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Interventional Cardiology

The Impact of Obesity on the Short-Term and Long-Term Outcomes After Percutaneous Coronary Intervention: The Obesity Paradox?

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OBJECTIVES The purpose of this study was to assess the impact of body mass index (BMI) on the short- and long-term outcomes after percutaneous coronary intervention (PCI).

BACKGROUND Obesity is associated with advanced coronary artery disease (CAD). However, the relation between BMI and outcome after PCI remains controversial.

METHODS We studied 9,633 consecutive patients who underwent PCI between January 1994 and December 1999. Patients were divided into three groups according to BMI: normal, BMI between 18.5 and 24.9 (n = 1,923); overweight, BMI between 25 and 30 (n = 4,813); and obese, BMI >30 (n = 2,897).

RESULTS Obese patients were significantly younger and had consistently worse baseline clinical characteristics than normal or overweight patients, with a higher incidence of hypertension, diabetes, hypercholesterolemia and smoking history ($p < 0.0001$). Despite similar angiographic success rates among the three groups, normal BMI patients had a higher incidence of major in-hospital complications, including cardiac death ($p = 0.001$). At one-year follow-up, overall mortality rates were significantly higher for normal BMI patients compared with overweight or obese patients ($p < 0.0001$). Myocardial infarction and revascularization rates did not differ among the three groups. By multivariate Cox regression analysis, diabetes, hypertension, age, BMI and left ventricular function were independent predictors of long-term mortality.

CONCLUSIONS In patients with known CAD who undergo PCI, very lean patients (BMI <18.5) and those with BMI within the normal range are at the highest risk for in-hospital complications and cardiac death and for increased one-year mortality. (J Am Coll Cardiol 2002;39:578–84)

Excess body fat is an increasingly prevalent metabolic disorder affecting both the U.S. population and several countries in the developing world. More than 50% of Americans are overweight, with 20% classified as obese by the National Institutes of Health body weight guidelines (1). Diets high in fat and calories and a sedentary lifestyle with reduced physical activity are usually blamed for this increase in the prevalence of obesity (2,3).

Obesity is considered a serious independent risk factor for coronary heart disease, on par with cigarette smoking, physical inactivity and elevated blood cholesterol levels (4). Long-term longitudinal studies have also shown that obesity is associated with excess cardiovascular morbidity and mortality (5,6). However, there is limited data on the effect of obesity on percutaneous coronary intervention (PCI) success. An early study in the pre-stent era, has shown a correlation between in-hospital mortality after PCI in both underweight and very obese patients (7). While there is a common clinical perception that markedly obese patients have a higher short- and long-term risk after PCI (e.g., access site bleeding and restenosis, respectively), there is no contemporary data assessing the effect of body mass index (BMI) on short- and long-term outcome after PCI in the modern interventional era.

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METHODS

Patients. Using our comprehensive interventional database, whereby charts from patients undergoing coronary intervention are reviewed by dedicated, independent research personnel unaware of the objectives or purpose of the study, we identified a total of 9,633 patients who underwent PCI between January 1994 and December 1999. Clinical follow-up was performed by either telephone contact or office visit at 6 and 12 months. The occurrence of major late clinical events was recorded including death, Q-wave myocardial infarction (MI) and revascularization procedures, whether percutaneous or surgical. All events were source documented and adjudicated.

Abbreviations and Acronyms

BMI = body mass index
CI = confidence interval
LVEF = left ventricular ejection fraction
MI = myocardial infarction
OR = odds ratio
PCI = percutaneous coronary intervention

Clinical definitions. The presence of obesity was assessed using BMI, which was defined as weight in kilograms divided by height in meters squared (kg/m^2). A BMI <24.9 was considered normal range (non-overweight and non-obese), a BMI between 25 and 30 was considered overweight and a BMI >30 was considered obese (8,9). For one-year mortality, BMI was further divided based on cut-off points proposed by the World Health Organization (10,11). Procedural success was defined as the absence of death, emergency coronary artery bypass grafting or Q-wave MI (presence of new pathological Q waves associated with an elevation of cardiac enzyme at least two times the upper normal value). Non–Q-wave MI after PCI was defined as a creatinine kinase-MB enzyme elevation at least three times the upper normal value without new Q waves. Major bleeding was defined as a reduction in hemoglobin >5 g/dl (or ≥15% in hematocrit), any intracranial bleeding or the need for >2 U of blood transfusion. Renal function deterioration was defined as an increase in serum creatinine levels ≥25% or the need for in-hospital dialysis. Vascular complications were defined as the presence of a large hematoma, retroperitoneal bleeding or the need for surgical repair. Hypercholesterolemia was defined as a serum cholesterol >240 mg/dl.

Procedure. All patients underwent PCI according to current clinical guidelines with conventional steerable guidewire systems (12). The operator selected interventional devices at the time of the procedure. All patients received aspirin 325 mg daily at least 24 h before the procedure and continued indefinitely afterwards. Patients who underwent stenting were treated concomitantly with an additional antiplatelet agent: either ticlopidine 250 mg twice daily or clopidogrel 75 mg daily for four weeks per the routine protocol. Weight-adjusted heparin dosage was administered during the procedure in order to maintain an activated clotting time 250 s to 300 s and was routinely discontinued at the end of the procedure. Of all patients, <5% were treated with glycoprotein IIb/IIIa inhibitors.

Angiographic analysis. An independent angiographic core laboratory, blinded to the clinical data and the purpose of this study, performed qualitative and quantitative coronary angiographic analysis. The analysis was done on end-diastolic cine frames demonstrating the stenosis in its more severe and nonforeshortening projection; using a computer-assisted, automated edge detection algorithm, quantitative coronary angiographic analysis was performed using the CMS-GFT system (Medis, Leiden, the Netherlands) and the CASS system (Maastricht, the Netherlands) using standard morphologic criteria (13). The contrast-filled catheter was used as the calibration standard, and a three-reader consensus was routinely employed.

Statistical analysis. Continuous variables are expressed as mean ± 1 SD and categorical variables as percentages. Comparisons among the three groups were performed by analysis of variance for independent samples and the chi-square test for comparison of categorical values. Cox multivariate analysis regression analysis was used to model independent predictors of late mortality. Variables included in the model were age, gender, diabetes, hypertension, previous PCI, smoking, saphenous vein graft intervention, left ventricular ejection fraction (LVEF) and BMI. Statistical analysis was performed with SAS software (SAS Institute, Cary, North Carolina). A p value <0.05 was considered significant.

Table 1. Clinical Characteristics

	Normal BMI (n = 1,923)	Overweight (n = 4,813)	Obese (n = 2,897)	p Value
Age (yrs)	68 ± 12	64 ± 11	61 ± 11	< 0.0001
Women (%)	40.3	25.6	34.9	< 0.0001
Unstable angina (%)	30.0	31.8	31.1	0.21
Acute MI (%)	2.9	2.5	3.0	0.20
Prior MI (%)	52.2	52.1	50.9	0.45
Prior CABG (%)	39.9	41.6	35.3	< 0.0001
Prior PTCA (%)	43.7	50.6	48.8	< 0.0001
Hypertension (%)	55.6	63.1	72.3	< 0.0001
Diabetes mellitus (%)	17.4	25.5	38.0	< 0.0001
Insulin treated (%)	7.3	10.8	19.2	< 0.0001
Oral hypoglycemic (%)	10.1	14.6	18.8	< 0.0001
Family history (%)	56.2	60.3	63.1	< 0.0001
Hypercholesterolemia (%)	63.1	71.3	73.6	< 0.0001
Smoking history (%)	54.3	57.1	59.2	0.0004
BMI	22 ± 2	27 ± 2	34 ± 5	< 0.0001

BMI = body mass index; CABG = coronary artery bypass graft surgery; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

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Table 2. Angiographic Characteristics (Lesion-Based)

	Normal BMI (n = 4,840)	Overweight (n = 12,266)	Obese (n = 7,149)	p Value
Target vessel				
Left main (%)	3.6	4.0	4.1	0.51
Left anterior descending (%)	31.1	30.1	29.9	0.46
Left circumflex (%)	22.0	23.2	28.9	0.006
Right coronary (%)	27.7	27.6	31.4	0.24
Saphenous vein graft (%)	15.6	15.1	5.7	< 0.0001
In-stent restenosis (%)	9.6	10.9	9.9	0.05
Total occlusion (%)	13.8	12.7	15.7	0.02
Thrombus (%)	5.9	6.7	5.7	0.39
Lesion length >20 mm (%)	13.7	11.6	14.2	0.07
Lesion type B or C (%)	80.2	81.3	80.7	0.74
Ejection fraction (%)	44 ± 14	46 ± 13	48 ± 12	< 0.0001
Preprocedural				
Reference vessel diameter (mm)	2.92 ± 0.96	2.95 ± 0.87	2.98 ± 0.87	0.20
Diameter stenosis (%)	62 ± 21	63 ± 21	64 ± 19	0.09
Minimal lumen diameter (mm)	1.06 ± 0.74	1.07 ± 0.69	1.06 ± 0.69	0.88
Postprocedural				
Diameter stenosis (%)	14 ± 19	14 ± 19	14 ± 19	0.88
Minimal lumen diameter (mm)	2.61 ± 1.04	2.60 ± 0.94	2.63 ± 0.92	0.64

BMI = body mass index.

RESULTS

Data on 9,633 consecutive patients who underwent PCI was available for complete analysis. Half of the patients (50%) were overweight, and 80% were either overweight (n = 4,813) or obese (n = 2,897), with only 20% having normal BMI (n = 1,923). The baseline clinical characteristics of the three groups differed significantly as shown in Table 1. Obese patients were younger and had more risk factors for coronary artery disease (CAD) than overweight or normal BMI patients; they had higher rates of hypertension, diabetes mellitus, hypercholesterolemia and smoking history. All of these differences were highly significant. Angiographic characteristics are shown in Table 2. There was a higher incidence of saphenous vein grafts treated in the normal and overweight BMI groups and also a higher rate of total occlusions in the normal and obese groups. Vessel dimensions were very similar among the three groups (Table 2). Device use was also similar among the three groups, 46% (range: 42% to 47%, p = 0.26) of the patients underwent stenting and 26% (range: 27% to 29%, p = 0.31) underwent lesion modification by athero-ablative devices. A total of 19% of normal BMI and overweight patients underwent rotational atherectomy, compared with 26% in the obese group (p = 0.002). Excimer laser angioplasty use was similar among the three groups, 8% (range: 6% to 9%, p = 0.10).

In-hospital clinical outcome. Table 3 summarizes the short-term clinical outcome. Despite similar procedural and angiographic success rates in all three groups, normal BMI was associated with significantly higher rates of periproce-

Table 3. In-Hospital Outcome

	Normal BMI (n = 1,923)	Overweight (n = 4,813)	Obese (n = 2,897)	p Value
Procedural success (%)	97.3	97.4	97.6	0.74
Clinical success (%)	93.8	94.2	95.0	0.09
Pulmonary edema (%)	4.0	2.8	2.6	0.002
Hypotension (%)	4.8	3.2	2.9	< 0.0001
Renal insufficiency (%)	6.6	4.8	5.2	0.005
Death (%)	1.3	1.0	0.7	0.06
Cardiac death (%)	1.0	0.7	0.4	0.001
Myocardial infarction (%)	14.8	14.7	13.7	0.41
Q-wave (%)	0.4	0.4	0.3	0.79
Non–Q-wave (%)	21.4	20.2	19.4	0.19
Emergency CABG (%)	1.6	1.6	1.7	0.99
Vascular complications (%)	5.9	3.6	3.9	< 0.0001
Major bleeding (%)	4.5	3.5	3.1	0.01

BMI = body mass index; CABG = coronary artery bypass grafting.

Table 4. 12-Month Outcome

	Normal BMI (n = 1,923)	Overweight (n = 4,813)	Obese (n = 2,897)	p Value
MACE (%)	25.8	23.1	22.7	0.02
Death (%)	10.6	5.7	4.9	< 0.0001
Cardiac death (%)	4.8	3.3	2.5	< 0.0001
Myocardial infarction (%)	7.4	7.0	6.7	0.66
Q-wave (%)	1.5	1.2	0.8	0.10
Non–Q-wave (%)	6.2	6.0	6.1	0.92
TLR (%)	17.4	18.6	19.0	0.37
TVR (%)	20.2	22.0	22.4	0.16

BMI = body mass index; MACE = major adverse cardiac events (death, myocardial infarction and target lesion revascularization); TLR = target lesion revascularization; TVR = target vessel revascularization.

dural complications and of cardiac-related death. Of note, the normal BMI patients also had a higher rate of major bleeding ($p = 0.01$) and major vascular complications ($p < 0.001$) than the overweight and obese patients. Cardiac mortality was higher in the normal BMI patients, and overall mortality tended to be higher in patients with normal BMI ($p = 0.055$).

Long-term outcome. One-year clinical outcomes for all three groups are shown in Table 4 and in Figure 1. Overall one-year mortality rates and cardiac-related deaths were significantly higher in patients with normal BMI ($p < 0.0001$) (Fig. 2). Because age is known to be such a strong predictor of mortality, analysis by age groups showed that one-year mortality rates were higher in patients with normal BMI for all age groups, except for patients <50 years old (Fig. 3). In order to assess the contribution of gender and BMI to overall mortality, we further distributed the BMI according to guidelines from the International Obesity Task Force by gender (12). Peak mortality rates were seen in female patients with BMI <18.5 and in male patients with a BMI <20 (Fig. 4). When patients who had never smoked were analyzed separately and compared with former and current smokers, the results did not change, and very lean patients still had the highest mortality rates. For patients who had never smoked, mortality rates were lowest at the same BMI as in the general population. There was no significant difference in MI and revascularization rates at one-year follow-up among the three groups. Multivariate regression analysis showed that diabetes (odds ratio [OR] = 1.97, 95% confidence interval [CI] = 1.61 to 2.41, $p < 0.0001$), hypertension (OR = 1.46, 95% CI = 1.16 to 1.83, $p = 0.001$), age (OR = 1.04, 95% CI = 1.03 to 1.06, $p <$

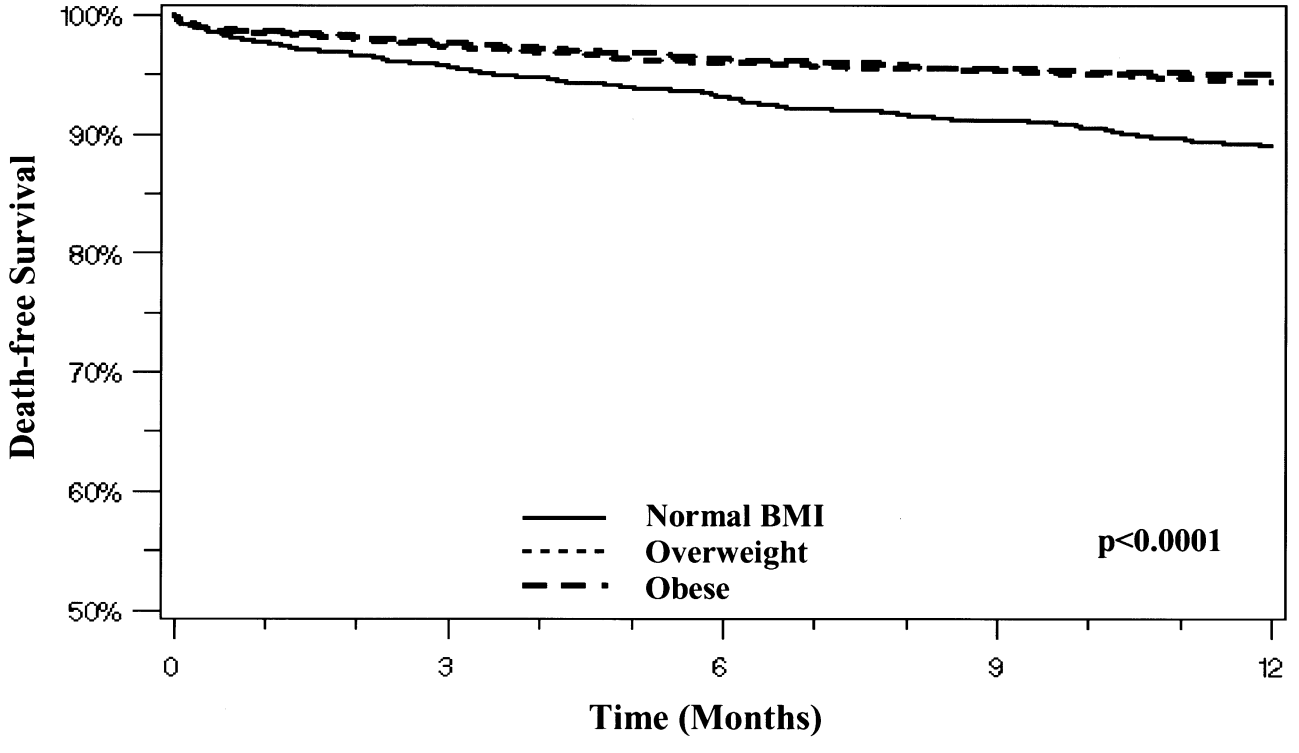

Figure 1. Kaplan-Meier curves illustrating death-free survival curves at 12 months follow-up. BMI = body mass index.

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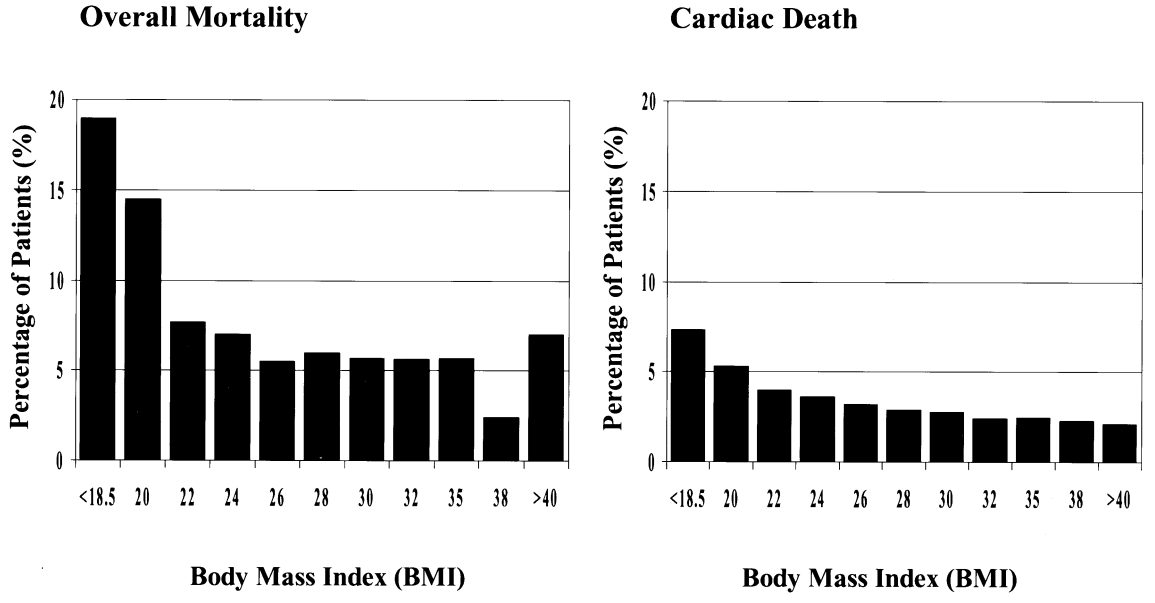

Figure 2. One-year overall and cardiac mortality rates among all patients according to body mass index (BMI).

0.0001), BMI (OR = 0.96, 95% CI = 0.94 to 0.98, p = 0.0003) and LVEF (OR = 0.05, 95% CI = 0.79 to 0.85, p < 0001) were independent predictors of long-term mortality.

DISCUSSION

In this study, we analyzed the impact of BMI on the in-hospital and one-year outcome of a large cohort of patients who underwent PCI. The working hypothesis was that overweight and obese patients have a worse in-hospital and long-term outcome after PCI. Contrary to our supposition, we found that normal BMI patients (male or female, smokers or nonsmokers) had higher in-hospital and one-year mortality rates when compared with overweight or obese patients, despite a better baseline clinical profile. Postprocedural complications, such as hypotension, pulmonary edema, renal function deterioration, major bleeding, access site hematoma, vascular complications and overall mortality rates were surprisingly higher in lean patients compared with overweight or obese patients. Furthermore, mortality rates were considerably higher for very lean female patients (<18.5 kg/m^2) compared with very lean male patients. At one-year follow-up, overall mortality rates were significantly higher in normal BMI patients, and cardiac-related deaths accounted for half of all deaths in all three groups.

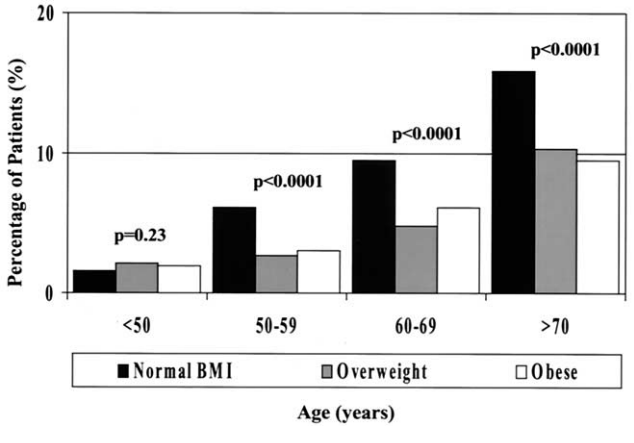

Figure 3. One-year mortality rates from all causes adjusted for age and body mass index (BMI) for all patients.

Mechanism. The mechanism by which normal BMI patients had an excess of these complications is not clear but could be related to the excessive anticoagulation in thin patients or the presence of severe, noncardiovascular, underlying diseases in very lean patients, as shown in previous trials (14,15). Overall in-hospital mortality rates were low, but there was an increased mortality in normal BMI patients; cardiac-and noncardiac-related deaths were significantly more frequent in normal BMI patients. When gender and smoking status were analyzed separately, higher mortality rates persisted in low and normal BMI patients at one-year follow-up.

Previous studies. These results are similar to those reported by Ellis et al. (7) from the pre-stent era, in which patients with low-normal BMI had worse in-hospital outcome after percutaneous balloon angioplasty than normal BMI patients. Such a trend was also seen in the British Regional Heart study, in which there was a U-shaped relation between BMI and mortality in middle-aged British men, with the highest mortality rates seen in very lean men (BMI < 20) (14). The very high mortality rate in this group was attributed to noncardiovascular causes, particularly digestive tract cancer, lung cancer and respiratory diseases, which could be associated with cigarette smoking (14,15). The lean population is often a combination of patients who have lost weight due to underlying debilitating diseases and

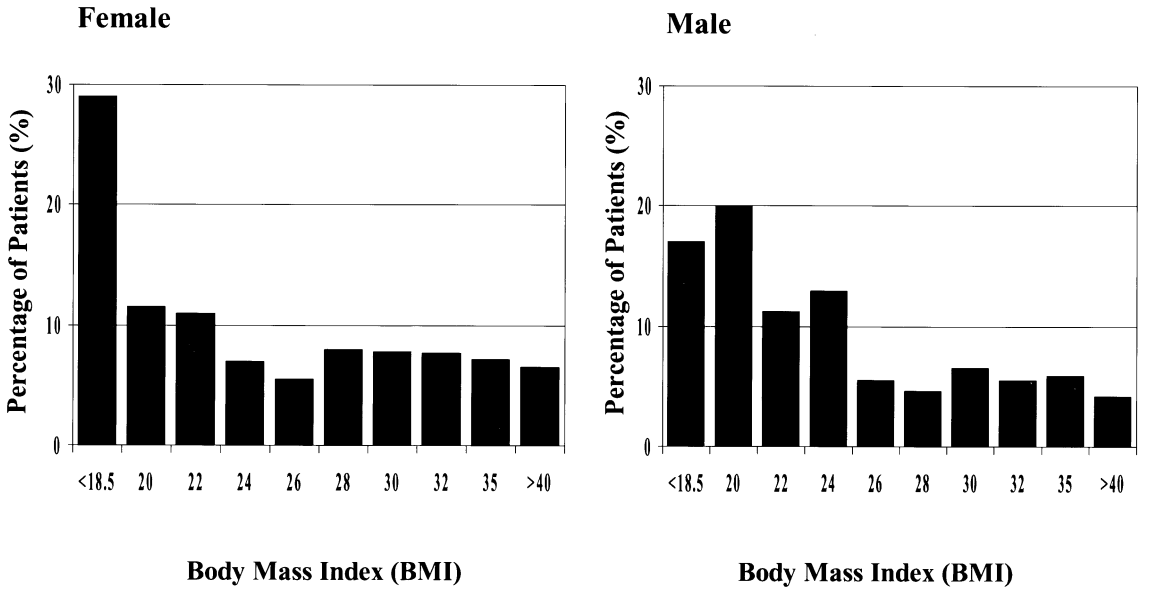

Figure 4. Gender-based one-year mortality rates from all causes according to body mass index (BMI).

smokers (who have a tendency to weigh less and have higher mortality rates compared with nonsmokers) (16–18). Mortality in these patients is usually related to cancer and "other" occult diseases rather than leanness per se. In this study, we also observed a poor outcome in the leanest patients. While it is possible that the poor outcome was due to other, noncardiac causes, low BMI was also related to cardiac-related death and was observed in smokers and nonsmokers alike.

It is important to take into account that most studies assessing the relationship between obesity and outcomes were prospective and performed in a large number of healthy subjects who were usually free of diagnosed chronic diseases and followed for a prolonged period of time. The consequence of excess body weight on mortality is delayed and may not be seen in short-term studies such as this one (19,20). The effects of obesity increase with the duration of follow-up and the age of the subjects, with increased mortality in the very lean patients during the first years of follow-up and increased mortality in the obese patients in subsequent years (20–24).

Study limitations. This was a retrospective analysis and, therefore, the results and conclusions are subject to the limitations inherent in all such reports. A BMI-based definition describes weight related to height and fails to take body fat distribution into account, which may be a better predictor for cardiovascular risk (25). Although there were significant differences in the baseline clinical characteristics among the three BMI groups, the known cardiovascular risk factors were not more common in obese patients and, therefore, cannot account for their lower mortality rates. The present study does not take into account recent weight loss and shifts in body weight, which may be associated with significant increases in risk, nor does it provide follow-up for >1 year. Patients with cancer or other serious comorbidities were not excluded from the analysis.

Conclusions. This study suggests the following: 1) in patients with known CAD who undergo PCI, very lean patients and patients with BMI within the normal range are at the highest risk for in-hospital major complications, including cardiac death; 2) the increased mortality in these patients is also seen at one-year follow-up, with a concomitant increase in major adverse cardiac events rates; 3) very lean female patients in this group seem to be at the highest risk; 4) the relatively short follow-up period (one year) does not allow for the assessment of long-term adverse effects of obesity; and 5) obese patients who undergo PCI are, on average, approximately seven years younger than their normal BMI counterparts.

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