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



Pradeep Narayan, FRCS[CTh], Sarang Naresh Kshirsagar, DNB, Chandan Kumar Mandal, FNB, Paramita Auddya Ghorai, MS, Yashaskar Manjunatha Rao, MBBS, Debasis Das, Mch, Atanu Saha, MS, Saibal Roy Chowdhury, FNB, Emmanuel Rupert, MD, and Mrinalendu Das, Mch

Departments of Cardiac Surgery, Anesthesia and Critical Care, and Bio-Statistics, NH Rabindranath Tagore International Institute of Cardiac Sciences, Kolkata, India

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 \geq 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 \geq 0.0%) 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%

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 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) © 2017 by The Society of Thoracic Surgeons

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-insulindependent [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

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.

Accepted for publication Dec 8, 2016.

Address correspondence to Dr Narayan, Department of Cardiac Surgery, NH Rabindranath Tagore International Institute of Cardiac Sciences, Mukundapur, Kolkata 700099, India; email: pradeepdoc@gmail.com.

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 post-operative 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,

additive EuroSCORE, recent myocardial infarction, unstable angina, peripheral vascular disease, hypertension, chronic obstructive airway disease, diabetes mellitus, preoperative renal dysfunction, preoperative neurologic event, ejection fraction <40%, presence of left main stem disease, presence of triple-vessel disease, LITA use and HbA1c level. Effect size was reported as an OR and its 95% confidence interval (CI). In a sensitivity analysis, HbA1c was tested as a continuous variable. All statistical tests were evaluated using a two-tailed .05 level of significance. The data were analyzed with SPSS version 22 (IBM Corp, Armonk, NY).

Results

A total of 4,678 patients (mean age, 58.8 years; male 4254) were included in the study. In this study group HbA1c was lower than 6.5% in 2,476 (52.93%) patients and 6.5% or higher in 2,202 (47.07%) patients; 3,045 (65%) of the study patients had known diabetes. Of these diabetic patients 1,867 (61.9%) had an HbA1c of 6.5% or higher. Out of 1,633 (34.9%) nondiabetic patients; 335 (7.16%) patients had an HbA1c of 6.5% or higher The group with an HbA1c of 6.5% or more had a significantly larger number of women, higher body mass index, and higher incidence of hypertension (Table 1). No other demographic differences were seen among the groups. The mean in-hospital blood glucose levels were 129.1 \pm 24.3 mg/dL and 133 \pm 27.4 mg/dL, respectively.

Operative characteristics in both groups were essentially similar. The numbers of grafts in the groups were 2.78 \pm 0.86 and 2.83 \pm 0.83, respectively. Radial artery

usage was similar (234 [9.45%] vs 195 [8.85%]; p = 0.52),
and similar numbers of LITA-to-left anterior descending
(LAD) artery anastomosis were performed in both groups
(2,086 [84.2%] vs. 1,847 [83.8%]; <i>p</i> = 0.74). Bilateral internal
thoracic artery was used in only 35 (0.74%) patients in
total, and was used predominantly (26 [72%]) in the group
with an HbA1c of less than 6.5%. The strategy of revas-
cularization was also similar in both groups and was off-
pump coronary artery bypass in most patients (1,869
[75.49%] vs 1,623 $[73.71]$; $p = 0.16$).

On univariate analysis, the incidences of deep sternal wound infections, sternal dehiscence, respiratory complications, neurologic complications, and renal complications were all significantly higher in the group with a preoperative HbA1c of 6.5% or higher (Table 2). However, the composite infection rate, comprising superficial and deep sternal wound infections, leg wound infections, respiratory infections, and urinary tract infections, was similar between the groups (Table 3).

The 30-day mortality was significantly higher in the group with a preoperative HbA1c of 6.5% or higher (76 [3.07%] vs 93 [4.22%]; p = 0.035). However, on multivariate analysis an HbA1c of 6.5% or higher was associated with an increase in only respiratory complications and sternal dehiscence (Table 4). Moreover, in nondiabetic patients an HbA1c of 6.5% or higher did not have any adverse affect on outcomes (Table 4). Detailed logistic regression analyses for postoperative sternal dehiscence, respiratory complications, neurologic complications, gastrointestinal complications, atrial fibrillation, and 30-day mortality, with the ORs, are enumerated in the Appendix.

Preoperative Variables	Glycosylated Hemoglobin $<6.5\%$ (n = 2,476)	Glycosylated Hemoglobin $\geq 6.5\%$ (n = 2,202)	p Value
Age (years)	58.8 ± 9.3	58.93 ± 8.51	0.624
Female sex	177 (7.15%)	247 (11.22%)	<0.001
Body mass index	23.54 ± 3.47	24.07 ± 3.6	<0.001
EuroSCORE			
0–2	1,243 (50.2%)	998 (45.32%)	0.195
3–5	949 (38.32%)	918 (41.68%)	
>5	284 (11.47%)	286 (12.98%)	
Recent myocardial infarction (between 8 and 21 days)	383 (15.47%)	352 (15.99%)	0.628
Unstable angina	798 (32.23%)	750 (34.06%)	0.184
Peripheral vascular disease	80 (3.23%)	95 (4.31%)	0.051
Hypertension	1,486 (60.02%)	1,560 (70.84%)	<0.001
Smoking	622 (25.12%)	579 (26.29%)	0.359
Chronic lung disease	183 (7.39%)	147 (6.68%)	0.34
Known diabetes	1,178 (47.58%)	1,867 (84.79%)	<0.001
Hypothyroidism	98 (3.96%)	109 (4.95%)	0.1
Preoperative renal impairment	97 (3.92%)	98 (4.45%)	0.363
Previous neurologic event	36 (1.45%)	31 (1.41%)	0.895
Ejection fraction <40%	243 (9.81%)	231 (10.49%)	0.444

Table 1. Baseline Characteristics

ADULT CARDIAC

Bold indicates significant values.

EuroSCORE = European System for Cardiac Operative Risk Evaluation.

Postoperative Complications	Glycosylated Hemoglobin $<6.5\%$ (n = 2,476)	Glycosylated Hemoglobin $\geq 6.5\%$ (n = 2,202)	p Value
High inotropic support	49 (1.98%)	52 (2.36%)	0.369
Atrial fibrillation	343 (13.85%)	314 (14.26%)	0.689
Need for intraaortic balloon pump	170 (6.87%)	166 (7.54%)	0.374
Respiratory complication	450 (18.17%)	468 (21.25%)	0.008
Renal failure	73 (2.95%)	96 (4.36%)	0.01
Gastrointestinal complications	49 (1.98%)	44 (2%)	0.963
Neurologic complications	45 (1.82%)	72 (3.27%)	0.001
Sternal dehiscence	11 (0.44%)	28 (1.27%)	0.002

Table 2. Univariate Comparison of Postoperative Outcomes

Diabetic patients with an HbA1c lower than 6.5% had a significantly lower incidence of respiratory complications (188 [16%] vs 394 [21.1%], p = 0.001), sternal dehiscence (6 [0.5%] vs 26 [1.4%]; p = 0.032); deep sternal wound infections (9 [0.8%] vs 36 [1.9%]; *p* = 0.015), and neurologic complications (26 [2.2%] vs 69 [3.7%]; p = 0.03) compared with diabetic patients who had an HbA1c level of 6.5% or higher on univariate analysis.

Nondiabetic patients with an HbA1c of 6.5% or higher revealed no increased risk compared with nondiabetic patients with an HbA1c lower than 6.5%. Both the groups were comparable in terms of mortality (37 [2.85%] vs 13 [3.88%]; p = 0.37) and postoperative adverse outcomes such as sternal dehiscence (5 [0.38%] vs 2 [0.59%]; p = 0.63), respiratory complications (262 [20.18%] vs 74 [22.08%]; p = 0.44), atrial fibrillation (193 [14.86%] vs 53 [15.82%]; p = 0.66), renal failure (27 [2.08%] vs 17 [2.68%]; p = 0.53), gastrointestinal complications (24 [1.84%] vs 7 [2.08%]; p = 0.82), and neurologic complications (19 [1.46%] vs 3 [0.89%]; p = 0.59). Multivariate analysis also did not reveal any differences between the groups (Table 4).

Unadjusted comparison of the three subgroups (HbA1c 6.5% to 7.4%; HbA1c 7.5% to 8.4%, and HbA1c ≥8.5%) showed that the incidence of atrial fibrillation was 154 (14.58%) versus 87 (17.46%) versus 73 (11.26%), respectively. Thus there was a significantly lower incidence of atrial fibrillation in the group with an HbA1c of 8.5% or higher (p = 0.01); there was no intergroup significant increase in mortality (48 [4.54%] vs 20 [4.01%] vs 23 [3.54%]; p = 0.59), sternal dehiscence (15 [1.42%] vs 8 [1.60%] vs 5 [0.77%]; p = 0.37) and neurologic complications (29 [2.74%] vs 16 [3.21%] vs 27 [4.16%]; p = 0.27), renal complications (46 [4.35%] vs 17 [3.41%] vs 33 [5.09%]; p = 0.49), or respiratory complications (25 [2.36%] vs 8 [1.60%] vs 11 [1.69%]; p = 0.49) among the three groups.

Multivariate analyses were undertaken at two different HbA1C levels (HbA1c >8.0% and HbA1c >9.0%). These analyses showed that although HbA1c was consistently an independent risk factor for respiratory complications, no additional adverse postoperative complications were seen with increasing HbA1c levels (Table 5). The protective effect of high HbA1c on atrial fibrillation was also not seen at any of the point estimates on multivariate analysis.

Comment

The main finding of our study was that a high preoperative HbA1c level (>6.5%) in patients undergoing CABG was associated with an increased risk of sternal dehiscence and respiratory complications. However, in nondiabetic patients the HbA1c level did not appear to influence adverse outcomes.

In this study we took HbA1c of 6.5% as a threshold to differentiate between optimal and suboptimal control of glycemia. HbA1c bears a very close correlation with glucose [10], and its main value lies in its use as a predictor of diabetic complications [9]. An HbA1c level of 6.5% yields a specificity of 99.6% and is currently the recommended diagnostic threshold [11-15].

The incidence of deep sternal wound infections, sternal dehiscence, postoperative respiratory complications, renal failure, and neurologic complications was higher in the group with an HbA1c of 6.5% or higher. These patients were more likely to have associated conditions such as high body mass index and hypertension. In addition, the number of female patients in this group was

ADULT CARDIAC

Tahle 3	Comparison	of	IInadiusted	In	fection Rate	20
Tuble 5.	Comparison	U	unuujusieu	m	јесноп кин	25

Infective Complications	Glycosylated Hemoglobin $<6.5\%$ (n = 2,476)	Glycosylated Hemoglobin \geq 6.5% (n = 2,202)	p Value
Superficial sternal wound infection	11 (0.44%)	15 (0.68%)	0.27
Deep sternal wound infection	13 (0.53%)	29 (1.32%)	0.004
Leg wound infection	24 (0.97%)	14 (0.64%)	0.20
Chest infection	54 (2.18%)	50 (2.27%)	0.84
Urinary tract infection	11 (0.44%)	13 (0.64%)	0.37
Composite infection rate	113 (4.5%)	123 (5.5%)	0.12

Postoperative Complications	Overall (n = 4,678) Odds Ratio (95% CI); p Value	Nondiabetic Patients (n = 1,633) Odds Ratio (95% CI); p Value	Diabetic Patients (n = $3,045$) Odds Ratio (95% CI); <i>p</i> Value
Respiratory complications	1.23 (1.04–1.45); <i>p</i> = 0.01	1.05 (0.78–1.42); $p=0.72$	1.28 (1.05–1.57); <i>p</i> = 0.13
Renal complications	1.20 (0.83–1.72); $p=0.31$	1.25 (0.55–2.86); $p=0.58$	1.16 (0.77–-1.74); $p=0.45$
Atrial fibrillation	1.07 (0.89–1.22); $p=0.44$	1.01 (0.71–1.44); $p=0.91$	1.12 (0.89–1.41); $p=0.31$
Gastrointestinal Complications	1.02 (0.64–1.61); $p=0.92$	1.22 (0.51–2.94); $p=0.65$	0.97 (0.56–1.66); $p=0.92$
Neurologic complications	1.38 (0.91–2.09); $p=0.12$	0.56 (0.16–1.96); $p=0.36$	1.57 (0.97–2.53); $p=0.06$
Sternal dehiscence	2.16 (1.008–4.63); $p=0.04$	1.52 (0.27–8.34); $p=0.62$	2.40 (0.96–5.98); $p=0.60$
Death	1.36 (0.95–1.95); $p = 0.08$	1.35 (0.67–2.72); $p = 0.39$	1.32 (0.86–2.02); <i>p</i> = 0.19

Table 4. Glycosylated Hemoglobin Adjusted Odds Ratios for Adverse Outcomes

CI = confidence interval.

significantly higher. Even after adjusting for all these demographic differences, the risk of sternal dehiscence and respiratory complications remained significantly high in these patients.

Our findings have been corroborated by other studies. Elevated HbA1c has been reported to be associated with increased early mortality rates, adverse postoperative outcomes, and shorter long-term survival [3, 4, 13, 16-18]. Rates of deep [3] as well as superficial [19] sternal wound infections were significantly increased with a higher HbA1c. High HbA1c, in essence, reflects poor glycemic control. There is substantial evidence that poor glycemic control is associated with worse outcomes in patients undergoing CABG. Impaired coronary flow reserve reflecting coronary microvascular dysfunction is common in diabetic patients [20]. Gene studies have revealed an upregulation of inflammatory mediators such as interleukin-6, E-selectin, and C-C motif chemokine ligand 2 (CCL2) in diabetic subjects that leads to an exaggerated postoperative inflammatory response [21]. There has also been evidence of morphologic changes in the internal thoracic artery graft in the presence of high HbA1c [22].

Although the association between HbA1c levels and adverse outcome in the group as a whole was quite clear in our study, the same relationship was not seen in nondiabetic patients. Similar findings have been reported by other studies investigating nondiabetic patients with a high HbA1c who are undergoing coronary operations [15], as well as those undergoing percutaneous coronary interventions [23]. The explanation for this observation is that there is a negative correlation between a high HbA1c level and intraoperative insulin sensitivity in diabetic patients but not in nondiabetic patients. Insulin sensitivity in turn has been shown to be significantly related to a proportional increase in major adverse outcomes. Investigators have suggested that in nondiabetic patients, preoperative HbA1c reflects their glucose tolerance, whereas in diabetic patients, HbA1c levels reflect impaired glucose tolerance as well as efficacy of the treatment [12].

Although high HbA1c levels have been reported to be associated with adverse outcomes, the assumption that a graded increase in HbA1c levels lead to worsening outcomes remains questionable. Some studies have reported certain point estimates at which the risk of death (HbA1c >8.6%) and deep sternal wound infections (HbA1c >7.8%) is significantly higher [3]. Other studies have reported worse outcomes with rising HbA1c levels in non-insulin-dependent patients but not in patients treated with insulin [24, 25]. Some other epidemiologic studies have reported a linear relationship between HbA1c levels and death, but these study subjects were largely nonsurgical patients [26].

In our study we performed multivariate analysis at two HbA1c levels (HbA1c $\geq 8.0\%$ and HbA1c $\geq 9.0\%$) and found no additional increase in the incidence of adverse postoperative outcomes with rising HbA1c levels. However, the number of female patients in our study was lower than usual. Also, most of our patients were younger (mean age, <60 years) and had a normal body mass index. As increased age, female gender and increased body mass index are independently related to adverse

Table 5. Adjusted Odds Ratios for Adverse Outcomes With Glycosylated Hemoglobin Levels of 8.0% and Higher and 9.0% and Higher

Postoperative Complications	Glycosylated Hemoglobin ≥8.0% Odds Ratio (95% CI); <i>p</i> Value	Glycosylated Hemoglobin ≥9.0% Odds Ratio (95% CI); <i>p</i> Value
Respiratory complications	1.28 (1.06–1.56); $p = 0.011$	1.34 (1.05–1.70); $p = 0.017$
Renal complications	1.19 (0.79–1.78); $p=0.39$	1.36 (0.84–2.22); $p=0.20$
Atrial fibrillation	0.95 (0.75–1.21); $p=0.7$	0.86 (0.63–1.18); $p = 0.37$
Gastrointestinal Complications	0.80 (0.43–1.46); $p=0.47$	0.64 (0.27–1.50); $p=0.30$
Neurologic complications	1.26 (0.81–1.97); $p=0.3$	1.61 (0.96–2.69); $p = 0.07$
Sternal dehiscence	0.66 (0.28–1.55); $p=0.34$	0.52 (0.15–1.76); $p = 0.29$
Death	1.28 (0.85–1.92); $p = 0.23$	1.25 (0.75–2.07); $p = 0.37$

CI = confidence interval.

outcomes after coronary artery operations the patient profile may have had a protective influence. In addition, overall more than 75% of the patients were operated using the off-pump coronary artery bypass technique.

The relationship between high HbA1c and postoperative atrial fibrillation is also controversial. Although some studies have shown that higher HbA1c levels were associated with a reduced incidence of atrial fibrillation [3, 16, 27] results of other studies suggested an increased incidence of atrial fibrillation in diabetic patients [28]. In our study, although a protective effect was seen on univariate analysis, this effect was not seen when the other covariates were accounted for in the analysis.

This large study has tried to correlate HbA1c as a risk factor for adverse outcomes in patients undergoing CABG. Our primary goal was to assess the effect of hyperglycemia irrespective of the cause, the type of diabetes, or the treatment strategy.

The insight that a high HbA1c level adversely affects outcome after CABG would allow surgeons to risk stratify patients. Moreover, because HbA1c is a modifiable factor, in patients with stable angina and without any anatomically critical lesions, attempts should be made to control blood glucose levels over a period of time, thereby reducing HbA1c levels preoperatively. However, when a surgical procedure is needed on a more urgent basis, admission to the hospital and stringent glycemic control are mandatory.

Limitations

This was a retrospective study and contains some of the problems inherent in such studies. Apart from this the demographic profile of our study population was slightly different from that of most reported series. The number of female patients in our study was low (<10%), the mean age was approximately 60 years, and most of the operations were performed on the beating heart (>75%). The rate of LITA-to-LAD anastomosis in our study was lower than usual at approximately 84%. The main reason for this was a higher than usual diabetic population (65%) in the study with a consequent increase in diffusely diseased LADs often requiring complex coronary reconstruction. In these cases the LITA was anastomosed to the diagonal or the circumflex artery as appropriate.

Conclusions

A high HbA1c level (\geq 6.5%) in diabetic patients presenting for CABG was associated with a significant increase in the incidence of sternal dehiscence and respiratory complications. Further increases in HbA1c levels were consistently associated with respiratory complications but were not associated with a further increase in any other postoperative morbidity or mortality. There was no protective relationship between HbA1c levels and atrial fibrillation.

References

1. Thourani VH, Weintraub WS, Stein B, et al. Influence of diabetes mellitus on early and late outcomes after coronary artery bypass grafting. Ann Thorac Surg 1999;67:1045-52.

- 2. Matsuura K, Imamaki M, Ishida A, Shimura H, Niitsuma Y, Miyazaki M. Off-pump coronary artery bypass grafting for poorly controlled diabetic patients. Ann Thorac Cardiovasc Surg 2009;15:18-22.
- 3. Halkos ME, Lattouf OM, Puskas JD, et al. Elevated preoperative hemoglobin A1c level is associated with reduced long-term survival after coronary artery bypass surgery. Ann Thorac Surg 2008;86:1431-7.
- 4. Carson JL, Scholz PM, Chen AY, Petersen ED, Gold J, Schneider SH. Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. J Âm Coll Cardiol 2002;40:418-23.
- 5. Holzmann MJ, Rathsman B, Eliasson B, et al. Long-term prognosis in patients with type 1 and 2 diabetes mellitus after coronary artery bypass grafting. J Am Coll Cardiol 2015;65: 1644-52
- 6. Lazar HL, Chipkin SR, Fitzgerald CA, et al. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. Circulation 2004;109:1497-502.
- 7. Gallagher S, Kapur A, Lovell MJ, et al. Impact of diabetes mellitus and renal insufficiency on 5-year mortality following coronary artery bypass graft surgery: a cohort study of 4869 UK patients. Eur J Cardiothorac Surg 2014;45:1075-81.
- 8. Mohammadi S, Dagenais F, Mathieu P, et al. Long-term impact of diabetes and its comorbidities in patients undergoing isolated primary coronary artery bypass graft surgery. Circulation 2007 Sep;116(Suppl):I220-5.
- 9. Saudek CD, Derr RL, Kalyani RR. Assessing glycemia in diabetes using self-monitoring blood glucose and hemoglobin A1c. JAMA 2006;295:1688-97.
- 10. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ, A1c-Derived Average Glucose Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care 2008;31:1473-8.
- 11. Saudek CD, Herman WH, Sacks DB, Bergenstal RM, Edelman D, Davidson MB. A new look at screening and diagnosing diabetes mellitus. J Clin Endocrinol Metab 2008;93:2447-53.
- 12. Tsuruta R, Miyauchi K, Yamamoto T, et al. Effect of preoperative hemoglobin A1c levels on long-term outcomes for diabetic patients after off-pump coronary artery bypass grafting. J Cardiol 2011;57:181-6.
- 13. Subramaniam B, Lerner A, Novack V, et al. Increased glycemic variability in patients with elevated preoperative HbA1C predicts adverse outcomes following coronary artery bypass grafting surgery. Anesth Analg 2014;118:277-87.
- 14. McGinn JT, Jr, Shariff MA, Bhat TM, et al. Prevalence of dysglycemia among coronary artery bypass surgery patients with no previous diabetic history. J Cardiothorac Surg 2011;6:104.
- 15. Sato H, Carvalho G, Sato T, Lattermann R, Matsukawa T, Schricker T. The association of preoperative glycemic control, intraoperative insulin sensitivity, and outcomes after cardiac surgery. J Clin Endocrinol Metab 2010;95:4338-44.
- 16. Tennyson C, Lee R, Attia R. Is there a role for HbA1c in predicting mortality and morbidity outcomes after coronary artery bypass graft surgery? Interact Cardiovasc Thorac Surg 2013;17:1000-8
- 17. Gumus F, Polat A, Sinikoglu SN, Yektas A, Erkalp K, Alagol A. Use of a lower cut-off value for HbA1c to predict postoperative renal complication risk in patients undergoing coronary artery bypass grafting. J Cardiothorac Vasc Anesth 2013;27:1167-73.
- 18. Hudson CC, Welsby IJ, Phillips-Bute, et al, Cardiothoracic Anesthesiology Research Endeavors (C.A.R.E.) Group. Glycosylated hemoglobin levels and outcome in non-diabetic cardiac surgery patients. Can J Anaesth 2010;57:565-72.
- 19. Alserius T, Anderson RE, Hammar N, Nordqvist T, Ivert T. Elevated glycosylated hemoglobin (HbA1c) is a risk marker in coronary artery bypass surgery. Scand Cardiovasc J 2008;42:392-8.
- 20. Erdogan D, Akcay S, Yucel H, et al. The effects of good glycaemic control on left ventricular and coronary

ADULT CARDIAC

endothelial functions in patients with poorly controlled type 2 diabetes mellitus. Clin Endocrinol (Oxf) 2015;82:388–96.

- **21.** Voisine P, Ruel M, Khan TA, et al. Differences in gene expression profiles of diabetic and nondiabetic patients undergoing cardiopulmonary bypass and cardioplegic arrest. Circulation 2004;110(Suppl 1):II280–6.
- 22. Bakuy V, Unal O, Gursoy M, et al. Electron microscopic evaluation of internal thoracic artery endothelial morphology in diabetic coronary bypass patients. Ann Thorac Surg 2014;97:851–7.
- 23. Verdoia M, Schaffer A, Barbieri L, et al. Glycosylated hemoglobin and the risk of periprocedural myocardial infarction in non-diabetic patients. J Diabetes Complications 2015;29:517–22.
- 24. Kuhl J, Sartipy U, Eliasson B, Nyström T, Holzmann MJ. Relationship between preoperative hemoglobin A1c levels and long-term mortality after coronary artery bypass grafting

in patients with type 2 diabetes mellitus. Int J Cardiol 2016;202:291-6.

- **25.** Sharma PK, Agarwal S, Ellis SG, et al. Association of glycemic control with mortality in patients with diabetes mellitus undergoing percutaneous coronary intervention. Circ Cardiovasc Interv 2014;7:503–9.
- **26.** Riddle MC, Ambrosius WT, Brillon DJ, et al. Epidemiologic relationships between A1c and all-cause mortality during a median 3.4-year follow-up of glycemic treatment in the ACCORD trial. Diabetes Care 2010;33:983–90.
- 27. Kinoshita T, Asai T, Suzuki T, Kambara A, Matsubayashi K. Preoperative hemoglobin A1c predicts atrial fibrillation after off-pump coronary artery bypass surgery. Eur J Cardiothorac Surg 2012;41:102–7.
- **28.** Huxley RR, Filion KB, Konety S, Alonso A. Meta-analysis of cohort and case-control studies of type 2 diabetes mellitus and risk of atrial fibrillation. Am J Cardiol 2011;108:56–62.