



Research Brief

Incidence of new diabetes following CABG surgery: Analysis of a single centre registry data

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ABSTRACT

Background: About 40–50% of patients undergoing coronary artery bypass graft (CABG) surgery have diabetes. The prevalence of impaired glucose tolerance (IGT) is also high in this group, however, incidence of new diabetes following CABG surgery is unknown. Objectives: To determine incidence of new diabetes and the impact on ICU and hospital stay in patients undergoing CABG surgery in India, we performed a registry-based study.

Methods: Prospectively collected data among consecutive adult cardiac surgical patients who underwent CABG surgery at a single hospital were analyzed. Descriptive statistics are reported.

Results: We recruited 1559 consecutive patients (men 1355, women 204) and analyzed data among 933 non-diabetic patients. Patients with known diabetes ($n = 626, 40\%$) were excluded. 57 (6.1%) of the 933 non-diabetic patients developed persistently high glucose levels at discharge with incidence rate of $61 + 5/1000$. Patients who developed diabetes had similar age and body mass index vs those who did not, but had greater preoperative IGT (44.6 vs 13.7%) and more time-period in intensive care unit ($102.0 + 75$ vs $80.2 + 29$ hours) as well as in hospital ($11.7 + 5.7$ vs $9.6 + 2.4$ days) ($p < 0.001$).

Conclusion: In a significant proportion of non-diabetic patients diabetes is unmasked after CABG. This is more likely in those with impaired glucose tolerance and prolonged period in intensive care and hospital.

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1. Background

Diabetes is an important cardiovascular risk factor and the prevalence of type 2 diabetes mellitus (T2DM) in patients undergoing coronary artery bypass graft (CABG) surgery is nearly 30–40%.¹ This proportion is greater in India where studies have reported that almost 40–50% have diabetes.² The prevalence of impaired glucose intolerance (IGT) is also high in Indians and the proportion of subjects with IGT that progress to T2DM varies from 13 to 52%, with a rate of progression of 1–6% per year.³ Diabetes mellitus is associated with a poorer clinical outcome and a longer hospital stay after cardiac surgery as compared to non-diabetic patients.⁴ In these patients there is greater incidence of wound infections, ischemic cardiovascular events, neurological and renal

complications which lead to morbidity and mortality.⁵ Hyperglycemia during immediate and early post-operative phase even in non-diabetics is associated with adverse outcomes.⁶ In non-diabetics undergoing CABG surgery the risk of developing diabetes postoperatively is not known. To determine incidence of new diabetes in a large cohort of patient undergoing CABG surgery, we performed a registry-based study.

Prospectively collected data among consecutive adult cardiac surgical patients who underwent CABG surgery between April 2012 and March 2014 was analyzed. We recorded clinical and biochemical parameters, obtained details of drug usage before, during and after CABG surgery. Details of time period (hours) in intensive care unit (ICU) and overall hospital stay (days) were recorded. All these CABG surgeries were off-pump (OPCAB). All patients were treated with intravenous insulin and epinephrine infusion for about 24–48 h in ICU after surgery and if needed basal-bolus insulin when shifted out to wards. All the patients who required insulin till the day of discharge were discharged on basal-

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Table 1
Comparison of anthropometric, biochemical, pharmacological and outcome variables in patients without and with post-CABG diabetes.

Variables	No diabetes (n = 877)	Post-CABG diabetes (n = 57)	p value
Age (years)	60.3 ± 9.1	61.0 ± 8.0	0.585
Body mass index (kg/m ²)	24.9 ± 4.0	25.9 ± 4.5	0.070
Current smoker	195 (22.2)	09 (16.1)	0.462
Hypertension	434 (49.4)	37 (64.9)	0.015
Preoperative pharmacological treatments:			
Anti-platelets	163 (18.5)	14 (24.5)	0.234
Renin-angiotensin system blockers	134 (15.3)	15 (26.3)	0.013
Beta blockers	194 (22.1)	16 (28.1)	0.268
Diuretics	36 (4.1)	03 (5.2)	0.648
Calcium channel blockers	22 (2.5)	02 (3.5)	0.607
Statins	161 (18.3)	13 (22.8)	0.366
Plasma glucose (random, mean, mg/dl)	115.3 ± 27.2	154.9 ± 67.0	<0.001
Preoperative random blood glucose ≥140 mg/dl	120 (13.7)	25 (44.6)	<0.001
Left ventricular ejection fraction (mean%)	50.0 ± 9.3	46.9 ± 9.2	0.015
Triple vessel disease	643 (73.3)	44 (77.1)	<0.001
Intra and postoperative treatments:			
Adrenaline, noradrenaline and other adrenergic drugs	877 (100.0)	54 (100.0)	1.00
Immediate post-operative hyperglycemia (≥200 mg/dl)	455 (51.8)	37 (64.9)	0.009
Duration of invasive ventilation (hours)	16.0 ± 7.6	19.9 ± 14.9	0.001
Intensive care unit stay (hours)	80.2 ± 28.5	102.0 ± 75.2	<0.001
Overall hospital stay (days)	9.6 ± 2.4	11.7 ± 5.7	<0.001

Numbers ± are 1 SD; Numbers in parentheses are percent.

bolus insulin regime. Diagnosis of new onset diabetes after CABG was made on the basis of insulin requirement to keep fasting plasma glucose <120 mg/dl and 2 h post meal <180 mg/dl at discharge from hospital. Variables are reported as percent for ordinal and mean±1SD for numerical variables. Inter-group comparisons were performed using *t*-test for numerical and X² test for ordinal variables. Logistic regression was performed to identify association of development of new diabetes with baseline risk factors and duration of ICU and hospital stay. Univariate and multivariate odds ratios (OR) with 95% confidence intervals (CI) are provided.

2. Findings

Baseline characteristics of 1559 CABG patients (men 1355, 86.9%; women 204, 13.1%) are in Table 1. The mean age of study population was 60.6 ± 8.7 years. Mean body mass index (BMI) was 25.4 ± 4.1 kg/m². Of these 626 (40.1%) had known diabetes and were excluded from further analyses. Data of 933 (59.9%) patients who were non-diabetic before CABG have been analyzed. Of these patients, 57 (6.1 ± 3%) had persistently high glucose levels at discharge from the hospital at a mean of 7.0 ± 4.0 days after CABG surgery, with incidence rate of 61/1000 (95% CI 50–85). These patients, as compared to those without diabetes, had greater BMI (25.9 ± 4.5 vs 24.9 ± 4.0 kg/m²) and lower left ventricular ejection fraction (46.9 ± 9.2 vs 50.0 ± 9.3%) at baseline, however the differences were not statistically significant. There was no difference in the prevalence of smoking, hypertension and pre-operative pharmacological treatments between these groups. The mean preoperative random plasma glucose in new onset diabetes patients was 154.9 ± 67 mg/dl as compared to 115.3 ± 27 mg/dl in those who remained non-diabetic (*p* < 0.001). Among new onset diabetes 44.6% patients had pre-operative random blood glucose of ≥140 mg/dl as compared to only 13.7% patients who remained non-diabetic (*p* < 0.001). There was no significant difference in intra-operative and immediate post-operative treatments in the two groups with similar use of adrenergic vasopressors and anti-arrhythmics. Patients who developed post CABG diabetes had greater duration of stay in ICU (102.0 ± 75.2 vs 80.2 ± 28.5 h) as well as in hospital (11.7 ± 5.7 vs 9.6 ± 2.4 days) (*p* < 0.001). Logistic regression analyses showed that the only significant determinant of

new onset diabetes was preoperative random blood glucose ≥140 mg/dl with univariate OR of 3.20 (CI 1.93–5.32) and multivariate (adjusted for age, sex, BMI, and baseline medicines) OR 5.4 (CI 3.04–9.63) (*P* < 0.001).

3. Comments

Our study shows that although CABG restores coronary vascularization it introduces a new cardiovascular risk factor—diabetes mellitus—in a small but significant proportion of patients. This new onset diabetes has incidence rate of 61/1000 and is an important finding. There are multiple mechanisms to explain this phenomenon. Norepinephrine and epinephrine are widely used in all patients during CABG as also in our cohort. Catecholamines inhibit insulin secretion and stimulate glucagon release.⁷ Stress hyperglycemia is dependent on underlying glucose tolerance, the severity of illness, and interactions of counter-regulatory hormones.⁸ Situations such as myocardial infarction, severe infections and trauma (all have catecholamine excess and hyperglycemia) are characterized by higher insulin resistance, fall in insulin secretion and higher glucagon concentration.^{8,9} Insulin resistance is known to worsen during cardiopulmonary bypass but there are scanty data of change in insulin resistance in normothermic surgeries.¹⁰

The degree of postoperative hyperglycemia in diabetic patients could be reflection of the severity of the patients' underlying glucose intolerance and a marker for increased comorbidities and greater insulin resistance. Hyperglycemia during cardiac bypass reflects a state of insulin resistance that develops during surgical intervention and that might contribute to poor outcome. In the present study greater ICU and hospital stay could be either a cause or an affect of the underlying conditions. Insulin resistance is also caused by catecholamines and cortisol secretion (surgical stress), accompanying systemic inflammatory response syndrome and/or the effects of systemic heparinization.¹¹ All our patients underwent normothermic CABG surgery. Higher blood glucose is observed in the hypothermic CABG suggesting etiological importance of factors discussed earlier.¹¹

Potential mechanisms of new onset diabetes in our patients could be extant prediabetes, inotropic usage, surgical stress and heparinization. Longer ventilatory support after CABG and prolonged ICU stay (hence likelihood of more inotrope usage) should

warn the treating team about impending emergence of new onset diabetes. As 45% of CABG patients on our cohort had preoperative glucose values more than 140 mg/dl, our study indicates importance of prediabetes in new onset diabetes. Although, the incidence rate of diabetes (6.1%) in our study is similar to annual conversion rate of impaired glucose tolerance to diabetes (5–6%/year),³ a shorter duration is a significant observation. This could be due to stress of CABG surgery, which has telescoped the duration. Long-term follow-up of this cohort would be more informative, and its absence is a study limitation. A study on South African Indians² has shown 50.4% conversion to T2DM at 4 years. Most prospective studies report that in <50% cases impaired glucose tolerance progresses to diabetes within 10 years while in a majority glucose tolerance returns to normal or persists unchanged following a surgical stress.¹² Unfortunately, in many of our subjects we do not know the preoperative fasting serum glucose, status of glucose intolerance, circulating insulin and HbA1c levels, and cannot conclusively address this issue. This is also a major limitation of our study.

Consequences of undetected pre-diabetes include prolonged and uncontrolled hyperglycemia, improper assignment of the patient to a lower risk group, failure to prevent progression from prediabetes to clinical diabetes, and underestimation of the hazard ratio for dysglycemia in conjunction with CABG.¹³ There is enough data supporting the role of hyperglycemia in post operative outcomes in the first 2–3 days after CABG¹⁴; however, there is no data to link blood glucose values on day 4–7 to the outcomes or the hospital stay. Also, there is no data showing conversion of prediabetes to overt diabetes after major surgery or CABG surgery. Our study provides a novel information in this regard and paves a way for future research. We recommend that in all patients undergoing CABG surgery and a preoperative impaired glucose tolerance with postoperative hyperglycemia should be evaluated for new onset diabetes to decide on a need for a proper glycemic control plan after discharge. These patients would require specialized diabetes education including self-monitoring of blood glucose, insulin adjustments and hypoglycemia management prior to discharge just like a known diabetic. Obtaining HbA1c prior to surgery in non-diabetic patients or in those patients who are at a risk for postoperative hyperglycemia will help to optimize glycemic control. It will also identify those patients who might require more aggressive glycemic control after surgery and at the time of hospital discharge.

Our study has multiple strengths and limitations. We used a large cohort of patients at a single centre. All the patients underwent similar type of surgery (normothermic off-pump CABG) and intra-operative and post-operative care. This has controlled multiple confounders. Limitations include study being confined to single hospital, absence of HbA1c data and only in-hospital follow-up. The present study thus, highlights that patients undergoing CABG surgery are probably at a higher risk for developing diabetes.

Fasting or random plasma glucose value alone may not be sufficient to diagnose all the patients with glucose metabolic disturbances. HbA1c measurement for patients who are undergoing CABG surgery may be useful and we recommend its inclusion in the routine preoperative workup.

Conflict of interest

None to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ihj.2018.11.017>.

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