

Study of association of preoperative glycosylated haemoglobin level and outcome after cardiac surgery

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Background: Diabetes mellitus involves 8.7% of the adult community in India, and its preponderance is rising. Diabetes is an independent risk factor for complications after open cardiac surgery. Poor glycaemic control, measured by glycosylated haemoglobin A_{1c} (HbA_{1c}), is associated with high incidence of micro and macroangiopathy. HbA_{1c} reflects the patient's prevailing sugar control over the previous 120-150 days. Perioperative cardiac surgical risk scoring systems like Euro Score and STS scoring systems do not include HbA_{1c} level as risk factor. We intended to study the correlation of preoperative HbA_{1c} level and outcome after cardiac surgery.

Methodology: A total of 350 patients who had undergone elective cardiac surgery were included. All patients were stratified into two groups, Group 1 with HbA_{1c} level < 7%, Group 2 >7%. Intraoperative and postoperative adverse events were documented retrospectively. The two groups of patients were compared with regard to their demographic data, operation risk, mortality and morbidity.

Results: Overall incidence of major adverse events (7.7%) and mortality (4.8%) were very low. Incidence of sternal wound infection and prolonged ventilator support (> 24hrs) were significant in group 2 compared to group 1 (p values were 0.03 and 0.01 respectively).

Conclusion: Preoperative HbA_{1c} level may provide more accurate prognostic information about outcomes after all major open cardiac surgeries compared with a diabetes status alone.

Keywords: Glycosylated haemoglobin (HbA_{1c}); cardiac surgery; post-operative complications; diabetes mellitus; glycaemia control

Introduction

Diabetes mellitus affects 8.7% of the adult community in India, and its preponderance is rising.¹ Diabetes is an independent risk factor for complications after cardiac surgery. Poor glycaemic control, measured by glycosylated haemoglobin A_{1c} (HbA_{1c}), is associated with high incidence of micro and macroangiopathy.¹ Glucose in the blood binds to haemoglobin irreversibly to form a stable HbA_{1c} complex. It

illustrates the patient's prevailing sugar control over the past 120-150 days. HbA_{1c} may be underestimated in few circumstances like haemolytic anaemia, chronic renal failure, and in patients who are on certain medications. (e.g. erythropoietin, iron and vitamin B₁₂ preparations).² The level of HbA_{1c} may be falsely increased due to hypertriglyceridaemia, hyperbilirubinaemia, alcoholism, previous splenectomy, pregnancy, and medications (e.g. opiates, vitamin C, salicylates).² HbA_{1c} levels less than 7% are recommended by The American Diabetes Association (ADA) and this is associated with reduced risk of complications related to diabetes mellitus.³ Euro SCORE and American STS SCORE do include diabetes in the risk factors,^{4,5} but HbA_{1c} level is not included as a risk indicator for cardiac surgery in any of the above mentioned preoperative risk scores.

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Methodology

Hospital Research Ethics Committee approval was obtained. Permission from Medical superintendent was obtained to access medical records and confidentiality was ensured by the use of indirect identifiers. Data of all patients who had undergone elective cardiac surgery (MVR, AVR, CABG, and DVR) was obtained from the hospital records section.

Study design: Data of all patients who had undergone elective cardiac surgery (MVR, AVR, CABG, and DVR) were included in the study. Patients who had undergone emergency cardiac surgeries, paediatric cardiac surgeries, and those with multiple comorbidities like severe renal, hepatic and CNS abnormalities (stroke, CKD stage 5 etc.) were excluded from the study. All patients were stratified into two groups, depending on their preoperative HbA1c, Group 1 with HBA1C level < 7%, and group 2 with level >7%.

Anaesthesia technique: All patients were given general anaesthesia with intravenous induction with fentanyl, propofol, midazolam and vecuronium. Anaesthesia was maintained with inhalation agent isoflurane and fentanyl bolus doses. Haemodynamic monitoring was done with radial arterial and central venous lines. All patients received intravenous antifibrinolytic agent (tranexamic acid 1g) before skin incision. All surgeries were done with midline sternotomy incision. Anticoagulation was achieved with intravenous heparin. In the off pump coronary artery bypass (OPCAB) patients, 150-200 IU/kg of heparin was administered before division of the internal mammary artery (IMA) to maintain an activated clotting time (ACT) between 250–350 seconds. Anticoagulation was reversed with protamine 1mg/100IU of heparin on completion of all anastomoses. In on pump cases (valves and combined valve and CABG), 300–400 IU/kg of heparin was given to target an ACT of at least 480 seconds before the commencement of cardiopulmonary bypass (CPB). Anticoagulation was reversed with protamine 3–4mg/100IU of heparin dose on termination of CPB. Intraoperative hyperglycaemia was managed with continuous insulin infusion to maintain target sugar level between 120mg/dl to 180mg/dl. Postoperative glycaemic control was managed with either continuous infusion or subcutaneous boluses according to sliding scale.

Intraoperative and postoperative adverse events were recorded from hospital data. Complications like arrhythmias, cerebrovascular accidents, bleeding, renal dysfunction, perioperative myocardial ischaemia, etc. were documented. The two groups of patients were analyzed concerning their demographic data, surgical risk, mortality, and morbidity. Following are the outcomes of cardiac surgery considered.

Primary outcomes:

- Death within six days of surgery
- Cardiac adverse events like new onset ST changes and arrhythmias, requiring more than two inotropes and the use of an intra-aortic balloon pump (IABP).
- Stroke or transient ischaemic attack (TIA)
- Post-operative renal dysfunction requiring dialysis
- Prolonged mechanical ventilation (more than 24 hours)
- Re-exploration

Secondary outcomes:

- Length of hospital stay.
- Sternal wound infection

Statistical analysis

All quantitative data were coded and transformed into an excel master sheet for computer programming. A chi-square test was used to evaluate categorical variables for analysis. For all practical analyses, $p < 0.05$ was accepted to be statistically significant. Statistical analysis of the data was done using SPSS (version 16) package.

Results

A total of 350 patients who underwent elective cardiac surgery from November 2017 to October 2018 in our hospital were analyzed in this study (219 patients with HbA1c < 7%, 131 patients with HbA1c level >7%). Preoperative demographics, clinical variables, and perioperative factors comparing patients with two groups are listed in Table 1. Sixty seven (30.59%) patients in group 1 were diabetic with HbA1c levels < 7%. In group two, 101 (77%) patients were known diabetics. Number of patients with severe LV dysfunction were considerably high in group two (11.4%) compared to group 1 (1.3%) (P value 0.03)

Table 1: Comparison of preoperative demographics, clinical variables and perioperative factors

Risk	HbA1c < 7.0%	HbA1c > 7 %	P value
TOTAL (n)	219(62.57%)	131(47.24%)	
Mean Age (yrs.)	58	63	0.09
Sex	M-141(64.38%)	84 (64.12%)	0.13
	F- 78(35.62%)	47(35.87%)	0.22
Diabetes Mellitus	67(30.59%)	101(77.09%)	0.001
Hypertension	94(42.95%)	78(59.54%)	0.05
CABG	140(63.92%)	92(70.22%)	0.56
MVR	30(13.69%)	14(10.68%)	0.62
AVR	10 (4.56%)	5(3.81%)	0.11
CABG ± MVR	3 (1.36%)	10(7.63%)	0.006
CABG ± AVR	6 (2.73%)	3(2.29%)	0.44
DVR	9(4.10%)	6(4.58%)	0.24
Others	21 (9.58%)	1(0.76%)	0.72
LMCA	44(31.20%)	33(25.19%)	0.35
EF ≥ 50% 35-50 ≤35	181(82.64%)	104(79.38%)	0.32
	35(15.98%)	12(9.16%)	0.88
	3(1.38%)	15(11.45%)	0.03
Arrhythmias	31(14.15%)	36(27.48%)	0.11
CPB	79(36.07%)	39(29.77%)	0.61

In-hospital outcomes are summarized by HbA1c subgroup in Table 2. For all the patients, the overall incidence of mortality was low (4.8%). Incidence of sternal wound infections and prolonged mechanical ventilation were significant in group 2 (2.29% and 20.6% respectively) compared to group 1 (0.45% and 8.2% respectively) (P value 0.03 and 0.01 respectively). Incidence of CVA (p value-0.52), renal failure (p value-0.06), re-exploration (p value- 0.59) and length of hospital (p value-0.15) stay were not statistically significant in both the groups. There was only one incidence of VAP found in group 2.

Table 2: In-hospital outcomes for all patients by HbA1c risk group

Outcome	HbA1c < 7.0% n=219	HbA1c >7.0% n=131	P value
Death	9 (4.10%)	8 (6.1%)	0.17
Renal failure	2 (0.91%)	4(3.05%)	0.06
CVA	2 (0.91%)	3(2.29%)	0.52
Cardiac accidents	4 (1.82%)	5(3.8%)	0.06
Infection(DSWI)	1 (0.45%)	3(2.29%)	0.03
Prolonged ventilation ≥ 24 hrs.	18(8.21%)	27(20.61%)	0.01
Re-exploration	2(0.91%)	3(2.29%)	0.59
Re intubation	3(1.36%)	4(3.05%)	0.07
VAP	0	1(0.7%)	
Tracheostomy	2 (0.91%)	1(0.7%)	0.83
Length of Hospital stay(mean) in days	5.8	6.3	0.15

Perioperative adverse events in HbA1c subgroups is analyzed in Table 3. Requirement

of IABP, unplanned CPB, blood transfusion requirement, new onset ST changes and mortality were compared. The study showed no significant difference in two groups concerning the above events.

Table 3: Perioperative events in all patients by HbA1c risk group

Events	HbA1c < 7.0% n=219	HbA1c > 7.0% n= 131	P value
Arrhythmias	78(35.61%)	46(35.11%)	0.57
Transfusion	44(20.09%)	29(22.13%)	0.77
New onset ST changes	12(5.47%)	10(7.63%)	0.35
Inotropes ≥ 2	88(40.18%)	56(42.74%)	0.26
Unplanned CPB	1(0.45%)	2(1.52%)	0.55
IABP	6(2.73%)	9(6.87%)	0.61
Deaths	9(4.10%)	8(6.1%)	0.17

Discussion

The majority of adult cardiac surgeries are CABGs, involving elderly patients with multiple comorbidities. Diabetes and hypertension are the known risk factors for coronary artery disease. Commonly, diabetes is diagnosed when the patient comes for CABG surgery. In the present study, we retrospectively evaluated 350 patients undergoing elective cardiac surgeries. Overall in-hospital mortality in all patients was 4.8%. In our study, 168 patients of 350 had diabetes. In patients with HbA1c >7 %, 77% of patients had diabetes and 23% of patients were undiagnosed diabetics, and they were not on any hypoglycaemic medication. Many studies, which compared diabetic and non-diabetic patients after coronary revascularization surgery have generated conflicting results.^{5,6} Calafiore and colleagues, in their study proved that diabetes mellitus was an independent risk factor for early cardiac mortality and morbidity.⁵ Rajakaruna et al, found comparable mortality outcomes in diabetic and non-diabetic patients.⁶ Study done by Kubal et al reported that diabetic patients who were on insulin had increased postoperative complications than the patients who had mere history of diabetes.⁷ The study done by Carson and colleagues compared outcomes in 41,663 diabetic patients with 1,05,123 non diabetic patients and found a near 30% increase in overall complications rate in diabetic patients compared non-diabetic patients.⁸ Furnary and colleagues, reported that glycaemic control by continuous insulin infusion in perioperative period reduced mortality and infection rate

among diabetic patients.^{9,10} We aimed to regulate glucose level between 120mg/dl to 180mg/dl in all the diabetic patients throughout perioperative period using continuous insulin infusion or bolus doses of insulin according to sliding scale. Once patients transferred post-operative intensive care unit, management was variable and dependent on their sugar level in the intensive care unit. Preoperative HbA1c level still emerged as an independent predictor of mortality and wound infection after CABG in the multivariate analysis, even after adjusting for mean glucose levels on the day of surgery and the first three postoperative days.¹¹

In the present study, we sought to determine whether these outcome differences could be explained by preoperative glycaemic control as measured by HbA1c rather than the mere history of diabetes mellitus. We agree with previous authors that strict intraoperative and postoperative glucose control is imperative to minimize postoperative morbidity and mortality after any open cardiac surgery. However, it is plausible from these data that HbA1c is also an independent predictor of postoperative adverse events that is not entirely due to intra and postoperative glucose control. It may be challenging to achieve intra and postoperative euglycaemia in patients with elevated HbA1c. Therefore, more aggressive glucose management should be used in these patients in the perioperative period. Current guidelines according to the American Diabetes Association recommend HbA1c screening of diabetic patients as frequently as every three months in patients with elevated HbA1c levels (>7%) or in patients with medication adjustments to ensure an adequate treatment regimen.¹²

Current recommendations suggest that patients with diabetes aim to achieve HbA1c levels of at least less than 7%. We chose to order HbA1c for all patients to determine whether this approach would identify patients who had uncontrolled hyperglycaemia without a previous diagnosis of diabetes mellitus.^{13,14} It is possible that a preoperative HbA1c level may provide more accurate prognostic information about outcomes after all major open cardiac surgeries compared with a diabetes status alone.

Conclusion

Our study showed that elevated preoperative HbA1c levels are associated with a significant

increase in sternal wound infection and prolonged mechanical ventilator support in patients undergoing elective cardiac surgery. A preoperative HbA1c level may provide more accurate prognostic information about outcomes after all major open cardiac surgeries compared with a diabetes status alone.

Limitations

The limitations in this study include, it was a retrospective, descriptive in nature, and a small cohort size. It is difficult to correlate all adverse outcomes on HbA1c levels by only one study. More prospective randomized long-term studies must be designed to study the adverse perioperative outcomes of diabetes in terms of preoperative HbA1c levels.

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