



# Obesity Paradox—PCI Outcomes

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Obesity is thought of as a growing health problem worldwide and a potential cardiovascular risk factor. The worldwide occurrence of obesity has become thrice than what it was in 1975, and there is a steeply inclining incidence of childhood obesity. Obesity is thought to increase insulin resistance causing type 2 diabetes mellitus (T2DM), dyslipidemia, hypertension (HT), and sleep-disordered breathing.

Several Western and Asian investigators have reported the “obesity paradox” following percutaneous coronary intervention (PCI), whereby overweight persons had a better clinical outcome post PCI when compared with normal weight counterparts. A report by Kosuge et al showed similar findings in obese subjects following PCI for acute myocardial infarction (MI).<sup>1</sup> The “obesity paradox” refers to the evidence which indicates that being overweight or obese based on the body mass index (BMI) is associated with a better outcome in a variety of diseases. This obesity paradox is not only applicable to coronary artery disease (CAD) but has also been observed in T2DM, HT, heart failure (HF), end-stage renal disease, peripheral arterial disease, and chronic obstructive pulmonary disease.

BMI is the body weight in kilograms divided by the square of the body height in meters. Subjects can be categorized as underweight (BMI <18.5 kg/m<sup>2</sup>), normal weight (BMI 18.5–25 kg/m<sup>2</sup>), overweight (25–30 kg/m<sup>2</sup>), or obese (>30 kg/m<sup>2</sup>) based on the BMI.

Hidehiro Kaneko, while researching the “obesity paradox,” studied 1,205 patients in the Shinken Database 2004 to 2010, undergoing PCI, and concluded that although classic coronary risk factors such as HT, T2DM, and dyslipidemia were more common in overweight and obese patients, these obese patients had experienced a significantly lesser incidence of major adverse cardiac events (MACE) and cardiac death, bleeding complications, and hospital admission or HF than lean patients. The obese patients were, however, younger and generally male. In contrast, lean patients had lesser number of conventional coronary risk factors, were most often older,

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of the female gender, had a higher prevalence of chronic kidney disease (CKD) and had the highest long-term mortality.<sup>2</sup>

Delhaye et al and investigators of other studies have also reported that the incidence of major bleeding following PCI increased at the two ends of the BMI spectrum, that is, in underweight and in class III obese patients, and the incidence of transfusion was the reverse across the BMI spectrum, irrespective of the anticoagulant used.<sup>3</sup> Similarly, other studies also showed that major in-hospital bleeding complications were higher in the lean when compared with overweight and obese patients, which is likely at least in part due to the increased use of radial access in obese patients.<sup>4</sup>

The Swedish coronary angiography registry had registered a total of 64,436 subjects who had undergone coronary angiography and who received medical therapy, PCI, or CABG, and who were followed-up for 3 years. Medical and PCI-treated patients who were moderately obese (26 kg/m<sup>2</sup>–28 kg/m<sup>2</sup>) had the lowest mortality and the graph was U-shaped, with the highest complication rate in the underweight and normal BMI persons at one end and the morbidly obese at the other end.<sup>5</sup>

Possible mechanisms contributing to the so-called obesity paradox is not clear; it is multifactorial and several hypotheses have been put forth, but more research is needed.

In most of the studies reporting “obesity paradox,” the higher BMI group were younger and most often males in contrast to the lean group. Earlier studies have also reported that elderly patients have poorer outcomes after PCI and although gender-related differences in PCI have reduced in the present era, previous investigators have reported worse outcomes after PCI, in females.

Although, the World Health Organization endorses BMI as a measure of obesity, BMI only reflects overall obesity and is not a measure of visceral adiposity which is now considered to correlate better with CAD. The role of visceral adipose tissue as an active endocrine organ secreting pro- and anti-inflammatory cytokines which are in perfect equilibrium

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under normal circumstances is increasingly being recognized. This equilibrium can be tilted with morbid increase in adipose tissue. Under normal conditions, adipose tissue has a cardioprotective effects by producing hormones such as leptin and adiponectin which have anti-inflammatory and antiapoptotic properties.<sup>6</sup> The increase in mortality seen in patients with extreme obesity suggests the protective effects of milder obesity was probably overruled by the deleterious effects of extreme obesity due to potentiation of an inflammatory and prothrombotic state and increased in comorbid conditions.

Increase in lean body mass and not fat, may be responsible for the increase BMI in overweight and mildly obese subjects which could explain the survival benefit; so “overweight paradox,” and not “obesity paradox,” would be a better term. Higher mortality in the low BMI group could be attributed to sarcopenia, wherein there is low muscle mass and insulin resistance which could contribute to the worse prognosis in the leaner. Several studies have reported waist to hip ratio, and not BMI, correlated better with cardiovascular disease.

Patients with normal BMI are less likely to receive appropriate secondary prevention therapy compared with their higher BMI counterparts. Lancefield et al reported that in spite of the more adverse risk profile of the overweight and obese at the time of PCI, aggressive treatment with multiple classes of cardiovascular medications like antiplatelet, lipid-lowering drugs,  $\beta$ -blockers, and angiotensin-converting enzyme inhibitors was probably responsible for the favorable outcome in all overweight and obese except the morbidly obese patients. Hirohisa Endo reported less use of guideline-recommended medical therapies like aspirin, RAAS inhibitors,  $\beta$ -blockers, and statins for underweight patients which may contribute to increase in mortality. Intensive lipid-lowering therapy have a significantly reduced plaque progression rates compared with moderate lipid-lowering therapy ( $p = 0.01$ )<sup>7</sup>. These results highlight the potential antiatherosclerotic benefits of lipid-lowering drugs in obese patients which may contribute to the obesity paradox.

High-risk coronary anatomy such as a thin-cap fibroatheroma (TCFA) is less common in obese individuals compared with nonobese patients. This association was studied by Rubinstein et al ( $p = 0.0002$ ).<sup>8</sup>

However, in the study under scrutiny and in a few others, the incidence of complications especially the post procedural bleeding as when compared with the lean group was higher in the obese and overweight. The population studied and the higher occurrence of risk factors in the obese group might have also contributed to the difference.

These findings indicate the need for careful follow-up of lean patients after PCI and the institution of optimal guideline-based medical therapy.

It has been hypothesized that in contrast to obese individuals, persons with low BMI may not have the functional ability and reserve to tolerate the stress and strain of an illness contributing toward higher mortality. Further, a low BMI could

mean a serious underlying illness and the Elixhauser index is considered as the best of comorbidity indices, especially when determining mortality beyond 30 days. The Elixhauser index was highest at the two extremes of weight, that is, the underweight and the morbidly obese, and indicated that the most independent predictor of mortality was low BMI.<sup>9</sup>

The level of cardiorespiratory fitness could also explain the “obesity paradox” because good cardiorespiratory fitness could be associated with better life expectancy.

Studies have revealed that larger coronary vessels are seen with higher BMI and the smaller the vessels, the greater is the risk for worse outcome after PCI and CABG.

Other hypotheses to explain the “obesity paradox” which are speculative include the mobilization of endothelial progenitor cells from the bone marrow reported by Aldhooon-Hainerova et al and the decreased production of thromboxane and thromboxane B<sub>2</sub>, may be responsible for the improved survival in the very obese.<sup>6</sup> Lund et al suggested a resistance to ghrelin (gastric peptide hormone) in the development of cardiac cachexia and a reduction of tumor necrosis factor which could contribute to the “obesity paradox” (24).

There have been some conflicting reports about the existence of “obesity paradox” and Diletti et al, Alidoosti et al, and a few other studies have found no relation between short-term and long-term clinical outcomes after coronary artery interventions and BMI.<sup>10</sup>

To conclude BMI is a crude and inaccurate anthropometric biomarker that does not demarcate fat mass/fat-free mass ratio or body fat distribution. The risk of cardiac death following any intervention be it PCI or surgery could be reduced by the long-term follow-up and guideline-based management of patients, irrespective of the BMI.

#### Conflict of Interest

None declared.

#### References

- 1 Kosuge M, Kimura K, Kojima S, et al; Japanese Acute Coronary Syndrome Study (JACSS) Investigators. Impact of body mass index on in-hospital outcomes after percutaneous coronary intervention for ST segment elevation acute myocardial infarction. *Circ J* 2008;72(4):521–525
- 2 Kaneko H, Yajima J, Oikawa Y, et al. Obesity paradox in Japanese patients after percutaneous coronary intervention: an observation cohort study. *J Cardiol* 2013;62(1):18–24
- 3 Cédric Delhay, Kohei Wakabayashi, Gabriel Maluenda, Loic Belle, Itsik Ben-Dor. Body mass index and bleeding complications after percutaneous coronary intervention: does bivalirudin make a difference? *Am Heart J* 2010;159(6):1139–1146
- 4 Holroyd EW, Sirker A, Kwok CS, et al; British Cardiovascular Intervention Society and National Institute of Cardiovascular Outcomes Research. The relationship of body mass index to percutaneous coronary intervention outcomes: does the obesity paradox exist in contemporary percutaneous coronary intervention cohorts? Insights from the British Cardiovascular Intervention Society Registry. *JACC Cardiovasc Interv* 2017;10(13):1283–1292

- 5 Angerås O, Albertsson P, Karason K, et al. Evidence for obesity paradox in patients with acute coronary syndromes: a report from the Swedish Coronary Angiography and Angioplasty Registry. *Eur Heart J* 2013;34(5):345–353
- 6 Hainer V, Aldhoon-Hainerová I. Obesity paradox does exist. *Diabetes Care* 2013;36(Suppl 2):S276–S281
- 7 Nicholls SJ, Tuzcu EM, Sipahi I, et al. Effects of obesity on lipid-lowering, anti-inflammatory, and antiatherosclerotic benefits of atorvastatin or pravastatin in patients with coronary artery disease (from the REVERSAL study). *Am J Cardiol* 2006;97(11):1553–1557
- 8 Rubinshtein R, Halon DA, Jaffe R, Shahla J, Lewis BS. Relation between obesity and severity of coronary artery disease in patients undergoing coronary angiography. *Am J Cardiol* 2006;97(9):1277–1280
- 9 Dixon JB, Lambert GW. The obesity paradox—a reality that requires explanation and clinical interpretation. *Atherosclerosis* 2013;226(1):47–48
- 10 Diletti R, Garcia-Garcia HM, Bourantas C. Impact of body mass index on long-term clinical outcomes after second-generation drug eluting stent implantation: Insights from the international global RESOLUTE program. *Am Heart J* 2008;156:13–22...–37