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The Effect of Body Mass Index on Bleeding After on Pump Coronary Artery Bypass Grafting

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ABSTRACT

Objective: To study the relationship of body mass index (BMI) and postoperative bleeding in patients undergoing isolated coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB).

Study Design: Analytical cross-sectional study.

Place and Duration of Study: Cardiothoracic services, Almana General Hospital, Al Khobar, Saudi Arabia, from Oct 2019 to Oct 2021.

Methodology: Two hundred and twenty (220) consecutive patients who underwent CABG using cardiopulmonary bypass were included in the study. Patients who had additional procedures, those who were operated in emergency and those with significant comorbidities like hepatic and liver dysfunction were excluded from the final analysis. Patients were divided into three groups according to their BMI, healthy weight (BMI 18.5 to <25), overweight (BMI 25 to <30) and obese (BMI >30). The world health organization (WHO) definition was used to define different categories of BMI. Various perioperative variables were recorded for all the patients. Only the immediate postoperative follow up period was included in the study. Data was analyzed using IBM SPSS-statistics 23.0 (IBM, SPSS Inc., Chicago, IL).

Results: Of the 220 patients included in the study, 184(83%) were male patients and 36(16%) female patients. There was no significant difference in the mean age of the patients in the three groups (p=0.481). There were significantly more hypertensive patients 46(45%) in the overweight group compared to other two groups (p=0.025). Baseline diabetic status was not significantly different among the three categories (p=0.978). Total mediastinal drainage in the first 24 hours was significantly less in the obese group (3.7±4.45 ml) compared to overweight (4.4±2.7 ml) and healthy weight (7.35±8.5 ml) patients (p=0.001). There was no mortality in the studied cohort.

Conclusion: Bleeding after isolated coronary artery bypass grafting is inversely related to BMI. Patients with healthy and overweight BMI are at higher risk of bleeding compared to obese patients.

Keywords: Body mass index, Coronary artery bypass grafting, Mediastinal drainage, Obesity.

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INTRODUCTION

An abnormal body mass index (BMI) is a known risk factor for coronary artery disease.[1] Many of these patients need coronary artery bypass grafting (CABG) due to the severity of the coronary disease. CABG has been performed traditionally through median sternotomy using cardiopulmonary bypass. Advances in minimally invasive techniques have allowed us to avoid median sternotomy in many types of open-heart surgeries including CABG. Minimally invasive techniques are known to reduce recovery time and wound complications.[2] Both minimally invasive and off pump techniques are known to mitigate the need for blood product usage due to less bleeding. But obesity has traditionally been considered a relative contraindication to minimally invasive procedures. Also, only select centers perform minimally invasive procedures. This leaves CABG with median sternotomy with or without the use of cardiopulmonary bypass as the most common approach for patients with high BMI.

Traditionally, obese patients have been considered high risk for open heart surgery especially diabetic patients. Complications like increased ventilation time, long ICU stay and sternal wound complications have been found to be associated with obesity when these patients are subjected to open heart surgery.[3] Paradoxically, obesity has an inverse relationship with adverse outcomes in patients with renal and pulmonary procedures. The concept of obesity paradox in cardiac surgery was described for the first time in 2003.[4] Since then, it has been extensively studied in the literature from various aspects. Whether an obesity paradox exists in cardiac surgery has been debated in the literature. Studies have shown that overweight and mild obesity is associated with better long-term survival after CABG.[5] The same benefit was not observed for patients with

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morbid obesity. Underweight patients have also been found to have high early mortality compared to overweight and obese patients.[6,7]

Bleeding is a common complication after cardiac surgery. Cardiac surgeries are mostly performed with the use of cardiopulmonary bypass which induces a generalized inflammatory state, platelets dysfunction and coagulation factors dysfunction and dilution. The resultant effect is increased propensity for bleeding in the immediate postoperative period. Additionally, many patients are already on antiplatelet medications or anticoagulants before the surgery, hence increasing the risk of bleeding postoperative. About 5% patients undergoing CABG are re-explored for bleeding.[8] Bleeding in the immediate postoperative period not only predisposes patients to complications like atrial fibrillation and wound infection but also the increased transfusion requirements as a result of bleeding increases the risks of graft failure and kidney injury.[9] Although increasing BMI has been associated with increased risk of acute kidney injury, increased ventilation time and ICU stay and significantly more chance of sternal wound complications, the effect of BMI on early postoperative mediastinal bleeding is less well described. The purpose of this work to study the association of BMI with bleeding after CABG in the immediate postoperative period.

METHODLOGY

An analytical cross sectional study was conducted at Almana General Hospital, Saudi Arabia from October 2019 to October 2021. Since this was a retrospective study and did not involve any new intervention, hence the need for individual consent from the patients was waivered. Data was recorded prospectively in the hospital database system after approval from institutional IERB(Ltr#21/21/ALM/21/1).

Sample Size: Sample size was calculated using 5% prevlence which was found to be 73, as it was retrospective study, we recrited all patients enrolled during the study duration.[8]

Inclusion Criteria: Consecutive patients who underwent CABG for atherosclerotic coronary artery disease using cardiopulmonary bypass through median sternotomy were included in the study.

Exclusion Criteria: Patients who had additional procedures like mitral or aortic valve replacement, emergency procedures and redo procedures were excluded from the study. Those with significant comorbidities like liver and hepatic derangements were also excluded from the final analysis.

All the patients were managed by the same heart team so standardized preoperative decision-making protocols were implied for all the patients. Body mass index was defined as weight in kilogram divided by height in meters square (Kg/m^2). Patients were divided into three categories according to their BMI as per the world health organization (WHO) definition. The normal BMI category included patients with BMI 18.5 to those less than 25. The overweight category included patients with BMI from 25 to less than 30. Patients with BMI more than 30 were categorized as obese. There was no patient with BMI below 18.5 (underweight) in our cohort. The use of preoperative medications was standardized with all the patients receiving β-blocker and Angiotensin Converting Enzyme (ACE) inhibitors preoperatively.

Patients underwent CABG through median sternotomy with general anesthesia and cardiopulmonary bypass (CPB). CPB was established after heparinization with unfractionated heparin targeting an activated coagulation time (ACT) of more than 450 seconds. Priming of CPB was done with crystalloids or blood depending the preoperative hemoglobin. CPB flows were calculated according to the weight and standardized for all the patients. Reversal of heparin was done through protamine sulphate in a dose-by-dose fashion. The conduits used for grafting were left internal mammary artery and one or more great saphenous veins.

Shedding of mediastinal blood was minimized through meticulous technique thus minimum of shed blood was returned to the CPB machine. The residual volume left in the CPB circuit was returned to the patient at the end of bypass as tolerated by the hemodynamics and loading conditions of the heart.

Postoperatively, mediastinal drainage was calculated from the drainage bottle system by an experienced staff. Total drainage in the first 24 hours was recorded.

Continuous variables were presented as mean and standard deviations and categorical variables as frequencies and percentages. Categorical variables were analyzed using chi square (χ^2) test. The three categories of BMI were analyzed in the context of postoperative bleeding ml/Kg using One Way ANOVA (Analysis of Variance) test. Linear correlation was calculated between BMI as a continuous variable and postoperative bleeding in ml/Kg. To assess the

effect of individual category of BMI, the three subsets were converted into dummy variables and linear regression was used to determine the category of BMI with significant effect on the outcome. Data was analyzed using IBM SPSS-statistics 23.0 (IBM, SPSS Inc., Chicago, IL).

RESULTS

Body mass index (BMI) was measured as a categorical variable with three levels across all the patients (n=220) included in the study i.e., healthy weight group BMI (18.5 to <25, n=73), overweight (25 to <30, n=103) and obese (BMI >30, n=44). There was no one in the underweight category (BMI<18.5) in our cohort.

Table-I: Important Demographic and Preoperative Characteristics of the Patients

Patient Characteristics		BMI Groups (n=220)			*p*-value
		Healthy weight (n=73)	Overweight (n=103)	Obese (n=44)	
Gender	Male 184 (83.64%)	51 (69.86%)	95 (92%)	38 (86%)	0.781
	Female 36 (16.36%)	22 (30.14%)	8 (8%)	6 (14%)	
Age (years)		52.6 ± 8.9	51.35 ± 7.9	52.84 ± 7.65	0.481
Diabetes		42 (57.53%)	58 (56.31%)	25 (56.82%)	0.978
Hypertension		38 (52.05%)	46 (44.66%)	30 (68.18%)	0.025
Current smokers		19 (26.02%)	21 (20.36%)	16 (37.36%)	0.112
Preoperative hemoglobin		13.65 ± 1.62	14.1 ± 1.54	13.4 ± 1.67	0.02
Preoperative platelet count (109/L)		248.3 ± 84.9	247.4 ± 68.04	248.7 ± 72.31	0.994
Preoperative HBA1c (%)		7.62 ± 2.06	7.16 ± 1.7	6.58 ± 1.23	0.039
Preoperative ejection fraction (%)		48.2 ± 9.7	51.6 ± 8.9	49.7 ± 10.3	0.066
MI within previous 7 days		30 (41.09%)	53 (51.45%)	14 (31.81%)	0.082
Initial Presentation	Stable angina	6 (8.3%)	12 (11.65%)	7 (15.90%)	0.432
	Unstable angina	14 (19.17%)	20 (19.14%)	12 (27.28%)	0.785
	NSTEMI	42 (57.53%)	57 (55.33%)	20 (45.46%)	0.079
	STEMI	11 (15.06%)	14 (13.61%)	5 (11.36%)	0.67
Preoperative Plavix taken within 5 days of surgery		21 (28.76%)	34 (33.00%)	9 (20.45%)	0.569

All the three categories were comparable with respect to age (*p*=0.481), diabetes (*p*=0.978), preoperative ejection fraction (*p*=0.066) and incidence of myocardial infarction in the previous 7 days (0.082). Hypertension was significantly more prevalent in obese patients (68.18%), compared to healthy (52.05%) and overweight patients (44.66%), (*p*=0.025). preoperative hemoglobin levels were significantly high in the overweight category (14.1±1.54, *p*=0.02) compared to obese and normal weight patients. Although, numerically more patients in the overweight category took clopidogrel in the previous 5 days of surgery 34(33%) compared to healthy weight patients 21(28.76%) and obese patients 9(20.45%), the comparison of the means was not statistically significant (*p*=0.569) (Table-I).

Intraoperatively, obese patients had high cross clamp time (144.17±70.6 minutes) compared to healthy (128±43.1 minutes) and overweight patients (119.98±32 minutes), (*p*=0.017). (Table-II) Cross clamp time was not significantly different among the three categories (*p*=0.15). Mean intraoperative hematocrit was significantly lower in people with healthy BMI (24.61±2.3, *p*=0.008).

There was no significant difference among the three categories with respect to total postoperative drainage (*p*=0.07), although patients with normal BMI had a trend towards higher bleeding (442±447 ml) (Table-III). But when drainage was calculated in ml/Kg body weight, postoperative drainage was significantly more (7.35±8.5 ml) compared to overweight (4.4±2.7 ml) and obese patients (3.7±4.45ml) (*p*=0.001). A negative correlation was observed between BMI as a continuous variable and postoperative bleeding (R2=0.07), (Figure-1). Multiple comparison analysis showed that this difference was mainly because of patients in the normal BMI category (normal vs Overweigh t=0.02 & normal vs obese, *p*=0.003).

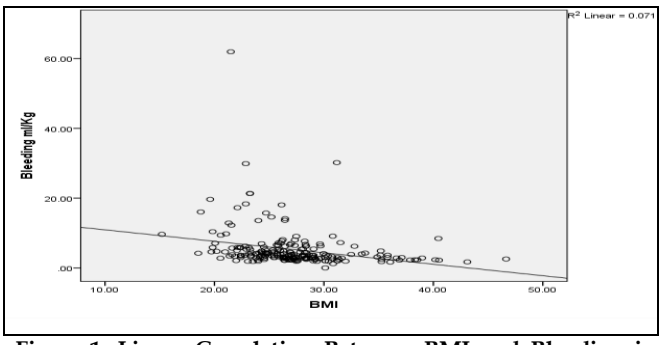

Figure-1: Linear Correlation Between BMI and Bleeding in ml/Kg

Table-II: Intraoperative Variables

Patient Characteristics	BMI Groups			*p*-value
	Healthy weight (n=73)	Overweight (n=103)	Obese (n=44)	
CPB time (minutes)	128 ± 43.1	119.98 ± 32	144.17 ± 70.6	0.017
Cross clamp time (minutes)	86.1 ± 30.9	78.4 ± 26	86.32 ± 31.1	0.15
Lowest intraoperative hematocrit during CPB (%)	24.61 ± 2.3	25.14 ± 3.22	26.6 ± 3.9	0.008
Urine output on CPB (ml)	544.9 ± 425	605.6 ± 357	625.8 ± 498.7	0.519

CPB: Cardiopulmonary Bypass,

Table-III: Important Postoperative Variables

Total mediastinal blood drainage in first 24 hours (ml)	442 ± 447	325 ± 195.2	361.1 ± 393.5	0.07
Total mediastinal drainage in first 24 hours in ml/Kg	7.35 ± 8.5	4.4 ± 2.7	3.7 ± 4.45	0.001
Re-exploration for bleeding	4 (5.4%)	2 (1.94%)	4 (9.09%)	0.140

DISCUSSION

Our study has brought some important findings into limelight. Our population cohort is young compared to most other major studies conducted in this context.[10] The cohort is predominantly male pointing to the high incidence of coronary artery disease in males and is consistent with literature in this regard.

Lower BMI, although in the healthy range, has been found to be associated with more bleeding postoperatively in the literature compared to the overweight and obese patients. This finding was confirmed in our study.[11] Obesity has been associated with lower rate of reoperation for bleeding post cardiac surgery.[12,13] Wang et al studied the outcomes of 1007 patients with respect to obesity and postoperative bleeding after open heart surgery.[14] They found higher bleeding rates in patient with BMI in the normal and overweight category. Similarly higher rates of blood transfusion were observed in patients who have BMI in the normal and overweight category. This finding was also confirmed in our study where the rate of bleeding, when considered as a function of ml/Kg, was more in patients with lower BMI. Hence, a negative correlation was observed between bleeding and BMI.

Many investigators have shed light on the procoagulant effect of obese patients undergoing cardiac surgery and the resultant lower bleeding risk in these patients. Kindo *et al*, assessed the various laboratory tests used to assess coagulation and found that obese patients after cardiac surgery have increased thrombin formation and reduced thrombolysis after cardiac surgery.[15] In their study, patients with severe obesity had high levels of fibrinogen even before the surgery. Fibrinogen plays an important role in coagulation. Another mechanism that may be responsible for this prothrombotic state in obese patients is described by Vilahur and colleagues.[16] They described the production of plasminogen activation inhibitor, an inhibitor of fibrinolytic system, by the adipose tissue as the contributing factor in decreasing blood loss after open heart surgery. It has also been suggested that a selection bias may be involved in the comparatively better outcome of obese patients when compared to non-obese patients. In their cohort of more than four thousand patients, Gao et al did not find obesity as a risk factor for early mortality or adverse events including bleeding.[17] Also, many studies have shown no protective effect of obesity according to bleeding.[18]

Although our study had a short term follows up, it showed that there was no difference in the outcome with respect to mortality when all the categories of BMI were compared. This is in agreement with the literature which largely favors the concept that the outcomes in obese patients after open heart surgery may not be as bad as thought previously.[19,20] Patients with obesity have been shown to be of younger age compared to patients with lower BMI.[21] This was not the case in our study where there was no significant difference in the age of all the three groups studied. This can be explained by the generally younger age of our patient cohort and hence the more aggressive nature of coronary artery disease in our population. Moreover, patients of Asian origin have generally been considered at high risk of coronary artery disease with worse demographic profile.[22] Questions have also been raised about the validity of the obesity classification system & its application to non-Caucasian population, proposing different definition of obesity and categorization of BMI.[23] Our study shows that the trends of bleeding post CABG in patients with different categories of BMI are not different from those in Caucasians as shown also by Hadjinikolaou and colleagues.[23]

LIMITATIONS OF STUDY

This was a non-controlled single center study which may be a source of bias in terms of the patient risk profile

and the operative technique which may differ from other centers. Our study did not include any patient in the underweight category which suggests the general prevalence of higher BMI in our cohort. Moreover, our study was based upon retrospective database review which has its inherent limitations. A prospectively conducted case-control study comparing the short as well as long term outcome of the effect of bleeding in various categories of BMI will be interesting to see. The limitation of our study was the uniformity of sample size. Unequal number of patients were present in both the groups because of the difference of hemodynamic status and cardiovascular disease of each patient, based on which the anesthesiologist would decide the need for either dexmedetomidine or propofol in real time. Limited sample size and duration were also contributing factors.

CONCLUSION

The obesity paradox seems to be real as for as postoperative bleeding and BMI are concerned in patients who have undergone isolated coronary artery bypass grafting using cardiopulmonary bypass. Larger sample sizes involving patients from many centers operated by surgical teams with varied surgical protocols may shed more light on this phenomenon.

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Author's Contribution

MS: Following authors have made substantial contributions to the manuscript as under:

MS: Concept, Manuscript drafting, analysis

IK: Manuscript writing, idea, review articles

FF: Intellectual contribution, critical review, Analysis

MAD: Data collection, data entry, data management

SMH: Manuscript writing, data management and analysis

HK: Data analysis, data management, critical review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work appropriately investigated & resolved.

REFERENCES

1. Carbone S, Canada JM, Billingsley HE, Siddiqui MS, Elagizi A, Lavie CJ. Obesity paradox in cardiovascular disease: where do we stand? Vasc Health Risk Manag 2019; 15(1): 89-100. doi: 10.2147/VHRM.S168946.
2. Davierwala PM, Verevkin A, Bergien L, von Aspern K, Deo SV, Misfeld M. Twenty-year outcomes of minimally invasive direct coronary artery bypass surgery: The Leipzig experience. J Thorac Cardiovasc Surg 2021; S0022-5223(21); 00343-3.
3. Uva MS, Rodrigues V, Monteiro N, Manuel Pedro A, Caria R, Mesquita A, Fernandes J, Pinho J, Bau J, Magalhães P. Cardiac surgery and morbid obesity. Rev Port Cardiol 2002; 21(3): 255-264; discussion 267-9. English, Portuguese.
4. Kalantar-Zadeh K, Block G, Humphreys MH. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. Kidney Int 2003; 63(1): 793–808.
5. Burgos LM, Gil Ramírez A, Seoane L, Espinoza J, Furmento JF, Costabel JP. Is the Obesity Paradox in Cardiac Surgery Really a Myth? Effect of Body Mass Index on Early and Late Clinical Outcomes. J Cardiothorac Vasc Anesth 2021; 35(2): 492-498. doi: 10.1053/j.jvca.2020.03.051. Epub 2020 Apr 19.
6. Dimberg A, Alström U, Janiec M. Re-exploration for bleeding associated with increased incidence of the need for reintervention after coronary artery bypass graft surgery. Interact Cardiovasc Thorac Surg 2019; 28(2): 214-221. doi: 10.1093/ icvts/ivy245.
7. Mariscalco G, Wozniak MJ, Dawson AG, Serraino GF, Porter R, Nath M, Klersy C, Kumar T, Murphy GJ. Body Mass Index and Mortality Among Adults Undergoing Cardiac Surgery: A Nationwide Study with a Systematic Review and Meta-Analysis. Circulation. 2017; 135(9): 850-863. doi: 10.1161/Circulationaha. 116.022840. Epub 2016 Dec 28.
8. Dimberg A, Alström U, Janiec M. Re-exploration for bleeding associated with increased incidence of the need for reintervention after coronary artery bypass graft surgery. Interact Cardiovasc Thorac Surg 2019; 28(2): 214-221. doi: 10.1093/ icvts/ivy245.
9. Özhan A, Akgül E, Parlar Aİ. The association of blood transfusion and acute kidney injury in diabetic coronary artery bypass grafting patients. Cardiovasc Surg Int 2021; 8(1): 13-19.
10. Zhang W, Chen S, Liu X, Wang L, Wang S, Yu Y. Can Higher Body Mass Index Patients Save Blood Following On-pump Coronary Artery Bypass Grafting? Heart Surg Forum. 2019; 22(5): E352-E356. doi: 10.1532/hsf.2559.
11. Elbaz-Greener G, Rozen G, Carasso S, Kusniec F, Yarkoni M. The Relationship Between Body Mass Index and In-Hospital Mortality in Patients Following Coronary Artery Bypass Grafting Surgery. Front Cardiovasc Med 2021; 8(1): 754934. doi: 10.3389/fcvm.2021.754934.
12. Birkmeyer NJ, Charlesworth DC, Hernandez F, Leavitt BJ, Marrin CA, Morton JR, et al. Obesity and risk of adverse outcomes associated with coronary artery bypass surgery. Northern New England Cardiovascular Disease Study Group. Circulation 1998; 97(1): 1689–1694.
13. Wagner BD, Grunwald GK, Rumsfeld JS, Hill JO, Ho PM, Wyatt HR, et al. Relationship of body mass index with outcomes after coronary artery bypass graft surgery. Ann Thorac Surg 2007; 84(1): 10–16.
14. Wang M, Chen M, Ao H, Chen S, Wang Z. The Effects of Different BMI on Blood Loss and Transfusions in Chinese Patients Undergoing Coronary Artery Bypass Grafting. Ann Thorac Cardiovasc Surg 2017; 23(2): 83-90. doi: 10.5761/ atcs.oa.16-00219. Epub 2017 Feb 8.
15. Kindo M, Minh TH, Gerelli S. The prothrombotic paradox of severe obesity after cardiac surgery under cardiopulmonary bypass. Throm Res 2014; 134(1): 346–353.
16. Vilahur G, Ben-Aicha S, Badimon L. New insights into the role of adipose tissue in thrombosis. Cardiovasc Res 2017; 113(9): 1046-1054. doi: 10.1093/cvr/cvx086. PMID: 28472252.
17. Gao M, Sun J, Young N, Boyd D, Atkins Z, Li Z, et al. Impact of Body Mass Index on Outcomes in Cardiac Surgery. J Cardiothorac Vasc Anesth 2016; 30(5): 1308-1316. doi: 10.1053/j.jvca. 2016.03.002. Epub 2016 Mar 4.

18. De Santo LS, Moscariello C, Zebele C. Implications of obesity in cardiac surgery: pattern of referral, physiopathology, complications, prognosis. J Thorac Dis 2018; 10(7): 4532-4539. doi: 10.21037/jtd.2018.06.104.
19. Chan PG, Sultan I, Gleason TG, Wang Y, Navid F, Thoma F, Kilic A. Contemporary outcomes of coronary artery bypass grafting in obese patients. J Card Surg 2020; 35(3): 549-556. doi: 10.1111/jocs.14415. Epub 2020 Jan 16.
20. Orhan G, Biçer Y, Aka SA, Sargin M, Simşek S, Senay S, et al. Coronary artery bypass graft operations can be performed safely in obese patients. Eur J Cardiothorac Surg 2004; 25(2): 212-217. doi: 10.1016/j.ejcts.2003.11.003.
21. Brister SJ, Hamdulay Z, Verma S, Maganti M, Buchanan MR. Ethnic diversity: South Asian ethnicity is associated with increased coronary artery bypass grafting mortality. J Thorac Cardiovasc Surg 2007; 133(1): 150-154.
22. Liu B, Du Y, Wu Y, Snetselaar LG, Wallace RB, Bao W. Trends in obesity and adiposity measures by race or ethnicity among adults in the United States 2011-18: population-based study. BMJ 2021; 372(2): n365. doi: 10.1136/bmj. n365.
23. Hadjinikolaou L, Klimatsidas M, Iacona GM. Short-and medium-term survival following coronary artery bypass surgery in British Indo-Asian and white Caucasian individuals: impact of diabetes mellitus. Interact Cardiovasc Thorac Surg 2010; 10(3): 389-393.