Abstract

Obesity increases the risk of hypertension, dyslipidemia, type 2 diabetes mellitus, insulin resistance, coronary artery disease, ischemic stroke, and heart failure. There is an association of obesity, particularly abdominal obesity and morbid obesity, with decreased survival. Yet, in many epidemiological studies, high BMI has been found to be associated with better survival, particularly in heart failure. This has been referred to as the “obesity paradox.” Improved survival of the obese is largely unexplained. A likely explanation may lie in limitations of BMI as a measure of obesity. So, BMI alone may not be a good indicator of cardiovascular risk and may confound the relation between adiposity and cardiovascular risk. Other factors that may result in an apparent improvement in survival in the obese may be high morbidity and mortality associated with cardiac cachexia of heart failure, early recognition of heart failure in the obese or confounding by smoking, inter-current illness, or intentional weight loss. Due to uncertainty of its existence and lack of firm biological explanation, the obesity paradox is at present just a hypothesis.

Introduction

Obesity is defined as an excess of body fat that is severe enough to increase health risks. For practical purposes, the line of demarcation between normal body fat levels and obesity is taken to be fat mass that exceeds 5% of the average value for age and gender in a given population. Not everybody agrees that higher fat content in older age is normal, and thus define overweight as having a fat content more than 20% in men and more than 30% in women, irrespective of the age during adulthood.

Body fat can be measured by several methods. None of these is in clinical use, except bioelectric impedance, because of the expense, lack of availability, or methodological issues. For clinical purposes, obesity is commonly measured by calculating body mass index (BMI). BMI is not a very accurate measure of total body fat, but despite its limitations, it is widely recommended in the clinical setting.

Obesity increases the risk of a number of medical and biochemical disorders including hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM), hyper-insulinemia/insulin resistance, coronary artery disease (CAD), ischemic stroke, and heart failure. There is an association of obesity, particularly abdominal obesity and morbid obesity, with decreased survival.
The obesity paradox

In many epidemiological studies, high BMI has been found to be associated with better survival, particularly in heart failure, but also in CAD, atrial fibrillation, and sudden cardiac death. This has been referred to as the “obesity paradox.” It is notable that the so-called obesity paradox is not observed in morbid obesity, in which 8–10 years of decrease in mean survival is observed.

An inverse relation between BMI and heart failure mortality has been observed in several studies. There may be a 10% lower mortality for every 5 unit increase in BMI. Similar results have been obtained in younger hospitalized people with lower mortality in those with higher BMI, despite a higher prevalence of T2DM.

In a large prospective study (n ~250,000; mean follow-up: 3.8 years), obese CAD patients had lower mortality compared with underweight and normal weight individuals. Similar findings were reported in a large cross-sectional study of ST-elevation myocardial infarction (STEMI) patients, and in another study of STEMI survivors.

Biological plausibility for the obesity paradox

Despite these observations, the obesity paradox may not be real. If it exists, there should be a biological explanation for it. If it does not, methodological limitations of studies may account for it.

A plausible explanation for improved survival in obesity is “good obesity” vs. “bad obesity.” “Good obesity” is characterized by adipocytes with efficient fuel storage capacity. “Bad obesity” is characterized by adipocytes that are inefficient in fuel storage and associated with inflammation. The differential location and type of adipocytes and their metabolic activity support the concept of “good obesity” vs. “bad obesity.” The majority of overweight and obese individuals have “bad obesity” associated with metabolic syndrome and T2DM, cardiovascular disease, and an increased mortality.

Improved survival of the obese in heart failure is largely unexplained. Preliminary observations indicate that adipocytes may secrete soluble tumor necrosis factor-α receptors that neutralize tumor necrosis factor-α. Higher levels of circulating lipoproteins in obese patients may also bind lipopolysaccharides, thereby decreasing inflammatory cytokine secretion.

Can obesity paradox be explained by methodological issues?

BMI as a measure of obesity

BMI is a convenient and inexpensive method of assessment for overweight and obesity. Nevertheless, it does not measure the body fat percentage, the type of fat, fat distribution, or its metabolic consequences. Despite having a high BMI, approximately 25% of the obese individuals are metabolically healthy without insulin resistance and may have low cardiovascular risk. At other extreme, nearly 23% of individuals with normal BMI have “metabolic obesity” with insulin resistance and dyslipidemia. Thus, BMI alone may not be a good indicator of cardiovascular risk and may confound the relation between adiposity and cardiovascular risk.

Confounding factors

It is possible that obesity really does protect against heart failure mortality. Heart failure is a catabolic state and may lead to cardiac cachexia. In contrast to those with cardiac cachexia, those with a preserved body fat and muscle may survive longer despite heart failure. However, this is just a hypothesis. Selection bias may be a contributory factor for the observed “obesity paradox” in many studies. Dyspnea or peripheral oedema due to obesity may prompt an early recognition and more effective treatment of heart failure, leading to better survival. Alternatively, only the healthiest obese without co-morbidities may survive long enough to develop heart failure. Other potential causes of bias may be smoking, inter-current illness, or intentional weight loss in heart failure patients.

Conclusions

At present, the obesity paradox is a hypothesis based on observations in epidemiological studies that have differentiated obese individuals from non-obese by BMI alone, without further exploration of the type of obesity and metabolic profile or accounting for co-morbidities or severity of illness. Unless these factors are taken into consideration, the observed improvement in survival in the obese is best not considered as a true paradox.

References


Address for correspondence:
Dr. Peeyush Jain
Email: dpn2005@gmail.com.