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Association of the body mass index with outcomes in elderly patients (≥80 years) undergoing percutaneous coronary intervention

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ABSTRACT

Background: The obesity paradox has been recognized in patients with cardiovascular disease. The association between obesity and outcomes in elderly patients undergoing percutaneous coronary intervention (PCI) has not been investigated, yet.
Methods: A total of 990 elderly (≥80 years) patients undergoing PCI at our institution between January 2009 and December 2017 and with available data on body mass index (BMI) were divided according to BMI tertiles (lowest BMI tertile: ≪24.1 kg/m^2, middle BMI tertile: 24.1–27.2 kg/m^2, and highest BMI tertile: ≫27.2 kg/m^2). The primary endpoint was all-cause mortality at a median follow-up of 233 [34–862] days.
Results: All-cause mortality was 11.2%, 7.6%, and 5.8% in the lowest, the middle, and the highest BMI tertiles (Log Rank p = 0.008). Belonging to the lowest BMI tertile was associated with an increased risk of all-cause mortality (HR 2.14, 95% CI 1.23–3.73, p = 0.007), and associations remained significant after multivariable adjustments (adjusted HR 1.92, 95% CI 1.05–3.52, p = 0.03). While belonging to the lowest BMI tertile was independently associated with an increased all-cause mortality in patients with acute coronary syndromes (HR 2.32, 95% CI 1.24–4.35, p = 0.009; adjusted HR 2.40, 95% CI 1.19–4.84, p = 0.01), relations were not significant in patients with stable coronary artery disease (HR 1.32, 95% CI 0.38–4.56, p = 0.67; adjusted HR 0.80, 95% CI 0.21–3.05, p = 0.75).
Conclusions: In elderly (≥80 years) patients undergoing PCI, belonging to the lowest BMI tertile was associated with an increased mortality, mainly in acute coronary syndromes. Hence, the BMI should be incorporated into the risk stratification of elderly patients with coronary artery disease.

1. Introduction

The number of elderly patients with coronary artery disease in need for coronary revascularization is steadily increasing given the ageing of the population [1,2]. This patient population represents a vulnerable and frail patient subgroup with mostly complex coronary artery disease, a substantial comorbid burden, and a high risk of adverse events [3–7]. Although elderly patients with coronary artery disease are increasingly being treated with percutaneous coronary intervention (PCI), dedicated randomized trials in these patients, along with large-scale registry data, are lacking [8–10].

Risk stratification in elderly patients is important. Obesity, being associated with an increased prevalence of cardiovascular risk factors, conveys an increased risk of cardiac events in the general population [11–13]. Recent research has indicated an inverse linear or U-shaped relation of obesity with outcomes in a variety of disease conditions. This phenomenon, known as the obesity paradox, has been described in different patient populations such as those with atrial fibrillation, heart failure, stable coronary artery disease, and acute coronary syndromes [14–18]. The role of obesity in the prognostication of elderly patients being referred for PCI is ill-defined.

This study therefore sought to investigate the impact of the body mass index (BMI) on outcomes in a large, unrestricted cohort of elderly (≥80 years) patients undergoing PCI.

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2. Material and methods

2.1. Study design

Out of 18′378 PCI procedures performed between January 2009 and December 2017 at our institution, a total of 1′238 (6.7%) patients were ≥80 years of age with information on BMI available for 990 patients [19,20]. All patients were treated according to current guidelines for stable coronary artery disease, acute coronary syndromes, and myocardial revascularization, and received evidence-based medical management [21–24]. Baseline characteristics and outcome data were collected from the clinical database system. Estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease (MDRD) equation. For the purpose of this study, patients were divided according to BMI tertiles (BMI tertile 1: ≪24.1 kg/m^2, BMI tertile 2: 24.1–27.2 kg/m^2, and BMI tertile 3: ≫27.2 kg/m^2).

The primary endpoint was all-cause mortality. Cardiac mortality included death from cardiac as well as unknown causes. Bleeding was defined as bleeding requiring red blood cell transfusion in line with the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) criteria [25]. The study was conducted in full conformance with the principles of the Declaration of Helsinki, and the study protocol approved by the institutional review board.

2.2. Statistical analysis

Continuous variables are presented as mean ± standard deviation or median (interquartile range). Categorical variables are presented as frequencies (percentages). The Shapiro-Wilk test was used to test for normality of distribution. The Mann-Whitney *U* test was used for comparison of continuous variables, and the Pearson's $\chi 2$ test or the Fisher's exact test for comparison of categorical variables, respectively. The Kaplan-Meier method was applied to generate survival curves of BMI tertiles with the Log Rank test used to assess differences between groups. Cox proportional hazards regression models were applied to estimate unadjusted and adjusted risks of all-cause mortality according to BMI tertiles. Models were adjusted for baseline variables significantly associated with all-cause mortality in univariate analysis with p-values ≪ 0.05. Cox proportional hazards regression test of interaction (BMI status by sex status) was performed to investigate a potential differential effect on the outcome measure. All testing was two-sided and conducted at the 0.05 significance level. Statistical analyses were performed using IBM-SPSS version 24 (IBM Corp.).

3. Results

3.1. Patient and procedural characteristics

Out of 990 patients, 442 (44.6%) were women. Median age of the patients was 83.4 [81.5–86.1] years and median BMI 25.5 [23.3–28.1] kg/m^2. Women had a lower BMI (24.8 [22.4–28.1]) than men (26.0, [24.0–28.0]), p ≪ 0.001, (Fig. 1).

Baseline characteristics according to BMI tertiles are given in Table 1. Age decreased with increasing BMI tertiles. Patients in BMI tertile 1 were more likely to be female, and less often suffered from cardiovascular risk factors such as type 2 diabetes and hypertension. They less often had known coronary artery disease and chronic obstructive pulmonary disease, but had a lower left ventricular ejection fraction as compared with patients in the higher BMI tertiles. With increasing BMI tertiles, patients less often presented with ST segment elevation myocardial infarction. Median Charlson Comorbidity Index (n = 597) was 2 [1–3] with lowest values observed for the BMI tertile 2 (2 [1, 2] versus 1 [1–3] versus 2 [1–3], p = 0.002). Median Barthel Index (n = 565) was 100 [80–100] without any differences among BMI tertiles (p = 0.09).

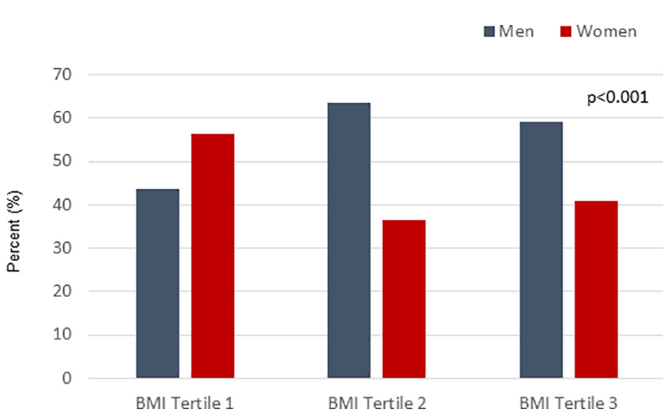

Fig. 1. Prevalence of women and men according to body mass index (BMI) tertiles.

Table 1
Baseline characteristics.

Variable	BMI tertile 1	BMI tertile 2	BMI tertile 3	p-Value
Clinical characteristics				
Body mass index (kg/m^2)	22.2 [20.9–23.3]	25.5 [24.7–26.2]	29.4 [28.1–32.0]	–
Age (years)	84.2 [81.7–87.0]	83.4 [81.4–86.0]	83.0 [81.2–85.1]	≪0.001
Female gender	186 (56.4)	121 (36.6)	135 (41.0)	≪0.001
Type 2 diabetes	64 (19.4)	97 (29.3)	159 (48.3)	≪0.001
Hypertension	267 (80.9)	288 (87.0)	300 (91.2)	0.001
Dyslipidemia	163 (49.5)	183 (55.3)	183 (55.6)	0.21
Known coronary artery disease	120 (36.6)	152 (46.1)	155 (47.4)	0.01
Prior myocardial infarction	58 (21.3)	61 (22.9)	82 (30.7)	0.03
Prior percutaneous coronary intervention	83 (25.4)	107 (32.5)	109 (33.1)	0.056
Prior coronary artery bypass grafting	41 (12.5)	53 (16.1)	43 (13.1)	0.36
Prior stroke	53 (16.1)	60 (18.1)	60 (18.2)	0.71
Peripheral arterial disease	43 (13.0)	33 (10.0)	28 (8.5)	0.16
Atrial fibrillation	129 (39.1)	111 (33.5)	121 (36.8)	0.33
Congestive heart failure	60 (18.2)	43 (13.0)	52 (15.8)	0.19
Chronic obstructive pulmonary disease	27 (8.2)	32 (9.7)	47 (14.3)	0.03
Dementia	9 (4.5)	8 (3.8)	4 (2.1)	0.43
Malignancy	24 (12.1)	37 (17.5)	35 (18.7)	0.16
Left ventricular ejection fraction (%)	52 [40–64]	58 [45–67]	57 [44–65]	0.02
Index event				
Stable coronary artery disease	77 (23.4)	90 (27.2)	105 (31.9)	0.05
Unstable angina	60 (18.2)	81 (24.5)	71 (21.6)	0.14
Non-ST segment elevation myocardial infarction	114 (34.5)	106 (32.0)	104 (31.6)	0.69
ST segment elevation myocardial infarction	79 (23.9)	54 (16.4)	49 (14.9)	0.006
Laboratory characteristics				
Hemoglobin (g/dl)	12.9 [11.5–14.1]	13.3 [12.1–14.5]	13.4 [12.0–14.1]	0.006
eGFR (MDRD, ml/min)	57 [44–74]	59 [46–74]	60 [45–72]	0.76
CRP (mg/dl)	2.6 [0.6–10.4]	2.1 [0.5–6.6]	2.8 [0.9–7.9]	0.10
CK (U/l)	103 [65–219]	110 [71–205]	116 [71–196]	0.82
Hs-cTnT (ng/l)	63 [23–287]	59 [20–143]	47 [17–187]	0.07
Medication at presentation				
Aspirin	109 (50.0)	122 (53.5)	130 (56.5)	0.38
Adenosine diphosphate inhibitor	38 (17.5)	33 (14.5)	28 (12.2)	0.29
Oral anticoagulation	50 (23.0)	49 (21.4)	58 (25.2)	0.56
Statins	79 (36.4)	102 (44.7)	122 (53.3)	0.002
Beta blocker	114 (53.0)	136 (59.6)	157 (68.6)	0.003
Renin-angiotensin system blockers	141 (65.6)	152 (66.4)	171 (74.3)	0.08
Calcium channel blocker	49 (22.8)	59 (25.9)	83 (36.2)	0.004
Diuretics	90 (41.9)	107 (46.7)	140 (61.1)	≪0.001
Medication at discharge				
Aspirin	297 (94.0)	306 (95.0)	303 (93.5)	0.70
Adenosine diphosphate inhibitor	315 (99.7)	223 (99.7)	234 (99.7)	1.00
Oral anticoagulation	90 (28.5)	92 (28.4)	121 (37.2)	0.02
Statins	268 (84.8)	287 (88.6)	291 (89.5)	0.16
Beta blocker	277 (87.7)	288 (88.9)	289 (88.9)	0.85
Renin-angiotensin system blockers	290 (92.1)	305 (94.1)	307 (94.5)	0.41
Calcium channel blocker	59 (18.7)	68 (21.0)	103 (31.7)	≪0.001
Diuretics	214 (67.7)	226 (70.0)	256 (78.8)	0.004

Values are given as median and interquartile range or numbers and percentages. CK = creatine kinase, CRP = C-reactive protein, eGFR = estimated glomerular filtration rate, hs-TnT = high-sensitivity cardiac troponin T.

A total of 225 (22.7%), 310 (31.3%), and 455 (46.0%) patients were treated for single, two, and three vessel disease, respectively. The prevalence of single, two, and three vessel disease did not differ among BMI tertiles ($p = 0.35$). A total of 64 (6.5%) patients suffered from left main disease, with equal distribution across BMI tertiles ($p = 0.64$). Drug-eluting and bare metal stent implantation was performed in 85.7% and 12.9% of patients without any differences among BMI tertiles ($p = 0.85$ and $p = 0.78$). Fluoroscopy time (13.4 [9.1–21.1] versus 13.7 [8.4–19.1] versus 14.0 [9.5–20.5] minutes, $p = 0.49$) and amount of contrast volume used (196 [159–250] versus 195 [160–249] versus 195 [160–249], $p = 0.98$) were similar among groups. Radiation exposure significantly increased across BMI tertiles (64 [40–94] versus 83 [57–112] versus 99 [66–147] cGy*cm^2, $p \ll 0.001$). Discharge medication is presented in Table 1.

3.2. Outcomes

Rates of bleeding requiring red blood cell transfusions differed across BMI tertiles with highest rates observed in BMI tertile 1 (31 [9.4%] versus 13 [3.9%] versus 17 [5.2%] patients, $p = 0.009$). Rates of vascular access site complications were similar among groups (21 [6.4%] versus 26 [7.9%] versus 21 [6.4%] patients, $p = 0.69$).

All-cause mortality was 8.2% at a median follow up of 233 [34–862] days. Cardiac death was observed in 46 (56.8%) patients, and death due to infections, malignancies, and gastrointestinal bleeding in 22 (27.2%), 3 (3.7%), and 2 (2.5%) patients, respectively. All-cause mortality was 11.2%, 7.6%, and 5.8% in BMI tertiles 1, 2, and 3 (Log Rank $p = 0.008$, Fig. 2). When including patients undergoing PCI for acute coronary syndromes only ($n = 718$), corresponding rates were 12.6%, 9.6%, and 6.3%, respectively (Log Rank $p = 0.02$). Using Cox regression analysis, belonging to BMI tertile 1 was related with an increased risk of all-cause mortality in univariate analysis (HR 2.14, 95% CI 1.23–3.73, $p = 0.007$), and associations remained significant after multivariable adjustments (adjusted HR 1.92, 95% CI 1.05–3.52, $p = 0.03$). Predictors of all-cause mortality are given in Table 2. While belonging to BMI tertile 1 was independently associated with an increased all-cause mortality in patients with acute coronary syndromes (HR 2.32, 95% CI 1.24–4.35, $p = 0.009$; adjusted HR 2.40, 95% CI 1.19–4.84, $p = 0.01$), relations were not significant in patients with stable coronary artery disease (HR 1.32, 95% CI 0.38–4.56, $p = 0.67$; adjusted HR 0.80, 95% CI 0.21–3.05, $p = 0.75$). There was no significant interaction of BMI tertiles and sex on all-cause mortality (interaction $p = 0.78$). Differences in cardiac death among BMI tertiles did not reach statistical significance (6.1%, 4.8%, and 3.0%, Log Rank $p = 0.18$).

4. Discussion

This study shows that a lower BMI independently determines the prognosis of patients ≥80 years of age with coronary artery disease and who are undergoing PCI. Significantly increased mortality rates were observed in the lowest tertile BMI group, mainly in those patients presenting with acute coronary syndromes.

4.1. Body mass index and PCI in elderly patients

Percutaneous coronary revascularization is increasingly being performed in an elderly patient population at increased risk of adverse events [26,27]. The prevalence of comorbidities observed in this patient cohort, being comparable to previously reported studies [1,27], differed across BMI groups. The occurrence of cardiovascular risk factors including type 2 diabetes and hypertension increased with higher BMI tertile groups, along with the prevalence of prior coronary artery disease, prior myocardial infarction, and chronic obstructive pulmonary disease [15,28]. Consistently, obesity seems to be related with a greater use of

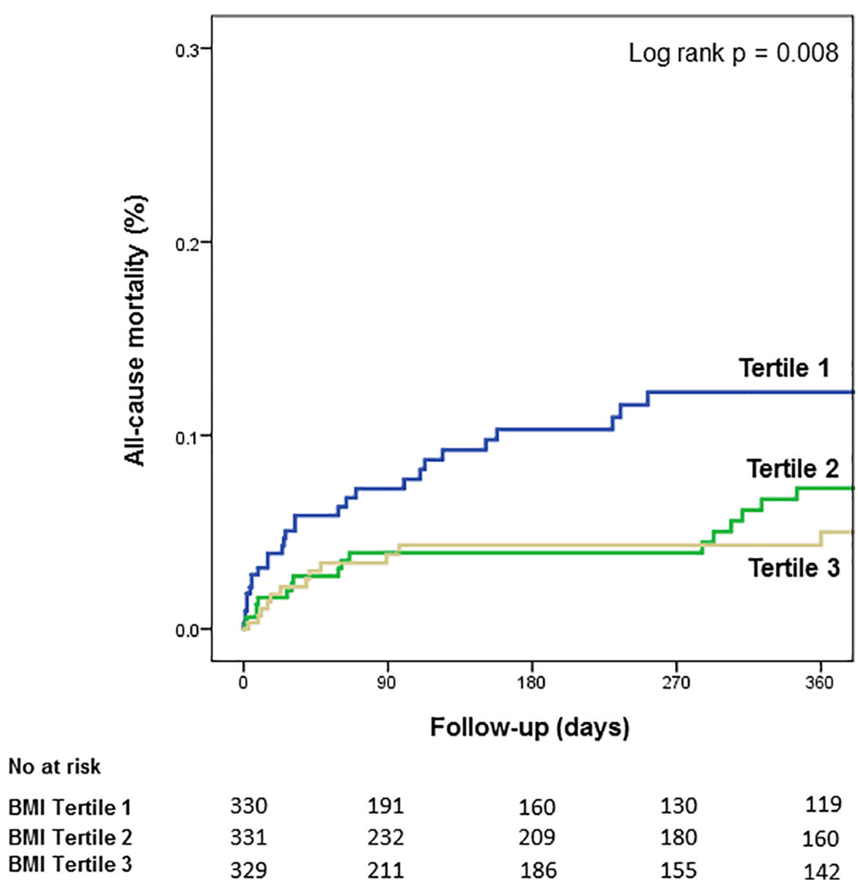

Fig. 2. Kaplan-Meier estimates for all-cause mortality according to body mass index (BMI) tertiles.

Table 2
Univariate and multivariate predictors of all-cause mortality.

Variable	Univariate analysis		Multivariate analysis	
	HR (90% CI)	p-Value	HR (90% CI)	p-Value
Age (years)	**1.16 (1.09–1.23)**	**≪0.001**	**1.09 (1.02–1.17)**	**0.01**
Female gender	1.12 (0.72–1.73)	0.62		
Diabetes mellitus	1.52 (0.97–2.38)	0.07		
Hypertension	0.68 (0.39–1.20)	0.19		
Dyslipidemia	0.78 (0.51–1.21)	0.27		
Known coronary artery disease	0.90 (0.58–1.40)	0.65		
Prior myocardial infarction	1.17 (0.71–1.95)	0.54		
Prior stroke	1.31 (0.77–2.24)	0.32		
Atrial fibrillation	**1.76 (1.14–2.73)**	**0.01**	1.60 (1.00–2.57)	0.051
Congestive heart failure	**1.94 (1.14–3.28)**	**0.01**	1.37 (0.76–2.45)	0.29
Chronic obstructive pulmonary disease	1.62 (0.88–2.99)	0.13		
STEMI at presentation	**1.76 (1.06–2.92)**	**0.03**	1.71 (0.94–3.09)	0.08
Hemoglobin (g/dl)	**0.83 (0.74–0.93)**	**0.001**	**0.88 (0.78–1.00)**	**0.048**
eGFR (MDRD, ml/min)	**0.98 (0.97–0.99)**	**≪0.001**	**0.99 (0.97–1.00)**	**0.03**
BMI (Tertile 1)	**2.14 (1.23–3.73)**	**0.007**	**1.92 (1.05–3.52)**	**0.03**

BMI = body mass index, CI = confidence interval, eGFR = estimated glomerular filtration rate, HR = hazard ratio, MDRD = Modification of Diet in Renal Disease, and STEMI = ST segment elevation myocardial infarction.

guideline-recommended therapy on admission. The lowest BMI tertile group was characterized by an increased prevalence of women, advanced age, reduced left ventricular systolic function, and lower hemoglobin levels at presentation. The increased prevalence of women in lower BMI groups has previously been described [16,28], and the inverse relation of age and BMI in coronary artery disease patients is consistent with other studies [16,28,29]. Interestingly, patients with lower BMI values were more likely to present with ST segment elevation myocardial infarction as index acute coronary syndrome event, an association which needs to be further defined [28].

4.2. Body mass index and outcomes following PCI in elderly patients

Rates of mortality following PCI were twice as high in the lowest as compared with the highest BMI tertile group, despite the increased comorbid burden including diabetes, hypertension, prior coronary artery disease, and chronic obstructive pulmonary disease in the highest BMI tertile group. The association between BMI and outcomes in coronary artery disease patients remains conflicting. While some studies failed to show any association between BMI and mortality after PCI or even suggested an increased long-term mortality in obese patients due to an accelerated cardiometabolic disease progression [30–33], favorable outcomes in obese patients were reported in others [15,16,34]. The decreasing mortality rates in elderly patients across BMI groups observed in this study support the theory of a linear inverse relation between body weight and mortality also in elderly coronary artery disease patients [16,28,34]. Pathophysiological mechanisms underlying this association remain to be determined. Although the biology of the obese phenotype may account at least in part for the survival benefit of patients with higher BMI values [35–37], mortality differences may be due to unmeasured confounding factors such as malignancy, autoimmune disorders, poor nutritional status or frailty, possibly predominating in lower weight elderly patients. In addition, differences in baseline characteristics – although integrated into the multivariate models - may have contributed to the observed findings, along with the increased bleeding risk attributed to patients with lower BMI values. It may further be hypothesized that obesity-related neuroendocrine alterations modulate myocardial remodeling following an acute coronary syndrome and thereby beneficially affect outcomes in patients with higher BMI values [35–37].

4.3. Limitations

Some limitations need to be considered. The study is a single center, retrospective analysis of a large, unrestricted cohort of patients ≥80 years of age undergoing PCI, with the limitations inherent to such a design. The exclusion of patients with missing baseline information on BMI could have introduced some selection bias. Although we used a comprehensive group of adjustment variables, the possibility of residual confounding by factors not incorporated into the multivariate models can not be excluded completely. As the BMI was not recorded during follow-up, effects of weight changes on outcomes could not be assessed.

4.4. Conclusions

This study for the first time reports the association between lower BMI values and increased mortality in elderly patients undergoing PCI. Our data therefore suggest that BMI should be incorporated into the risk stratification of elderly patients with coronary artery disease.

Declaration of Competing Interest

No conflict of interest regarding the content of the paper.

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