

Impact of Body Mass Index on the Clinical Outcomes after Percutaneous Coronary Intervention in Patients ≥ 75 Years Old

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Abstract

Background: The impact of body mass index (BMI) on the clinical outcomes after percutaneous coronary intervention (PCI) in patients ≥ 75 years old remained unclear.

Methods: A total of 1098 elderly patients undergoing PCI with stent implantation were recruited. Patients were divided into four groups by the value of BMI: Underweight (≤ 20.0 kg/m²), normal weight (20.0–24.9 kg/m²), overweight (25.0–29.9 kg/m²) and obese (≥ 30.0 kg/m²). Major clinical outcomes after PCI were compared between the groups. The primary endpoint was defined as in-hospital major adverse cardiovascular events (MACEs), which included death, myocardial infarction (MI) and target vessel revascularization. The secondary endpoint was defined as 1 year death. Logistic regression analysis was performed to adjust for the potential confounders.

Results: Totally, 1077 elderly patients with available BMIs were included in the analysis. Patients of underweight, normal weight, overweight and obese accounted for 5.6%, 45.4%, 41.5% and 7.5% of the population, respectively. Underweight patients were more likely to attract ST-segment elevation MI, and get accompanied with anemia or renal dysfunction. Meanwhile, they were less likely to achieve thrombolysis in MI 3 grade flow after PCI, and receive beta-blocker, angiotensin converting enzyme inhibitor or angiotensin receptor blocker after discharge. In underweight, normal weight, overweight and obese patients, in-hospital MACE were 1.7%, 2.7%, 3.8%, and 3.7% respectively ($P = 0.68$), and 1 year mortality rates were 5.0%, 3.9%, 5.1% and 3.7% ($P = 0.80$), without significant difference between the groups. Multivariate regression analysis showed that the value of BMI was not associated with in-hospital MACE in patients at 75 years old.

Conclusions: The BMI “obese paradox” was not found in patients ≥ 75 years old. It was suggested that BMI may not be a sensitive predictor of adverse cardiovascular events in elderly patients.

Key words: Aged; Angioplasty; Body Mass Index; Outcomes

INTRODUCTION

A number of studies have proved body mass index (BMI) as a risk factor in predicting cardiovascular disease.^[1,2] People with higher value of BMI usually had more cardiovascular comorbidities, such as diabetes, hypertension or hyperlipidemia. These comorbidities further increased the development of coronary artery disease (CAD) afterward.^[1,2] Among already CAD established patients, recent studies showed a lower rate of death in patients undergoing percutaneous coronary intervention (PCI) with a higher value of BMI categorized as overweight (25 kg/m² < BMI < 30 kg/m²) or obese (BMI ≥ 30.0 kg/m²).^[3-5] This phenomenon is called “obesity paradox”. It was also observed that patients categorized as

underweight (BMI ≤ 20 kg/m²) showed a higher mortality rate compared with normal weight (20 kg/m² < BMI < 25 kg/m²).^[6] So does that mean the excess fat is protective in predicting cardiovascular events? Numbers of studies were performed to test the “obesity paradox.” However, most of the studies were carried among unselected patients.^[7,8] Elderly patients had quite different lipid concentration and BMI profiles compared with younger ones. So we decided to test the association between BMI and the clinical outcomes after PCI specifically in patients ≥ 75 years old.

METHODS

Patient selection

From June 1, 2006 to April 30, 2011, 1098 elderly patients (≥ 75 years old) who had PCI and stent implantation

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were included. Twenty-one patients were excluded in the analysis because of incomplete BMIs. Patients were divided into four groups by the value of BMI: Underweight (≤ 20.0 kg/m²), normal weight (20.0–24.9 kg/m²), overweight (25.0–29.9 kg/m²) and obese (≥ 30.0 kg/m²).

Data collection and follow-up checkup

For the calculation of BMI, height and weight were acquired from patients' direct measurement. Clinical characteristics and in-hospital outcomes were extracted from the medical record by a group of trained medical students. Angiographic characteristics were obtained from the laboratory database. Clinical follow-up was performed at 6 months and 1 year after patients' discharge. In-hospital major outcomes were adjudicated by the data monitoring committee, which was composed by four senior clinical fellows. Data extraction was reviewed by the random inspection for the quality control.

Variable definition

Body mass index was used as a surrogate to indicate patient's adiposity level, which was calculated as weight in kilograms divided by height squared in meters. The primary endpoint was defined as in-hospital major adverse cardiovascular event (MACE), which included death, myocardial infarction (MI) and target vessel revascularization (TVR). The secondary endpoint was defined as death after 1 year discharge. Major bleeding at hospital was also compared, which was defined as bleeding met Bleeding Academic Research Consortium ≥ 3 grade.^[9] MI was defined by meeting at least 2 of the following criteria: (1) unrelieved onset of chest pain over 20 min; (2) significant new changes of ST-segment or new Q waves in the electrocardiograms; (3) elevation of myocardial enzymes that are more than three times the upper reference limit. TVR referred to any percutaneous or surgical revascularization of a previously treated vessel. Anemia was determined by the hemoglobin value, hemoglobin <120 g/L in male and <110 g/L in female was defined as anemia. Glomerular filtration rate was calculated with serum creatine, age, BMI and sex, an estimated glomerular filtration rate <60 ml/min per 1.73 m² was defined as renal dysfunction.

Percutaneous coronary intervention procedure

Before PCI, patients were pretreated with 300 mg loading dose of aspirin and clopidogrel. And prior to the catheterization, patients were administrated with weight-adjusted loading dose of heparin. Glycoprotein IIb/IIIa inhibitor and low molecule weight heparin were administrated optionally at the doctor's discretion. Sustained dual antiplatelet therapy including both aspirin and clopidogrel was prescribed after PCI for 1 year in patients receiving drug-eluting stents (DESs), and for 1 month in patients receiving bare metal stents.

Statistics

Continuous variables were expressed as mean values \pm standard deviation and compared using Student's *t*-test. Categorical variables were expressed as frequencies

with percentages and compared using Chi-square test or Fisher's exact test when appropriate. Logistic regression analysis was performed to adjust for the potential confounders in predicting the association between BMI and in-hospital MACE. Clinical relevant variables or baseline variables compared between the groups with a $P < 0.1$ entered the logistic model, which included: age, sex, BMI categories, hypertension, diagnosis of ST-segment elevation MI, left ventricular ejection fraction, anemia, renal dysfunction, left main disease, use of DESs, and the achievement of final thrombolysis in MI (TIMI) 3 flow. The analyses were performed using SPSS 18.0 (SPSS Inc., Chicago, IL, USA). A two-sided $P \leq 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

Totally, 1077 elderly patients included in the analysis. According to the BMI value, 60 patients (5.6%) were underweight, 489 (45.4%) were normal weight, 447 (41.5%) were overweight, and 81 (7.5%) were obese. Patients' baseline characteristics are shown in Table 1. Prior medical histories were comparable between the groups, except that hypertension was more frequent in overweight patients. Underweight patients were more likely to attract ST-elevation myocardial infarction, and overweight patients were more likely to attract stable angina. Underweight patients had higher rates of anemia, and renal dysfunction ($P < 0.01$), and overweight patients had a lower value of left ventricular ejection fraction ($P < 0.01$). In-hospital medication usage was similar between the groups, but overweight or obese patients were more likely to receive beta-blocker, angiotensin-converting enzyme inhibitor or angiotensin receptor blockers at discharge compared with other patients. On the contrary, underweight patients were least likely to receive both drugs ($P < 0.05$). The extent of atherosclerosis was similar between the BMI groups [Table 2]. Overweight group was most likely to have left main disease, and underweight group was least likely to have DES. The achievement of final TIMI 3 flow was significantly lower in underweight patients than in normal weight, overweight and obese patients (91.7% vs. 99.0% vs. 97.8% vs. 100%, $P < 0.01$).

In-hospital outcomes

The rates of in-hospital MACE were similar between underweight, normal weight, overweight and obese patients (1.7% vs. 2.7% vs. 3.8% vs. 3.7%, $P = 0.677$) [Table 3]. No significant difference was detected in each component of MACE between the groups ($P > 0.05$). Major bleeding was similar between the groups ($P > 0.05$). PCI complications including coronary dissection and thrombosis were also similar between the groups ($P > 0.05$). When combining underweight and normal weight patients as one group, there was no difference in MACE between the new three groups. When combining overweight and obese patients as one group, the rates of MACE were still the same. In the multivariate regression analysis [Table 4], the

Table 1: Baseline characteristics

Variables	BMI (%)				P
	(≤20 kg/m ²) (n = 60)	(20.0–24.9 kg/m ²) (n = 489)	(25.0–29.9 kg/m ²) (n = 447)	(≥30.0 kg/m ²) (n = 81)	
Male	37 (61.7)	331 (67.7)	304 (68.0)	47 (58.0)	0.262
Prior MI	16 (26.7)	123 (25.2)	105 (23.5)	25 (30.9)	0.547
Prior CABG	1 (1.7)	22 (4.5)	31 (6.9)	4 (4.9)	0.210
Prior PCI	8 (13.3)	98 (20.0)	94 (21.0)	13 (16.0)	0.433
Prior stroke	2 (3.3)	40 (8.2)	43 (9.6)	10 (12.2)	0.251
Prior heart failure	3 (5.0)	37 (7.6)	32 (7.2)	12 (14.8)	0.090
Diabetes	11 (18.3)	134 (27.4)	118 (26.4)	20 (24.7)	0.497
Hypertension	26 (43.3)	307 (62.8)	341 (76.3)	59 (72.8)	<0.01
Hyperlipidemia	27 (45.0)	238 (48.7)	228 (51.0)	41 (50.6)	0.786
Smoking	13 (21.7)	80 (16.4)	61 (13.6)	12 (14.8)	0.358
Anemia	19 (31.7)	91 (18.6)	65 (14.5)	11 (13.6)	<0.01
Renal dysfunction	52 (86.7)	334 (68.3)	196 (43.8)	25 (30.9)	<0.01
LVEF	61.65 ± 8.12	61.701 ± 7.93	61.21 ± 8.56	60.08 ± 8.62	<0.01
PCI indication					
STEMI	18 (30.0)	96 (19.6)	53 (11.9)	8 (9.9)	<0.01
NSTEMI	4 (6.7)	34 (7.0)	30 (6.7)	7 (8.6)	0.939
Unstable angina	30 (50.0)	239 (48.9)	229 (51.2)	42 (51.9)	0.892
Stable angina	8 (13.3)	115 (23.5)	134 (30.0)	23 (28.4)	0.015
Other	0 (0.0)	5 (1.0)	1 (0.2)	1 (1.2)	0.372
Periprocedure medication					
GP IIb/IIIa inhibitor	3 (5.0)	20 (4.1)	9 (2.0)	3 (3.7)	0.271
Warfarin	0 (0.0)	6 (1.2)	2 (0.4)	1 (1.2)	0.498
LMWH	47 (78.3)	370 (75.7)	332 (74.3)	57 (70.4)	0.682
Fondaparinux	0 (0.0)	7 (1.4)	5 (1.1)	3 (3.7)	0.236
Medication at discharge					
Aspirin	59 (98.3)	483 (98.8)	443 (99.1)	81 (100)	0.715
Clopidogrel	60 (100)	487 (99.6)	447 (100)	80 (98.8)	0.223
Cilostazole	1 (1.7)	4 (0.8)	1 (0.2)	0 (0.0)	0.350
Statin	60 (100)	487 (99.6)	446 (99.8)	81 (100)	0.863
Beta blocker	46 (76.7)	421 (86.1)	394 (88.1)	66 (81.5)	0.059
ACEI/ARB	36 (60.0)	338 (69.1)	327 (73.2)	62 (76.5)	0.088

ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CABG: Coronary artery bypass graft; GP IIb/IIIa inhibitor: Glycoprotein IIb/IIIa inhibitor; LMWH: Low molecular weight heparin; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction; NSTEMI: Non-ST segment elevation myocardial infarction; PCI: Percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction; BMI: Body mass index.

achievement of final TIMI 3 flow was associated with a lower rate of MACE (odds ratio: 0.23, 95% confident interval: 0.05–0.96, $P = 0.04$). However, BMI was not associated with MACE in this population.

One year outcomes

In underweight, normal weight, overweight and obese patients, the mortality rate after one year discharge was 3.3%, 1.8%, 1.8% and 0 respectively, with no significant difference between the groups ($P = 0.508$). When combining underweight with normal weight, or overweight with obese patients, the outcomes difference between the new generated three groups was still not significant ($P > 0.05$).

DISCUSSION

The purpose of the study was to assess the association between BMI and clinical outcomes after PCI in elderly patients. Previous studies showed an “obesity paradox”

among unselected patients.^[1] The “obesity paradox” indicates that the rate of MACE decreased as BMI increased, which contradicts to the traditional recognition of BMI as a risk factor of CAD. This phenomenon was consistent in unselected patients undergoing primary or elective PCIs.^[3,10] However, elderly patients hold quite different BMI profiles compared with the younger ones. If they shared the same weight as younger patients, they held a quite smaller percentage of body weight as fat.^[5] We assumed the “obesity paradox” is not applicable in elderly patients, and as expected, the main findings of this study did not find the paradox. Instead, it showed patients ≥75 years old with different BMIs had similar outcomes during hospitalization and at 1 year follow-up.

Our study was one of the limited studies in evaluating the association between BMI and clinical outcomes in elderly patients. Mehta *et al.*^[11] showed that the mortality rate of the

Table 2: Angiographic results

Variables	BMI (%)				P
	(≤20 kg/m ²) (n = 60)	(20.0–24.9 kg/m ²) (n = 489)	(25.0–29.9 kg/m ²) (n = 447)	(≥30.0 kg/m ²) (n = 81)	
Left main disease	0 (0.0)	48 (9.8)	52 (11.6)	6 (7.4)	0.033
Vessel involved					
1 vessel disease	7 (11.7)	93 (19.0)	77 (17.2)	12 (14.8)	0.472
2 vessel disease	17 (28.3)	151 (30.9)	120 (26.8)	24 (29.6)	
3 vessel disease	36 (60.0)	245 (50.1)	250 (55.9)	45 (55.6)	
Type C lesion	36 (60.0)	267 (54.6)	247 (55.3)	36 (44.4)	0.247
CTO lesion	14 (23.3)	82 (16.8)	69 (15.4)	9 (11.1)	0.250
Ostium lesion	6 (10.0)	69 (14.1)	61 (13.6)	10 (12.3)	0.830
Bifurcation lesion	22 (36.7)	172 (35.2)	199 (31.1)	30 (37.0)	0.480
Use of DES	52 (86.7)	467 (95.5)	430 (96.2)	79 (97.5)	<0.01
Number of stents					
1	30 (50.0)	230 (47.0)	190 (42.)	36 (44.4)	0.685
2	18 (30.0)	161 (32.9)	147 (32.9)	26 (32.1)	
≥3	12 (20.0)	98 (20.0)	110 (24.6)	19 (23.5)	
Use of IVUS	3 (5.0)	21 (4.3)	22 (4.9)	3 (3.7)	0.945
Use of IABP	3 (5.0)	15 (3.1)	13 (2.9)	1 (1.2)	0.631
Final TIMI 3 flow	55 (91.7)	484 (99.0)	437 (97.8)	81 (100)	<0.01
Radial route	47 (78.3)	378 (77.3)	345 (77.2)	62 (76.5)	0.996
Coronary dissection	0 (0.0)	8 (1.6)	4 (0.9)	0 (0.0)	0.393
Coronary thrombosis	0 (0.0)	4 (0.8)	2 (0.4)	0 (0.0)	0.685
Access site complications	4 (6.7)	21 (4.3)	14 (3.1)	3 (3.7)	0.544

CTO: Chronic total occlusion; DES: Drug-eluting stent; IABP: Intra-aortic balloon pump; IVUS: Intravascular ultrasound; TIMI: Thrombolysis in myocardial infarction.

Table 3: Major outcomes

Variables	BMI (%)				P
	(≤20 kg/m ²) (n = 60)	(20.0–24.9 kg/m ²) (n = 489)	(25.0–29.9 kg/m ²) (n = 447)	(≥30.0 kg/m ²) (n = 81)	
In-hospital outcomes					
MACE	1 (1.7)	13 (2.7)	17 (3.8)	3 (3.7)	0.677
Death	0 (0.0)	5 (1.0)	2 (0.4)	0 (0.0)	0.521
MI	1 (1.7)	8 (1.6)	13 (2.9)	3 (3.7)	0.477
TVR	0 (0.0)	3 (0.6)	2 (0.4)	0 (0.0)	0.826
Major bleeding	2 (3.3)	13 (2.7)	6 (1.3)	2 (2.5)	0.486
1-year outcomes					
Death	2 (3.3)	9 (1.8)	8 (1.8)	0 (0.0)	0.508

MACE: Major adverse cardiovascular events; MI: Myocardial infarction; TVR: Target vessel revascularization; BMI: Body mass index.

obese patient was significantly lower than normal weight or underweight patient at hospital, and at 6 or 12 month follow-up. However, in the multivariate analysis, only older age (not the increased BMI value) was the strongest predictor of mortality at 1 year. Elderly patients are more likely to have normal weight or underweight while younger patients are more likely to find “fatter.” Adverse cardiovascular events occurred more in older patients than in younger ones regardless of the treatment.^[12] So the better outcomes in patients with high value of BMIs might attribute to the benefit of their young age. We also observed that the medication prescriptions varied in patients with different BMIs. Diercks *et al.* reported that obese patients with acute coronary syndrome were more likely to receive aggressive medication than normal weight and underweight patients,

and adverse cardiovascular events also occurred less in those patients.^[13] Steinberg *et al.* reported a lineal association between increased use of guideline-based medications and increased value of BMIs in 130,139 CAD patients.^[14] So the “obese paradox” could be mistakenly interpreted by confounders, such as age or medications.

In the present study, normal weight (45.4%) and overweight (41.5%) patients accounted the majority parts of all the patients. Obese and underweight patients only accounted about 10% of all the patients. This composition in the elderly patients in China is different from the younger patients and western patients. In the United States or Europe, approximately 70% of the patients are overweight or obese, whereas only 30% of the patients had normal or lower

Table 4: Logistic regression analysis for the predictors of in-hospital MACE

Variables	B	SE	Wald	HR (95% CI)	P
Age	0.052	0.067	0.603	1.054 (0.923 – 1.203)	0.438
Sex (female vs. male)	0.654	0.368	3.151	1.923 (0.934 – 3.958)	0.076
Hypertension	-0.751	0.444	1.652	0.565 (0.237 – 1.349)	0.199
STEMI	0.620	0.452	1.878	1.859 (0.766 – 4.513)	0.171
LVEF	-0.016	0.023	0.459	0.984 (0.941 – 1.030)	0.498
Anemia	-0.930	0.632	2.167	0.395 (0.114 – 1.361)	0.141
Renal dysfunction	-0.588	0.430	1.864	0.556 (0.239 – 1.292)	0.172
DES	-0.815	0.631	1.670	0.443 (0.129 – 1.524)	0.196
Final TIMI 3 flow	-1.491	0.738	4.082	0.225 (0.053 – 0.956)	0.225
Left main disease	-0.051	0.630	0.007	0.950 (0.276 – 3.268)	0.935
BMI (underweight vs. normal weight)	-0.678	1.111	0.372	0.508 (0.058 – 4.483)	0.542
BMI (overweight vs. normal weight)	0.349	0.391	0.795	1.418 (0.658 – 3.053)	0.373
BMI (obese vs. normal weight)	0.346	0.668	0.269	1.414 (0.382 – 5.233)	0.604

BMI: Body mass index; DES: Drug-eluting stent; LVEF: Left ventricular ejection fraction; STEMI: ST-segment elevation myocardial infarction; TIMI: Thrombolysis in myocardial infarction; SE: Standard error; CI: Confidence interval; HR: Hazard ratio; MACE: Major adverse cardiovascular events.

BMI. [15] A number of risk factors did not increase as BMI raised. [16] Nikolsky *et al.* [10] recently evaluated the association between BMI and clinical outcomes in patients undergoing primary PCI, and found the better outcomes in obese patients attributed to their better renal function. The present study showed that the rates of renal dysfunction (glomerular filtration rate <60 ml/min) in underweight, normal weight, overweight, and obese patients were 86.7%, 68.3%, 43.8% and 30.9%, respectively, which confirmed previous findings. Meanwhile, a higher rate of anemia in patients with a lower value of BMI was also observed in the elderly patients. So the obesity paradox indicating the protective status of BMI may not be precise as it could also be confounded by patients' comorbidities.

Since the association between BMI and the new developed cardiovascular events are not agreed in different studies. [17] Researchers assumed that BMI may not be an appropriate predictor for MACE. The deficiency of BMI is the inability of it in discriminating between an excess weight in body fat and in lean mass. Increased weight as body fat was harmful but increased lean mass was associated with better fitness and exercise capacity. [18] Thus, BMI may not be a reasonable surrogate to represent adiposity. [19] Romero-Corral *et al.* showed that when BMI >25 kg/m², it showed poor specificity to detect excess body fat. [20] On the contrary, waist circumference and waist-hip-ratio were more representative of lipid level, also sensitive and accurate in predicting short-and long-term cardiovascular events. [21] Underweight patients are usually at higher risk of heart failure and mortality, [6] and we assumed it attributed to the low value of lean mass, which still needed to be confirmed.

Several limitations have to be taken into consideration. First, this study only used BMI as surrogate for the lipid level, while waist circumference and waist-hip-ratio have shown to be more accurate in predicting MACE. However, due to the retrospective design, the capacity of those surrogates could not be compared. Second, the outcomes of extremely obese

patients (BMI > 35 kg/m²) were not separately analyzed due to the limited number of the patients. As data from the National Cardiovascular Data Registry in the US showed that extremely obese patients had higher in-hospital mortality, [22] we believe that it has the same trend in elderly patients. Third, the sample size was still limited, which restricted the statistical power in discriminating the differences. Finally, the secondary endpoint was defined as the incidence rate of 1 year death. However, changes in BMI after patients' discharge were not measured. Previous study suggested that patients with higher BMIs were more aware of CAD, and more willing to adapt lifestyle and taking drugs. [23] This could affect the comparison of 1 year outcomes between the groups.

Elderly patients of underweight, normal weight, overweight and obese had similar in-hospital MACE after PCI. The "obesity paradox" should be interpreted with caution, thus BMI may not be a sensitive predictor of cardiovascular events in elderly patients.

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