The obesity paradox: does it carry weight in percutaneous coronary interventions?

“...the perception of obesity as a protective condition of outcomes after PCI is shattered...”

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Obesity is associated with significant morbidity and mortality and is becoming increasingly prevalent in western societies, with two thirds of this population classified as overweight or obese [1]. Overweight and obese individuals are at a greater risk of developing coronary artery disease, primarily because of obesity-related conditions, such as diabetes mellitus, hypertension and dyslipidemia [2]. Although the impact of obesity on clinical outcomes after percutaneous coronary intervention (PCI) with stents has been investigated by several studies, the issue remains complex and controversial [3–7].

A decade ago, several studies had reported better clinical outcomes in overweight and obese subjects after PCI, compared with normal and underweight subjects; an interaction termed the ‘obesity paradox’ [3–7]. Present data, derived from a large registry in the modern era of interventional cardiology, dismantled any ‘obesity paradox’ as a misnomer in the context of PCI and drug-eluting coronary stents [8]. Compared with overweight and obese patients, those with normal body weight had similar rates of all-cause mortality and major adverse cardiovascular and cerebrovascular events, as well as target-vessel revascularization, myocardial infarction, stroke and stent thrombosis, even after risk adjustment.

These contemporary documented findings from the German Drug-Eluting Stent Registry neutralize any previously suggested benefit for the overweight, but underline the role of obesity as a risk factor for cardiovascular events [9–11], and corroborates recent findings that the mortality risk after an acute infarction is not affected by the weight of a given patient population [12]; essentially supporting the role of obesity as a risk factor for cardiovascular events [9–11]. Nevertheless, one recent interventional study seemed to support the concept of an ‘obesity paradox’ in a large cohort of patients undergoing PCI [13]. Upon closer examination, however, the retrospective association study just claimed a U-shaped nonsignificant trend towards lower survival among the underweight patients, compared with normal or mildly overweight patients. However, 1.2% of patients who were underweight were likely to suffer from comorbid conditions, including malignancies and heart failure, and happened to be significantly older than the normal and obese patients. Moreover, antithrombotic medications, potentially causing post-PCI bleeding complication, were more likely to be overdosed in the underweight patients. In addition, obese patients are usually younger and associated with a lower risk of high-risk coronary anatomy than underweight patients who are older [14,15]. Along these lines, another important confounding observation was the fact that obese patients tended to be diagnosed and treated at an earlier stage in the atheromatous disease process than lean patients. Furthermore, the ‘obesity paradox’ is clearly challenged by a survey on >130,000 patients, revealing that adherence to guidelines was better with higher BMI concerning standard medication such as aspirin, β-blockers, acetylsalicylic acid and angiotensin II receptor blockers, as well as lipid lowering drugs [16]. In the same survey a relationship between obesity and an increased prevalence of diabetes and hypertension were also confirmed.

So what is left to support the so-called ‘obesity paradox’, or is it just a paradoxical concept? Protagonists claim that adipose tissue is being recognized as an endocrine organ, producing higher serum levels of low-density lipoproteins to scavenge unbound circulating lipopolysaccharides with subsequent anti-inflammatory effect [17–19]. Low levels of inflammatory cytokines or tumour necrosis factor have only been suggested in the
context of obesity and coronary artery disease [20].

Thus, on aggregate, while early studies may have suggested an inverse relationship between being underweight with outcomes in heart failure, which led to the coining of the obesity paradox, such ‘obesity paradox’ failed to show in the context of coronary artery disease and modern coronary interventions. In fact there is no plausible concept to turn away from the classic relationship between risk factors, confounding variables and prognostic outcomes. The limitations of such association studies are not only the lack of a pathophysiologic underpinning, but moreover the mere association with descriptive notions and the unknown effect of confounding variables. In view of the neutralizing results from a recent survey [13] and the German Drug-Eluting Stent Registry [8], the perception of obesity as a protective condition of outcomes after PCI is shattered and the provocative construct of an ‘obesity paradox’ evaporates, as such hypothesis was never confirmed in the clinical setting of coronary artery disease and PCI. Finally, as it turns out, such associative studies that eventually lead to the creation of the ‘obesity paradox’ can at best suffer from various serious limitations and be hypothesis-generating; their message will eventually survive only if supported by plausible physiology. In the context of coronary artery disease and PCI, there is hardly any plausible explanation and eventually no clinical data to justify it. Thus, it’s the ‘obesity paradox’ that looks paradoxical!

Synthesis

The initiators of the ‘obesity paradox’ intuitively called it a paradox, which is what it really is! However, a sober analysis of data reveals that there is not any paradox.

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