

Analysis of Preoperative Hba1c Levels as Outcome Predictor after off Pump Coronary Artery Bypass Graft Surgery

Govindaiah Satish¹, Pangi Manish², Lakshman Sudheer³

Authors Affiliation:

^{1,2}Associate Professor ³Postgraduate Student Cardiac surgery, Sri Jayadeva Institute of Cardiovascular sciences & Research, Bangalore, Karnataka 560069, India.

Corresponding Author: Pangi Manish,

Associate Professor, Cardiac surgery, Sri Jayadeva Institute of Cardiovascular sciences & Research, Bangalore, Karnataka 560069, India.

E-mail: mnpangi@gmail.com

Received on 09.08.2018

Accepted on 24.08.2018

Abstract

Context: Diabetes Mellitus is a proven risk factor for adverse events for coronary artery disease and its prevalence among patients continues to rise. Hemoglobin A1c (HbA1c) is an accepted marker for adequacy of glycemic control. But it is not known whether it could be used to predict outcome after off pump coronary artery bypass graft (OPCAB) surgery. *Aims:* To study adequacy of using baseline HbA1c levels to predict outcome after coronary artery bypass graft especially in OPCAB surgery. *Settings and Design:* Retrospective observational study. *Methods and Material:* Diabetic patients undergoing isolated OPCAB surgery from 2015 to 2018, done by a single surgical team in a tertiary care institution, were included. The cohort of 310 patients was then grouped into three groups depending upon their HbA1c levels. The patient data, operative factors and 30 day post operative outcomes were compared. *Statistical analysis used:* variables were compared using student's t test and paired t test. A p value <0.05 was considered significant. *Results:* Of the 310 patients, there were no significant differences in the baseline and angiographic characteristics. Mortality was observed in 2 patients in group I, 3 in Group II and 4 in group III corresponding to 3% among the groups, hence not significant. The only significant differences in morbidity were found to be higher superficial surgical site infection (p value 0.0039) and duration of post operative stay (p value 0.0032) in group III patients. *Conclusions:* Preoperative baseline HbA1c levels can be used to predict minor morbidity but are not suitable for predicting mortality in OPCAB surgery.

Keywords: HbA1c; Outcome; Coronary Revascularisation; Opcab.

Introduction

There has been a steady increase in the prevalence of diabetes among patients suffering from ischemic heart disease with more than 40% recently [1,2]. It is also known that diabetic patients tend to have more adverse cardiovascular events after coronary revascularisation [3]. This has resulted in various strategies for avoiding hyperglycemia, intra operatively and in the post operative period. However the usefulness in the preoperative period is unclear. Additionally, the optimal timing of surgery has to be balanced with strategies for intense glycemic control. Hemoglobin A1c (HbA1c) is an accepted marker used for assessing adequacy of glycemic control [4]. Therefore there is a need for study to assess relationship between glycemic

control (measured by HbA1c) with outcome after coronary revascularisation. Additionally with the increasing usage of off pump CABG (OPCAB), which avoids cardio pulmonary bypass and its attendant inflammatory response and renal impairment, there is a need to study its effect on preoperative HbA1c levels predicting outcome after surgery.

Materials and Methods

A total of 310 patients with diabetes undergoing isolated off pump CABG from 2014 to 2018 were included in the study. This was a retrospective study of prospectively collected data. Patients were defined as diabetics if they were known to have high blood glucose (> 126mg/dl fasting, >200mg/dl after

glucose tolerance test, HbA1C >6.5) or receiving treatment for the same. Exclusion criteria included any concomitant surgery, patients receiving dialysis and salvage surgery. Demographic data (age, gender, body mass index), cardiac risk factors (smoking, hypertension, hyperlipidemia, COPD, serum creatinine, ejection fraction, NYHA class) and operative data were studied. Patients were then divided into three groups according to their preoperative HbA1c levels: Group I (standard-HbA1c less than 6.5%), Group II (moderate- 6.5% to 7.5%) and Group III (high- more than 7.5%).

Surgical technique

All patients underwent OPCAB by a single surgical team using a standard approach. OPCAB was performed under normothermia with warm intravenous fluids administration. All cases underwent OPCAB without conversion to on-pump CABG. Median sternotomy was used to expose the heart. The pericardium was opened with an inverted T-shaped incision and then the Left internal mammary artery was harvested as a pedicled graft. After placing deep pericardial sutures to expose target coronary vessels, the heart was stabilized with a suction-irrigation tissue stabilization system (Octopus evolution 2000; Medtronic, Minneapolis, MN, USA). After the arteriotomy, intracoronary shunts were used without proximal snaring. Proximal anastomosis of the saphenous vein to the ascending aorta was performed with side clamping. Normal saline, Pottasium, Insulin and Magnesium insulin was started in all patients and additional insulin dose was titrated as per blood glucose levels. Only the left internal mammary was harvested. Saphenous vein was harvested by open technique in all patients.

Outcomes

The 30 day post operative data was included to assess outcome. Primary endpoints being mortality and cardiac morbidity. Definitions for variables like renal failure, chronic lung disease, deep sternal wound infection, superficial surgical site infection, sternal dehiscence, respiratory complications, myocardial infarction were according to The Society of Thoracic Surgeons National Database.

Statistical analysis

The continuous variables were expressed as mean±standard deviation. The baseline variables were compared using student's t test. Chi square test was used to compare data among the three groups and p value <0.05 was considered significant.

Results

Data from all 310 patients was available for analysis. Group I consisted of 60 patients, Group II of 108 and Group III 142 patients. In the preoperative data, there was slightly increased number of patients with higher body mass index in group III (p value 0.0487). No other demographic differences were seen among the groups and the angiographic features were also comparable.

On comparing the treatment for diabetes among the patients, a significantly higher number of patients were found to be in the newly diagnosed group (diagnosed during evaluation of the patients presenting cardiac condition) in group II and group III (p value 0.0221) (Table 1).

Table 1: Baseline characteristics and demographic data

	Group I (n=60)	Group II (n=108)	Group III (n=142)	P value	Inference
Age (years)	48 ±9	50 ±8.5	52 ±9.9	0.5114	NS
Male	81%	70%	66%	0.0590	NS
Body Mass Index (kg/m ²)	25 ±0.3	26 ±0.3	27 ±0.3	0.0487	significant
Hypertension	79%	70%	70%	0.0624	NS
Hyperlipidemia	70%	69%	76%	0.1013	NS
Fasting Blood Glucose (mg/dl)	117±16	130±24	220±36	0.0276	Significant
HbA1c	5.8 ±0.3	7.1 ± 0.2	9.3 ± 0.7	0.0007	Significant
Smoking	70%	60%	59%	0.0664	NS
LVEF (%)	52.4 ± 10	54 ± 12	53.5 ± 12	0.1258	NS
Creatinine (mg/dl)	1 ± 0.6	1 ± 0.5	1.1 ± 0.5	0.1297	NS
Vessels affected	2.5 ± 0.1	2.7 ± 0.2	2.7 ± 0.3	0.0993	NS

Abbreviations: NS: Not Significant, LVEF: Left Ventricular Ejection Fraction

Table 2: Diabetes status

	Group I	Group II	Group III	P value	Inference
Insulin	15	27	40	0.4719	NS
OHA	30	45	62	0.3187	NS
Newly diagnosed	15	36	40	0.0221	significant

Abbreviations: NS: Not Significant

Table 3: Postoperative outcome in 30 day period

	Group I	Group II	Group III	P value	Inference
Myocardial Infarction	3	5	5	0.9983	NS
Mediastinitis	0	0	0	1.0000	NS
Pneumonia	4	4	6	0.9897	NS
Renal Failure	1	2	2	0.9913	NS
Stroke	1	0	2	0.9901	NS
Superficial Surgical site Infection	0	4	20	0.0039	Significant
ICU stay	2.3	2.2	2.3	0.9911	NS
Post op stay	5.6	8.1	8.8	0.0032	Significant
Mortality	2	3	4	1	NS

Abbreviations: NS: Not Significant

Operative characteristics in all the groups were similar. Only 5 patients (1 in group I, 2 in group II and 2 in group III) did not undergo arterial grafting (Table 2).

On comparing the 30 day outcome after OPCAB surgery, mortality was observed in 2 patients in group I, 3 patients in group II and in 4 patients in group III resulting in mortality of 3% in all the groups, hence not significant. On comparing the 30 day morbidity, significant differences were noted only in case of superficial surgical site infection in 20 patients in group III (p value 0.0039) and duration of post operative stay which was higher in both group II and group III (p value 0.0032). There was difference with respect to other complications.

Discussion

Diabetes mellitus is a proven risk factor for developing ischemic heart disease [5], and can result in a 2-4 fold higher cardiovascular risk correlating with the degree of hyperglycemia [6]. A statement from the American Heart Association and the American Diabetes Association has recommended for the benefit of glycemic control on cardiovascular disease in diabetic patients [7]. HbA1c values have been widely investigated as an index of long term blood glucose control and outcome predictors in diabetic patients [4]. However, it is unknown whether adequacy of diabetic control, measured by HbA1c, is a reliable predictor of adverse outcomes

after CABG surgery. It is to answer this question that our study was done.

Our study showed a positive association between high preoperative HbA1c levels and superficial surgical site infections. Studies by Farsky PS et al. [8] and Lola I et al. [9] showed similar findings of diabetic patients had higher incidence of infective complications. It was shown that the diabetic patients had a higher incidence of infective complications. Alserius et al. [10] conducted a prospective study correlating HbA1c concentrations with infection rate and mortality outcomes in 605 patients. Rates of superficial sternal wound infection were significantly increased in patients with HbA1c $\geq 6\%$ (13.9% HbA1c $\geq 6\%$ vs 5.2% when HbA1c $< 6\%$, $p=0.007$). Similar findings were noted in the study by Narayan et al. [11], where the incidence of infective complications like deep sternal wound infection and respiratory complications were higher.

We did not find any increase in other morbidities with high HbA1c levels. This could be because of our multi disciplinary team approach to prevent post operative morbidity. There was a increase in the length of stay, which could be due to management of superficial site infections and time taken to achieve adequate post operative glycemic control.

Our study was able to show that preoperative HbA1c was not associated with increase in 30 day mortality among diabetic patients undergoing coronary revascularisation using OPCAB technique.

Halkos et al studied the association of elevated preoperative HbA1c level after CABG among over 3000 patients [2,12]. Perioperatively, for each unit increase in HbA1c, risks of Myocardial Infarction and deep sternal wound infection increased significantly. As for long-term impact on mortality, patients with HbA1c $\geq 7\%$ showed lower unadjusted 5-year survival compared to patients with HbA1c $< 7\%$. Narayan et al. [11] in a retrospective study showed association of high HbA1c with significant morbidity after CABG while effect on mortality elevation was not statistically significant. However they included non diabetic patients also, which could have effected their analysis as In all the above studies. All these studies included CABG surgeries done using cardio pulmonary bypass technique which could have altered the patients inflammatory reaction thereby resulting in higher mortality in patients with inadequate glycemic control. Indeed, gene studies have shown up regulation of inflammatory mediators like interleukin-6, E-selectin and C-C motif chemokine ligand secondary to diabetes that can result in an exaggerated inflammatory response [13]. All this coupled with activation of inflammatory reaction secondary to bypass can alter the outcome.

Tsuruta et al. studied the effect of preoperative HbA1c on long term outcome in diabetic patients after OPCAB [14]. They found that HbA1c levels might not predict long term outcomes. This was similar to our study findings, except we studied only the 30 day mortality as long term mortality will be affected by adequacy of controlling hyperglycemia which depends on a multitude of factors. However the effect of using OPCAB technique could be important. It could be because the OPCAB technique by avoids a systemic inflammatory cascade reaction which would have affected diabetic patients more. Whether diabetic patients are better benefited by exclusively using OPCAB technique needs to be studied more.

Our study has several limitations being a retrospective study with a relatively small sample size. Our study does not dispute the importance of achieving glycemic control in the preoperative period. However, intensive glycemic control may not be useful for diabetic patients with elevated HbA1c levels. Instead of delaying surgery to achieve glycemic control, these patients are better served by undergoing early surgery preferably using OPCAB technique.

Conclusion

Preoperative baseline HbA1c levels can be used

to predict minor postoperative morbidity in diabetic patients undergoing coronary revascularisation, but are not suitable for early predicting mortality after OPCAB surgery. Regimen of early surgery rather than intense glycemic control maybe beneficial.

Acknowledgement: NIL

Conflict of Interest: NIL

References

1. Thourani VH, Weintraub WS, Stein B, Gebhart SS, Craver JM, Jones EL, Guyton RA. Influence of diabetes mellitus on early and late outcome after coronary artery bypass grafting. *Ann Thorac Surg*. 1999;67(4):1045-52.
2. Halkos ME, Lattouf OM, Puskas JD, Kilgo P, Cooper WA, Morris CD, Guyton RA, Thourani VH. Elevated preoperative hemoglobin A1c level is associated with reduced long-term survival after coronary artery bypass surgery. *Ann Thorac Surg* 2008;86:1431-7.
3. Carson JL, Scholz PM, Chen AY, Peterson ED, Gold J, Schneider SH. Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. *J Am Coll Cardiol* 2002;40:418-23.
4. Elley CR, Kenealy T, Robinson E, Drury PL. Glycated haemoglobin and cardiovascular outcomes in people with Type 2 diabetes: a large prospective cohort study. *Diabet Med* 2008;25:1295-301.
5. Fox CS. Cardiovascular disease risk factors, type 2 diabetes mellitus, and the Framingham Heart Study. *Trends in Cardiovascular Medicine* 2010;20(3): 90-95.
6. The Emerging Risk Factors Collaboration, N. Sarwar, P. Gao et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* 2010;375(9733):2215-22.
7. J.B. Buse, H.N. Ginsberg, G.L. Bakris et al. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. *Circulation*, 2007;115(1); 114-126.
8. Farsky PS, Graner H, Duccini P, Zandonadi Eda C, Amato VL, Anger J, Sanches AF, Abboud CS. Risk factors for sternal wound infections and application of the STS score in coronary artery bypass graft surgery. *Rev Bras Cir Cardiovasc* 2011;26(4):624-29.
9. Lola I, Levidiotou S, Petrou A, Arnaoutoglou H, Apostolakis E, Papadopoulos GS. Are there independent predisposing factors for postoperative infections following open heart surgery? *J Cardiothorac Surg* 2011;6:151.

10. Alserius T., Anderson R.E., Hammar N., Nordqvist T., Ivert T. Elevated glycosylated hemoglobin (HbA1c) is a risk marker in coronary artery bypass surgery. *Scand Cardiovasc J.* 2008;42:392-98.
 11. Narayan P., Kshirsagar S.N., Mandal C.K., Ghorai P.A., Rao Y.M., Das D., et al. Preoperative Glycosylated Hemoglobin: A Risk Factor for Patients Undergoing Coronary Artery Bypass. *Annals of Thoracic Surgery* 2017,104(2),606-12.
 12. Halkos ME, Puskas JD, Lattouf OM, Kilgo P, Kerendi F, Song HK, Guyton RA, Thourani VH. Elevated preoperative hemoglobin A1c level is predictive of adverse events after coronary artery bypass surgery. *J Thorac Cardiovasc Surg* 2008;136:631-40.
 13. Voisine P., Ruel M., Khan T.A. et al, Differences in gene expression profiles of diabetic and nondiabetic patients undergoing cardiopulmonary bypass and cardioplegic arrest. *Circulation* 2004;110:II280-II286.
 14. 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;57:181-86.
-

SUBSCRIPTION FORM

I want to renew/subscribe international class journal "**Journal of Cardiovascular Medicine and Surgery**" of Red Flower Publication Pvt. Ltd.

Subscription Rates:

- Institutional: INR10000/USD781

Name and complete address (in capitals): _____

Payment detail:

Online payment link: <http://rfppl.co.in/payment.php?mid=15>

Cheque/DD: Please send the US dollar check from outside India and INR check from India made payable to 'Red Flower Publication Private Limited'. Drawn on Delhi branch.

Wire transfer/NEFT/RTGS:

Complete Bank Account No. 604320110000467

Beneficiary Name: Red Flower Publication Pvt. Ltd.

Bank & Branch Name: Bank of India; Mayur Vihar

MICR Code: 110013045

Branch Code: 6043

IFSC Code: BKID0006043 (used for RTGS and NEFT transactions)

Swift Code: BKIDINBBDOS

Term and condition for supply of journals

1. Advance payment required by Demand Draft payable to **Red Flower Publicaion Pvt. Ltd.** payable at **Delhi**
2. Cancellation not allowed except for duplicate payment.
3. Agents allowed 10% discount.
4. Claim must be made within six months from issue date.

Mail all orders to

Subscription and Marketing Manager

Red Flower Publication Pvt. Ltd.

48/41-42, DSIDC, Pocket-II

Mayur Vihar Phase-I

Delhi - 110 091(India)

Phone: 91-11-45796900, 22754205, 22756995, Cell: +91-9821671871

E-mail: sales@rfppl.co.in