

EDITORIAL COMMENT

# Percutaneous Coronary Intervention and the Obesity Paradox



## Fat Chance\*

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We do not need a review of the epidemiological literature to know what a casual stroll along the downtown streets of any major city in the United States will attest. We are a fat society. With no immediate solution on the horizon, the problem is only getting worse. Since 1980, the prevalence of obesity in the United States has more than doubled in adults and tripled in children (1). Nearly 70% of adults in this country are either overweight or obese (2). Worldwide, this has reached epidemic proportions. In 2015, more than 800 million people were obese, and high body mass index (BMI) accounted for 4 million deaths globally (3).

Obesity is a risk factor for a number of illnesses including cardiovascular disease, sleep apnea, kidney failure, cancer, and musculoskeletal ailments. The risk of developing cardiovascular disease in the overweight patient is compounded by the frequent coexistence of risk factors such as diabetes, hyperlipidemia, and hypertension. The ultimate health consequence is a shortened life expectancy. The relation of BMI and mortality is classically a J-shaped curve with increased mortality in underweight individuals and progressively increasing mortality for BMI >25 kg/m<sup>2</sup> (4). It has been speculated that the unremitting surge in obesity might bring a halt to the continuous rise in life expectancy that has occurred over the last century.

Given the mountainous evidence of the adverse health consequences of obesity, where's the paradox?

The coinage of the term “obesity paradox” is generally ascribed to Gruberg et al. (5). They retrospectively studied 9,633 patients who had undergone percutaneous coronary intervention (PCI). Of these, 30% were obese (BMI >30 kg/m<sup>2</sup>), 50% were overweight (BMI 25 to 30 kg/m<sup>2</sup>), and only 20% were normal weight (BMI 18.5 to 24.9 kg/m<sup>2</sup>). Patients with normal or low BMI had a higher risk of in-hospital complications and 1-year mortality. The mortality rates at 1 year in the normal, overweight, and obese groups were 10.6%, 5.7%, and 4.9%, respectively (p < 0.0001). Thus, the paradox is that although obesity is a major risk factor for developing coronary artery disease, it is associated with better outcomes after PCI procedures used to treat the disease. As counterintuitive as this might seem, these results have been replicated by several other (6–11), but not all investigators (12). Furthermore, evidence of an obesity paradox has been reported for other cardiac conditions including congestive heart failure and atrial fibrillation (13).

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In this issue of *JACC: Cardiovascular Interventions*, the study by Faggioni et al. (14) is a valuable addition to the literature on the obesity paradox. The authors note that there are limited data on whether the obesity paradox pertains to PCI in women. The investigators pooled data from 26 randomized trials and identified 9,420 women who underwent PCI. On the basis of BMI assessment, 1% were underweight, 29% were normal weight, 36% were overweight, 20% were obese, and 13% were severely obese (BMI >35 kg/m<sup>2</sup>). Women with higher BMI were significantly younger, but were more likely to have diabetes, hyperlipidemia, and hypertension. Conversely, underweight patients were more likely to have a history of smoking. Patients with higher BMI were less likely to

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have acute coronary syndromes, multivessel disease, or complex lesions undergoing PCI. The primary endpoint of risk-adjusted cardiac events at 3 years did not differ across BMI groups. However, all-cause mortality was significantly higher in underweight patients. Compared with the normal weight group, all-cause mortality was 28% lower ( $p = 0.02$ ) in the overweight group, and 24% lower ( $p = 0.10$ ) in the obese group. On the other hand, severely obese patients showed a trend towards increased mortality. The authors conclude that these results refine the concept of an obesity paradox in a large female cohort treated with PCI.

Previous meta-analyses support the existence of an obesity paradox in patients undergoing PCI (10,11). However, published studies uniformly suffer from important limitations. They are all retrospective in design and have relatively short follow-up durations (on average, <2 years). Nevertheless, it's hard to refute that at least for the short term, overweight and mildly obese patients seem to fare better after PCI. Longer-term studies are needed to determine whether higher BMI patients demonstrate a clinical catch-up during later follow-up due to excess cardiovascular risk factors.

What are the clinical implications of the obesity paradox? The issue at hand is the cause-and-effect relationship between weight and clinical outcomes. One possible interpretation is that being overweight or modestly obese confers a protective effect through some yet to be determined mechanisms. If this is the case, then clinicians worldwide may be practicing bad medicine in recommending weight reduction to patients after cardiac procedures. If big is indeed better, then do we need to revise current attitudes and guidelines on secondary prevention? This question is the elephant in the room rarely addressed in publications on the obesity paradox. In our opinion, it is far too premature to change clinical practice especially since there are alternative explanations for the apparent paradox.

The many studies of the obesity paradox consistently report that obese patients are very different from lower weight patients in terms of prognostic factors. Obese patients are significantly younger, have less complex disease, and more likely to have

PCI for stable disease. Conversely, lower weight patients are more likely to smoke and to undergo PCI for higher risk acute coronary syndromes. Because of the numerous differences between the obese and nonobese patient groups, statistical adjustment of risk factors is necessary. However, given the substantial intergroup differences, it is a legitimate question as to whether all confounding variables are adequately accounted for.

The presence of obesity could affect the selection process with respect to performing the PCI. In the study by Faggioni et al. (14), high BMI patients were less likely to have multivessel disease or complex lesions. Although it may be that obese patients have less advanced disease, there also could be a technical reason why fewer obese patients were selected for complex PCI. Angiographic resolution can be significantly degraded in larger patients, making operators averse toward attempting higher risk procedures. Another potentially confounding factor is the higher use of radial access in obese patients (9). Radial access has been associated with less bleeding and lower mortality in selected patients undergoing PCI (15,16). Finally, there is a medication treatment bias pertaining to obese patients that may paradoxically be beneficial. Several studies have reported that guideline-directed intensive medical therapies are more frequently prescribed in obese than nonobese patients undergoing PCI (8,11,17). This phenomenon of a beneficial treatment bias towards obese patients could contribute to the favorable outcomes in this population.

Like the waistline of the average American, evidence for the obesity paradox continues to grow. Overweight and obese patients undergoing PCI appear to have better outcomes, at least over the short term. The clinical implications could have potentially disruptive ramifications. Further research is clearly needed to unravel the cause-and-effect conundrum of the obesity paradox.

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