The obesity paradox: weighing the benefit

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This editorial refers to ‘Obesity paradox in a cohort of 4880 consecutive patients undergoing percutaneous coronary intervention’, by C.E. Hastie et al. on page 222

Obesity has become a medical and socioeconomic burden of epidemic proportions and the World Health Organization (WHO) has marked obesity as one of the most blatantly visible but most neglected public health problems. Indeed, being overweight is an established risk factor for the development of many different diseases including cardiovascular, metabolic, and orthopaedic illnesses.

In contrast, obesity has not been associated with a worse outcome in all patient populations. In fact, substantial data have accumulated suggesting a survival benefit in patients with existing chronic cardiovascular diseases for patients who are overweight and moderately obese. In chronic heart failure (CHF), convincing evidence has accumulated from studies including >30 000 patients over a broad spectrum of disease severity, that being overweight is associated with decreased mortality.¹–⁴ Similarly, in patients with acutely decompensated heart failure, higher body mass index (BMI) is associated with lower in-hospital mortality.⁵ Despite the known role of obesity as a major risk factor for cardiovascular events,⁶–⁸ the mortality risk after an acute myocardial infarction is no higher in overweight and obese patients compared with lighter patients.⁹ In a systematic review of 40 studies including a total of >250 000 patients with coronary artery disease, a better outcome for cardiovascular and total mortality was seen in the overweight and mildly obese groups compared with normal weight patients.¹⁰ Furthermore, in the INVEST study including >22 500 patients with advanced cardiovascular risk profile of hypertension plus documented coronary artery disease, there was a lower risk of death and major cardiovascular events in overweight and obese patients compared with those of normal weight.¹¹ The accumulated findings stimulated a vivid discussion on the impact of weight and obesity in a range of chronic and acute diseases. The ‘obesity paradox’ has been proposed as a label for these unexpected observations and to highlight the surprising contrast with the overwhelming evidence for the detrimental impact of obesity on individual and population health.

Hastie and colleagues have reported a further manifestation of the obesity paradox.¹² From the Scottish Coronary Revascularisation Register, the authors found than among patients undergoing elective percutaneous intervention for coronary artery disease those patients with BMI between 27 and 30 kg/m² had a significantly lower all-cause mortality compared with normal weight patients. Moreover, whilst there might be a U-shaped relationship between BMI and mortality, obese patients with BMI >30 kg/m² did not show a significant increase in risk. The study is well in line with a number of previous reports on patients undergoing percutaneous intervention, but, in contrast to most previous studies, Hastie et al. have studied a homogenous study population as only elective and first time interventions were included. Exclusion of very early events (<30 days) or adjustment for various confounders including age, sex, smoking status, left ventricular impairment, previous myocardial infarction, or severity of the coronary artery disease did not affect this outcome of the study.

Speculating on the underlying mechanisms to explain this finding, the authors consider a higher bleeding risk among the underweight patients from relative overdosing of anticoagulant therapy. Whilst the hypothesis cannot, of course, be excluded, the similar observations in CHF patients as well as in other patient populations where anticoagulant therapy is not a factor suggest that bleeding is unlikely to be a major mechanism of the obesity paradox in this study. As a key additional analysis on the data of Hastie et al., the cause of death would indeed be interesting to see.

An interesting observation is that overweight patients may be more likely to receive appropriate medication for their cardiovascular disease.¹³ Hastie et al. have not provided an analysis of this potential confounding effect, but it could perhaps be that the presence of obesity triggers prescribing; or, by its association with hypertension, makes it easier for the prescribing physician to introduce new medication.

One question in the ongoing discussion of the ‘obesity paradox’ may refer to the term itself: why do we address it as a ‘paradox’?
The data from a considerable spectrum of diseases and conditions and in various study populations repeatedly verified the association. It might be that this observation is truly a reflection of the interaction between host metabolism and disease, and should not be regarded as an unexpected and surprising paradox. This label, in fact, reveals much more about our expectations that have become irrevocably ingrained by considering primary prevention and epidemiological data. The perception that obesity is a plague of modern society, injurious to health, has become translated into an omnipresent appeal to achieve leanness regardless of potential co-existing conditions such as chronic disease or advanced age. We should recognize that in patients with some diseases, both acute and chronic, being overweight and even obese may be protective rather than harmful.

Whilst aiming for a lean body composition and preventing (and reversing) obesity are repeated like a Hindu mantra, it may be the time to consider a more differentiated strategy towards weight recommendations in patients with chronic ailments such as cardiovascular disease. Current data as confirmed again by Hastie et al. suggest that being overweight might not be the most important factor of concern in many patients. We have previously shown a marked survival benefit associated with increasing weight in patients with CHF\textsuperscript{14,15} and a relationship between improving survival and higher cholesterol.\textsuperscript{16} Similar findings apply to an older population without overt coronary disease.\textsuperscript{17} The U-shaped relationship between body mass and age (Figure 1),\textsuperscript{18} and perhaps with chronic illness is moved to the right. Why is obesity helpful with regard to mortality risk? As Hastie et al. point out, ‘Adipose tissue is now recognized as a major endocrine organ’, and it might simply be that chronic illness is a metabolically demanding state, and people who are overweight have greater metabolic reserves to deal with the demand.

’Let me have men about me that are fat/Sleek-headed men and such as sleep a-nights’.\textsuperscript{19}

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References

The ‘left’ ventricle during pulsatile mechanical assistance: reliability of cardiac output monitoring with an uncalibrated pulse contour method

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The determination of cardiac output (CO) during mechanical circulatory support (MCS) is crucial since low-output syndrome is the main cause of death in such patients.

A new uncalibrated pulse contour method (PCM) named PRAM (pressure recording analytical method) has recently been introduced in the clinical practice and validated in animals, humans, and patients assisted with axial flow pumps.

The figure illustrates CO monitoring by PRAM in a patient during pulsatile left ventricular assist device assistance (HeartMate-I Thoratec Corporation, Pleasanton, CA, USA) (Panel A). The discrepancy between pump (operating in fixed-rate mode at 50 b.p.m.) and patient heart rate (paced at 85 b.p.m.) shows that some spontaneous ventricular contraction still occurred and resulted in a residual ventricular ejection (Panel B).

A good agreement between PRAM-CO and ThD-CO estimations was found in all the determinations whereas an apparent bias (about 10% overestimation) with respect to values of pump console (device calculated output) was observed (Panel C).

A retrospective analysis by PRAM (Panel D) demonstrated that, depending on loading conditions, each residual systolic-arterial wave resulted from an adjunctive ventricular stroke volume of about 5–8 mL. Although this is relatively small, with a heart rate of 85 b.p.m., left ventricle actually contributed to ‘total’ CO with 400–600 mL/min (about 10% of ‘total’ PRAM estimated CO).

PRAM technique overcomes the limitations inherent to thermodilution (ThD)-based devices (unreliable during right or biventricular support because of the ‘indicator loss’ occurring in right heart sections) and other PCMs based on ‘cold bolus’ trans-pulmonary thermodilution calibration which are not applicable during any type of MCS. It allows a less-invasive, beat-by-beat monitoring, deriving CO values from peripheral arterial pressure waves (radial artery), and seems to provide an actual estimation of the ‘total’ systemic blood flow (device derived plus residual ventricular ejection) in patients assisted with pulsatile VADs.

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