Elevated preoperative HBA1C: Could off-pump CABG improve the surgical outcome?

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KEYWORDS
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ABSTRACT
Background: Dysglycemia is a well-established risk factor for coronary artery disease (CAD). Numerous studies have found a substantial link between uncontrolled diabetic mellitus (DM) and adverse outcomes following Coronary artery bypass grafting (CABG).
Aim of study: We aimed to disclose if off-pump CABG (OP-CAB) has a better outcome than on-pump CABG (ON-CAB) in patients with elevated glycated hemoglobin (HBA1C).
Methods: Perioperative Data regarding 945 diabetic patients with elevated HBA1C (> 6 mmol/L) who underwent CABG between January 2020 and July 2024 in Kasr-alainy, Fayoum, Beniseuf University Hospitals and Naser National Institute were gathered and patients were divided into two groups; Group A or the ON-CAB group that included 477 patients and Group B or the OP-CAB group that included 468 patients.
Results: Compared to ON-CAB group, OP-CAB group showed statistically significant (P value < 0.05) shorter post-operative intensive care unit (ICU) stay (3.02± 0.60 vs. 6.13± 1.65), Hospital stays (5.8 ± 3.4 vs. 6.7 ± 4.5), less need for Intra-Aortic Ballon Pump; IABP (76 vs 110), High vasopressor therapy (69 vs 98), lower incidence of Re-sternotomy (12 vs. 25), Mediastinitis (6 vs.16), new Renal Dialysis (3 vs. 11) and Early Mortality (7 vs.17). Although there were differences between both groups in terms of less postoperative myocardial infarction (MI) and unstable angina (UA) in Group A, as well as a lower incidence of post-operative stroke, blood transfusion, and renal failure (needing no dialysis) in Group B, the differences were not statistically significant (P value > 0.05).
Conclusion: Whenever possible, we recommend the OP-CAB technique in diabetic patients with elevated HBA1C who are candidates for CABG.

INTRODUCTION

Cardiovascular derangements commonly affect diabetic patients, especially those with long-standing dysglycemia. Diabetes mellitus is a well-known risk factor for IHD, found in more than 25 percent of patients demanding revascularization[1].

Diabetes mellitus is associated with a two- to fourfold increase in morbidity and death rates following surgical coronary revascularization. Strict glycemic control is necessary to improve the surgical outcome[2-3].

Glycated hemoglobin is a common laboratory test that reflects the average blood glucose level over the previous three to four months[3] and has been approved by many studies as a preoperative predictor of post-CABG morbidity and mortality[4-7].

Despite the abundance of data about the hazards of diabetes after CABG, there are still further relationships to elucidate, including ways to improve outcomes in such patients through proper preoperative glycemic control that requires sufficient time to reach satisfactory levels of HBA1C (below 6 mmol/mol)[8-9].

The severity of ischemic heart symptoms and the pressing need for surgical revascularization can sometimes allow for inadequate preoperative glucose control. Surgeons may rely on intraoperative strategies to mitigate the negative effects of dysglycemia, particularly when using the cardio-pulmonary bypass (CPB) machine, which has been shown to exacerbate hyperglycemia and trigger a systemic inflammatory response that is detrimental to surgical outcomes[10].

Hypothetically, we propose that using the OP-CAB approach whenever possible could reduce the burden of preoperative dysglycemia. In this study, we attempted to analyze the benefits of the OP-CAB approach by comparing results to those of the ON-CAB in patients with preoperatively high levels of HBA1C.

PATIENTS AND METHODS

Study design:

Data on 945 CABG patients from Kasr Al-Ainy, Fayoum, Beniseuf University Hospitals, and Naser National Institute were collected and analyzed between January 2020 and July 2024.

Patients were divided into two groups: Group A (control, 477 patients) and Group B (OP-CAB, 468 patients).

Definitions:

- Ischemic heart disease mandating CABG, Dyslipidemia, prolonged ICU stay, post-operative hospital stay, post-operative renal failure, new-onset post-operative dialysis, sternal wound infection, and mediastinitis were defined regarding the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)[11].
- Elevated HBA1C denoting prolonged poor glycemic control (more than 3 months duration) was defined as HBA1C level more than 6mmol/L[12].

Exclusion criteria:

We excluded patients with concurrent cardiac lesions needing on-pump repair, low ejection fraction <30%, acute ischemic mechanical and mitral lesions, and OP-CAB patients who were converted to the ON-CAB technique during surgery.

Study endpoints:

- The primary endpoints: Early mortality and Cerebro-vascular stroke.
- Secondary endpoints: Post-operative ICU stay, post-operative hospital stay, Re-sternotomy for bleeding, Disturbed renal function with or without need for new onset dialysis, sternal wound infection and Recurrence of ischemic heart symptoms after the operation.

Ethical approval:

The study protocol was accepted by the ethics council of Fayoum University hospitals "Ethical Approval Number: R-604". Every patient provided an informed written permission to accept the operation. This study was conducted in compliance with the World Medical Association's Code of Ethics (Declaration of Helsinki) for human subjects[13].

Statistical analysis:

Sampling method: With an alpha error of 5%, a 95% confidence level, and an 80% power sample, the Medcalc 19 program was used to determine the appropriate sample size population (945 patients) (Equations are provided by Machin et al. [14]).

Data analysis: The data was coded, processed, and analyzed using IBM SPSS Inc.'s version 24.0 for Windows®. Continuous data were expressed as mean±standard deviation or median with the interquartile range and categorical data as percentages. All reported P values are two-sided, and P values of ≤ 0.05 were considered statistically significant.

RESULTS

[Data presented as mean± SD, mean (interquartile range), or n (%)]

- Demographic and pre-operative variables; Table 1:

  A total of 945 patients (237 females) were divided into two groups: Group A (the control group of 477 patients with ON-CAB) and Group B (the OP-CAB of 468 patients). Our sample's mean age was 51.88 (± 9.456) years old. There was no significant difference between both groups regarding all demographic and clinical baseline characteristics ($p > 0.05$).
- Intraoperative variables; Table 2

The number of coronary arteries grated using the ON-CAB technique exceeded those in the other group (3.3 ± 0.8 vs. 2.8 ± 0.8), culminating in a shorter operative time when utilizing the OP-CAB approach (158 ± 42.64 vs. 172 ± 52.94).

Circulatory support using IABP and high vasopressor therapy was needed in 110 and 98 patients, respectively, among group A, compared to only 76 and 69 patients in the other group, denoting a statistically significant difference (P value <0.05).

- Post-operative variables; Table 3

Regarding our primary endpoints, early mortality in Group A significantly exceeded that in the Group B population (17 (3.56%) vs. 7 (1.50%), and despite a higher incidence of cerebrovascular strokes in Group A (8 (1.67%) vs. 5 (1.06%), the difference was not statistically significant (P > 0.05).

Considering our secondary endpoints, group B had significantly shorter post-operative ICU and hospital stays (3.02 ± 0.60 and 5.8 ± 3.4, respectively) compared to those in group A (6.13 ± 1.65 and 6.7 ± 4.5).

Only 12 (2.56%) patients in group B, compared to 25 (5.24%) patients in group A, had an exploratory re-sternotomy for bleeding, denoting statistical significance. Renal dysfunction affected 23 patients in Group A; 11 of them needed new post-operative renal dialysis. The number of patients who suffered a recurrence of myocardial ischemia symptoms in Group A surpassed that in Group B, although the difference was not statistically significant (65 (13.63%) vs. 52 (11.11%), P value > 0.05).

Table 1: Preoperative parameters.

Preoperative parameter	**Group A (477)**	**Group B (468)**	**P Value**
Baseline HBA1C	6.5 ± 1.82	6.7 ± 1.63	P = 0.0757
Age	57.6 ± 7.5	56.8 ± 8.5	P = 0.1251
Male sex	370 (77.56%)	341 (72.86%)	P = 0.0944
Other Comorbidities			
BMI > 25 kg/m^2	225 (47.16%)	198 (42.30%)	P = 0.1332
Previous M.I.	380 (79.66%)	391 (83.55%)	P = 0.1467
Smoking	382 (80.08%)	355 (75.85%)	P = 0.1168
Hypertension	376 (78.83%)	388 (82.91%)	P = 0.1112
Dyslipidemia	437 (91.61%)	423 (90.38%)	P = 0.5091
Renal Dysfunction (Serum creatinine >1.5 mg/dL)	29 (6.07%)	21 (4.49%)	P = 0.2781
Medications			
Insulin	202 (42.35%)	225 (48.08%)	P = 0.0770
OHGs	306 (64.15%)	99 (63.88%)	P = 0.9337
Beta Blockers	401 (84.07%)	410 (87.61%)	P = 0.1190

BMI; Body Mass Index, MI; Myocardial Infarction, OHG; Oral Hypo-Glycemics.

Table 2: Intraoperative parameters.

	Group A (477)	**Group B (468)**	**P Value**
Total operation time	172± 52.94	158± 42.64	P < 0.0001
Number of distal anastomoses	3.3 ± 0.8	2.8 ± 0.7	P < 0.0001
Intraoperative Use of IABP	110 (23.06%)	76 (16.24%)	P = 0.0083
High vasopressor therapy (>0.5 mcg/kg/min of norepinephrine to maintain target BP[15])	98 (20.55%)	69 (14.74%)	P = 0.0193

IABP: Intra-Aortic Ballon Pump

Table 3: Postoperative Parameters.

	Group A (477)	Group B (468)	P Value
Early mortality	17 (3.56%)	7 (1.50%)	P = 0.0437
Cerebro-vascular stroke	8 (1.67%)	5 (1.06%)	P = 0.4283
Post-operative ICU stay	6.13± 1.65	3.02± 0.60	P = 0.0573
Post-operative Hospital stays	6.7 ± 4.5	5.8 ± 3.4	P = 0.0006
Re-sternotomy for bleeding	25 (5.24%)	12 (2.56%)	P = 0.0337
Disturbed renal function	23 (4.82%)	18 (3.85%)	P = 0.4646
New Post-Operative Dialysis	11 (2.31%)	3 (0.64%)	P = 0.0338
sternal wound infection	16 (3.35%)	6 (1.28%)	P = 0.0348
Recurrence of ischemic heart symptoms	65 (13.63%)	52 (11.11%)	P = 0.2399

ICU: Intensive Care Unit

DISCUSSION

Over the last 2 decades, many studies and meta-analyses have examined the effect of preoperative Dysglycemia on cardiac surgeries[16-19]. Many other studies searched for significance of HBA1C as a predictor of hazardous outcome following CABG in diabetic patients[5, 20-21]. However, only few data are available on superiority of certain CABG technique over the other one, namely ON-CAB and OP-CAB techniques in patients with prolonged Dysglycemia.

In this study, we evaluated the cumulative hazardous effects of utilizing the CPB on the protracted preoperative condition of dysglycemia, as well as the benefits that patients may receive by avoiding the ON-CAB technique whenever possible.

In 2022, Ansari et al.[19] concluded that Close perioperative monitoring of the patient's glycemic condition is advised to prevent postoperative complications, since preoperative prolonged dysglycemia and elevated HbA1c levels can significantly affect morbidity and mortality following cardiac surgeries.

In 2013, Tennyson et al. [5] concluded that elevated HbA1c is a strong predictor of mortality and morbidity irrespective of previous diabetic status. In particular, the mortality risk for CABG is quadrupled at HbA1c levels >8.6%, and in 2022, after examining data from nearly 7000 CABG patients, Haqzad et al.[22] reported considerably worse outcomes among diabetes patients, albeit without taking into account the technique of the CABG procedure.

Our sample's mean age (51.88± 9.456) was much lower than the average reported in several other studies[23-25]. This could be explained by the fact that we limited our study to people with uncontrolled diabetes. Moreover, diabetes and hypertension are common among Egyptian patients, which accelerates the degenerative processes associated with atherosclerosis.

Other preoperative parameters showed no significant differences among our patients that correlated well with data reported by Shroyer et al.[26]. Singh et al. [27], on the other hand, reported younger age, less obese patients, a higher glomerular filtration rate, lower serum creatinine levels, better LV function, and higher HbA1c among the OP-CAB patient group.

Data on our ON-CAB patients showed significantly longer operative time, more grafted coron1aries, need for mechanical support and high vasopressor therapy (P value < 0.05), that couped with data informed by Singh et al.[27], Emmert et al.[28] and Cooke et al.[29].

Regarding post-operative mortality, we found that OP-CAB patients had a significantly lower early mortality rate (1.50% vs. 3.56%), and Emmert et al.[28] documented similar results (1.1% vs. 3.8%). In contrast, Magee et al. [24] and Srinivasan et al. [25] found no in-hospital mortality difference.

Comparing postoperative morbidity among our population to data reported by similar researchers; *Cerebrovascular stroke*: OP-CAB patients showed statistically insignificantly lower incidence of postoperative stroke (1.06% vs. 1.67%) that coincided with results reported by Cooke et al.[29]. However, the difference was statistically significant in many other papers[24-25].

ICU and Hospital stay: Many papers reported significantly shorter ICU and hospital stays using the OP-CAB technique[23-28] that fits well with our results (6.13± 1.65 vs. 3.02± 0.60 and 6.7 ± 4.5 vs. 5.8 ± 3.4, respectively).

Other complications: Wang et al.[21], Magee et al.[24] and Raja et al.[30] reported lower rates of procedural complications such as postoperative bleeding, need for high vasopressor support, renal dialysis, and sternal wound infection that are similar to our results.

In contrast, some papers reported no difference regarding postoperative mortality and morbidity, including anginal pains and myocardial infarction, among their off-pump patients, including Wang et al.[21], Shroyer et al.[26], and Singh et al.[27].

CONCLUSION

The OP-CAB technique provides better outcomes regarding postoperative morbidity and mortality compared to the ON-CAB technique in diabetic patients with pre-CABG elevated HBA1C and should be the preferred technique whenever possible in such cases.

CAD	Coronary Artery Disease
DM	Diabetes Mellitus
CABG	Coronary Artery Bypass Grafting
HBA1C	Glycated Hemoglobin
OP-CAB	Off bypass CABG
ON-CAB	On bypass CABG
ICU	Intensive Care Unit
IABP	Intra-Aortic Ballon Pump
MI	Myocardial Infarction
UA	Unstable Angina

Conflict of interest: None

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REFERENCES

1. Crisafulli A, Pagliaro P, Roberto S, Cugusi L, Mercuro G, Lazou A, Beauloye C, Bertrand L, Hausenloy DJ, Aragno M, Penna C. Diabetic Cardiomyopathy and Ischemic Heart Disease: Prevention and Therapy by Exercise and Conditioning. Int J Mol Sci. 2020 Apr 21;21(8):2896.
2. Padovani C, Arruda RMDC, Sampaio LMM. Does Type 2 Diabetes Mellitus Increase Postoperative Complications in Patients Submitted to Cardiovascular Surgeries? Braz J Cardiovasc Surg. 2020 Jun 1;35(3):249-253.
3. D'Emden M. Diagnostic tests: Glycated haemoglobin for the diagnosis of diabetes. Australian Prescriber [Internet]. 2014 Jun 1;37(3):98–100.
4. Deo S, Sundaram V, Sheikh MA, Sahadevan J, Selvaganesan P, Mohan SKM, et al. Pre-operative glycaemic control and long-term survival in diabetic patients after coronary artery bypass grafting. European Journal of Cardio-thoracic Surgery [Internet]. 2021 May 10;60(5):1169–77.
5. 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 Dec;17(6):1000-8.
6. Abu Tailakh M, Ishay SY, Awesat J, Poupko L, Sahar G, Novack V. Hemoglobin A1c in Patients with Diabetes Predict Long-Term Mortality Following Coronary Artery Surgery. J Clin Med. 2021 Jun 21;10(12):2739.
7. Natarajan K, Narayanan A, Hemapriya R, Swetha S, Jayashree R, Ninan B. Impact of elevated glycosylated hemoglobin (HbA1c) on the outcome following coronary artery bypass graft surgery. Journal of Cardiothoracic and Vascular Anesthesia [Internet]. 2019 Sep 1;33:S158.
8. Chen J, Yin D, Dou K. Intensified glycemic control by HbA1c for patients with coronary heart disease and Type 2 diabetes: a review of findings and conclusions. Cardiovascular Diabetology [Internet]. 2023 Jun 22;22(1).
9. Gaudino M, Chadow D, Perezgrovas R. Is lower better? JACC Asia [Internet]. 2022 Apr 1;2(2):207–8.
10. Doenst T, Wijeysundera D, Karkouti K, Zechner C, Maganti M, Rao V, et al. Hyperglycemia during cardiopulmonary bypass is an independent risk factor for mortality in patients undergoing cardiac surgery. Journal of Thoracic and Cardiovascular Surgery/ˆthe ‰Journal of Thoracic and Cardiovascular Surgery/˜the œJournal of Thoracic and Cardiovascular Surgery [Internet]. 2005 Oct 1;130(4):1144.e1-1144.e8.
11. Franz-Josef Neumann and others, 2018 ESC/EACTS Guidelines on myocardial revascularization, European Heart Journal, Volume 40, Issue 2, 07 January 2019: 87–165.

12. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. 2. Classification and Diagnosis of diabetes: Standards of Care in Diabetes—2023. Diabetes Care [Internet]. 2022 Dec 12;46(Supplement_1):S19–40.
13. World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. JAMA. 2013;310(20):2191–2194.
14. Machin, David & Campbell, Michael & Tan, Say & Tan, Sze-Huey. (2009). Sample Size Tables for Clinical Studies, Third Edition.
15. Bassi E, Park M, Azevedo LC. Therapeutic strategies for high-dose vasopressor-dependent shock. Crit Care Res Pract. 2013;2013:654708.
16. Bauters C, Lamblin N, Mc Fadden EP, Van Belle E, Millaire A, de Groote P. Influence of diabetes mellitus on heart failure risk and outcome. Cardiovasc Diabetol. 2003 Jan 8;2:1.
17. McCullough PA. Coronary artery disease. Clin J Am Soc Nephrol. 2007 May;2(3):611-6.
18. Aldea GS, Bakaeen FG, Pal J, Fremes S, Head SJ, Sabik J, Rosengart T, Kappetein AP, Thourani VH, Firestone S, Mitchell JD; Society of Thoracic Surgeons. The Society of Thoracic Surgeons Clinical Practice Guidelines on Arterial Conduits for Coronary Artery Bypass Grafting. Ann Thorac Surg. 2016 Feb;101(2):801-9.
19. Ansari DM, Harahwa T, Abuelgasim E, Harky A. Glycated Haemoglobin Levels and Its Effect on Outcomes in Cardiac Surgery. Braz J Cardiovasc Surg. 2022 Oct 8;37(5):744-753.
20. Bauters C, Lamblin N, Fadden EPM, Van Belle E, Millaire A, De Groote P. Influence of diabetes mellitus on heart failure risk and outcome. Cardiovascular Diabetology [Internet]. 2003 Jan 1;2(1):1.
21. Wang Y, Shi X, Du R, Chen Y, Zhang Q. Off-pump versus on-pump coronary artery bypass grafting in patients with diabetes: a meta-analysis. Acta Diabetol. 2017 Mar;54(3):283-292.
22. Haqzad Y, Hobkirk J, Ariyaratnam P, Chaudhry M, Carroll S, Loubani M. Outcomes following coronary artery bypass surgery in diabetic treatment sub-groups. A propensity matched analysis of >7000 patients over 18 years. Asian Cardiovascular and Thoracic Annals. 2022;30(2):131-140.
23. Renner A, Zittermann A, Aboud A, Pühler T, Hakim-Meibodi K, Quester W, Tschoepe D, Börgermann J, Gummert JF. Coronary revascularization in Diabetic Patients: Off-Pump versus On-Pump surgery. The Annals of Thoracic Surgery [Internet]. 2013 Aug 1;96(2):528–534.
24. Magee MJ, Dewey TM, Acuff T, Edgerton JR, Hebeler JF, Prince SL, Mack MJ. Influence of diabetes on mortality and morbidity: off-pump coronary artery bypass grafting versus coronary artery bypass grafting with cardiopulmonary bypass. The Annals of Thoracic Surgery [Internet]. 2001 Sep 1;72(3):776–781.
25. Srinivasan AK Grayson AD Fabri BM . On-pump versus off-pump coronary artery bypass grafting in diabetic patients: a propensity score analysis . Ann Thorac Surg 2004 ;78 :1604 –9.
26. Shroyer AL, Hattler B, Wagner TH et al (2014) Comparing off-pump and on-pump clinical outcomes and costs for diabetic cardiac surgery patients. Ann Thorac Surg 98:38–44.
27. Singh A, Schaff HV, Mori Brooks M, Hlatky MA, Wisniewski SR, Frye RL, Sako EY; BARI 2D Study Group. On-pump versus off-pump coronary artery bypass graft surgery among patients with type 2 diabetes in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial. Eur J Cardiothorac Surg. 2016 Feb;49(2):406-16.
28. Emmert MY, Salzberg SP, Seifert B, Rodriguez H, Plass A, Hoerstrup SP, Grünenfelder J, Falk V. Is off-pump superior to conventional coronary artery bypass grafting in diabetic patients with multivessel disease? European Journal of Cardio-Thoracic Surgery [Internet]. 2011 Jul 1;40(1):233–239.
29. Cooke B, Williams L, Delay TK, Xie R, Cornelius K, Davies JE, Vardas PN. Effect of elevated HbA1c on outcomes in on-pump versus off-pump coronary artery bypass grafting. The Cardiothoracic Surgeon [Internet]. 2023 Oct 18;31(1).
30. Raja SG, Shah J, Navaratnarajah M, Amin F, Amrani M. Outcomes and predictors of mortality and stroke after on-pump and off-pump coronary artery bypass surgery in octogenarians. Innovations (Phila). 2013 Jul-Aug;8(4):269-75.