Association of Body Mass Index With Major Cardiovascular Events and With Mortality After Percutaneous Coronary Intervention

Duk-Woo Park, MD; Young-Hak Kim, MD; Sung-Cheol Yun, PhD; Jung-Min Ahn, MD; Jong-Young Lee, MD; Won-Jang Kim, MD; Soo-Jin Kang, MD; Seung-Whan Lee, MD; Cheol Whan Lee, MD; Seong-Wook Park, MD; Seung-Jung Park, MD

Background—Conflicting data exist regarding the relation between body mass index (BMI) and cardiovascular events and mortality after percutaneous coronary intervention.

Methods and Results—We performed pooled analyses to evaluate the association between BMI (weight in kilograms divided by the square of the height in meters) and the risks of major cardiovascular events (defined as death from cardiovascular causes, nonfatal myocardial infarction, stent thrombosis, or stroke) and death among 23 181 patients from 11 prospective percutaneous coronary intervention studies. Overall, mean (±SD) BMI was 24.9±3.0. During follow-up (median, 2.1 years), 2381 patients had a major cardiovascular event, and 1004 patients died. After adjusting covariates, there was an inverse relationship between BMI and adverse outcomes. With a BMI of 22.5 to 24.9 as the reference category, the risk of major cardiovascular events was elevated among patients with a lower BMI (by a factor of 1.52 for a BMI <18.5; 1.05 for a BMI of 18.5–19.9; 1.03 for a BMI of 20.0–22.4); by contrast, the risk declined among patients with a higher BMI (by a factor of 0.97 for a BMI of 25.0–27.4; 0.97 for a BMI of 27.5–29.9; and 0.78 for a BMI of ≥30.0). In general, the hazard ratios for deaths were similar.

Conclusions—Among patients undergoing percutaneous coronary intervention, a low BMI was associated with increased risks of major cardiovascular events and death. However, there were no excess risks of these events associated with a high BMI. **(*Circ Cardiovasc Interv*. 2013;6:146-153.)**

Key Words: body mass index ■ outcomes ■ percutaneous coronary intervention

Overweight or obesity are increasing in epidemic prevalence throughout the world.[1] Among the general population, it is well established that overweight or obese people with a high body mass index (BMI; weight in kilograms divided by the square of the height in meters) have a higher risk of cardiovascular disease and death from heart disease or stroke.[2–5]

Despite known adverse effects of overweight or obesity as risk factor for coronary artery disease (CAD) and cardiovascular mortality, once CAD has been established, the close relation of obesity with total or cardiovascular mortality and cardiovascular events is unclear.[6] Moreover, several studies have suggested that overweight or obese groups seem to have a better prognosis compared with normal or lower BMI groups in patients with established CAD and heart failure,[6–8] a phenomenon termed as the obesity paradox.

BMI is associated with atherosclerotic burden of CAD, plaque vulnerability, and adjunct drug responses affecting clinical outcomes, especially among patients with documented CAD undergoing percutaneous coronary intervention (PCI).[9,10] However, conflicting data exist regarding the relation between BMI and the risks of cardiovascular events and mortality after PCI.[11–16] Pooled analyses provide the opportunity to address these issues carefully in a large dataset with the use of a standard analytic approach across studies, providing a reliable estimate of the link between BMI and clinical outcomes. We examined, therefore, the relation between BMI and risks of major cardiovascular events and mortality after PCI using patient-level data from 11 prospective clinical studies, predominantly designed to study PCI outcomes.

Methods

Study Population and Procedures

For the present analysis, databases from 11 independent, prospective clinical studies (8 randomized clinical trials and 3 registries) were pooled to provide a patient-level data analysis. All studies were conducted in South Korea and performed in Asian population. The study designs and results of individual studies have been published previously.[17–27] Among all studies included, the baseline BMI was calculated with the use of weight and height measured at enrollment and data on adverse cardiovascular events and mortality were prospectively collected. These studies contain information on

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From the Departments of Cardiology, Asan Medical Center, (D.-W.P., Y.-H.K., J.-M.A., J.-Y.L., W.-J.K., S.-J.K., S.-W.L., C.W.L., S.-W.P., S.-J.P.), and Division of Biostatistics, Center for Medical Research and Information (S.-C.Y.), University of Ulsan College of Medicine, Seoul, Korea.

Correspondence to Dr Seung-Jung Park, Department of Cardiology, University of Ulsan College of Medicine, Asan Medical Center, 388-1 Poongnap-dong, Songpa-gu, Seoul 138–736, Korea. E-mail sjpark@amc.seoul.kr

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WHAT IS KNOWN

- A high body mass index is associated with a higher risk of cardiovascular disease and mortality.
- Once coronary artery disease has been established, the obesity paradox has been reported with overweight or obese patients having a better prognosis compared with normal or lower body mass index groups.
- The relationship between body mass index and adverse cardiovascular events after percutaneous coronary intervention is unknown.

WHAT THE STUDY ADDS

- This study supports the inverse relationship of body mass index with major cardiovascular events and all-cause mortality after percutaneous coronary intervention.
- The mechanism for the obesity paradox is not clear and further studies are needed.

patient demographics, cardiac or coexisting risk factors, clinical manifestations, left ventricular function, angiographic and procedural characteristics, and in-hospital and follow-up outcomes. Relevant data were prospectively collected using a dedicated, electronic case report form by specialized personnel at each center, and the Internet-based system provides each center with immediate and continuous feedback on processes and quality-of-care measures. All databases are maintained at the Clinical Research Center of Asan Medical Center, Seoul, Korea, and therefore a convenience sample of 11 clinical studies was available in existing merged data sets. As each study enrollment criteria, patients with cardiogenic shock, terminal illness, or malignancy at baseline were excluded. All of these studies were approved by the local institutional review board, and all patients provided written informed consent.

Among studies, PCI was performed according to current standard guidelines. Antiplatelet therapy and periprocedural anticoagulation were administered according to standard regimens. All patients were prescribed aspirin (loading dose, 200 mg) plus clopidogrel (loading dose, 300 or 600 mg) before or during PCI. After the procedure, aspirin (100–200 mg per day) was continued indefinitely, patients treated with drug-eluting stents were prescribed clopidogrel (75 mg/d) for at least 12 months, and patients treated with bare-metal stents were prescribed clopidogrel for at least 1 month.

Outcomes, Definitions, and Follow-Up

Two outcomes were assessed for inclusion in the current analysis: major cardiovascular events and death from any cause. Major cardiovascular event was defined as a composite of death from cardiovascular causes, nonfatal myocardial infarction (MI), stent thrombosis, or stroke. All deaths were considered to be a result of cardiovascular causes unless an unequivocal noncardiovascular cause could be established. The diagnosis of MI was based on the universal definition of MI.[28] Stent thrombosis was defined as the definite or probable events, according to the Academic Research Consortium criteria.[29] Stroke, as detected by the occurrence of a new neurological deficit, was confirmed by a neurologist and on imaging. For each study, an independent clinical events committee adjudicated all clinical end points of the study, and all outcomes of interest were confirmed by source documentation collected at each hospital.

Among studies, clinical follow-up was performed via office visit or telephone contact at 1, 6, and 12 months and then every 6 or 12 months, thereafter, according to the study protocol. All other possible information derived from outpatient visits, hospital readmission, or by the referring physician, patients, or relatives were entered into the dedicated database. For validation of complete follow-up data, information on vital status was obtained from the National Population Registry of the Korea National Statistical Office with the use of a unique personal identification number.

Statistical Analysis

Continuous variables are described as mean and SD, and dichotomous variables are described as counts and percentages. Baseline clinical, angiographic, and procedural characteristics were described for each group according to BMI categories.

The association between BMI, and the risks of major cardiovascular events and death was analyzed using Cox proportional-hazards regression models, with a categorical representation of BMI as the predictor variable. Based on cutoff points in previous studies,[3,4] analyses of BMI used the following predefined categories: <18.5, 18.5 to 19.9, 20.0 to 22.4, 22.5 to 24.9, 25.0 to 27.4, 27.5 to 29.9, and ≥30.0. Using the BMI range of 22.5 to 24.9 as the referent category, we estimated hazard ratios and 95% confidence interval for the other BMI ranges. To account for between-study heterogeneity, *P* value and confidence interval were calculated using robust standard errors based on sandwich estimators.[30]

We planned to accomplish this first by unadjusted analysis and then using a multivariable model to adjust potentially confounding factors, which were clinically relevant or were significantly associated with outcomes ($P<0.05$) (*P* study, age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking status, previous MI, previous stroke, peripheral vascular disease, renal dysfunction, acute coronary syndrome, ejection fraction, multivessel disease, left main disease, bifurcation disease, long disease, stent type, and number of stents). The assumptions of the proportional hazards were statistically assessed on the basis of Schoenfeld residuals and graphically using log–log plots. No significant deviations from the assumptions were noted. Cumulative probability and survival curves according to BMI categories were constructed from Kaplan–Meier estimates and compared using log-rank test. Additionally, to minimize the influence of possible reverse causation of low BMI and to assess the baseline BMI as a risk factor for nonprocedure cardiovascular events, sensitivity analyses were conducted excluding adverse events that occurred at <7 days after the procedure. All reported *P* values are 2-sided, and *P* values of <0.05 were considered to indicate statistical significance. SAS software, version 9.1 (SAS Institute, Cary, NC) was used for all statistical analysis.

Results

Study Population and Baseline Characteristics

A total of 23 604 subjects were pooled from 11 PCI clinical studies. Major clinical and demographic features of the combined population and that of each study are provided in Table 1. All the population had a mean age of 62 years, 70% of patients were men, 30% had diabetes mellitus, and 58% presented with acute coronary syndromes. For the devices of PCI, 82% patients received implantation of drug-eluting stents. Follow-up among studies varied from 1 to 5 years.

After exclusion of 423 (1.8%) subjects without baseline BMI data in merged population, 23 181 were included in the final analysis evaluating the association between BMI and outcomes. Overall, the mean (±SD) BMI for the study population was 24.9±3.0. Detailed data on baseline, angiographic, and procedural characteristics according to the BMI categories are shown in Table 2. With increasing BMI, patients were younger, but the prevalence of diabetes mellitus, hypertension, and hyperlipidemia, and history of MI and PCI increased. Previous congestive heart failure, renal dysfunction, and left main disease were slightly more common in the lower BMI categories.

Table 1. Major Baseline Characteristics of Each Study

Variable	Overall	ZEST[17]	ZEST-AMI[18]	LONG-DES II[19]	LONG-DES III[20]	LONG-DES IV[21]	ESSENCE-Diabetes[22]	DECLARE-LONG II[23]	REAL-LATE[24]	ASAN-PCI[25]	ASAN-VERIFY[26]	IRIS-DES[27]
No. of subjects	23 604	2645	328	500	450	500	300	499	1625	7221	3370	6166
Age, y	62 (10)	62 (10)	60 (11)	61 (9)	63 (10)	63 (10)	63 (8)	62 (9)	63 (10)	60 (10)	62 (10)	63.6 (11)
BMI, kg/m^2	25 (3)	25 (3)	24 (3)	25 (3)	25 (3)	25 (3)	25 (3)	25 (3)	25 (3)	25 (3)	25 (3)	24.7 (3)
Men	16 424 (70)	1759 (67)	270 (82)	321 (64)	314 (70)	365 (73)	177 (59)	353 (71)	1156 (71)	5132 (71)	2446 (73)	4131 (67)
Diabetes mellitus	6995 (30)	760 (29)	85 (26)	166 (33)	133 (30)	144 (29)	300 (100)	176 (35)	426 (26)	1700 (24)	956 (28)	2149 (35)
Hypertension	13 101 (56)	1609 (61)	153 (47)	275 (55)	265 (59)	285 (57)	212 (71)	307 (62)	917 (56)	3273 (45)	1958 (58)	3847 (62)
Hyperlipidemia	9752 (41)	1363 (52)	148 (45)	146 (29)	255 (57)	277 (55)	115 (38)	218 (44)	609 (38)	2228 (31)	1996 (59)	2397 (39)
Previous MI	2249 (10)	110 (4)	5 (2)	12 (2)	17 (4)	8 (2)	5 (2)	18 (4)	63 (4)	1426 (20)	201 (6)	384 (6)
ACS	13 656 (58)	1463 (55)	328 (100)	273 (55)	190 (42)	180 (36)	125 (42)	263 (53)	1102 (68)	4579 (64)	1616 (48)	3537 (57)
Follow-up (median, month)	25	25	13	13	12	13	12	12	39	59	25	16

Data are shown as mean (SD) for continuous variables and absolute number (percentage) for dichotomous variables, unless otherwise stated. ACS indicates acute coronary syndrome; ASAN-PCI, Asan Medical Center-Percutaneous Coronary Intervention Registry; ASAN-VERIFY, Asan Medical Center-VerifyNow Registry; BMI, body mass index; DECLARE-LONG, Drug-Eluting Stenting Followed by Cilostazol Treatment Reduces Late Restenosis in Patients with Long Coronary Lesions; ESSENCE-DM, Randomized Comparison of Everolimus-Eluting Stent Versus Sirolimus-Eluting Stent Implantation for De Novo Coronary Artery Disease in Patients With Diabetes Mellitus; IRIS-DES, Interventional Cardiology Research In-cooperation Society-Drug-Eluting Stents Registry; LONG-DES, Percutaneous Treatment of Long Native Coronary Lesions With Drug-Eluting Stent; MI, myocardial infarction; REAL-LATE, Correlation of Clopidogrel Therapy Discontinuation in Real-World Patients Treated with Drug-Eluting Stent Implantation and Late Coronary Arterial Thrombotic Events; ZEST, Comparison of the Efficacy and Safety of Zotarolimus-Eluting Stent with Sirolimus-Eluting and Paclitaxel-Eluting Stent for Coronary Lesions; and ZEST-AMI, Comparison of the efficacy and safety of zotarolimus-, sirolimus-, and paclitaxel-eluting stents in patients with ST-elevation myocardial infarction.

Table 2. Baseline Characteristics of Patients According to Categories of Body Mass Index

	Body Mass Index						
Variable	<18.5	18.5–19.9	20.0–22.4	22.5–24.9	25.0–27.4	27.5–29.9	≥30.0
No. of patients	339	652	3670	7771	6703	2933	1113
Demographics							
Age (y)	68±12	66±11	64±10	62±10	61±10	60±10	59±11
Sex							
Men	196 (58)	445 (68)	2549 (70)	5572 (72)	4794 (72)	1965 (67)	641 (58)
Women	143 (42)	207 (32)	1121 (31)	2199 (28)	1909 (29)	968 (33)	472 (42)
Clinical characteristics or coexisting conditions							
Diabetes mellitus	72 (21)	149 (23)	1030 (28)	2310 (30)	1980 (30)	897 (31)	424 (38)
Hypertension	148 (44)	288 (44)	1778 (48)	4119 (53)	3886 (58)	1861 (64)	788 (71)
Current smoker	114 (34)	214 (33)	1219 (33)	2357 (30)	1976 (30)	856 (29)	325 (29)
Hyperlipidemia	83 (25)	228 (35)	1324 (36)	3174 (41)	2921 (44)	1309 (45)	567 (51)
Previous MI	17 (5)	57 (9)	331 (9)	718 (9)	702 (11)	300 (10)	106 (10)
Previous PCI	18 (5)	65 (10)	406 (11)	933 (12)	924 (14)	358 (12)	152 (14)
Previous CABG	4 (1)	11 (2)	89 (2)	127 (2)	116 (2)	44 (2)	18 (2)
Previous CHF	18 (5)	19 (3)	55 (2)	88 (1)	68 (1)	26 (1)	18 (2)
Previous stroke	16 (5)	27 (4)	218 (6)	464 (6)	371 (6)	157 (5)	68 (6)
Peripheral vascular disease	4 (1)	14 (2)	67 (2)	132 (2)	111 (2)	38 (1)	23 (2)
Chronic lung disease	19 (6)	20 (3)	82 (2)	136 (2)	92 (1)	41 (1)	21 (2)
Renal dysfunction	14 (4)	15 (2)	111 (3)	160 (2)	135 (2)	42 (1)	21 (2)
Acute coronary syndrome	234 (69)	433 (66)	2332 (64)	4483 (58)	3714 (55)	1544 (53)	636 (57)
Ejection fraction, %	56±12	57±11	58±10	59±9	60±9	60±8	59±8
Angiographic and procedural characteristics, n (%)							
Multivessel disease	174 (51)	314 (48)	1878 (51)	3896 (50)	3464 (52)	1442 (49)	578 (52)
Left anterior descending artery disease	210 (62)	386 (59)	2223 (61)	4705 (61)	4045 (60)	1741 (59)	657 (59)
Left main disease	28 (8)	48 (7)	263 (7)	493 (6)	404 (6)	145 (5)	47 (4)
Bifurcation lesion	80 (24)	132 (20)	854 (23)	1815 (23)	1574 (24)	651 (22)	235 (21)
Long lesion (>20 mm)	216 (64)	427 (66)	2486 (68)	5279 (68)	4636 (69)	2026 (69)	759 (68)
Total occlusion	47 (14)	68 (10)	389 (11)	882 (11)	787 (12)	345 (12)	137 (12)
Stent type							
Bare-metal stents	64 (19)	131 (20)	670 (18)	1390 (18)	1214 (18)	545 (19)	210 (19)
Drug-eluting stents	275 (81)	521 (80)	3000 (82)	6381 (82)	5489 (82)	2388 (81)	903 (81)
No. of stents	1.7±0.9	1.7±1.0	1.7±1.0	1.8±1.0	1.8±1.1	1.7±1.0	1.7±1.0
Total stent length (mm)	39±26	39±27	41±27	42±27	42±28	41±27	42±28

Data are shown as mean (SD) for continuous variables and absolute numbers (percentage) for dichotomous variables. CABG indicates coronary artery bypass grafting; CHF, congestive heart failure; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

Association Between BMI and the Risks of Major Cardiovascular Events and Mortality

The median follow-up was 2.1 years (25th and 75th percentiles; 1.2 and 3.9 years). During follow-up, a total of 2381 major cardiovascular events (392 cardiovascular deaths, 1954 MI, 181 stent thrombosis, and 167 strokes) were reported and 1004 total deaths occurred. Cumulative incidence curves of major cardiovascular events and all-cause mortality are presented in Figure 1. Overall, the rates of major cardiovascular events and mortality have significantly increased with decreasing BMI categories. The cumulative incidence of major cardiovascular events over time showed an initial steep rise, followed by a continuous separation of the curves, with a significantly higher rate of events in a low-BMI group. The incidence of mortality did continuously diverge over time, with a higher rate in a low-BMI group and a lower rate in a high-BMI group.

In unadjusted Cox regression analysis, as compared with the reference range of 22.5 to 24.9, the hazard ratios for the risk of major cardiovascular event increased with progressively lower levels of BMI, whereas the hazard ratios decreased with progressively higher levels of BMI (Table 3). A similar association was also seen between BMI and the risk of all-cause mortality.

To determine the independent association between BMI and clinical outcomes, we performed a multivariable Cox regression analysis after adjusting for a wide range of confounding

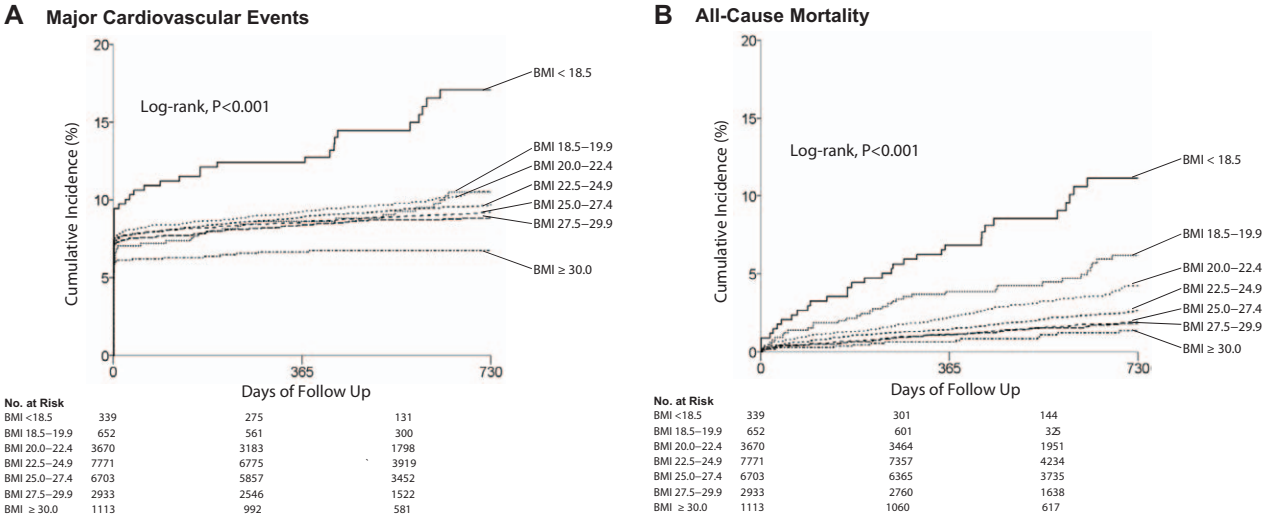

Figure 1. Kaplan–Meier curves of the cumulative probability of major cardiovascular events and death according to body mass index categories. Major cardiovascular event was defined as a composite of death from cardiovascular causes, nonfatal myocardial infarction, stent thrombosis, or stroke. *P* values were calculated with the use of the log-rank test.

factors. Even after multivariable adjustment, the inverse relationship of BMI with major cardiovascular events and with all-cause mortality were maintained (Table 4 and Figure 2). As compared with the reference of 22.5 to 24.9, the risks of major cardiovascular events were higher among patients with a lower BMI (by a factor of 1.52 for a BMI <18.5; 1.05 for a BMI of 18.5–19.9; 1.03 for a BMI of 20.0–22.4), but the risks of these events were lower among patients with a higher BMI (by a factor of 0.97 for a BMI of 25.0–27.4; 0.97 for a BMI of 27.5–29.9; and 0.78 for a BMI of ≥30.0). The adjusted hazard ratios for all-cause mortality were also similar.

In sensitivity analyses excluding events at <7 days, overall findings suggesting the inverse relationship of BMI with major cardiovascular events and all-cause mortality were consistent (Table 5).

Discussion

This is the largest study to evaluate systematically the relationship of BMI with major cardiovascular events and total mortality after PCI using individual patient-level data from several prospective PCI clinical studies. As a result, the study shows that after adjusting for potential confounding factors, a low BMI is significantly associated with increased risks of major cardiovascular events and all-cause mortality. The excess risks for these outcomes associated with a high BMI, however, were not observed.

Obesity involves hyperinsulinemia and insulin resistance, enhances free fatty acid turnover, increases sympathetic tone activity, induces platelet and clotting system activation, and causes chronic low-grade inflammation, all of which increase the risks for developing CAD and adverse cardiovascular events.[31] And also, a greater BMI was significantly associated with poorer response of clopidogrel and aspirin, which are mandatory adjunct drugs for PCI.[10,32] Contrary to these pathophysiology mechanisms induced by obesity, several studies suggested that overweight or obese patients have better PCI outcomes than do normal or leaner patients, supporting protective effect of obesity, known as the obesity paradox.[11–14] These studies were, however, hampered by limited

Table 3. Crude Association Between Body Mass Index and Risk of Major Cardiovascular Events and All-Cause Mortality*

	Body Mass Index						
Outcome	<18.5	18.5–19.9	20.0–22.4	22.5–24.9	25.0–27.4	27.5–29.9	≥30.0
No. of patients	339	652	3670	7771	6703	2933	1113
Major cardiovascular events							
Total number of events	60	77	412	797	665	281	89
Cumulative rate at 2 y†	17.1	10.9	10.5	9.7	9.2	8.9	6.8
Hazard ratio (95% CI)	1.82 (1.38–2.39)	1.16 (0.77–1.74)	1.10 (0.98–1.24)	Reference	0.96 (0.90–1.03)	0.93 (0.84–1.02)	0.77 (0.63–0.95)
All-cause mortality							
Total number of events	43	69	225	321	221	87	38
Cumulative rate at 2 y†	11.1	6.2	4.2	2.7	1.9	1.8	1.4
Hazard ratio (95% CI)	3.70 (3.30–4.14)	2.72 (2.24–3.32)	1.52 (1.36–1.69)	Reference	0.78 (0.72–0.84)	0.69 (0.62–0.78)	0.81 (0.58–1.12)

Major cardiovascular events were defined as a composite of cardiovascular death, nonfatal myocardial infarction, stent thrombosis, or stroke. CI indicates confidence interval.
*The hazard ratios represent the effect per category of body mass index relative to the reference category (22.5–24.9).
†Cumulative event rates are derived from Kaplan–Meier estimates.

Table 4. Adjusted Hazard Ratios for Major Cardiovascular Events and All-Cause Mortality, According to Body Mass Index*

	Body Mass Index						
Outcome	<18.5	18.5–19.9	20.0–22.4	22.5–24.9	25.0–27.4	27.5–29.9	≥30.0
Major cardiovascular events							
Hazard ratio (95% CI)	1.52 (1.16–1.99)	1.05 (0.83–1.33)	1.03 (0.92–1.17)	Reference	0.97 (0.87–1.07)	0.97 (0.85–1.11)	0.78 (0.62–0.98)
All-cause mortality							
Hazard ratio (95% CI)	2.93 (2.63–3.27)	2.44 (1.95–3.05)	1.39 (1.24–1.56)	Reference	0.79 (0.72–0.87)	0.76 (0.67–0.85)	0.79 (0.61–1.04)

Major cardiovascular events were defined as a composite of cardiovascular death, nonfatal myocardial infarction, stent thrombosis, or stroke. CI indicates confidence interval.

*The hazard ratios represent the effect per category of body mass index relative to the reference category (22.5–24.9). This model were adjusted for study, age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking status, previous myocardial infarction, previous stroke, peripheral vascular disease, chronic lung disease, renal dysfunction, acute coronary syndrome, ejection fraction, multivessel disease, left main disease, bifurcation disease, long disease, stent type, and number of stents.

number of patients, a relatively short follow-up period, or a retrospective observational study design. A recent large-sized meta-analysis, including >250 000 patients with documented CAD, showed that a low-BMI group had the highest all-cause and cardiovascular mortality, whereas better survival was observed in higher BMI groups.[6] Especially, these trends were mostly prominent in patients who received PCI than in those who underwent coronary artery bypass grafting or had a history of MI. Consistent with these findings, our patient-level pooled analysis of PCI patients also showed that there was an inverse relationship between BMI and mortality after PCI. Apart from the association between BMI and total mortality, an inverse relationship of BMI with major cardiovascular events, which are more specific measure of PCI outcomes, was also demonstrated.

Our study does not fully clarify the exact mechanism of an absence of association or an inverse association of BMI and clinical outcomes after PCI. However, there could be some possible explanations for this phenomenon. First, the discriminatory ability of BMI is relatively limited to make a clear distinction between body fat, which have negative impact on prognosis, and lean body mass, which is associated with better prognosis in patients with cardiovascular disease.[6] Therefore, a high BMI does not solely imply excess body adiposity, and may reflect a preserved or increased lean body mass. It would be a plausible explanation of the better outcomes in overweight or obese patients. Second, higher BMI groups were associated with a higher prevalence of coexisting cardiovascular conditions, such as diabetes mellitus, hypertension, hyperlipidemia, and history of MI and PCI. Therefore, there is the possibility that patients with a high BMI were on more aggressive secondary preventive drug therapies rather than those with a normal or low BMI. Previous study demonstrated that overweight or obese patients were more likely to be adherent to guideline-recommended medical treatment.[13] Third, although our analysis excluded patients with terminal illness or cancer to minimize the influence of possible reverse causation, other unmeasured factors that influence a low BMI, presumably, remain to be identified. Lastly, further studies are warranted to address the novel suggested mechanisms; a higher BMI is related to larger vessels treated with larger stent diameter[33] or to the cardio-protective effect of adipokines.[34,35]

The current analysis includes a large number of patients specifically treated with PCI in which contemporary devices and techniques were used. From the clinical standpoint, an important issue that deserves comment is that most devices used in PCI have been manufactured targeting patients with the average BMI. Although exact mechanism linking low BMI

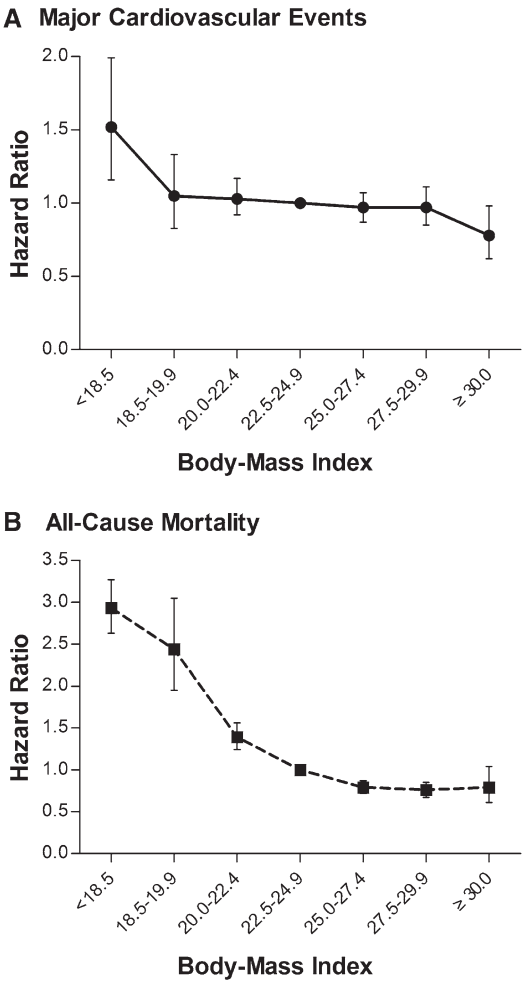

Figure 2. Adjusted hazard ratios for major cardiovascular event and death according to body mass index categories. Major cardiovascular event was defined as a composite of death from cardiovascular causes, nonfatal myocardial infarction, stent thrombosis, or stroke. The reference category was a body mass index of 22.5 to 24.9. **A** and **B** have different scales for hazard ratios. *Hazard ratios were adjusted for study, age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking status, previous myocardial infarction, previous stroke, peripheral vascular disease, chronic lung disease, renal dysfunction, acute coronary syndrome, ejection fraction, multivessel disease, left main disease, bifurcation disease, long disease, stent type, and number of stents.

Table 5. Crude and Adjusted Hazard Ratios for Clinical Outcomes Among Patients Who Did Not Experience Events or Survived 7 Days, According to Body Mass Index*

	Body Mass Index						
Outcome	<18.5	18.5–19.9	20.0–22.4	22.5–24.9	25.0–27.4	27.5–29.9	≥30.0
Major cardiovascular events							
Crude hazard ratio (95% CI)	3.36 (1.93–5.86)	2.06 (1.19–3.56)	1.33 (1.11–1.61)	Reference	0.83 (0.64–1.09)	0.78 (0.63–0.96)	0.64 (0.41–1.01)
Adjusted hazard ratio† (95% CI)	2.32 (1.58–3.43)	1.63 (1.16–2.30)	1.14 (0.92–1.40)	Reference	0.86 (0.71–1.05)	0.88 (0.67–1.14)	0.70 (0.45–1.07)
All-cause mortality							
Crude hazard ratio (95% CI)	3.70 (3.20–4.27)	2.86 (2.36–3.47)	1.53 (1.37–1.71)	Reference	0.80 (0.74–0.86)	0.69 (0.62–0.77)	0.83 (0.58–1.19)
Adjusted hazard ratio† (95% CI)	2.98 (2.57–3.45)	2.60 (2.10–3.21)	1.41 (1.23–1.60)	Reference	0.81 (0.73–0.89)	0.75 (0.67–0.85)	0.82 (0.60–1.11)

Major cardiovascular events were defined as a composite of cardiovascular death, nonfatal myocardial infarction, stent thrombosis, or stroke. CI indicates confidence interval.

*The hazard ratios represent the effect per category of body mass index relative to the reference category (22.5–24.9).

†This model were adjusted for study, age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking status, previous myocardial infarction, previous stroke, peripheral vascular disease, chronic lung disease, renal dysfunction, acute coronary syndrome, ejection fraction, multivessel disease, left main disease, bifurcation disease, long disease, stent type, and number of stents.

with poorer PCI outcomes is still unclear, future studies are needed to determine whether patients with extreme small BMI may specifically need tailored PCI devices or not.

Potential limitations of the current study warrant discussion. First, the database merged several clinical studies and interstudy variability may exist that could have influenced results in the pooled patient population. Second, although we adjusted possible confounding factors, unmeasured confounders associated with BMI still exist. Third, we did not capture the measurements of body composition or body fat distribution (ie, waist circumference or waist-to-hip ratio regarding central obesity), which are suggested to be more closely related with adiposity-related outcomes. Fourth, as this analysis was performed in Asian population, it is uncertain whether this finding can be directly applied to other ethnic groups. Compared with Western population,[15] the proportion of severe or extreme obese patients was too small in our population; 0.3% (59) patients with class II obese (35 kg/m^2 ≤ BMI <40 kg/m^2) and 0.02% (4) patients with class III obese (BMI ≥40 kg/m^2). In addition, it has been suggested that the relationship between BMI and mortality may differ across racial and ethnic groups.[36] Fifth, we did not perform serial measurements of BMI during follow-up. There has been report suggesting a relation between weight change and cardiovascular events.[37] Finally, longer term follow-up are needed to evaluate very long-term effect of BMI on outcomes after PCI.

Conclusions

In this large, pooled population of CAD patients receiving PCI in contemporary practice, patients with a low BMI had a higher risk of major cardiovascular events and death than patients with a normal BMI. However, no elevated risk of major cardiovascular events and mortality were seen in high-BMI groups. Before presumably drawing a conclusion that obesity is protective or harmless for cardiovascular risk among patients receiving PCI, more reliable surrogate markers differentiating excess body fat and muscle mass are needed for future risk stratification in such population, and additional clinical studies are needed to test different methods reflecting adiposity.

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Disclosures

None.

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