

Obesity and Long-Term Survival in Acute Myocardial Infarction Patients with and without Diabetes Mellitus

Anand Shankar

Associate Professor, Department of Medicine, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India

Received: 25-08-2023 / Revised: 28-09-2023 / Accepted: 30-10-2023

Corresponding Author: Dr Anand Shankar

Conflict of interest: Nil

Abstract

Background: Ironically, patients who have experienced cardiovascular events like acute myocardial infarction (AMI) have been found to benefit from being overweight or obese in terms of survival. Regardless of the fact that AMI individuals with diabetes had more deaths from cardiovascular disease than their counterparts without diabetes, this obesity paradox has not been examined in this population. Thus, examining the relationship among BMI and death from all causes in AMI individuals who have or do not have diabetes mellitus was the aim of this long-term study.

Methods: 12 individuals with diabetes and 28 patients without it, ages 28 to 75, were enrolled in the study. They were drawn from a population-based AMI registry in India. Individuals with their first AMI were monitored until December 2022. Structured interviews and review of charts were used in the data collection process. The relationship between BMI and mortality over the long-term from all causes was also analyzed.

Results: Patients with AMI who were of average weight had the greatest long-term mortality rates (5 deaths per 100 person years) in both the diabetes and non-diabetic groups. Following covariate adjustments, patients with AMI who did not have diabetes showed a substantial protective impact from overweight and obesity on all-cause mortality (overweight: hazard ratio (HR) 0.74, obesity: HR 0.65). On the other hand, individuals with diabetes who had AMI did not exhibit an obese paradox. Nevertheless, stratified studies revealed survival advantages in diabetic over-weight AMI individuals who had been taken statins before developing AMI (HR 0.50) or four evidence-based drugs when they were discharged from the hospital (HR 0.53).

Conclusion: Unlike AMI patients with no diabetes, AMI individuals who have diabetes have no advantage from an increased BMI in terms of survival. More research that stratifies its samples according to diabetes status is required to look into the underlying causes of these findings.

Keywords: Acute Myocardial Infarction, Diabetes, BMI.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

In the overall population, having a higher body mass index (BMI) is a separate risk indicator for higher all-cause death. Furthermore, as compared to one's having normal wt., those who are over-weight or obese have a higher risk of cardiovascular events. Overweight and obese individuals have been found to have a contentious survival advantage following cardiac events such as acute myocardial infarction (AMI) [1].

Diabetes mellitus is a significant risk contributor to cardio-vascular disease and death in addition to being overweight [2]. Individuals diagnosed with diabetes have a markedly raised risk of cardiovascular death, which is further enhanced following a documented cardiovascular event like an AMI. Furthermore, compared to individuals without diabetes, they have poorer short- and long-term results following cardiovascular treatments.

Few research, however, have looked specifically at patients who have or do not have diabetes to determine the association among obesity and mortality over the long term following a cardiovascular incident, and their findings have been mixed [3].

Therefore, there is presently no comprehensive elucidation for the cause of the obesity dilemma in AMI patients. Furthermore, there haven't been any long-term studies on this subject that account for significant comorbidities, treatment before and after AMI, or complications that arise while the patient is in the hospital.

Thus, the aim of this long-term observational study was to examine the relationship among BMI and mortality from all causes in individuals with and without diabetes.

Methods

Study Population: This study comprises all successively registered patients who arrived at the hospital alive and whose survival duration after acute myocardial infarction (AMI) was longer than 28 days, for 5 years. Patients were tracked through the end of December 2022. 50 patients, ages 28 to 75, who had their first non-fatal AMI were included in the data set. Patients having insufficient information on any of the significant covariates ($n = 3$) and patients with lacking information on smoking, diabetes, and BMI ($n = 6$) were eliminated. Moreover, patients with a BMI of less than 18.5 kg/m^2 were excluded. There were 40 patients in the final data set.

When compared to individuals who were included in the trial, those who were omitted had a much higher crude hazard ratio (HR) for long-term death (HR 2.37).

Data Collection: During their hospital stay, study nurses interviewed patients in a standardized manner to gather information on their pre-AMI medication, comorbidities, risk factors, and demographics. Medical charts provided details about AMI features, medical interventions, and problems that occurred while the patient was in the hospital.

Participants were categorized as normal wt., overweight, or obese grounded on their BMI. According to WHO recommendations, BMI was computed using height and weight measures taken during hospitalization (overweight: $25.0\text{-}29.9 \text{ kg/m}^2$, normal: $18.5\text{-}24.9 \text{ kg/m}^2$, obese: $\geq 30.0 \text{ kg/m}^2$) [4]. Patient self-reports were used to assess the patient's diabetes mellitus status, which was then verified by chart review.

Data Analysis: Whereas constant data were given as mean \pm SD, categorical variables were shown as percentages. Participants were categorized into two groups: those with diabetes and those without it. Potential confounders were cross-tabulated against the normal weight, overweight, and obese BMI categories among these groups. The effects of interaction were assessed for variables associated to AMI therapy, age, sex, and BMI group. Significant relationships between the BMI group, statin therapy before to AMI, and receiving all evidence based medication 4 EBMs at discharge were observed in diabetic patients. We computed distinct parsimonious models for each of these subgroups. For all data analysis, SAS software version 9.2 (SAS Institute) was utilized.

Results

The sample included 12 diabetic patients (28.4%) and 28 non-diabetic patients (Table 1). Both groups had a substantial percentage of overweight individuals (42.4% for diabetics and 48.3% for non-diabetics). Among normal weight patients, those with a LVEF $< 30\%$ were more common, and they were less likely to have PCI or any re-perfusion therapy compared to overweight or obese people. Individuals classified as overweight or obese, particularly those diagnosed with diabetes, exhibited a greater prevalence of prior administration of angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) or beta-blockers. The administration of discharge medication exhibits a preference for overweight and obese patients with regards to ACEIs/ARBs, all four evidence-based medications (EBMs), antiplatelet agents (limited to individuals with diabetes), and beta-blockers (limited to individuals without diabetes).

Table 1: Attributes of individuals categorized by diabetes status and further segmented into BMI categories

	Diabetes			Non- Diabetes		
	Normal weight	Overweight	Obesity	Normal weight	Overweight	Obesity
	BMI 18.5-24.9 kg/m^2	BMI 25-29.9 kg/m^2	BMI $\geq 30 \text{ kg/m}^2$	BMI 18.5-24.9 kg/m^2	BMI 25-29.9 kg/m^2	BMI $\geq 30 \text{ kg/m}^2$
Sociodemographic characteristics						
Female	26.76	18.96	36.72	28.34	15.84	24.95
Age [years], mean	62.81	61.86	60.96	58.55	58.56	57.98
Risk factors and co-morbidities						
Angina pectoris	22.11	22.35	25.69	15.78	16.10	19.58
Hypertension	79.75	85.62	89.40	61.97	72.36	85.12
Hyperlipidemia	63.16	73.03	79.80	63.86	71.94	74.81
Stroke	10.95	8.66	6.59	5.01	4.86	4.45
Smoking	29.97	26.71	24.89	46.52	36.77	33.88
Clinical characteristics						
Re-infarction during hospitalization	12.27	15.09	15.52	9.28	9.04	8.75
AMI type						

ST-segment elevation MI	35.65	37.98	34.07	42.38	37.23	37.09
Non-ST-segment elevation MI	52.39	55.10	56.98	51.29	55.37	55.88
Bundle branch block	8.95	3.95	6.94	3.34	5.30	4.84
Left ventricular ejection fraction < 30%	20.88	11.74	8.93	11.16	12.34	6.82
Diabetes treatment						
Oral antidiabetic agents	56.70	62.64	51.77			
Insulin therapy	31.00	26.27	27.08			
Both antidiabetic agents and insulin therapy	9.40	8.09	18.19			
Long-term mortality	28.26	20.51	20.43	14.92	11.05	9.05

Patients diagnosed with diabetes mellitus exhibited a significantly elevated long-term mortality rate of 4 deaths per 100-person years, in contrast to individuals without diabetes, who experienced a comparatively lower mortality rate of 2 deaths per 100-person years. In a cohort comprising both diabetic and people without diabetes, it was observed that individuals with normal weight exhibited a greater long-term mortality rate. Specifically, the mortality rate was found to be 5 deaths per 100 person-years among diabetic patients and 3 deaths per 100 person-years among non-diabetic patients.

The unadjusted analyses revealed a discernible shielding effect of over-weight and obesity on mortality over the long-term among non-diabetic individuals, whereas no such benefit was found in those with diabetes. In the study, it was observed that overweight individuals without diabetes exhibited a statistically substantial 0.74-fold increased risk of mortality. Furthermore, obese individuals without diabetes displayed an even lower HR of 0.65 when compared to non-diabetic individuals with normal weight. Nevertheless, the aforementioned protective effects exhibited a reduction in magnitude in both BMI cohorts upon accounting for confounding factors. Notably, these effects failed to reach statistical significance specifically in individuals diagnosed with diabetes.

Parsimonious models were computed to assess various observation periods, spanning from 1 to 12 years at one-year intervals. These models aimed to compare the HRs between patients who were overweight or obese, with or without diabetes. The aforementioned models have exhibited a noteworthy safeguarding impact of excessive wt. and obesity on mortality from all causes in patients with AMI who do not have diabetes. However, it is important to note that this protective effect gradually diminishes over the course of time, while still maintaining

statistical significance. In contradistinction, the presence of excessive wt. or obesity did not yield a favorable outcome in terms of survival for patients diagnosed with AMI and concomitant diabetes mellitus.

Discussion

This population-based study found that among AMI patients without diabetes, a higher BMI significantly impacted long-term survival. On the other hand, no such correlation was seen in individuals with diabetes. Interestingly, overweight diabetic patients who were taken statins prior to AMI or 4 EBMs at hospital discharge seemed to benefit significantly in terms of survival. Moreover, the benefit of overweight and obesity on death was found to decrease with longer observation periods in people without diabetes.

Adamopoulos *et al.* [5] identified no obesity dilemma in diabetes and chronic coronary artery disease individuals, as did our investigation. However, our study only compared obese and non-obese BMI categories, limiting comparability. Normal-weight diabetics with pre-existing CVD events had the greatest all-cause death rates when associated to obese and over-weight individuals [3]. Japanese research indicated a higher 30-day death rate for normal-wt. diabetic individuals compared to over-weight patients (BMI ≥ 25 kg/m²) [6]. These inconsistencies may be due to statistical strength and study design. When BMI groups vary widely, mortality relationships resemble U- or J-shaped curves instead of linear increases [7].

For patients without diabetes, our findings match prior AMI investigations [8] and current comprehensive reviews of CVD individuals [9]. Stratified analyses showed that overweight diabetics administered statins before AMI and those discharged with all four EBMs had a survival advantage. Statin medication in diabetics without

cardiovascular disease may benefit, and giving all four EBMs at discharge may minimize long-term mortality and morbidity [10]. Hypertension (ACEIs, beta-blockers, ARBs) and cholesterol (statins) medications may affect the remodeling of myocardium and post-AMI mortality [10].

Over-weight and obese individuals without diabetes had less survival benefit with extended follow-up. Earlier studies on short-term mortality may have over-estimated overweight and obesity's protective effect after AMI, which may only be valid for a short time, possibly due to patients' weight loss [11] or their resilience to acute cardiovascular events.

Diabetes and non-diabetes may have different long-term survival rates due to several causes. First, diabetes and its comorbidities, together with obesity, can be harmful. Overweight and obese people may have normal cardiometabolic health [12]. Some normal-weight cardiometabolic dysfunction patients have similar or higher cardiac morbidity and mortality from all causes than overweight and obese individuals [13]. Differentiating metabolically good and unhealthy BMI groups may also address the obesity paradox.

Secondly, the study didn't take into account cancer, weight gain or loss, or post-discharge drug adherence. BMI may affect long-term cardiovascular mortality, according to recent research [14].

Finally, the obesity paradox might rely on the indices used to assess and define normal wt., overweight, and obesity [15]. BMI and body fat distribution indices like WHR or WC may improve cardiovascular event mortality estimates [16]. Cardiovascular disease mortality is higher with abdominal obesity. Indicators that distinguish fat from lean mass and analyze body fat distribution may provide more information. [17]

This is the first study to examine BMI with mortality over the long term in AMI patients who have or do not have diabetes. It uses consecutive recruitment from a population-based registry, includes important covariates, has a longer follow-up period, and excludes cachexic patients. Diabetes was established by chart review.

However, constraints should be considered. Weight changes throughout the extensive follow-up were ignored. Patients above 9 were eliminated. Individuals who died prior to reaching the medical center or during the 28 days had been unaccounted for. Malignant illness and renal dysfunction, which impact AMI survival, were excluded. A tiny percentage of diabetics in our study had type 1 diabetes. Finally, treatment time span, pre- and post-AMI therapies, and drug compliance were unknown.

Conclusion

The study found a substantial protective impact of over-weight and obesity on mortality from all causes in AMI individuals having no diabetes, which diminished with longer observation periods but remained statistically significant. Nonetheless, being over-weight or obese did not enhance survival in AMI patients with diabetes. Remarkably, a counterintuitive correlation was discovered in over-weight AMI individuals having diabetes who were prescribed four EBMs at hospital discharge and had previously received statins.

More research is required to fully inspect the association among BMI and mortality from all causes in individuals with and without diabetes.

References

1. Buchholz EM, Rathore SS, Reid KJ, Jones PG, Chan PS, Rich MW, *et al.* Body mass index and mortality in acute myocardial infarction patients. *Am J Med.* 2012;125(8):796–803.
2. Gregg EW, Gu Q, Cheng YJ, Narayan KM, Cowie CC. Mortality trends in men and women with diabetes, 1971 to 2000. *Ann Intern Med.* 2007;147(3):149–55.
3. Dallongeville J, Bhatt DL, Steg PH, Ravaud P, Wilson PW, Eagle KA, *et al.* Relation between body mass index, waist circumference, and cardiovascular outcomes in 19,579 diabetic patients with established vascular disease: the REACH Registry. *Eur J Prev Cardiol.* 2012;19(2):241–9.
4. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organization technical report series 2000, 894:i-xii, 1-253.
5. Adamopoulos C, Meyer P, Desai RV, Karatzidou K, Ovalle F, White M, *et al.* Absence of obesity paradox in patients with chronic heart failure and diabetes mellitus: a propensity-matched study. *Eur J Heart Fail.* 2011;13(2):200–6.
6. Ikeda N, Nakajima R, Utsunomiya M, Hori M, Itaya H, Makino K, *et al.* Higher body mass index at the time of acute myocardial infarction is associated with a favorable long-term prognosis (8-year follow-up). *Heart Vessels.* 2011;26(5):495–501.
7. Prospective Studies C, Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, *et al.* Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet.* 2009;373(9669):1083–96.
8. Chakdoufi, S., Moumen, A., & Guerboub, A. (2023). Dyslipidemia and Diabetic Retinopathy in Moroccans Type 2 Diabetics Patients: A Cross-Sectional Study. *Journal of Medical Research and Health Sciences*, 6(3), 2471–2479.

9. Mehta L, Devlin W, McCullough PA, O'Neill WW, Skelding KA, Stone GW, *et al.* Impact of body mass index on outcomes after percutaneous coronary intervention in patients with acute myocardial infarction. *Am J Cardiol.* 2007;99(7):906–10.
10. McAuley PA, Blair SN. Obesity paradoxes. *J Sports Sci.* 2011;29(8):773–82.
11. Porter KE, Turner NA. Cardiac fibroblasts: at the heart of myocardial remodeling. *Pharmacol Ther.* 2009;123(2):255–78.
12. Doehner W, Erdmann E, Cairns R, Clark AL, Dormandy JA, Ferrannini E, *et al.* Inverse relation of body weight and weight change with mortality and morbidity in patients with type 2 diabetes and cardiovascular co-morbidity: an analysis of the PROactive study population. *Int J Cardiol.* 2012;162(1):20–6.
13. Mourmoura E, Chate V, Couturier K, Laillet B, Vial G, Rigaudiere JP, *et al.* Body adiposity dictates different mechanisms of increased coronary reactivity related to improved in vivo cardiac function. *Cardiovasc Diabetol.* 2014; 13:54.
14. Van Der Leeuw J, Van Der Graaf Y, Nathoe HM, De Borst GJ, Kappelle LJ, Visseren FL, *et al.* The separate and combined effects of adiposity and cardiometabolic dysfunction on the risk of recurrent cardiovascular events and mortality in patients with manifest vascular disease. *Heart.* 2014;100(18):1421–9.
15. Bodegard J, Sundstrom J, Svennblad B, Ostgren CJ, Nilsson PM, Johansson G. Changes in body mass index following newly diagnosed type 2 diabetes and risk of cardiovascular mortality: a cohort study of 8486 primary-care patients. *Diabetes Metab.* 2013;39(4):306–13.
16. De Schutter A, Lavie CJ, Kachur S, Patel DA, Milani RV. Body composition and mortality in a large cohort with preserved ejection fraction: untangling the obesity paradox. *Mayo Clin Proc.* 2014;89(8):1072–9.
17. Clark AL, Chyu J, Horwich TB. The obesity paradox in men versus women with systolic heart failure. *Am J Cardiol.* 2012;110(1):77–82.