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Periprocedural Risk Predictors and Body Mass Index Impact Long-Term Prognosis in Patients Undergoing Coronary Artery Bypass Grafting

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Abstract

Objective: The main goal of this study is to identify risk predictors for all-cause mortality in patients undergoing Coronary Artery Bypass Grafting (CABG) based on Body Mass Index (BMI).

Methods: All consecutive 4,871 patients undergoing isolated CABG between 2005 and 2021, were included in the study. Underweight (<19 kg/m^2) (n=42), normal/obese (BMI= 19-39.9 kg/m^2) (n=4,622), and morbidly obese (BMI ≥ 40 kg/m^2) (n=215) patients were compared for preoperative characteristics. A propensity-adjusted analysis was used to compare the groups. Primary outcome were long-term incidence of death and Major Adverse Cardiovascular and Cerebrovascular Events (MACCE).

Results: Preoperatively, mean age was 71.2 (normal/obese), *vs.* 75.5 (underweight) *vs.* 65.9 (morbidly obese) years old. Intraoperatively, morbidly obese patients had higher operating room time. Postoperatively, morbidly obese, and underweight patients had higher blood product transfusion and 30-day readmission rate. Primary outcome of all-cause mortality was normal/obese 528/4622 (11.3%) *vs.* underweight 11/42 (26.2%) *vs.* morbidly obese 32/215 (14.9%), p=0.003. MACCE was significantly higher in morbidly obese patients 17/215 (7.9%), p=0.024. Predictors for all-cause mortality in morbidly obese patients were non-white patients, diabetes, Peripheral Vascular Disease (PVD), STS ≥ 4%, dialysis, hypertension, Chronic Obstructive Pulmonary Disease (COPD), Ejection Fraction (EF) <50%, and Atrial fibrillation (Afib). Predictors for all-cause mortality in underweight patients were male gender, white race, STS ≥ 4%, dialysis, EF<50%, and hypertension.

Conclusion: Death rate in underweight patients was two-fold compared to normal/obese patients and 57% higher compared to morbidly obese patients. MACCE rate was significantly higher in morbidly obese patients.

Keywords: Obesity; BMI; Underweight; CABG; Risk Factors: Long-Term Prognosis

Abbreviations

CABG: Coronary Artery Bypass Grafting; CAD: Coronary Artery Disease; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; PVD: Peripheral Vascular Disease; OR: Operating Room; ICU: Intensive Care Unit; BMI: Body Mass Index; BSA: Body Surface Area; SVG: Saphenous Venous Grafting; IMA: Internal Mammary Artery; MI: Myocardial Infarction; CBVD: Cerebrovascular Disease; RBC: Red Blood Cells; FFP: Fresh Frozen Plasma; PCI: Percutaneous

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Coronary Intervention

Introduction

Impact of obesity and undernourishment in short- and long-term outcomes after Coronary Artery Bypass Grafting (CABG) has been widely studied [1-4]. In this context, the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II does not include Body Mass Index (BMI) among risk factors [5] while the Society of Thoracic Surgeons (STS) risk score includes Body Surface Area (BSA) among risk factors [6]. While impact of BMI in valve surgery remains controversary [7,8], an analysis of the National Cardiac Surgery Database of the Society of Thoracic Surgeons, using data from CABG operations in over 300,000 patients, indicated that morbid obesity remains an independent predictor of increased operative mortality in patients undergoing CABG [9]. In addition, the Reduction of Atherothrombosis for Continued Health (REACH) Registry [10] reported that secondary prevention after CABG should focused on more comprehensive risk factor modifications to bring patients to target goals specified by clinical guidelines [11,12] and to reduce variability in risk factor control. In this context, primary prevention is essential for improving clinical outcomes. In addition, interaction between BMI and pre-operative risk predictors in patients undergoing isolated CABG and their influence on long-term prognosis remain hindered. The main goal of this study is to identify risk predictors that interact with BMI and to analyze their impact on long-term prognosis in patients undergoing isolated CABG.

Methods

Study population

We identified all consecutive patients who underwent CABG between May 2005 and June 2021 at Lankenau Heart Institute (Lankenau Medical Center, PA, USA). The study protocol was approved by the Main Line Health Hospitals Institutional Review Board (IRB 45CFR164.512). Patients individual consent was waived due to the retrospective nature of the study. Inclusion criteria was all patients who underwent an isolated CABG. Normal/obese, underweight, and morbidly obese patients were compared by all demographics and preoperative characteristics. Patients were identified *via* operation codes in a digital operation registry. Clinical data were collected retrospectively from medical records.

Patients Follow-up

Follow-up was done at our outpatient's clinic and from the hospital registry. All patients had at least one follow-up time point available. In case a patient did not show up at a follow-up visit, we called the referring cardiologist to acquire the information for this study. During the study period, eleven surgeons performed CABG procedures in our institution.

Primary and secondary outcomes

Primary outcome was long-term incidence of all-cause death in underweight and morbidly obese patients undergoing isolated CABG. Secondary outcome was Major Adverse Cardiovascular and Cerebrovascular Events (MACCE) including all-cause death, stroke, and Myocardial Infarction (MI).

Covariates included in the study

Covariate included in the study were age, gender, race, STS-PROM risk score, Chronic Obstructive Pulmonary Disease (COPD), obesity, creatinine level, comorbidities such as preoperative dialysis, smoking, hypertension, dyslipidemia, Cerebrovascular Disease (CBVD), Peripheral Vascular Disease (PVD), liver disease, diabetes, mediastinal radiation, prior Percutaneous Coronary Intervention (PCI), prior CABG, prior MI, prior valve surgery, Atrial fibrillation (Afib), Ejection Fraction (EF), number of diseased vessels, left main coronary artery stenosis, severe proximal Left Anterior Descending (LAD) lesion.

Statistical analysis

Groups were compared by two-sample t-tests or Wilcoxon Rank Sum Test for continuous variables and chi-square test of independence for categorical variables. A propensity-adjusted matching was used *via* a multiple logistic regression with normal/obese as the dependent variable and all demographics and preoperative variables added to the model. A 1:1 greedy nearest neighbor with no replacement match and caliper width of 0.2 produced three groups. Success of matching was assessed by computing the percent bias (similar to standardized mean difference) of each covariate with a cut-off of 10% to denote acceptable balance. Matched samples were compared with McNemar's test and marginal homogeneity tests for categorical variables and matched paired t-tests and signed rank tests for continuous variables.

Adjusted survival functions for these interactions were plotted using Stata's stcurve command. To illustrate the effect of underweight and morbid obesity on long-term survival, Kaplan–Meier cumulative curves were constructed and compared by log-rank test. All analyses were performed in Stata 17.0 (Statacorp, LLC. College Station, TX). 95% confidence intervals and p-values are reported with a p-value <0.05 considered significant.

Propensity-adjustment significance compared to propensity-score matching

Propensity-matching provides excellent matching before the analysis, while the propensity-adjustment accounts for biases during the analysis. Therefore, while seeing significant differences among preoperative variables with propensity-adjustment analysis, these differences are adjusted during the modeling process. In addition, propensity-matching reduces the size of the groups while propensity-adjustment retains the sample size of the groups. As shown by multiple studies, propensity-adjustment analysis provides similar or better adjustment for biases when compared to propensity-matching because the sample size was maintained, therefore increasing the statistical power of the analysis. This statistical analysis is particularly suitable for smaller sample sizes [13].

Rationale in combining normal and obese patients in a one group

Several studies have shown minor differences in outcomes among normal and obese patients while often obese patients tend to have better outcomes when compared to normal weight patients (''obesity paradox'') [14]. Therefore, considering minor differences among these two subgroups, we combined them into one group (normal + obese group) and compared it with the underweight group and the morbidly obese groups. Underweight and morbidly obese patients tend to have worst outcomes compared to normal/obese patients.

Results

Preoperative characteristics

There was a total of 4,871 consecutive unique surgical patients while the matched sample had three groups of patients including underweight (n=42), morbidly obese (n=215) and normal/obese

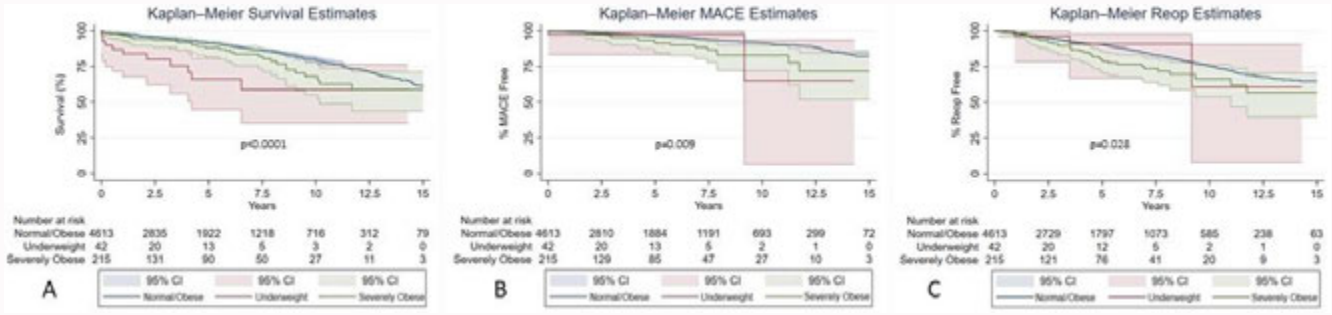

Figure 1: Matched Kaplan -Meier survival curves.
legend: A) Survival; B) MACE; C) Reoperation

Table 1: Preoperative characteristics.

Preoperative Characteristics	Normal/Obese n=4622	Underweight n=42	Morbidly Obese n=215	p-value
Age Years (mean/SD)	71.2 (11.0)	75.5 (10.4)	65.9 (10.4)	**<0.0001**
Gender				**<0.001**
Female n (%)	1061 (23.0%)	26 (61.9%)	90 (41.9%)	
Male n (%)	3553 (77.0%)	16 (38.1%)	125 (58.1%)	
Race				**<0.001**
White n (%)	4088 (88.6%)	29 (69.0%)	188 (87.4%)	
Black or African American n (%)	424 (9.2%)	12 (28.6%)	25 (11.6%)	
Other n (%)	102 (2.2%)	1 (2.4%)	2 (1.0%)	
STS Risk of Mortality % (median/IQR)	0.97 (0.5-2.1)	3.8 (2.2-8.5)	1.1 (0.6-2.0)	**<0.0001**
BMI kg/m² (Mean/SD)	28.6 (4.5)	17.4 (1.4)	45.9 (29.7)	**<0.001**
Obese n (%)	1643 (35.6%)	0 (0.0%)	215 (100.0%)	**<0.001**
Creatinine Level (Median/IQR)	1 (0.9-1.2)	1 (0.8-1.3)	1 (0.8-1.3)	0.113
Dialysis n (%)	111 (2.4%)	3 (7.1%)	5 (2.3%)	0.140
Smoking n (%)	2180 (47.2%)	19 (45.2%)	68 (31.6%)	**<0.001**
COPD n (%)	701 (15.2%)	16 (38.1%)	50 (23.3%)	**<0.001**
Hypertension n (%)	3970 (86.0%)	33 (78.6%)	202 (93.9%)	**0.001**
Dyslipidemia n (%)	4006 (86.8%)	36 (85.7%)	189 (87.9%)	0.878
CBVD n (%)	849 (18.4%)	11 (26.2%)	38 (17.7%)	0.413
PVD n (%)	685 (14.8%)	10 (23.8%)	27 (12.6%)	0.168
Liver disease n (%)	61 (1.3%)	1 (2.4%)	0 (0.0%)	0.195
Diabetes n (%)	1858 (40.3%)	11 (26.2%)	150 (69.8%)	**<0.001**
Mediastinal Radiation n (%)	43 (0.9%)	0 (0.0%)	2 (0.9%)	0.821
Previous PCI n (%)	1708 (37.0%)	12 (28.6%)	98 (45.6%)	**0.020**
Prior CABG n (%)	107 (2.3%)	0 (0.0%)	5 (2.3%)	0.607
Prior MI n (%)	2572 (55.7%)	26 (61.9%)	126 (58.6%)	0.523
Prior Valve Surgery n (%)	30 (0.6%)	0 (0.0%)	0 (0.0%)	0.431
Atrial Fibrillation n (%)	558 (12.1%)	2 (4.8%)	33 (15.3%)	0.122
EF % (mean/SD) n (%)	52.5 (13.4)	44.6 (16.5)	52.9 (12.8)	**<0.001**
EF<50% (Yes) n %	1335 (28.9%)	21 (50.0%)	56 (26.0%)	**0.007**
Diseased Vessels				0.766
<3 n (%)	1590 (34.5%)	16 (38.1%)	78 (36.3%)	
≥ 3 n (%)	3024 (65.5%)	26 (61.9%)	137 (63.7%)	
Left Main Coronary Artery Stenosis >50% n (%)	1166 (25.3%)	15 (35.7%)	50 (23.3%)	0.236
Severe Proximal LAD Lesion >70% n (%)	3870 (83.9%)	32 (76.2%)	185 (86.0%)	0.275

IMA				**0.001**
Both n (%)	536 (11.6%)	4 (9.5%)	7 (3.3%)	
Single or None n (%)	4078 (88.4%)	38 (90.5%)	208 (96.7%)	
Radial Artery Graft, n (%)	852 (18.5%)	3 (7.1%)	38 (17.7%)	0.163

EF: Ejection Fraction; IMA: Internal Mammary Artery; LAD: Left Anterior Descending; MI: Myocardial Infarction; CABG: Coronary Artery Bypass Grafting; COPD: Chronic Obstructive Pulmonary Disease; HTN: Hypertension; PVD: Peripheral Vascular Disease; CBVD: Cerebrovascular Disease; RIMA: Right Internal Mammary Artery; PCI: Percutaneous Coronary Intervention

Table 2: Procedural characteristics.

	Unmatched			Matched		
Procedural Characteristics	**Not Obese n=3013**	**Obese n=1858**	**p-value**	**Not Obese n=1600**	**Obese n=1600**	**p-value**
SVG, n (%)	1492 (49.6%)	953 (51.29%)	0.247	799 (49.9%)	832 (52.0%)	0.246
Number of Grafts (median/IQR)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.383	2 (1-3)	2 (1-3)	0.734
Number of Grafts			**0.276**			**0.205**
1 n (%)	1240 (41.1%)	798 (42.9%)		676 (42.2%)	673 (42.1%)	
2 n (%)	536 (17.8%)	292 (15.7%)		287 (17.9%)	252 (15.7%)	
3 n (%)	723 (24.0%)	465 (25.0%)		378 (23.6%)	406 (25.4%)	
4 n (%)	383 (12.7%)	232 (12.5%)		186 (11.6%)	209 (13.1%)	
5+ n (%)	131 (4.3%)	71 (3.8%)		73 (4.6%)	60 (3.7%)	
On-Pump	398 (13.2%)	293 (15.8%)	0.013	233 (14.6%)	252 (15.7%)	0.343
Multiarterial CABG n (%)	757 (25.1%)	421 (22.7%)	0.051	378 (23.6%)	370 (23.1%)	0.742
Total Arterial CABG n (%)	823 (27.3%)	454 (24.4%)	0.026	420 (26.2%)	390 (24.4%)	0.218
Surgery Priority			**0.305**			**0.676**
Elective n (%)	1589 (52.7%)	1022 (55.0%)		869 (54.3%)	876 (54.7%)	
Urgent n (%)	1397 (46.4%)	820 (44.1%)		721 (45.1%)	710 (44.4%)	
Emergent n (%)	27 (0.9%)	16 (0.9%)		10 (0.6%)	14 (0.9%)	

SVG: Saphenous Venous Graft; CABG: Coronary Artery Bypass Grafting

(n=4,622) (Table 1).

Intraoperative outcomes

Intraoperatively, morbidly obese patients had a significantly higher Operating Room (OR) time (p<0.001) and a lower platelets transfusions rate (p=0.042). In addition, number of grafts (p=0.028), multiarterial (p=0.022) and elective surgery (p=0.049) was higher in the normal/obese group compared to the other groups (Table 2).

Postoperative outcomes

After propensity-adjustment, morbidly obese patients had a lower rate of blood utilization and blood products transfusion (p<0.05) (Table 3), as well as a higher rate of deep sternal wound infections (p=0.036), Postoperative Atrial Fibrillation (POAF) (p=0.015), and 30-days readmission (p=0.006).

Follow-up

The median follow-up survival for the three groups were normal/obese 3.9 (1.1-7.8), underweight 2.0 (0.5-6.3), and morbidly obese 3.9 (1.1-7.3) years, p=0.111. Primary outcome of death was normal/obese 528/4622 (11.3%) vs underweight 11/42 (26.2%) *vs.* morbidly obese 32/215 (14.9%), p=0.003; [HR: 2.35 (1.2, 4.4)]. MACCE was significantly higher in morbidly obese patients 17/215 (7.9%), p=0.024, [HR: 1.92 (1.1, 3.2)] (Table 4, Figure 1).

Risk predictors for all-cause mortality in morbidly obese patients

New risk predictors for all-cause mortality in morbidly obese patients were non-white patients (HR: 3.6 [1.8, 7.0]), diabetes (HR: 2.1 [1.4, 3.2]), PVD (HR: 2.5 [1.2, 5.4]), STS ≥ 4% (HR: 4.4 [2.1, 9.0]), dialysis (HR: 4.5 [1.3, 15.3]), hypertension (HR: 1.7 [1.1, 2.8]), COPD (HR: 2.1 [1.1, 4.2]), EF<50% (HR: 2.8 [1.7, 4.7]), and Afib (HR: 2.3 [1.0, 5.1] (Table 5).

Risk predictors for all-cause mortality in underweight patients

New risk predictors for underweight patients were male gender (HR: 3.2 (1.3, 7.9]), white race (HR: 2.6 [1.2, 5.6]), STS ≥ 4% (HR: 5.2 [2.5, 10.9]), dialysis (HR: 15.3 [2.6, 88.3]), EF<50% (HR: 2.9 [1.2, 7.1]), hypertension (HR: 2.5 [1.2, 5.5]), (Table 6).

Comparison of risk predictors for all-cause mortality in morbidly obese and underweight patients

Common predictors for all-cause mortality among the two groups were STS ≥ 4%, dialysis, hypertension, and EF<50%. Risk predictors for all-cause mortality present only in morbidly obese patients were non-white patients, diabetes, PVD, COPD, and Afib (Table 7). Risk predictor for all-cause mortality present only in underweight patients was male gender.

Discussion

Summary of findings:

1) Underweight patients had a higher incidence of mortality compared to normal/obese patients.

2) MACCE was higher in morbidly obese patients compared to normal/obese patients.

Table 3: Intra-operative and postoperative outcomes.

Outcomes	Normal/ Obese n=4622	Underweight n=42	Morbidly Obese n=215	p-value	Propensity Score Adjusted			
					Underweight		Morbidly Obese	
Intra-operative					**Adj. Mean Difference (95% CI)***	**p-value**	**Adj. Mean Difference (95% CI)***	**p-value**
Time in OR (Hours) Mean/SD	6.03 (1.3)	6.01 (1.7)	6.6 (1.3)	<0.0001	0.01 (-0.39, 0.41)	0.965	0.57 (0.39, 0.75)	**<0.001**
Blood Transfusion n (%)	853 (18.5%)	16 (38.1%)	29 (13.5%)	0.001	1.46 (0.72, 2.97)	0.293	0.67 (0.45, 1.01)	0.057
RBC Units n (%)	727 (15.8%)	16 (38.1%)	29 (13.5%)	<0.001	1.65 (0.80, 3.41)	0.173	0.80 (0.53, 1.20)	0.285
Cryoprecipitate Units n (%)	184 (4.0%)	1 (2.4%)	2 (0.9%)	0.066	0.63 (0.08, 4.70)	0.652	0.25 (0.06, 1.03)	0.055
Platelet Units n (%)	328 (7.1%)	6 (14.3%)	7 (3.3%)	0.017	1.84 (0.74, 4.57)	0.189	0.45 (0.21, 0.97)	**0.042**
FFP Units n (%)	103 (2.2%)	1 (2.4%)	3 (1.4%)	0.713	0.98 (0.13, 7.55)	0.983	0.61 (0.19, 1.96)	0.404
Extubated in OR n (%)	3582 (77.6%)	28 (66.7%)	145 (67.4%)	0.001	0.82 (0.41, 1.63)	0.577	0.62 (0.46, 0.84)	**0.002**
Post-operative					**Adj. Mean Difference (95% CI)***	**p-value**	**Adj. Mean Difference (95% CI)***	**p-value**
Total ICU (Hours) (Median/ IQR)	44.8 (25-74)	72.3 (27.8-142.0)	46.8 (25-76)	0.411	-3.75 (-44.54, 37.03)	0.857	-6.23 (-24.51, 12.04)	0.504
Total LOS (Days) (Median/IQR)	5 (4-7)	7 (5-11)	5 (4-8)	0.164	0.26 (-1.73, 2.24)	0.799	0.32 (-0.57, 1.21)	0.486
Blood Transfusion n (%)	1467 (31.8%)	26 (61.9%)	47 (21.9%)	<0.001	2.06 (1.05, 4.04)	**0.035**	0.61 (0.43, 0.85)	**0.004**
RBC Units n (%)	1426 (30.9%)	26 (61.9%)	47 (21.9%)	**<0.001**	2.16 (1.11, 4.25)	**0.024**	0.63 (0.45, 0.88)	**0.007**
Cryoprecipitate Units n (%)	194 (4.2%)	3 (7.1%)	3 (1.4%)	0.078	1.80 (0.53, 6.08)	0.345	0.41 (0.13, 1.32)	0.135
Platelet Units n (%)	269 (5.8%)	4 (9.5%)	3 (1.4%)	**0.013**	1.41 (0.48, 4.16)	0.531	0.29 (0.09,0.92)	**0.036**
FFP Units n (%)	172 (3.7%)	2 (4.8%)	2 (0.9%)	0.092	0.83 (0.18, 3.74)	0.804	0.26 (0.06, 1.05)	0.059
Stroke n (%)	26 (0.6%)	1 (2.4%)	1 (0.5%)	0.293	5.53 (0.68, 44.82)	0.109	0.62 (0.08, 4.81)	0.649
Superficial Infection n (%)	15 (0.3%)	0 (0.0%)	2 (0.9%)	0.315	N/A		2.67 (0.56, 12.66)	0.217
Deep Sternal Infection n (%)	13 (0.3%)	0 (0.0%)	3 (1.4%)	**0.019**	N/A		4.25 (1.10, 16.41)	**0.036**
Reoperation for Bleeding n (%)	47 (1.0%)	0 (0.0%)	0 (0.0%)	0.267	N/A		N/A	
Prolonged Ventilation (>24 hours) n (%)	187 (4.0%)	3 (7.1%)	13 (6.0%)	0.225	0.66 (0.16, 2.6)	0.558	1.37 (0.76, 2.50)	0.297
Renal Failure n (%)	87 (1.9%)	1 (2.4%)	4 (1.9%)	0.972	0.73 (0.09, 6.03)	0.772	0.94 (0.33, 2.65)	0.908
Dialysis n (%)	24 (0.5%)	0 (0.0%)	1 (0.5%)	0.891	N/A		0.95 (0.12, 7.31)	0.958
Atrial Fibrillation	1033 (22.4%)	10 (23.8%)	53 (24.6%)	0.724	1.03 (0.49, 2.13)	0.943	1.50 (1.08, 2.09)	**0.015**
30 Day Readmit	355 (7.7%)	8 (19.0%)	28 (13.0%)	**0.001**	1.77 (0.76, 4.14)	0.184	1.82 (1.19, 2.78)	**0.006**
Operative Death	46 (1.0%)	2 (4.8%)	2 (0.9%)	0.054	2.61 (0.51, 13.37)	0.248	0.97 (0.23, 4.16)	0.97

Table 4: Cumulative long-term outcomes.

Cumulative Long-term Outcomes	Matched Cohort			
	Normal/Obese N=4,622	Underweight N=42	Morbidly Obese N=215	p-value
Long-Term Outcomes				
Survival all Cause n (%)	4094 (88.7%)	31 (73.8%)	183 (85.1%)	**0.003**
Mortality all Cause n (%)	528 (11.3%)	11 (26.2%)	32 (14.9%)	
MACCE n (%)	188 (4.1%)	2 (4.8%)	17 (7.9%)	**0.024**
Stroke n (%)	92 (2.0%)	0 (0.00)	5 (2.3%)	0.614
MI n (%)	104 (2.2%)	2 (4.8%)	13 (6.0%)	0.001
Reoperation n (%)	530 (11.5%)	3 (7.1%)	35 (16.3%)	0.067
Angina n (%)	504 (10.9%)	1 (2.4%)	29 (13.5%)	0.101
Follow-up (Years/Median/IQR)				
Survival	3.9 (1.1-7.8)	2.0 (0.5-6.3)	3.9 (1.1 -7.3)	0.111
MACE	3.8 (1.1-7.7)	2.0 (0.2-6.3)	3.5 (1.1-7.3)	0.084
Stroke	3.8 (1.1-7.7)	2.0 (0.5-6.3)	3.8 (1.1-7.3)	0.124
MI	3.8 (1.1-7.7)	2.0 (0.2-6.3)	3.5 (1.1-7.3)	0.076
Reoperation	3.5 (1.1-7.1)	2.0 (0.5-5.5)	3.3 (1.1-6.8)	0.092
Angina	3.5 (1.1-7.3)	2.0 (0.5-5.5)	3.4 (1.1-6.9)	0.131

Table 5: Univariate and multivariate Cox proportional hazard of long-term outcomes by BMI status. (HR: Hazard Ratio).

	Mortality		MACCE		Reoperation	
Long-term Outcomes	**Underweight¥ HR (95% CI)**	**Morbidly Obese¥ HR (95% CI)**	**Underweight¥ HR (95% CI)**	**Morbidly Obese¥ HR (95% CI)**	**Underweight¥ HR (95% CI)**	**Morbidly Obese¥ HR (95% CI)**
Model 1						
Univariate	**3.33 (1.8, 6.0)****	1.43 (0.99, 2.0)	1.75 (0.4, 7.1)	**2.10 (1.3, 3.4)***	0.87 (0.3, 2.7)	**1.58 (1.1, 2.2)***
Model 2						
Multivariate	1.73 (0.9, 3.3)	1.42 (0.98, 2.0)	0.96 (0.2, 4.1)	**1.98 (1.2, 3.3)***	0.93 (0.3, 2.9)	1.29 (0.9, 1.8)
Model 3						
P Score	**1.91 (1.0, 3.6)***	1.40 (0.97, 2.0)	1.50 (0.4, 6.3)	**1.93 (1.1, 3.2)***	0.88 (0.3, 2.8)	1.33 (0.9, 1.9)
Model 4						
Double Robust	**2.35 (1.2, 4.4)***	**1.49 (1.0, 2.1)***	1.48 (0.3, 6.3)	**1.92 (1.1, 3.2)***	0.88 (0.3, 2.8)	1.33 (0.9, 1.9)

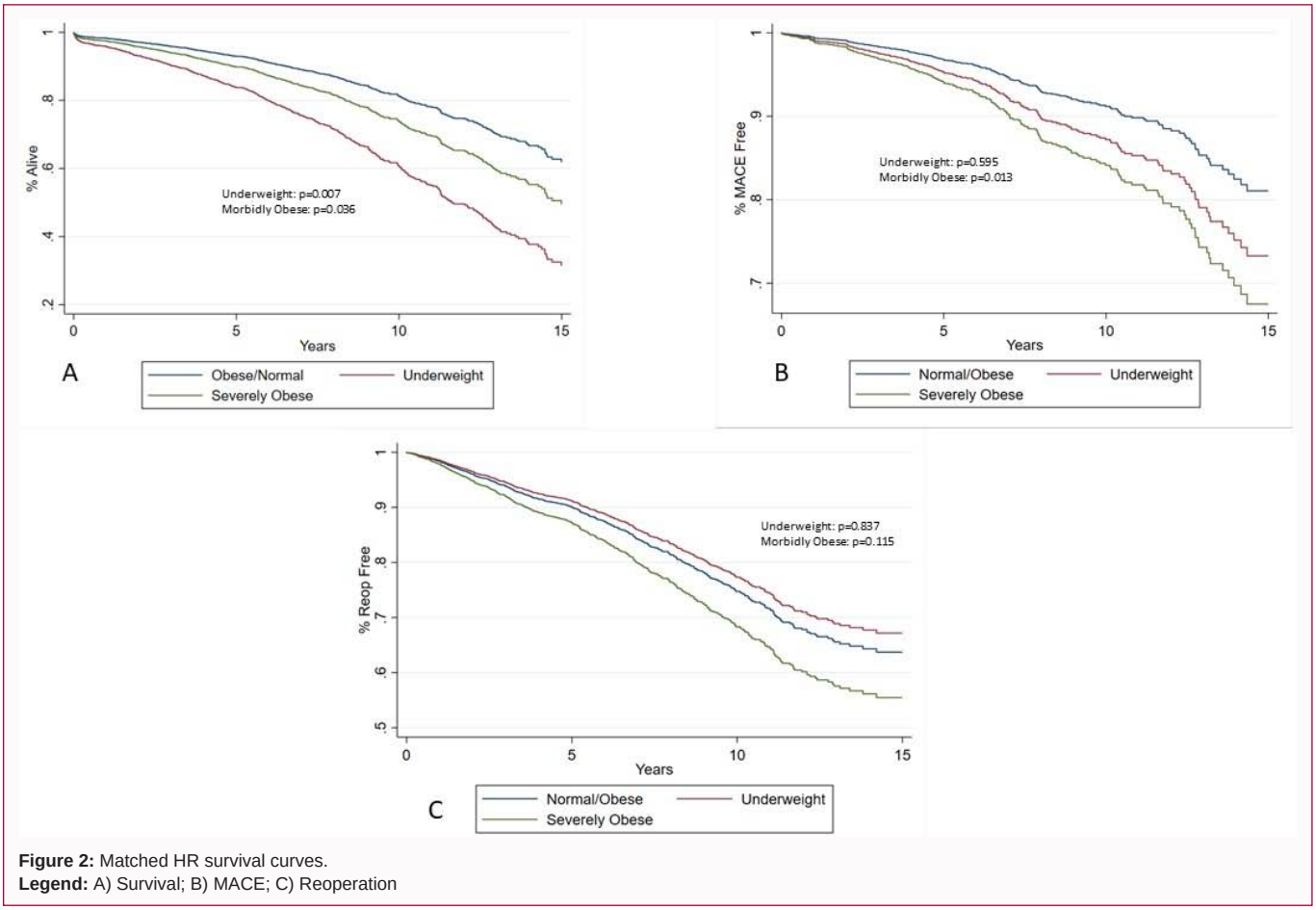

Figure 2: Matched HR survival curves.
Legend: A) Survival; B) MACE; C) Reoperation

3) New risk predictors for underweight patients after isolated CABG were male gender, white race, STS ≥ 4%, dialysis, EF<50%, and hypertension.

4) New risk predictors for morbidly obese patients were non-white patients, diabetes, PVD, STS ≥ 4%, dialysis, hypertension, COPD, EF<50%, and Afib.

Comments

This analysis provided several novel insights in the fragile underweight and morbidly obese groups undergoing isolated CABG. Firstly, mortality and MACCE were higher in underweight and morbidly obese compared to normal/obese patients after isolated CABG. Secondly, new predictors that impact long-term prognosis appear associated with underweight and morbidly obese patients after isolated CABG.

Risk predictors for long-term outcomes analysis from other clinical studies

The seminal INTERHEART case–control study demonstrated that potentially modifiable risk factors account for most of the population attributable risk of a first MI, consistent across all geographic regions, ethnic groups, and genders [15]. These modifiable risk factors should be targeted by early lifestyle modification and drug-based interventions, at both individual and population levels. The role of secondary prevention measures risk-factor control in reducing adverse cardiovascular events and mortality is well established, including after cardiac surgery [16], as highlighted by international guidelines

Table 6: Cumulative incidence of long-term outcomes.

Long-term Outcomes	Unweighted analysis				Weighted analysis			
	Underweight HR (95% CI)	p- value	Morbidly Obese HR (95% CI)	p-value	Underweight HR (95% CI)	p-value	Morbidly Obese HR (95% CI)	p-value
All-Cause Mortality								
1-year	6.1 (2.5, 15.1)	**<0.001**	1.3 (0.6, 3.1)	0.483	4.9 (1.9, 12.5)	**0.001**	1.2 (0.5, 2.8)	0.663
2-years	5.1 (2.2, 11.6)	**<0.001**	1.5 (0.8, 2.8)	0.213	4.2 (1.8, 9.7)	**0.001**	1.4 (0.7, 2.7)	0.333
5-years	4.9 (2.6, 9.2)	**<0.001**	1.4 (0.8, 2.2)	0.213	3.6 (1.8, 7.1)	**<0.001**	1.3 (0.8, 2.2)	0.235
10-years	3.8 (2.1, 7.0)	**<0.001**	1.5 (1.03, 2.2)	0.035	2.8 (1.5, 5.2)	**0.001**	1.5 (1.03, 2.2)	**0.035**
MACCE								
1-year	5.1 (0.7, 37.7)	0.111	N/A		4.9 (0.6, 37.4)	0.128	N/A	
2-years	3.4 (0.5, 24.7)	0.229	1.2 (0.3, 4.8)	0.841	3.7 (0.5, 28.0)	0.197	1.04 (0.2, 4.5)	0.957
5-years	1.49 (0.2, 10.7)	0.692	2.1 (1.1, 4.3)	0.028	1.2 (0.2, 9.7)	0.841	1.8 (0.9, 3.6)	0.112
10-years	2.0 (0.5, 8.0)	0.335	2.2 (1.3, 3.7)	0.004	1.6 (0.4, 6.8)	0.521	1.9 (1.1, 3.3)	**0.020**
REOPERATION								
1-years	1.9 (0.3, 13.5)	0.531	0.7 (0.2, 2.7)	0.569	2.0 (0.3, 14.7)	0.498	0.5 (0.1, 1.9)	0.284
2-years	0.9 (0.1, 6.4)	0.914	1.4 (0.7, 2.7)	0.325	0.9 (0.1, 6.7)	0.933	1.1 (0.5, 2.2)	0.776
5-years	0.9 (0.2, 3.8)	0.925	2.0 (1.3, 2.9)	**0.001**	0.8 (0.2, 3.6)	0.827	1.6 (1.04, 2.4)	**0.030**
10-years	0.9 (0.3, 2.9)	0.913	1.6 (1.1, 2.3)	**0.007**	0.9 (0.3, 2.9)	0.885	1.3 (0.9, 2.9)	0.107

Table 7: Comparison of risk factors for all-cause mortality underweight *vs.* morbidly obese.

Predictors for all-cause mortality	Underweight HR (95% CI)	Morbidly Obese HR (95% CI)
Male	**3.2 (1.3, 7.9)**	1.5 (0.9, 2.5)
Female	1.6 (0.7, 4.0)	1.2 (0.7, 2.2)
White	**2.6 (1.2, 5.6)**	1.2 (0.8,1.8)
Non-White	1.9 (0.6, 5.6)	**3.6 (1.8, 7.0)**
Diabetes	**4.1 (2.0, 8.5)**	**2.1 (1.4, 3.2)**
STS-PROM ≥ 4%	**5.2 (2.5, 10.9)**	**4.4 (2.1, 9.0)**
Dialysis	**15.3 (2.6, 88.3)**	**4.5 (1.3, 15.3)**
Hypertension	**2.5 (1.2, 5.5)**	**1.7 (1.1, 2.8)**
COPD	2.6 (1.02, 6.9)	**2.1 (1.1, 4.2)**
PVD	**2.8 (1.3, 6.0)**	**2.5 (1.2, 5.4)**
EF <50%	**2.9 (1.2, 7.1)**	**2.8 (1.7, 4.7)**
Atrial Fibrillation	**2.9 (1.5, 5.5)**	**2.3 (1.1, 5.1)**

COPD: Chronic Obstructive Pulmonary Disease; PVD: Peripheral Vascular Disease; EF: Ejection Fraction

for cardiovascular prevention and myocardial revascularization [17-20]. In this context, most of our risk factors are modifiable, including BMI.

This manuscript provides valuable data on the interaction among risk predictors and BMI in patients undergoing isolated CABG.

Risk for mortality

The increased hazard ratio and mortality rate in underweight patients has been previously described [21]. However, persistence of the increased hazard ratio over time reflects the frailty of this population. The reasons behind these outcomes remain hindered. However, we hypothesize that the underlying catabolism in underweight patients may impact long-term outcomes, possibly unrelated to CABG procedure itself. Learning the cause of death of this group of patients could be helpful, however, these data were not available in our database.

Given the apparent adequacy of our propensity-score weighting (with minimal standardized mean differences) based on elements available in claims data, it is likely that underweight and morbidly obese patients undergoing isolated CABG may benefit from these outcomes.

Limitations

This retrospective study was subject to all limitations inherent to a non-randomized study, including potential selection bias regarding which patients underwent CABG depending on the BMI group. However, the rigorous propensity-adjusted analysis limited these biases. In addition, the study includes a large timeframe (2005-2021) and many advanced techniques and changes in medical treatments have occurred in this period. Another limitation is the single-center data; therefore, our analysis needs further validation from multicenter studies.

Conclusion

Overall death was higher in underweight patients after isolated CABG compared to normal/obese patients. MACCE was higher in morbidly obese compared to normal/obese patients after isolated CABG. Herein, we describe new risk predictors that impact long-term prognosis in underweight and morbidly obese patients after isolated CABG.

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