shown that uncontrolled hyperglycemia is associated with poor clinical outcomes after surgical interventions.[1-7] Likewise, control of glucose can improve outcomes in critically ill patients. Since the landmark study by Van den Berghe and colleagues[2] in 2001, there have been guidelines for strict glycemic control in the intensive care unit (ICU). Over the past several years, the debate has been which patient population (surgical or medical) will benefit most from strict glycemic control and how strict a protocol is required.[1-7]

Hyperglycemia is commonly encountered after cardiac surgery, whether a patient has a history of diabetes or not.[1] Hyperglycemia has been associated with increased perioperative morbidity and mortality; several studies have demonstrated that glycemic control using insulin protocols improves operative mortality, lowers operative morbidity, and improves long-term survival.[2-4]

Although the consensus is that hyperglycemia should be managed after surgery, the optimal target serum glucose level that minimizes both perioperative complications and hypoglycemic events has yet to be established. In 2004, Lazar and colleagues[6] demonstrated that maintaining the serum glucose between 120 and 180 mg/dL in diabetic patients undergoing cardiac surgery is safer and that a stricter regimen did not contribute to improved outcome. However, their study dealt only with diabetic patients, who comprise less than 50% of the operated population in the majority of centers. The Society of Thoracic Surgeons (STS) recommends that insulin infusions be titrated to maintain serum glucose at less than 180 mg/dL for the duration of the perioperative ICU stay.[2,4] The recently completed Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial found that intensive glucose control (81–108 mg/dL) actually increased 90-day mortality compared with a more liberal glucose

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Abbreviations and Acronyms

BG = blood glucose
CABG = coronary artery bypass grafting
ICU = intensive care unit
NICE-SUGAR = Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation
STS = Society of Thoracic Surgeons

target (<180 mg/dL) in patients in the ICU.[7] However, this study was not focused solely on patents undergoing cardiac surgery and was mainly comprised of nonoperative patients, often with sepsis and multiorgan dysfunction.

Lazar and colleagues[8] recently completed a prospective, randomized trial in diabetic patients undergoing coronary artery bypass grafting (CABG) to determine whether tight glycemic control (90–120 mg/dL) would result in more optimal clinical outcomes than a more moderate glycemic control (120–180 mg/dL). They found that tight glycemic control increased the incidence of hypoglycemic events, but did not result in any significant improvement in clinical outcomes that was achieved with the more moderate control; however, this study also dealt only with diabetic patients. For the past several years, our patient management has dictated strict glycemic control with blood glucose (BG) levels maintained in the range of 90 to less than 120 mg/dL for all patients undergoing cardiac surgery. Our study aimed to compare the current practice of strict control with a liberal strategy: BG maintained at less than 180 mg/dL (121–180 mg/dL).

MATERIALS AND METHODS

A randomized controlled study was performed to test the hypothesis that a liberal strategy of serum glucose control (BG 121–180 mg/dL) is not inferior to a strict strategy (BG 90–120 mg/dL) in patients after first-time isolated CABG for complications and outcomes and is superior for glucose control and target BG management.

This study was a prospective, randomized controlled single-center clinical trial that examined adult patients undergoing first-time isolated CABG in whom hyperglycemia developed, thus requiring insulin therapy for treatment. All patients, regardless of a history of diabetes, were eligible for inclusion in this trial if they had 3 or more blood glucose readings of more than 150 mg/dL or 1 BG reading more than 200 mg/dL (considered our standard of care). The study was approved by the Human Research Protection Program at Inova Heart and Vascular Institute (institutional review board number 09.111), and informed consent was obtained from all patients. This study was also registered on ClinicalTrials.gov.

INCLUSION CRITERIA

1. All diabetic patients who underwent first-time, isolated, nonemergency CABG.
2. Nondiabetic patients who underwent first-time, isolated, nonemergency CABG who were found to have had 3 consecutive BG readings greater than 150 mg/dL or any 1 BG reading greater than 200 mg/dL perioperatively, which is aligned with the current STS guidelines.
3. Patients who were started on an insulin infusion while in the operating room.

EXCLUSION CRITERIA

1. Patients who underwent open surgery other than isolated CABG.
2. Patients who were found not to require an insulin infusion post-CABG.
3. Patients who underwent a concomitant procedure in addition to CABG (eg, CABG + valve repair).

STUDY TREATMENT AND INTERVENTION

Once enrolled, patients underwent a series of preoperative blood tests, anthropomorphic measurements, and assessment scales and inventories as noted in Figure 1. Questionnaires assessing depression (Patient Health Questionnaire 9), health-related quality of life (Short Form-12), diet, and physical activity (Duke Activity Score) were filled out by patients preoperatively, although these results will not be included in the present analyses.

Intraoperative glucose measures and interventions were under the purview of the anesthesiologist, whose goal was to maintain a BG level between 100 and 180 mg/dL. Maintenance of BG levels according to their randomized arm was started in the ICU using the programmed Glucommander (Gluco Tec, Greenville, SC) to adjust the BG level to patients' assigned range. The nursing staff was not blinded to treatment group allocation. Hourly BG monitoring was performed with blood obtained from a patient's arterial line and analyzed by point of care testing through Glucose Accu-Chek Advantage with the AccuData GTS/GTS manufactured by Roche (Basel, Switzerland). BG levels less than 40 mg/dL or greater than 500 mg/dL were sent to the laboratory for further analysis; however, treatment was initiated for low BG if indicated. Patients were maintained on the electronic-based protocol of intravenous insulin for a minimum of 72 hours perioperatively.

GLUCOMMANDER

The Glucommander is a Food and Drug Administration–approved computer software system for controlling BG designed to assist clinicians in obtaining and then maintaining glucose control by calculating the insulin dose required to achieve the target range in response to measurement of BG at the patient's bedside, but does not administer the insulin. It is the current method of glycemic control for patients post-CABG at our institution. We previously validated[9] increased efficiency and efficacy of Glucommander data.

The Glucommander uses the variables of patients' height, weight, HbA_{1C}, and current and cumulative BG values to