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CLINICAL INVESTIGATIONS

Effect of body mass index on survival after sudden cardiac arrest

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Background: Although elevated body mass index (BMI) is a risk factor for cardiac disease, patients with elevated BMI have better survival in the context of severe illness, a phenomenon termed the "obesity paradox."

Hypothesis: Higher BMI is associated with lower mortality in sudden cardiac arrest (SCA) survivors.

Methods: Data were collected on 1433 post-SCA patients, discharged alive from the hospitals of the University of Pittsburgh Medical Center between 2002 and 2012. Of those, 1298 patients with documented BMI during the index hospitalization and follow-up data constituted the study cohort.

Results: In the overall cohort, 30 patients were underweight (BMI <18.5 kg/m^2), 312 had normal weight (BMI 18.5–24.9 kg/m^2), 417 were overweight (BMI 25.0–29.9 kg/m^2), and 539 were obese (BMI ≥30 kg/m^2). As expected, the prevalence of coronary artery disease, myocardial infarction, diabetes mellitus, and hypertension increased significantly with increasing BMI. Over a median follow-up of 3.6 years, 602 (46%) patients died. Despite higher prevalence of cardiovascular comorbidities in more obese patients, a higher BMI was associated with lower all-cause mortality on univariate analysis (hazard ratio: 0.86 per increase by 1 BMI category, 95% confidence interval: 0.78-0.94, P = 0.002) and multivariate analysis after adjusting for unbalanced baseline comorbidities (hazard ratio: 0.86 per increase by 1 BMI category, 95% confidence interval: 0.77-0.96, P = 0.009).

Conclusions: Higher BMI is associated with lower all-cause mortality in survivors of SCA, suggesting that the obesity paradox applies to the post-arrest population. Further investigation into its mechanisms may inform the management of post-SCA patients.

KEYWORDS

Body Mass Index, Mortality, Sudden Cardiac Arrest

1 | INTRODUCTION

An estimated 15% to 20% of all deaths result from sudden cardiac death,[1] nearly half of which occur in patients with no prior history of heart disease.[2] Studies examining the outcomes of sudden cardiac arrest (SCA) victims by body mass index (BMI), a known modulator of cardiovascular (CV) risk,[3] have shown conflicting results.[4–9] Overweight patients have exhibited lower mortality after SCA in the presence of a shockable rhythm,[4] in cases where extracorporeal cardiopulmonary resuscitation[5] or temperature management[6] were used, and following in-hospital cardiopulmonary resuscitation.[7] Conversely, mortality rates in other studies were higher for obese patients following therapeutic hypothermia,[8] both at 30 days and 1 year after the index SCA event.[7] Differences in prognosis by BMI after SCA may result from impediments to hospital care due to a larger body habitus as well as from any direct impact of increased or decreased BMI on

recovery. Though studies often align with a trend known as the "obesity paradox," whereby obese and overweight patients have better survival outcomes than normal-weight or underweight patients, there are also studies that show a direct relationship between a higher BMI and higher mortality rates due to post-arrest treatment differences.

Given these conflicting results, we investigated the association between BMI and mortality in a large, unselected population of consecutive SCA survivors at a network of hospitals in western Pennsylvania, using all-cause mortality after hospital discharge as the primary outcome of interest.

2 | METHODS

2.1 | Study design and population

This is a retrospective, observational study conducted at the hospitals of University of Pittsburgh Medical Center. This study was approved by the institutional review board of the University of Pittsburgh. Data were collected from the electronic medical records of all patients age > 18 years who had survived an in-hospital or out-of-hospital SCA between 2002 and 2012. Of the initial 1433 consecutive patients admitted into the database, BMI data were unavailable for 135 patients, leaving 1298 patients comprising the study cohort.

The dates of BMI recording were manually selected based on proximity to the date of SCA event. Using the World Health Organization classifications, BMI was calculated by weight in kilograms divided by the square of height in meters, with categories of underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30 kg/m^2). Baseline data were collected for all patients, including demographics, clinical data, and survival outcomes. Details of SCA location and presenting rhythm were ascertained from emergency department and inpatient records. Death was confirmed from institutional medical records as well as from the Social Security Death Index database.[10] Patients were followed to the endpoint of death or last follow-up, through February 20, 2017.

2.2 | Statistical analysis

Continuous variables are presented as mean ± SD and were compared between BMI groups using analysis of variance (ANOVA) test. Categorical variables are presented as numbers and frequencies and compared between BMI groups using the χ^2 test. Survival curves were constructed using the Kaplan–Meier method and compared by BMI strata using the log-rank test. Multivariate survival analyses adjusting for unbalanced baseline variables between BMI groups were performed using Cox proportional hazard models. Statistical analyses were performed using SPSS software version 25.0 (IBM Corp., Armonk, NY). A 2-sided *P* value <0.05 was considered statistically significant.

3 | RESULTS

Baseline characteristics of the overall cohort and the 4 BMI categories are shown in Table 1. The overall cohort was largely Caucasian (82%) and majority male (58%), with a mean age of 62 ± 15 years. The mean BMI was 29.9 ± 7.9 kg/m^2, with 74% of the overall cohort categorized as overweight or obese.

As expected, the prevalence of CV comorbidities, including coronary artery disease (CAD), myocardial infarction, diabetes mellitus (DM), and hypertension (HTN), increased significantly with increasing BMI. In addition, there were significant differences in age, sex, surface electrocardiographic parameters, serum electrolyte markers, and first documented systolic blood pressure between the BMI categories.

Over a mean follow-up of 3.5 ± 3.1 years (median, 3.6 years), 602 (46%) patients died (67% in the underweight, 54% in normal-weight, 42% in overweight, and 44% in obese categories; *P* = 0.001). Despite higher prevalence of CV comorbidities in more obese patients, a higher BMI was associated with lower all-cause mortality (hazard ratio [HR]: 0.86 per increase by 1 BMI category, 95% confidence interval [CI]: 0.78-0.94, *P* = 0.002; Figure 1). After adjusting for all unbalanced comorbidities between BMI categories, including age, sex, and presenting rhythm; the presence of CAD, HTN, DM, chronic obstructive pulmonary disease, or malignant cancer; the location of SCA; the first documented systolic blood pressure after SCA; and the width of the P-R interval and QRS complex in a Cox multivariate model, higher BMI remained a strong predictor of survival during follow-up (HR: 0.86 per increase by 1 BMI category, 95% CI: 0.77-0.96, *P* = 0.009; Table 2). Figure 2 shows the direct relation between BMI and survival.

4 | DISCUSSION

We report that elevated BMI is associated with reduced long-term mortality in survivors of SCA. Despite a higher burden of comorbidities including CAD and CV risk factors such as HTN and DM, and other recognized predictors of sudden cardiac death,[11–13] obese and overweight patients lived longer than patients who were of normal weight or underweight. These data further support the "obesity paradox" documented in other conditions, although the mechanisms of this paradox remain speculative.

Earlier studies relating BMI to survival after SCA have examined immediate and short-term mortality in the context of specific resuscitation methods, such as extracorporeal cardiopulmonary resuscitation[5] or temperature management.[6] Although these approaches provide insight into the effectiveness of specific post-SCA interventions, they fail to examine the effect of BMI on long-term survival. In addition, most prior data were derived from single centers, whereas our data were extracted from a network of 25 urban, suburban, and rural hospitals spanning western Pennsylvania.

There are several potential explanations for why the obesity paradox applies to survivors of SCA. Higher BMI may allow for the use of higher doses of cardioprotective medications, such as β-adrenergic blockers, in CAD patients who undergo bypass surgery, thus accounting for the better outcome of more obese patients.[14] There are also reports on metabolically healthy obesity, where individuals have the blood pressure, cholesterol, and glucose levels of normal-weight individuals despite being obese and therefore may not be at an increased

TABLE 1 Baseline characteristics of cardiac arrest patients for the overall cohort and by BMI status

	Total, N = 1298	Underweight, n = 30	Normal Weight, n = 312	Overweight, n = 417	Obese, n = 539	*P* Value
Demographics						
Age, y	62 ± 15	60 ± 20	63 ± 18	61 ± 14	62 ± 15	0.032
Female sex, %	42	53	46	35	43	0.005
Race, %						0.25
White	82	73	81	83	83	
Black	12	17	43	10	12	
Cardiac disease, %						
Any CAD	65	37	57	70	66	0.002
Any MI	49	27	42	54	51	0.002
Any CABG	22	8.0	18	26	22	0.09
Any PCI	32	10	25	38	33	0.007
AF	31	27	27	31	34	0.18
LVEF, %	45 ± 16	43 ± 19	45 ± 17	44 ± 16	47 ± 15	0.13
NYHA class	2.0 ± 0.9	1.3 ± 0.6	2.2 ± 1.0	2.0 ± 0.9	2.0 ± 0.9	0.42
NYHA class, %						0.93
I	35	67	30	38	33	
II	29	33	30	26	30	
III	34	0	33	36	35	
IV	2.0	0	7.0	0	2.0	
Comorbidities, %						
DM	33	13	25	28	43	<0.001
HTN	63	50	57	63	68	<0.001
Peripheral vascular disease	10	7.0	11	12	8.0	0.33
COPD	33	53	36	27	35	0.005
CKD or dialysis	17	13	18	14	18	0.85
Moderate/severe liver disease	1.2	0.0	1.3	0.7	1.7	0.39
Dementia	2.0	13	5.0	4.0	2.0	0.003
Malignancy	11	23	14	8.0	11	0.08
Tobacco use	35	37	37	32	35	0.49
Alcohol use	17	30	19	17	15	0.13
BMI, kg/m^2	29.9 ± 7.9	16.9 ± 1.5	22.3 ± 1.7	27.4 ± 1.7	36.9 ± 7.0	<0.001
CCI	2.74 ± 2.35	2.77 ± 2.85	2.74 ± 2.37	2.56 ± 2.35	2.88 ± 2.31	0.23
ECG parameters						
P-R interval, ms	167 ± 41	152 ± 38	162 ± 31	167 ± 45	171 ± 42	0.010
QRS duration, ms	106 ± 30	91 ± 20	102 ± 27	109 ± 30	107 ± 32	0.001
QT interval, ms	400 ± 71	373 ± 58	396 ± 73	403 ± 71	401 ± 71	0.11
QTc interval, ms	473 ± 55	458 ± 37	474 ± 55	475 ± 56	472 ± 54	0.43
Laboratory values						
Serum potassium, mEq/L	4.3 ± 1.7	4.1 ± 0.9	4.1 ± 0.8	4.2 ± 1.0	4.4 ± 2.4	0.11
Serum magnesium, mEq/L	2.0 ± 0.5	1.9 ± 0.5	2.0 ± 0.5	2.0 ± 0.5	2.1 ± 0.5	0.06
Serum bicarbonate, mmol/L	24 ± 5	24 ± 7	23 ± 6	23 ± 5	24 ± 5	0.039
TnI, μg/L	10 ± 41	0.5 ± 0.99	9 ± 58	9 ± 30	11 ± 44	0.64
CK-MB, μg/L	56 ± 129	3 ± 1	43 ± 111	70 ± 145	56 ± 131	0.39
Vital signs at admission						
Heart rate, bpm	89 ± 26	95 ± 24	91 ± 26	89 ± 27	88 ± 25	0.18
SBP, mm Hg	127 ± 31	136 ± 39	122 ± 31	130 ± 31	127 ± 31	0.010
DBP, mm Hg	71 ± 27	74 ± 21	71 ± 39	71 ± 22	70 ± 22	0.81
Cardiac arrest						
Location (out of hospital)	42	67	46	41	38	0.002
Initial rhythm of cardiac arrest						0.05

(*Continues*)

TABLE 1 (Continued)

	Total, N = 1298	Underweight, n = 30	Normal Weight, n = 312	Overweight, n = 417	Obese, n = 539	*P* Value
VT/VF	53	17	50	59	53	
Asystole/PEA	25	40	26	21	26	
Unspecified	22	43	24	20	21	
Index hospitalization						
LOS, d	16 ± 16	19 ± 21	16 ± 17	15 ± 16	16 ± 18	0.54
ICD implantation	26	7	25	30	25	0.010

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; CK-MB, creatine kinase MB; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; DM, diabetes mellitus; ECG, electrocardiographic; HTN, hypertension; ICD, implantable cardioverter-defibrillator; LOS, length of stay; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PEA, pulseless electrical activity; QTc, corrected QT interval; SBP, systolic blood pressure; TnI, troponin I; VF, ventricular fibrillation; VT, ventricular tachycardia. Data are presented as % or mean ± standard deviation.

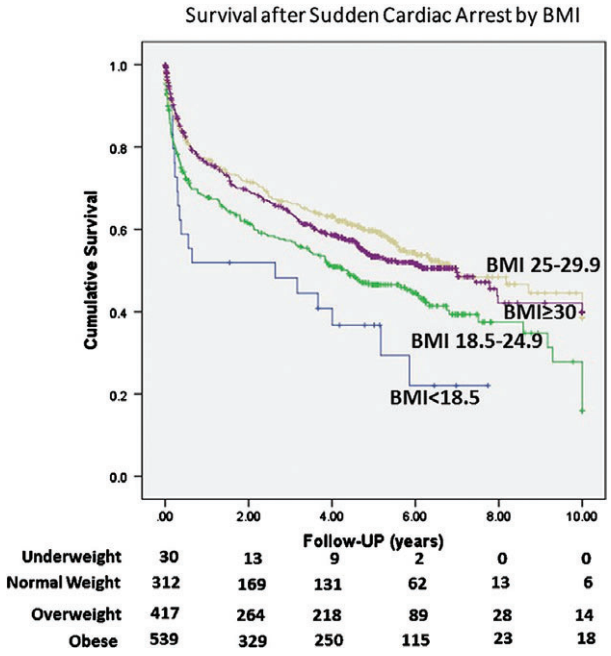

FIGURE 1 Kaplan–Meier curves for all-cause mortality in survivors of SCA by BMI category. Note that patients with higher BMI have better survival. Abbreviations: BMI, body mass index; SCA, sudden cardiac arrest

risk for CV disease.[15] Lastly, in the context of colorectal and lung cancer or advanced kidney disease, overweight patients tend to live longer as they may have more body weight and caloric reserves to sustain them during the course of the illness and its treatment.[16–18] Some or all these mechanisms may apply to the post-SCA setting.

4.1 | Study limitations

The present study has several limitations. First, it is a retrospective analysis that is subject to bias. We have, however, included all consecutive SCA survivors in our analysis without any selection to minimize bias and have used multivariate models to adjust for any unbalanced covariates. Second, although our study is a single-institution study and its results may not apply to patients in other settings or geographical areas, our patient population was derived from 25 different hospitals across western Pennsylvania, with patients being treated in different settings, which reduces any bias related to its single-institutional nature. Lastly, although we report all-cause mortality as our primary endpoint, the cause of death is not available as part of this dataset.

TABLE 2 Baseline factors associated with all-cause mortality in SCA survivors

Variable	HR	95% CI	*P* Value
BMI (per category increase)	0.86	0.77-0.96	0.009
Age at SCA (per 1-year increase)	1.03	1.02-1.04	<0.001
Female sex	1.05	0.86-1.28	0.62
HTN	0.83	0.67-1.02	0.08
CAD	0.94	0.75-1.16	0.55
DM	1.72	1.40-2.11	<0.001
Chronic pulmonary disease	1.50	1.23-1.83	<0.001
Presence of malignant cancer	1.89	1.46-2.44	<0.001
First SBP after SCA	1.00	1.00-1.00	0.74
PR duration (per 1-ms increase)	1.00	1.00-1.00	0.003
QRS duration (per 1-ms increase)	1.00	1.00-1.01	0.14
Implantation of defibrillator	0.70	0.54-0.92	0.009
Out-of-hospital SCA	1.09	0.88-1.34	0.42
Initial documented rhythm is nonshockable[a]	1.59	1.23-2.06	<0.001
First serum Mg level after SCA	1.11	0.92-1.33	0.27
First serum bicarbonate level after SCA	1.01	0.99-1.03	0.29

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio; HTN, hypertension; Mg, magnesium; SBP, systolic blood pressure; SCA, sudden cardiac arrest; VF, ventricular fibrillation; VT, ventricular tachycardia.

[a] A shockable rhythm is defined as VF or VT.

5 | CONCLUSION

A higher BMI among survivors of SCA is associated with longer survival. Further research on the underlying mechanisms of this finding is needed before interventions can be implemented to improve the outcome of SCA victims.

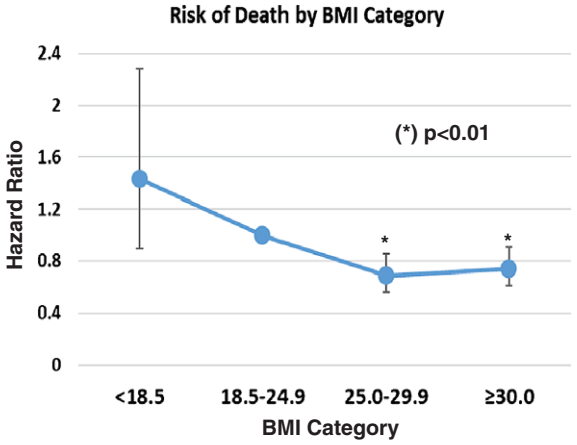

FIGURE 2 Plot of HRs and 95% CIs for all-cause mortality by category of BMI, using the normal BMI category (BMI = 18.5–24.9 kg/m^2) as a reference. Note that underweight patients have the worst outcome, followed by normal-weight patients, and then overweight and obese patients. Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio

Author contributions

Sayna Matinrazm and Adetola Ladejobi contributed equally to this article.

Conflicts of interest

S. Saba reports research support and consultation services from Boston Scientific; E. Adelstein reports research support from Medtronic; and S.K. Jain reports research support from Boston Scientific and Medtronic. The authors declare no other potential conflicts of interest.

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