Preoperative Glycosylated Hemoglobin: A Risk Factor for Patients Undergoing Coronary Artery Bypass

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Background. **The prevalence of diabetes in the population of patients presenting with coronary artery disease continues to rise. The aim of this study was to assess whether high Glycosylated hemoglobin (HbA1c) was associated with adverse outcomes in patients undergoing elective coronary artery bypass grafting.**

Methods. **A retrospective observational study on prospectively collected data in 4,678 patients undergoing elective, isolated coronary artery bypass graft procedures in a single institution over a 4-year period was conducted. Patients were grouped into those with adequate preoperative control of hyperglycemia (HbA1c <6.5%) and those with suboptimal control (HbA1c ≥6.5%). Multivariable analysis using HbA1c as a binary independent variable was undertaken in the whole group. A subgroup analysis in diabetic patients and in nondiabetic patients was performed. The effect of HbA1c on outcomes at higher levels (HbA1c ≥8.0% and HbA1c ≥9.0%) was also assessed.**

Results. **A total of 4,678 patients (mean age, 58.8; male, 4,254) were included in the study. HbA1c was less than 6.5% in 2,476 (52.93%) patients and 6.5% or higher in 2,202 (47.07%) patients. On multivariate analysis, there was no difference in mortality rates between the groups (odds ratio, 1.36; 95% confidence interval [CI], 0.95 to 1.953; $p = 0.08$). Overall, an HbA1c of 6.5% or higher was an independent risk factor for respiratory complications (odds ratio, 1.05; 95% CI, 1.008 to 4.631; $p = 0.01$) and sternal dehiscence (odds ratio, 2.161; 95% CI, 1.008 to 4.63; $p = 0.04$). An association between HbA1c levels and adverse outcomes was not seen in nondiabetic patients. No additional adverse postoperative complications were seen with increasing HbA1c levels (HbA1c ≥8.0% and HbA1c ≥9.0%).**

Conclusions. **An HbA1c level of 6.5% or higher in patients presenting for coronary artery bypass grafting was associated with a significant increase in the incidence of deep sternal wound infection and respiratory complications.**

(Ann Thorac Surg 2017;104:606–12)

The relationship between diabetes and adverse outcomes after coronary artery bypass continues to be a subject of interest and research. The prevalence of diabetes in the population of patients presenting with coronary artery disease continues to rise, from 19% in the past to more than 40% more recently [1–3]. Many studies have reported an association between diabetes and postoperative morbidity, short-term mortality, and reduced long-term survival after coronary operations [4, 5].

This knowledge has led to the development of protocols that ensure strict glycemic control during the intraoperative and the immediate postoperative periods, and improved outcomes have been seen with this strategy [6]. Although the relevance of maintaining in-hospital glycemic control is well established, the importance of optimal glycemic control before the operative procedure has been confounded by various other considerations. Most studies of preoperative hyperglycemia have categorized patients into diabetic patients and nondiabetic patients [7], or insulin-dependent versus non–insulin-dependent [8], or by the type of diabetes, either type 1 or type 2 [5]. Very few studies have categorized diabetic patients with good versus suboptimal preoperative glycemic control irrespective of the type of diabetes or the treatment strategy.

Glycosylated hemoglobin (HbA1c) is considered to be the best marker to assess glycemic control because it reflects a time-weighted mean over the previous 3 to 4

Accepted for publication Dec 8, 2016.

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The Appendix can be viewed in the online version of this article [http://dx.doi.org/10.1016/j.athoracsur.2016.12.020] on http://www.annalsthoracicsurgery.org.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.12.020

months and is also a good predictor of complications [9]. Therefore the main aim of this study was to assess whether a high HbA1c level was associated with adverse postoperative outcomes in patients undergoing coronary artery bypass grafting (CABG). We also sought to examine whether an incremental HbA1c level led to increased adverse outcomes in the study population.

Material and Methods

A total of 4,678 consecutive patients undergoing primary, isolated, elective CABG at a single tertiary care center (NH Rabindranath Tagore International Institute of Cardiac Sciences, Kolkata, India) between 2011 and 2014 were included in the study. This was a retrospective study of prospectively collected data. Ethical approval was obtained from the institutional ethics committee.

The exclusion criteria included patients requiring emergency operations, patients with history of previous cardiac surgical procedures, and patients with any concomitant valvular involvement.

Patients were stratified, based on the presence or absence of elevated preoperative HbA1c levels ($\geq$6.5%) and not on the basis whether they were known diabetic patients. Therefore patients having an HbA1c of less than 6.5%, included both patients with known but well-controlled diabetes and nondiabetic patients. Patients with an HbA1c of 6.5% or higher in turn included known diabetic patients whose blood glucose control was not satisfactory as well as previously undiagnosed diabetic patients.

Comparison of the two groups was made in terms of baseline characteristics, operative details, and postoperative outcomes. Multivariate analysis using the HbA1c as a binary independent variable was undertaken, and adjusted odds ratios (ORs) for adverse outcomes were calculated. A multivariate subgroup outcome analysis for known diabetic patients and nondiabetic patients was also undertaken.

To assess whether rising HbA1c levels increased the risk of adverse outcomes, the group with an HbA1c of 6.5% or higher was further subdivided into three subgroups based on a 1% increase in HbA1c levels (6.5% to 7.4%; 7.5% to 8.4% and $\geq$8.5%). Moreover, multivariate outcome analysis at two different HbA1c levels ($\geq$8.0% and $\geq$9.0%) was undertaken.

Definitions

Patients were defined as diabetics if they were known to have high blood glucose or HbA1c levels in the past and were receiving some form of treatment for the condition. Definitions for variables such as renal failure, chronic lung disease, deep sternal wound infection, sternal dehiscence, postoperative myocardial infection, respiratory complications, neurologic complications, and gastrointestinal complications were determined according to The Society of Thoracic Surgeons National Database.

Surgical Techniques

The strategy of revascularization, off-pump coronary artery bypass, or coronary artery grafting with conventional cardiopulmonary bypass, was at the discretion of the operating surgeon. The left internal thoracic artery (LITA) was harvested as a pedicle graft in almost all the cases. Proximal anastomoses were performed using a partial occlusion aortic clamp.

Anesthetic Techniques

A standard anesthetic technique was used throughout. Briefly, fentanyl (20 to 35 mg/kg) and pancuronium (0.1 mg/kg) were used in all cases along with isoflurane or propofol. An individualized calculation of heparin and protamine dose was carried out using the R_xD_x system (International Techidyne Corp, NJ) to minimize protamine-induced complement activation. Intraoperative transesophageal echocardiography was used in the event of any hemodynamic instability to assess regional wall motion abnormality.

Blood Glucose Control

In the preoperative period we aimed at keeping the blood glucose level lower than 180 mg/dL. Oral antidiabetic agents were stopped 24 hours before the operation. Subcutaneous insulin was used as required to maintain blood glucose levels lower than 180 mg/dL. All patients were treated with a uniform perioperative intravenous insulin protocol. In the operating room, an insulin infusion was premixed with 80 units of insulin in 40 mL 0.9% normal saline solution. Routine measurement of blood glucose was obtained from serial arterial blood gases measured every 30 minutes intraoperatively. In the intensive care unit, glucose levels were obtained from arterial blood gas samples every 2 hours. Patients with intraoperative blood glucose levels higher than 180 mg/dL were treated with insulin infusion. Once started, the infusion was continued in the intensive care unit. If no insulin infusion was required in the operating room, insulin was started only if the blood glucose level was found to be more than 180 mg/dL in the intensive care unit and was adjusted to target intraoperative blood glucose between 150 and 180 mg/dL. If the blood glucose level fell to less than 150 g/dL, the insulin infusion was stopped. In the ward, blood glucose values were obtained every 4 to 6 hours, and a euglycemic state was maintained with the help of a sliding scale and additional subcutaneous insulin if required. Endocrinology review was obtained for patients with newly diagnosed or poorly controlled diabetes in the postoperative period.

Statistical Analysis

All continuous variables were expressed as mean $\pm$ SD and compared across the two groups using unpaired t test. All categorical variables were expressed as numbers and percentages. The two groups (patients with HbA1c $<$6.5% vs those with HbA1c $\geq$6.5%) were compared using Pearson's χ^2 test. Fisher's exact test was used if the expected frequencies were lower than 5. Univariate logistic regression was performed to identify predictors of adverse outcomes. In the multivariate model HbA1c was the variable of interest. The full multivariate model included 17 covariates: age, sex, body mass index,