Obesity Pillars 11 (2024) 100114

Contents lists available at ScienceDirect

Obesity Pillars

journal homepage: www.journals.elsevier.com/obesity-pillars

In-hospital outcomes in metabolically healthy and unhealthy individuals over 65 years of age with obesity undergoing percutaneous intervention for acute coronary syndrome: A nationwide propensity-matched analysis (2016–2020)

Rupak Desai [a,1], Aobo Li [b,1], Avilash Mondal [c], Sashwat Srikanth [d], Alka Farmer [b,e], Lin Zheng [b,e,*]

[a] Independent Researcher, Atlanta, GA, USA
[b] Department of Medicine, Inspira Health Network, Vineland, NJ, USA
[c] Department of Medicine, Nazareth Hospital, PA, USA
[d] Department of Medicine, East Carolina University Health Medical Center, NC, USA
[e] Division of Hospital Medicine, Department of Medicine, Cooper Medical School of Rowan University, NJ, USA

ARTICLE INFO

Keywords:
Metabolically healthy obesity
Metabolically unhealthy obesity
Obesity
Acute coronary syndrome
Percutaneous coronary intervention
Mortality/outcomes

ABSTRACT

Background: The obesity paradox in patients with coronary artery disease is well established, but the role of the metabolic syndrome associated with obesity is not well studied. Our study aims to evaluate the in-hospital outcomes of percutaneous coronary intervention (PCI) in metabolically healthy individuals with obesity (MHO) and metabolically unhealthy (MUHO) individuals with obesity over 65 years of age with acute coronary syndrome (ACS) between 2016 and 2020.

Methods: This was a retrospective and observational study. Patients were identified through utilizing the National Inpatient Sample (NIS) Database (2016–2020) and ICD-10 codes. By employing a *t*-test and Pearson's Chi-square test, we assessed and contrasted the initial attributes, concurrent conditions, and results pertaining to all-cause mortality (ACM), cardiogenic shock (CS), length of stay (LOS), and hospitalization expense. Moreover, propensity score matching was conducted in a 1:1 ratio with respect to age, gender, and race. We also utilized multivariable logistic regression to compare MHO and MUHO in terms of the impact on all-cause mortality.

Results: Out of a total of 135,395 patients identified, 2995 patients with MUHO were matched with 2995 MHO patients. Patients in the MUHO group had a higher prevalence of chronic pulmonary disease (24.9 % vs. 19.5 %), peripheral vascular disease (9.3 % vs. 6.7 %), hypothyroidism (16 % vs. 11.5 %), prior myocardial infarction (15.9 % vs. 6.2 %), and prior stroke (7.5 % vs. 2.8 %). Patients in the MHO group had a higher ACM (12.4 % vs. 2.8 %, $p < 0.001$), CS (18.55 % vs. 7 %, $p < 0.001$), stroke (2.2 % vs. 1 %, $p < 0.001$), ventricular assist device insertions (5.2 % vs. 2.7 %, $p < 0.001$), and IABP insertions (8.8 % vs. 3.8 %) compared to the MUHO cohort.

Conclusion: Our study revealed an obesity paradox in individuals over 65 years of age undergoing PCI demonstrating worse outcomes, including higher in-hospital mortality, CS, stroke, Ventricular assist device and IABP insertion in MHO patients compared to the MUHO cohort.

1. Introduction

Obesity is associated with an increased risk of cardiometabolic risk factors such as hypertension, diabetes, metabolic syndrome, and dyslipidemia. The risk factors are shared commonly by coronary artery disease and acute coronary syndrome (ACS). Mechanisms explaining this link include but are not limited to, elevated circulatory pro-inflammatory markers and hormonal and upregulated enzyme

* Corresponding author. Department of Internal Medicine, Inspira Health Network, Vineland, NJ, USA.
E-mail addresses: drrupakdesai@gmail.com (R. Desai), lia@ihn.org (A. Li), avilashmandal98@gmail.com (A. Mondal), sashwath17@gmail.com (S. Srikanth), Farmer-Alka@Cooperhealth.edu (A. Farmer), zheng-lin@cooperhealth.edu (L. Zheng).
[1] R.D. and A.L. share equal contributions to the manuscript as first authors.

https://doi.org/10.1016/j.obpill.2024.100114
Received 5 May 2024; Received in revised form 23 May 2024; Accepted 24 May 2024
Available online 25 May 2024

activities, including increased clotting factors, decreased fibrinolysis, increased TNF-a and leptin levels associated with poor outcomes in CAD and in-stent restenosis [1]. Obesity is an independent risk factor for coronary artery disease (CAD). However, upon analyzing epidemiological data, mostly from hospitalized registries, in recent studies, it is linked to enhanced survival ("obesity paradox"). Studies have described the obesity paradox, where obesity appears to offer protective benefits in terms of in-hospital mortality and adverse outcomes in certain populations with CAD, heart failure, atrial fibrillation, post-PCI, and post-CABG patients [2–5]. In our study, we set out to analyze the impact of metabolic health on in-hospital adverse outcomes, including mortality, and discuss the potential mechanisms and biases that might explain why metabolically healthy (MHO) patients with obesity undergoing percutaneous coronary intervention (PCI) experienced worse outcomes compared to their metabolically unhealthy (MUHO) counterparts.

2. Methods

This was a retrospective and observational study. In this study, we utilized data from the National Inpatient Sample (NIS) for the years 2016–2019 to identify patients with ACS aged ≥65 years undergoing PCI into MHO and MUHO using the International Classification of Diseases, 10th Revision-Clinical Modification (ICD-10- CM) codes. Of which those without concomitant metabolic risk factors were defined as metabolically healthy (MHO) (no hypertension, diabetes, or hyperlipidemia), and the other cohort was defined as metabolically unhealthy obesity (MUHO).

The data selection process involved 1:1 propensity score matching, with age, sex, race, median household income, primary payer, location and region of hospital, and type of admissions, whether elective or non-elective as matching criteria with a caliper width of 0.01 and near neighbor matching method. Comorbid conditions such as hypothyroidism, chronic pulmonary disease, peripheral vascular disease, alcohol and drug abuse, depression, history of prior MI, transient ischemic attack (TIA), or stroke were also matched.

All-cause mortality (ACM) was the primary outcome of interest, while cardiogenic shock (CS), use of mechanical circulatory devices (MCDs) such as Ventricular assist device and intra-aortic balloon pump (IABP), post-PCI related bleeding, and patient disposition were considered secondary outcomes. We conducted descriptive and inferential statistical analyses to compare outcomes between the two cohorts. Descriptive statistics were used to summarize patient characteristics, while inferential statistics were used to compare outcomes between the two cohorts. Mann-Whitney test was used to compare continuous variables given a non-normal distribution curve, and Pearson chi-square was utilized to compare categorical variables. We utilized multivariable logistic regression to compare MHO and MUHO in terms of the impact on all-cause mortality, while controlling for all confounding variables, including age at admission, sex, race, payer status, median household income quartile, hospital location/teaching status, and comorbidities including, hypertension, diabetes, hyperlipidemia, depression, drug abuse including alcohol and tobacco use disorder, COPD, peripheral vascular disease, thyroid disorders, prior history of myocardial infarction, prior history of bariatric surgery, valvular heart diseases and cancer. The outcome was deemed to be non-significantAll analyses were interpreted with a significance level of 0.05. IBM Statistical Package for the Social Sciences (SPSS) v25.0 (IBM Corp., Armonk, NY, USA) was utilized to perform the analyses.

3. Results

Out of a total of 135,395 individuals over 65 years of age with obesity, (97.8 % were MUHO, and 2.2 % were MHO) admitted for ACS undergoing PCI, 2995 patients with MUHO were matched with 2995 MHO patients after propensity matching. Baseline characteristics, including sex, race, insurance, and median household income, were comparable in both groups. Patients in the MUHO group had a higher prevalence of depression (12.7 % vs. 6.5 %), drug use (2.3 % vs. 1.5 %), chronic pulmonary disease (24.9 % vs. 19.5 %), peripheral vascular disease (9.3 % vs. 6.7 %), hypothyroidism (16 % vs. 11.5 %), prior myocardial infarction (15.9 % vs. 6.2 %), and prior stroke (7.5 % vs. 2.8 %).

Patients in the MHO group had a higher ACM (12.4 % vs. 2.8 %, $p < 0.001$), CS (18.55 % vs. 7 %, $p < 0.001$), stroke (2.2 % vs. 1 %, $p < 0.001$), Ventricular assist device insertions (5.2 % vs. 2.7 %, $p < 0.001$), and IABP insertions (8.8 % vs. 3.8 %) compared to the MUHO cohort. We utilized multivariable logistic regression to compare MHO and MUHO in terms of the impact on ACM, while controlling for all confounding variables, which failed to show any significant difference in outcomes between MHO vs. MUHO cohorts (OR 2.00; 95%CI 0.47–8.61, $p = 0.35$) [Table 1].

4. Discussion

Our nationwide analysis from 2016 to 2020 of individuals over 65 years of age undergoing PCI for ACS highlights a nuanced understanding of the obesity paradox, where MHO patients exhibited worse in-hospital outcomes compared to their MUHO counterparts. Individuals in the MHO group had notably elevated rates of ACM (12.4 % vs. 2.8 %) and complications such as cardiogenic shock (18.55 % vs. 7 %), stroke (2.2 % vs. 1 %), and implantation of mechanical circulatory devices. This finding is consistent with other studies suggesting that obesity, especially in relation to metabolic health, has a multifaceted impact on cardiovascular disease results [3,4].

Some of the biological mechanisms of metabolically healthy obesity involve reduced levels of ectopic fat (visceral and liver), increased leg fat deposition, enhanced expandability of subcutaneous adipose tissue, maintained insulin sensitivity, beta-cell function, and improved cardiorespiratory fitness when compared to unhealthy obesity [6]. In pooled data analysis of 1.46 million individuals, it was noted that among metabolically healthy non-smokers, there was a J-shaped relationship between BMI and ACM, with the lowest odds of ACM seen at a BMI range of 20.0–24.9, on a long-term follow up [7]. However, such studies on long-term follow-up are subject to limitations given their reliance on anthropometric measurements and disease conditions at a single point in time. The concept of BMI is not optimal since it has limitations in differentiating between fat and lean body mass. Our study is also similar in the sense, ninety percent of the population is also white, as in the study by Gonzalez et al. [7]. The obesity paradox might be explained through various mechanisms: Individuals with obesity often possess greater metabolic reserves and exhibit less cachexia, potentially contributing to better outcomes in certain conditions. They tend to present with coronary artery disease (CAD) at a younger age, which might lead to more aggressive medical therapy and diagnostic/revascularization procedures. Increased muscle mass and potentially better cardiorespiratory fitness, despite obesity, could offer advantages. Additionally, an attenuated hormonal response, particularly within the renin-angiotensin-aldosterone system, might play a role. However, unmeasured confounders, including selection bias, where the etiology of CAD in individuals with obesity versus lean individuals differs, could influence these observations. A stronger evidence can be noted from this study by Cortigiani et al. as a more robust evidence of protective effect of obesity (BMI ≥30) in patients with stress-induced ischemia and/or coronary microvascular dysfunction [8].

Many studies have disclosed the obesity paradox in CAD, but most are based on the BMI group. A cohort study found that a higher BMI was linked to a reduced risk of all-cause mortality over 3 years, even after adjusting for age, renal function, history of stroke, coronary artery bypass graft, peripheral arterial disease, heart failure, and CTO revascularization status [9]. Explanations for the obesity paradox have pointed out confounding factors that can introduce bias, which is linked to the perceived survival advantage of individuals with obesity [10,11].

Table 1
Baseline Characteristics and In-hospital outcomes following PCI for Acute coronary syndrome-related Hospitalizations in Individuals over 65 years of age with Metabolically Healthy vs. Metabolically Unhealthy Obesity: A Nationwide Propensity Score Matched Analysis [2016–2020].

Variables		MUHO (n = 2995)	MHO (n = 2995)	P-value
Age (years) at admission, median [IQR]		70	70	0.599
Sex	Male	56.8 %	58.8 %	0.117
	Female	43.2 %	41.2 %	
Race	White	89.5 %	90.7 %	0.422
	Black	3.0 %	3.0 %	
	Hispanic	6.2 %	5.0 %	
	Asian/PI	0.7 %	0.7 %	
	Native American	0.7 %	0.7 %	
Elective	Non-elective	94.8 %	96.0 %	0.033
	Elective	5.2 %	4.0 %	
Payer Type	Medicare	85.4 %	85.0 %	0.969
	Medicaid	0.5 %	0.5 %	
	Private	13.2 %	13.7 %	
	Self-pay	0.9 %	0.9 %	
Median household income national quartile for patient ZIP Code	0-25th	27.0 %	25.7 %	<0.001
	26-50th	27.2 %	27.9 %	
	51-75th	26.5 %	22.6 %	
	76-100th	19.3 %	23.8 %	
Comorbidities				
Alcohol abuse		1.8 %	2.2 %	0.356
Depression		12.7 %	6.5 %	<0.001
Drug abuse		2.3 %	1.5 %	0.019
Chronic pulmonary disease		24.9 %	19.5 %	<0.001
Peripheral vascular disease		9.3 %	6.7 %	<0.001
Hypothyroidism		16.0 %	11.5 %	<0.001
Prior MI		15.9 %	6.2 %	<0.001
Prior TIA/Stroke without Neurologic deficit		7.5 %	2.8 %	<0.001
Cancer		2.8 %	3.7 %	0.069
In-hospital outcomes				
All-cause mortality		2.8 %	12.4 %	<0.001
Cardiogenic Shock		7.0 %	18.5 %	<0.001
Ventricular assist device		2.7 %	5.2 %	<0.001
IABP		3.8 %	8.8 %	<0.001
Post PCI related bleeding		0.8 %	1.7 %	0.004
Postprocedural stroke		1.0 %	2.2 %	<0.001
Disposition of patient	Routine	72.4 %	63.1 %	<0.001
	Transfer to Short-term Hospital	1.8 %	2.5 %	
	Transfer Other: SNF, ICF, another type of facility	10.4 %	11.5 %	
	HHC	12.4 %	10.2 %	
Length of Stay (days), Median [IQR]		3 [2–5]	3 [2–6]	0.189
Cost (USD), Median [IQR]		104338 [74706–167415]	112714 [75536–195398]	<0.001
Multivariable Odds Ratios MHO vs MUHO				
All-cause mortality	Odds Ratio	95 % CI UL	59 % CI LL	P-value
	2.00	0.47	8.61	0.35

Abbreviations: PCI Percutaneous coronary intervention; MUHO Metabolically unhealthy obese; MHO Metabolically healthy obese; PI Pacific Islanders; IQR Interquartile range; MI Myocardial infarction; TIA Transient ischemic attack; IABP Intraortic balloon pump; SNF Skilled Nursing Facility; ICF Intermediate Care Facility; HHC Home Health Care.
Multivariable logistic regression was adjusted for age at admission, sex, race, payer status, median household income quartile, hospital location/teaching status, and comorbidities including, hypertension, diabetes, hyperlipidemia, depression, drug abuse including alcohol and tobacco use disorder, COPD, peripheral vascular disease, thyroid disorders, prior history of myocardial infarction, prior history of bariatric surgery, valvular heart diseases and cancer.
$P < 0.05$ was considered statistically significant.

The paradox regarding the independent association of elevated BMI with reduced mortality after PCI was also evident in contemporary U.K. and Japan based studies [12,13].

Evidenced by all these studies, we are bound to come up with a new assessment standard for obesity, or more precisely, measuring the cardiovascular comorbidity of a person that makes him prone to cardiovascular adverse events. Critics contend that a more significant indicator of obesity, as indicated by several studies, should be assessed by waist circumference, waist-to-hip ratio, or body fat [3]. A recent study introduced a new scoring system, the Relative Fat Mass (RFM) Index, to assess body fat percentage (BFP). This index was found to be a more accurate and consistent indicator of obesity and the severity of CAD compared to BMI [14]. Adjusting BMI parameters to classify obesity based on ethnic variations may help identify different CAD risk categories within diverse ethnic populations.

5. Limitation

Our study, although hypothesis generating, is not without limitations. Our study sample included more white and less black patients in MHO group. It potentially could have introduced sampling bias. The use of the NIS database restricts our analysis to hospitalized individuals only, limiting generalizability of the findings to the wider population. Furthermore, given the cross-sectional design of the study, it's difficult to establish causality. The study lacks longitudinal data, which would be crucial to understand the long-term outcomes and the potential transition from metabolically healthy obesity to metabolically unhealthy states. Our study relies on administrative codes for categorizing obesity and metabolic health, which has been primarily established for a white population, and not for black population as mentioned earlier. This method might not capture the nuances of metabolic health and obesity, particularly in a diverse population, who may have different metabolic profiles at lower BMI levels. Although we attempted comprehensive multivariable regression assessing the primary endpoint—all-cause mortality, it was not possible to evaluate all end-points while controlling for confounding variables, which in fact necessitates larger-scale investigations.

6. Conclusion

Our study illuminates the complexity of the obesity paradox in individuals over 65 years of age undergoing PCI for ACS, revealing that

metabolically healthy obesity is associated with poorer in-hospital outcomes compared to metabolically unhealthy obesity, challenging conventional perceptions, and highlighting the need for nuanced clinical strategies.

Key takeaway clinical message

- Metabolically healthy obesity in individuals over 65 years of age undergoing PCI for ACS is associated with higher risk of in-hospital mortality, cardiogenic shock, post-PCI stroke events, and requirement for mechanical circulatory devices.
- Contrary to conventional beliefs, metabolically healthy obesity does not confer protective effects in cardiovascular interventions, emphasizing the importance of metabolic health status in predicting patient outcomes post-PCI.
- This paradox within a paradox underscores the complex interplay between obesity, metabolic health, and cardiovascular outcomes, necessitating tailored clinical approaches for optimal patient management.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of artificial intelligence (AI) and AI-assisted technologies

During the preparation of this work the author(s) used AI, *Grammarly* to enhance the vocabulary and correct grammatical errors in the manuscript. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

CRediT author statement

Rupak Desai, Aobo Li, Li Zheng: Conceptualization, Methodology, Software, Formal Analysis, Resources, Data Curation, Writing-Original Draft, Writing - Review & Editing, Project administration.

Aobo Li, Avilash Mondal, Sashwath Srikanth, and Alka Farmer: Writing-Original Draft, Writing - Review & Editing, Visualization.

Funding source

None.

Declaration of competing interest

All authors have no conflict of interest to disclose.

Acknowledgment

None.

References

[1] Rader DJ. Effect of insulin resistance, d., and intra-abdominal adiposity on the development of cardiovascular disease and diabetes mellitus. Am J Med 2007;120 (3):S12–8.
[2] Badheka A RA, Kizilbash M, et al. Influence of obesity on outcomes in atrial fibrillation: yet another obesity paradox. Am J Med 2010;123(7):646–51. https://doi.org/10.1016/j.amjmed.2009.11.026.
[3] Lavie Cj MR, Ventura HO, Romero-Corral A. Body composition and heart failure prevalence and prognosis: getting to the fat of the matter in the "obesity paradox.". Mayo Clin Proc 2010;85(7):605–8. https://doi.org/10.4065/mcp.2010.0333.
[4] Martin JLJG, Martin SS, et al. The relationship of obesity to ischemic outcomes following coronary stent placement in contemporary practice. Cathet Cardiovasc Interv 2006;67(4):563–70.
[5] Romero-Corral A MV, Somers VK, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. Lancet 2006;368(9536):666–78. https://doi.org/10.1016/s0140-6736(06)69251-9.
[6] Wu Ah PB, Anker SD, Vincent J, Mujib M, Ahmed A. Association of obesity and survival in systolic heart failure after acute myocardial infarction: potential confounding by age. Eur J Heart Fail 2010;12(6):566–73. https://doi.org/10.1093/eurjhf/hfq043.
[7] De González Ab HP, Cerhan JR, et al. Body-mass index and mortality among 1.46 million white adults. N Engl J Med 2010;363(23):2211–9. https://doi.org/10.1056/nejmoa1000367.
[8] Cortigiani LHM, Ciampi Q, Bovenzi F, Villari B, Picano E. The obesity paradox in the stress echo lab: fat is better for hearts with ischemia or coronary microvascular dysfunction. Int J Obes 2021;45:308–15.
[9] Tsai CHW, Lu Y, Teng H, Huang S, Tsai Y, Lee W, Lu T. Obesity paradox in patients with chronic total occlusion of coronary artery. Eur J Clin Invest 2022;52:e13698.
[10] Goel KL-JF, De Schutter A, Coutinho T, Lavie CJ. Obesity paradox in different populations: evidence and controversies. Future Cardiol 2014;10:81–91.
[11] Rubinshtein RHD, Jaffe R, Shahla J, Lewis BS. Relation between obesity and severity of coronary artery disease in patients undergoing coronary angiography. Am J Cardiol 2006;97:1277–80.
[12] Holroyd Ew SA, Kwok CS, et al. The relationship of body mass index to percutaneous coronary intervention outcomes. JACC Cardiovasc Interv 2017;10 (13):1283–92. https://doi.org/10.1016/j.jcin.2017.03.013.
[13] Morishita TUH, Mitsuke Y, Tada H. Relationship of body mass index to clinical outcomes after percutaneous coronary intervention. Eur J Clin Invest 2022;52(8). https://doi.org/10.1111/eci.13789.
[14] Efe Sç KA, Doğan C, et al. Relative Fat Mass Index can be solution for obesity paradox in coronary artery disease severity prediction calculated by SYNTAX Score. Postgrad Med 2020;97(1149):434–41. https://doi.org/10.1136/postgradmedj-2020-138926.