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REVIEW

Obesity paradox and aging

Ottavio Bosello[1] · **Angiola Vanzo**[2]

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Abstract

Background In association with the rapid lengthening of life expectancy and the ever-rising prevalence of obesity, many studies explored in the elderly the phenomenon usually defined as the obesity paradox.

Objective and methods This article is a narrative overview of seventy-two papers (1999–2019) that investigated the obesity paradox during the aging process. Twenty-nine documents are examined more in detail.

Results The majority of studies suggesting the existence of an obesity paradox have evaluated just BMI as an index of obesity. Some aspects are often not assessed or are underestimated, in particular body composition and visceral adiposity, sarcopenic obesity, and cardio fitness. Many studies support that central fat and relative loss of fat-free mass may become relatively more important than BMI in determining the health risk associated with obesity in older ages.

Conclusion Inaccurate assessments may lead to a systematic underestimation of the impact of obesity on morbidity and premature mortality and, consequently, to clinical behaviors that are not respectful of the health of elderly patients. Knowledge of the changes in body composition and fat distribution will help to better understand the relationship between obesity, morbidity, and mortality in the elderly.

Level of evidence Level V, narrative overview.

Keywords Aging · Body mass index · Body composition · Fat distribution · Morbidity · Mortality · Obesity · Obesity paradox · Sarcopenia · Sarcopenic obesity · Waist circumference (WC) · Waist-to-hip ratio (WHR)

Introduction

Since the earliest times, excess weight has been considered a risk factor for health: from the Greek Hippocrates to the Indian Suśruta, from the Greek–Roman Galeno [1] to the Persian Avicenna [2], all the way up to the evaluations of the MLICs of the middle of the last century [3]. Although the role of obesity in causing multiple diseases is definitively recognized, once these conditions have been met, some observations seem to indicate that overweight may provide some protective benefits.

In 1999, Fleischmann et al. first described the phenomenon in patients undergoing hemodialysis. They studied 1346 patients attending limited-care hemodialysis units and found that the 1-year survival rate was significantly higher in the overweight patients as compared with the normal weight (BMI < 27.5) and lower in the underweight patients (BMI < 20) [4].

However, the term "obesity paradox" was coined only in 2002, by Gruberg et al. to describe their counterintuitive finding that overweight and obese patients with coronary artery disease had better outcomes than their normal-weight counterparts [5].

In the last two decades, many articles have been published regarding obesity paradox in several different diseases. Furthermore, in association with the rapid lengthening of life expectancy, in some studies a question arose: is excess body weight a protective factor in the elderly?

The matter is, therefore, very complex and deserves a close examination of the multiple intersection between obesity, obesity paradox, aging, morbidity and mortality.

This article is a narrative overview on obesity paradox in aging. We used as sources MEDLINE/PubMed, CINAHL, EMBASE, and Cochrane Library, from inception to May 2019.

✉ Ottavio Bosello
ottavio.bosello@univr.it

[1] Department of Medicine, University of Verona, Verona, Italy

[2] SIAN AULSS 8, Vicenza, Veneto, Italy

Aging and obesity

Although the number of available studies on the epidemiology of obesity in the elderly is still limited [6], the few available allow us to state that an increase in prevalence has emerged and must be seen as the most serious health epidemic in the world [7–12].

One of the problems that are still very much debated in the medical field is to recognize obesity as a disease. The American Medical Association in a 2013 Statement stated that obesity is a disease [13]. Someone still poses the problem [14], but there is now a substantially good agreement [15, 16] that obesity is a disease [17, 18].

Regarding health and the related risk of mortality due to obesity, an analytical study was carried out on 10,625,411 subjects in Asia, Australia and New Zealand, Europe and North America, from 239 prospective studies. The main analysis covered mortality risk, equated by sex and age, compared to BMI 22.5–25.0. The associations of both overweight and obesity, with increased mortality from any cause, were indisputable and substantially in line with the four continents. These observations support strategies to combat the entire spectrum of excess fat in multiple populations. These research findings also seem to question the recent hypotheses that overweight and moderate obesity are not associated with higher mortality, bypassing speculations about hypothetical protective metabolic effects of an increase in body fat in seemingly healthy individuals [19].

Therefore, it is arguable that the incessant increase in prevalence and incidence of obesity suggests that the strategies used to date for prevention and treatment simply do not work. The physical, emotional, and financial cost to the obesity-related society is astounding [20]. The approach to the prevention and treatment of obesity must be rethought completely.

New approaches are needed and these must include a realistic assessment of why the population has become obese and what needs to be done to reverse this trend [21].

The prevalence of obesity is growing even among the most advanced age groups. The potential damage of obesity in the elderly is a controversial point. Some studies suggest that the advancing years make the association between obesity and mortality risk less crucial [22–24].

Bender and coworkers made a large study (6193 obese patients) with a long mortality follow-up (median follow-up time of 14.8 years) of a cohort of patients with obesity (BMI 32–39.9 kg/m^2) and morbid obesity (BMI $\geq$ 40 kg/m^2) subjects. They tried to assess the effect of age on the excess mortality associated with all degrees of obesity.

They found that the excess mortality associated with obesity diminished considerably with age in all degrees of obesity and for both sexes [25]. However, models failed to account for some possible confounding factors and the estimates of the obesity–mortality relationship could be biased.

The relationship between obesity in old age and total or specific disease mortality is still the subject of debate, as is the definition of obesity in the elderly, its clinical relevance and the need for its treatment.

Knowledge of the changes of age-related body composition and fat distribution will help to better understand the relationships between obesity, morbidity, and mortality in the elderly. Many studies support that central fat and relative loss of fat-free mass may become relatively more important than BMI in determining the health risk associated with obesity in older ages.

It is important to consider the problem of sarcopenia, a decline in skeletal muscle mass associated with age and functional deterioration. Sarcopenia can be exacerbated by obesity leading to higher disability, frailty, morbidity and mortality rates. In the association between sarcopenia and obesity, the so-called sarcopenic obesity (SO), some key factors mediated by age and obesity can aggravate sarcopenia [26].

In the context of the progressive aging of the population, there is a growing appearance of "sarcopenic obesity" (SO), characterized by low muscle mass and reduced skeletal strength, combined with excess body fat, most of which is visceral. Surrounding the critical organs of the body, visceral fat stimulates inflammatory processes, constituting an increasingly serious risk factor for cardiovascular diseases and diabetes [27, 28].

Stoklossa et al. [29] found that the prevalence of SO increases with age but is extremely variable in older individuals: it ranged from 0 to 100% in males and from 0 to 84.5% in females, depending on the applied definition, with greater prevalence when the definition takes into account the measurement of fat mass.

Cruz-Jentoft et al. [30] for the European Sarcopenia Working Group in the elderly have recently updated the definition of sarcopenia which aims to promote progress in the identification and treatment of people with sarcopenia. The presence of sarcopenic obesity complicates the discussion about a possible paradoxical effect of obesity, but it does not go unnoticed that it certainly aggravates the risks of excess weight.

Bowman et al. followed for 8.3 years 130,473 subjects aged 60–69 years. Current smokers and individuals with recent or disease-associated weight loss were excluded.

Survival models were adjusted for a number of factors (sex, age, smoking history, alcohol intake, etc.). The authors studied the association between mortality and incident coronary artery disease (CAD) with combined measurements of BMI and waist-to-hip ratio (WHR). They found that central

adiposity was associated with substantial excess mortality also in subjects with a BMI corresponding to normal-weight or overweight.

They concluded that the obesity paradox in the elderly may result from failing to account for central adiposity [31].

In old age, weight gain or fat redistribution may still pose health risks (early mortality and comorbidity resulting in independent adverse health risks or functional decline). In the elderly, a careful assessment of comorbidity and weight history should be performed to generate a complete framework for potential adverse health effects of overweight or obesity.

The risks of obesity in the elderly have been underestimated by a number of confounders such as survival effect, competing mortalities, relatively shortened life expectancy in older persons, smoking, weight change, and unintentional weight loss.

Studies on the effect of voluntary weight loss in the elderly are scarce, but they suggest that even small amounts of weight loss (between 5 and 10% of initial body weight) may be beneficial. In the elderly as well as in adults, moderate voluntary weight loss may help to prevent the adverse health consequences of obesity.

Therefore, even if an intentional weight loss by obese older people can be safe and likely to be beneficial when obesity-related conditions exist, rigorous caution is advised in recommending weight loss to older overweight people based on body weight alone [32].

The system for achieving weight loss in elderly patients is substantially the same as in other age groups. It is, however, categorical that caloric reduction is associated with a physical activity program, especially of resistance, to preserve muscle mass. In fact, it is well known that weight loss induces loss of muscle mass in addition to that of fat: this phenomenon would be of serious damage to older people who already have decreased skeletal muscle mass as compared to younger adults.

Lifestyle modification should always be the main intervention; the knowledge of physical inactivity constraints and modulators should help to involve older people in physical activity [33].

It should be kept in mind that the prevalence of obesity increases up to 69 years in both men and women and, therefore, tends to decrease. However, comparing the period 1999–2000 with the period 1988–1994, it can be seen that the prevalence of obesity tends to increase even in the most advanced ages. It is still to be underlined that the central fat and the relative loss of lean mass can become, in old age, relatively more important than the BMI in determining the health risk associated with obesity [34].

To determine the most valid, practical definition of 'obesity' in the elderly is difficult because it is also difficult to measure body fat and fat distribution in the clinical practice.

But indices of fat distribution such as waist circumference appear to be relatively more important than BMI.

In old age, many health risks, which entail independent adverse health risks or functional decline, are linked to weight gain or fat redistribution and affect both early mortality and comorbidity.

A complete assessment of the potential adverse health effects of overweight or obesity in elderly patients can only be obtained by assessing comorbidity and weight history.

An important and confusing factor is the underestimation of health risks related to obesity in the elderly.

Older obese people involved in epidemiological studies may have high mortality and relatively low life expectancy for diseases that are not related to obesity. As a result, these individuals may die before obesity and weight gain can determine their health effects in later life.

The longitudinal effects of confounding factors (smoking, weight variation, etc.) are difficult to measure and separate from the independent effects of obesity itself.

Furthermore, it should not be forgotten that the distribution of fat can give a greater risk to health than BMI.

It can be argued that a voluntary loss of weight can have beneficial effects on health in the elderly as in younger adults. However, studies on the effect of weight loss in the elderly are still unclear, but suggest that even small amounts of voluntary weight loss may be useful (even less than 5% of initial body weight). Treatment should be prudent to avoid loss of lean mass and bone mass. On the contrary, involuntary weight loss is always dangerous and deserves careful clinical evaluation for the search for the underlying causes. Probably, in elderly subjects, it is clinically important to try to diagnose sarcopenic obesity.

In fact, as previously stated, the presence of sarcopenic obesity makes it difficult to evaluate the type of excess body weight and exposes the data analysis to significant methodological biases.

Therefore, further studies are needed for the clinical diagnosis and definition of sarcopenic obesity and its relation to the clinical consequences [30, 34–36].

Recent findings suggest that survey-based estimates of age patterns in the obesity–mortality relationship are significantly confounded by disparate cohort mortality and age-related survey selection bias. When these factors are accounted for in Cox survival models, the obesity–mortality relationship is estimated to grow stronger with age [37, 38].

Obesity paradox and aging

In the recent years, analyses of large clinical trials mostly conducted in patients with chronic conditions, such as heart failure, coronary artery diseases, chronic kidney disease, and stroke, have reported an inverse relationship

between obesity and mortality [36, 39–43]. The survival advantage of obese patients has been confirmed also in older patients with non-cardiovascular chronic disease, like cancer [44, 45].

However, special care must be taken when considering the available studies on the obesity paradox in subjects with chronic diseases, such as those in old age.

The great number of biases and confounding factors, as mentioned above, makes the relation between BMI and mortality very complex, particularly in older subjects. At least the following points should be considered:

- low weight and weight loss in the elderly could be signs of underlying diseases, often difficult to detect;
- patients with normal BMI and high WC may have lower lean mass, lower cardiorespiratory fitness together with higher visceral fat and ectopic fat deposition [46]. At the same BMI, the ratio between lean to fat mass may be different, and this is particularly true in older ages;
- presence of obesity makes the patients symptomatic for chronic conditions at earlier stages of the diseases and, consequently, they could be treated earlier, more aggressively for coexisting diseases (for example diabetes) than their normal-weight counterparts [40];
- it is indubitable that higher adiposity may confirm higher protection against catabolic stress by supplying nutritional reserve.

Information from long-term prospective studies with more detailed assessment of all patients (for example with simultaneous evaluation of weight, BMI, WC, cardio- respiratory fitness, nutritional status, weight change) is needed to better understand the complexity of obesity paradox.

The phenomenon of the obesity paradox in relation to aging may be discussed retracing about body weight changes during the years, which are a relative trend of obesity and clinical relationships between obesity and aging. In Table 1, we reported the publications in which the phenomenon of obesity paradox was observed; in Table 2, those in which it was not found.

Some authors claim that a modest excess weight is useful in advanced age and others instead claim that excess weight is harmful at any age.

Flegal et al. in a study in 2013, concluded that grade 1 obesity overall was not associated with higher mortality and overweight was associated with significantly lower all-cause mortality [47]. In reality, that work was immediately challenged by Willet et al. who claimed that Flegal et al. study was deeply flawed [48]. According to Walter Willet,

Table 1 Sixteen selected articles supporting the existence of the obesity paradox in the elderly

References	Sample size	Outcome	Body mass and/or composition assessment
Antonopoulos and Tousoulis [59]	Review	CVD	BMI
Bender et al. [25]	6193	Age-related mortality	BMI
Chapman [32]	Review	Age-related diseases and mortality	BMI, WC
Curtis et al. [41]	7767	Mortality	BMI
Fleischmann et al. [4]	1346	Mortality in hemodialysis	BMI
Flegal et al. [47]	Metanalysis: 2.880 million individuals and more than 270,000 deaths	All-cause mortality	BMI
Gruberg et al. [5]	9633	Mortality and PCI	BMI
Hainer and Aldhoon-Hainerova [39]	Review	Mortality	BMI
Lee et al. [54]	14,345 men	Mortality	BMI, Fitness
McAuley and Beavers [60]	30,104	Age-related mortality	BMI, CRF
McAuley et al. [22]	12,417	Age-related diseases	BMI, CRF
Oesch et al. [66]	Systematic review: Twenty-five studies (299,750 patients)	Clinical outcomes after stroke	BMI
Rios-Diaz et al. [40]	14,080	Mortality and cancer	BMI
Spelta et al. [68]	Narrative review	Mortality in patients with COPD	BMI
Strulov Shachar and Williams [45]	Review	Cancer-moving	BMI
Trestini et al. [67]	Review	Cancer risk and mortality	BMI

BMI body mass index, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *CRF* cardiorespiratory fitness, *CVD* cardiovascular disease, *FMI* fat mass index, *LMI* lean mass index, *PCI* percutaneous coronary intervention, *WC* waist circumference

Table 2 Thirteen selected articles non-supporting the obesity paradox in the elderly

References	Sample size	Outcome	Body mass and/or composition assessment
Bosello et al. [58]	Narrative overview	Mortality	BMI
Bowman et al. [31]	130,473	Mortality	BMI and WC
Coutinho et al. [50]	Systematic review	CAD and mortality	BMI, WC, WHR
Das et al. [35]	50,149	STEMI	BMI
De Schutter et al. [51]	519	Mortality and CRP	BMI, LMI
Di Angelantonio et Al [19]	Metanalysis: 239 prospective studies in four continents	Mortality	BMI
Global BMI Mortality Collaboration [69]	Metanalysis: 239 prospective studies in four continents	Mortality	BMI
Harris et al. [64]	1723 non-smokers	CRF	BMI
Jahangir et al. [55]	Review	CVD mortality and morbidity	BMI and LBM
Romero-Corral et al. [36]	Metanalysis: 40 studies with 250,152 patients	Mortality	BMI
Sandbakk et al. [53]	417 men aged 70–77	Cardiometabolic risk	BMI
Masters et al. [37]	373,185 US adult men and 416,908 US adult women	Mortality	BMI
Zamboni et al. [34]	Editorial	Mortality in the elderly	BMI

BMI body mass index, *CAD* coronary artery disease, *CRF* cardiorespiratory fitness, *CRP* C-reactive protein, *CVD* cardiovascular disease, *FMI* fat mass index, *FFMI* fat-free mass index, *LBM* lean body mass, *LMI* lean mass index, *STEMI* ST-segment elevation myocardial infarction, *TAT* total adipose tissue, *WC* waist circumference, *WHR* waist-to-hip ratio

the comparison group (BMI of 18.5–25) contains skinny and active people, heavy smokers and serious patients with weight loss, as well as Asian populations. Overweight (BMI of 25–30) and obese groups (BMI > 30) are compared with a heterogeneous group so that the relative risks of higher BMI groups are underestimated, creating an artifact of reducing mortality in the overweight group.

Adiposity indicators other than BMI should also be considered, including abdominal circumference and weight gain. In Flegal study [47], there are no details on previous weight changes over the years, smoking, clinical conditions and age. Contrary to Flegal''s findings, the literature provides clear evidence that even a modest adiposity excess has many adverse health consequences, negative social outcomes, including low quality of life, higher costs of health care, as well as high mortality [49–51].

At this point, some specific considerations should be pointed out. First of all, there is evidence that the prevalence of obesity is growing progressively even among the most advanced age groups [6]. This aspect intensifies the problem, because the decision to intervene or not becomes crucial. If the phenomenon of obesity paradox was real even in older people, then nobody should intervene because excess weight could be considered a protective factor. On the other hand, if adiposity was dangerous even in advanced age and considered an illness even in the elderly, then a modest weight loss should be taken into consideration. Some aspects are often not evaluated or are underestimated by studies that report the phenomenon of obesity paradox even in the elderly: possibility of sarcopenic obesity, presence or absence of visceral adiposity and evaluation of cardio fitness [52].

Sarcopenia

A skeletal muscle-mass reduction is a physiological event linked to aging, usually associated with an increase of adipose tissue. The configuration of real sarcopenia, and consequently of sarcopenic obesity, is a risk factor that upsets the interactions between body mass, high adipose mass and clinical events connected to age-related pathology.

These aspects also raise the question regarding the criteria for a possible weight loss intervention. In fact, weight loss involves a portion of lean mass even in a correct therapeutic approach.

It is a fact that this loss, especially if associated with overweight subjects at an advanced age, will, above all, affect individual autonomy.

The distribution of fat

Another aspect, now consolidated, is body fat distribution that over the years becomes increasingly visceral, especially when a subject also gains weight.

Scientific evidence has now clarified that android-visceral phenotype is associated with major pathophysiological and clinical complications at all ages. This consequence becomes more and more evident as age progresses when, in addition to the centripetal tendency of body fat, the so-called ectopic fat distribution manifests itself, which in turn is related to the

inflammatory component that is currently considered crucial in obesity complications.

Cardio fitness

Levels of physical activity and cardiorespiratory fitness decrease with age [53].

Some long-term follow-up studies show that fitness significantly affects the unfavorable association between obesity and cardiovascular health and being fit is more important than weight loss in the reduction of CVD mortality risk [54].

The "fat but fit paradigm" refers to people with obesity who have a good level of fitness.

Fat but fit persons have lower mortality rates than lean but unfit individuals, in old age as well [55].

To evaluate the possible protective effect of excess weight on morbidity and mortality, all physio-pathological aspects of aging must be taken into consideration: in particular, body composition, modifications of body compartments, and cardio fitness.

Discussion and conclusive remarks

Whether obesity is a disease or just a risk factor is still a matter of debate [56]. The discussion becomes even more intense when excess weight in the elderly comes into the picture.

The Medical Association of the USA (AMA) has already issued a statement that recognizes obesity as a disease [13]; Canadian Medical Association joined the American Medical Association and the Canadian Obesity Network in declaring obesity a chronic disease. Despite this, there is still considerable skepticism linked to the diagnosis of obesity using merely BMI, which is biologically a continuum such as blood pressure, blood sugar or cholesterol in the blood.

However, beyond this discussion, the problem seems to be overcome when it is recognized that excess body weight is generally harmful to health, in the same way as smoking may be [57].

On the other hand, several studies suggest that there is a metabolically benign adipose phenotype, which may explain the paradoxically low risk of cardiovascular diseases of some obese individuals [58]. Therefore, adiposity is not always and necessarily unhealthy.

Health risks depend on many other factors (e.g., the regional distribution of fat, the adaptations of fatty tissue to excess calories) [59].

Fitness, however, seems crucial. Five cohort studies of 30,104 patients (87% men) with CVD show that cardiorespiratory fitness (CRF) significantly modifies the obesity paradox. However, among patients with high CRF, studies show that the risk of all-cause mortality is not always the lowest in the overweight category. The interactions between obesity and CRF in different ages are still insufficiently understood [60].

In contrast to the convincing evidence that obesity (measured by body mass index, BMI) increases the risk of many different types of cancer, there is an ambiguity in the role of obesity in survival among cancer patients. The false-positive association between BMI and cancer survival is likely to be explained by several methodologic limitations including confounding, reverse causation, collider stratification bias and the inadequacy of BMI as a measure of body fatness [61].

There is growing evidence that body composition may in part explain the paradox [62].

One can also point out the recent observation that shows obesity in some types of tumors capable of promoting the therapeutic efficacy of immunotherapy slowing the progression of tumors [63].

Some years ago, Andres et al. [24] argued that although the health risks due to excessive obesity and excessive thinness are both multiple and different, weight recommendations for older people are based primarily on the risk of mortality. He argues that weight assessment tables, which were then almost universal in use, had been derived from the life insurance industry experience. Those boards had not recommended weight adjustments for age. According to Andres, an analysis of actuarial data, on which more recent tables are based, shows that minimal mortality occurs, with a progressive increase in body weight, with advancing age (from 20 to 29, from 60 to 69 years). Furthermore, there was no systematic difference by gender. Andres draws attention to age-specific weight-height tables, eliminating sex and constitutional biotype as variables. These weight standards are lower for young adults and higher for older people than those previously recommended. According to Andres, these considerations confirm the need to adjust age weight standards.

Tamara Harris and coworkers [64], in a paper on the Framingham Heart Study, found that overweight is a significant health problem for older people, especially those that have suffered long lasting excess weight.

Chapman IM pointed out that although obesity in young people is a risk factor for morbidity and mortality, the effect of obesity in the elderly is much more complex [32].

He claims that the body weight associated with maximum survival increases as age increases. According to Chapman, even more surprising is the "obesity paradox" in the elderly, where overweight is associated with an increased risk of cardiovascular disease, but also a reduction in mortality due to these diseases.

It cannot be forgotten that there is no generally agreed criterion for the definition of "older persons". A 65-year limit is often used; however, in the developed world, the most

relevant syndromes for the geriatricians are more common after the 80s. Even when older people are recruited, there is evidence of selection bias, that is patients are included rather than those in routine clinical practice. Scientific studies generally recruit healthier, better-educated people with a higher socioeconomic status. This makes very difficult to interpret and compare studies that support the non-danger of excess weight in the most advanced ages and, consequently, the conclusion is that strict criteria must be imposed when conducting studies in old age [65].

For example, some observational data indicate a survival benefit of obese patients after stroke, but data analysis reveals some methodological concerns, including the discovery that obesity paradox is not observed in patients after thrombolysis. There is, therefore, the need for well-designed randomized controlled trials that evaluate, among other things, the effects of weight reduction on the risk of stroke and cancer in obese patients [66, 67]. Similar considerations must be made for the pulmonary chronic obstructive disease [68].

In a recent paper, on a large sample of non-smokers aged 60–69 without previous weight loss for age-related disease, Bowman et al. [31] have concluded that models of mortality risk estimation by combining BMI and waist circumference give more complete and more reliable information than models with only BMI measurements.

According to these authors, the paradox of the risk of overweight based on the Body Mass Index reported in old age seems to be attributable in part to the central adiposity, which is not measured by BMI. The healthiest elderly (that is, non-smokers and elderly people who have not lost weight in relation to age-related diseases) with central fat that are in the overweight BMI category have significant excess mortality and risk of heart disease. Bowman et al. did not find evidence of a risk paradox with moderate obesity, but instead observed a general increase in mortality compared to individuals with a normal BMI and low waist circumference. Higher levels of physical activity are also an independent protective factor in this case, but this does not diminish the adverse effects of overweight and obesity class I. Overall, these results do not support the paradox of risk of overweight as a real protective effect in the oldest study group [31].

Although the debate on the relative risk of mortality due to obesity still exists, the message that comes from the above mentioned analytical study conducted in Asia, Australia and New Zealand, Europe and North America seems a decisive one. The study critically evaluated 239 prospective studies: the main analysis concerned the risk of mortality, equated with sex and age, as compared to BMI 22.5–25.0. Overweight and obesity were associated with increased mortality for any cause, unquestionably and substantially in line with the four continents [69]. These observations seem to decisively refute the hypothesis that overweight and moderate obesity are not associated with higher mortality, denying speculations about hypothetical protective metabolic effects of an increase in body fat in apparently healthy subjects of all ages, especially the more advanced ones.

Ultimately, the problem of the relationship between body weight and health in the more advanced ages is very complex, as is the problem of aging in good or ill health. Excess weight is a risk factor of morbidity and premature mortality at all ages: this is an irrefutable fact. The reports of a protective effect of overweight or moderate obesity in relation to multiple morbid states, including tumors, are now to be considered contradicted by the more accurate analyses that have highlighted the above-mentioned methodological biases [70–72]. In the more advanced age groups, there are still some unclear aspects, which are also related to the scarcity of studies conducted with an accurate and complete methodology.

It is, however, very significative to recognize that even in the elderly, the paradox of the overweight risk defined by the BMI alone seems attributable to some bias, mainly not taking into account the central adiposity, rather than reflecting a physiological protective effect of the higher content of body fat in old age [73]. The danger may come from the fact that the presence of these incorrect assessments leads to a systematic underestimation of the impact of obesity on morbidity and premature mortality and consequently to clinical behaviors that do not respect the health of the elderly patient.

According to the editorial of 2017 on the Lancet Diabetes & Endocrinology, we can declare that "until obesity is universally recognized as a chronic disease, not a lifestyle choice, its prevalence is unlikely to be reduced" [17] (p. 483).

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Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflict of interest.

Ethical approval The study is a review article. It did not involve human participants and does not require ethics approval.

References

1. di Pergamo G (1989) La dieta dimagrante. S.E. Flaccovio Editore, Palermo
2. Avicenna (Ibn Sina) Il canone della medicina. Romae, In Typographia Medicea, MDXCIII, AUB Libraries, 2002–2007. American University of Beirut Libraries. https://www.aub.edu.lb/. Accessed 15 Apr 2019

3. Dublin LI (1953) Relation of obesity to longevity. N Engl J Med 248:971–9744
4. Fleischmann E, Teal N, Dudley J et al (1999) Influence of excess weight on mortality and hospital stay in 1346 hemodialysis patients. Kidney Int 55(4):1560–1567. https://doi.org/10.1046/j.1523-1755.1999.00389.x
5. Gruberg L, Weissman NJ, Waksman R et al (2002) The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? J Am Coll Cardiol 39(4):578–584
6. Samper-Ternent R, Snih SA (2012) Obesity in older adults: epidemiology and implications for disability and disease. Rev Clin Gerontol 22(1):10–34
7. Drazen JM (2017) Notable articles of 2017, NEJM. http://cdn.nejm.org/pdf/NEJM-Notable-Articles-2017.pdf. Accessed 28 Jan 2018
8. Di Q, Yang Wang, Zanobetti A et al (2017) Air pollution and mortality in the medicare population. N Engl J Med 376:2513–2522. https://doi.org/10.1056/NEJMoa1702747
9. The GBD 2015 Obesity collaborators health effects of overweight and obesity in 195 countries over 25 years (2017) N Engl J Med 377:13-27. https://doi.org/10.1056/nejmoa1614362
10. Gregg EW, Shaw JE (2017) Global health effects of overweight and obesity. N Engl J Med 377(1):80–81. https://doi.org/10.1056/NEJMe1706095
11. Ward ZJ, Long MW, Resch SC, Giles CM, Cradock AL, Gortmaker SL (2017) Simulation of growth trajectories of childhood obesity into adulthood. N Engl J Med 377:2145–2153. https://doi.org/10.1056/NEJMoa1703860
12. Swinburn BA, Sacks G, Hall KD et al (2011) The global obesity pandemic: shaped by global drivers and local environments. Lancet 378(9793):804–814. https://doi.org/10.1016/S0140-6736(11)60813-1
13. Frellick M (2013) AMA declares obesity a disease. https://www.medscape.com/viewarticle/806566. Accessed 28 Jan 2018
14. Stoner L, Cornwall J (2014) Did the American Medical Association make the correct Decision classifying obesity as a disease? AMJ 7(11):462–464. https://doi.org/10.4066/AMJ.2014.2281
15. Kyle TK, Dhurandhar EJ, Allison DB (2016) Regarding obesity as a disease: evolving policies and their implications. Endocrinol Metab Clin N Am 45(3):511–520. https://doi.org/10.1016/j.ecl.2016.04.004
16. Apovian CM, Mechanick JI (2013) Obesity is a disease! Curr Opin Endocrinol Diabetes Obes 5:367–368. https://doi.org/10.1097/01.med.0000433068.09294.a1 (**PMID:23974762**)
17. Editorial (2017) Should we officially recognize obesity as a disease? Lancet Diabetes Endocrinol 5(7):483. https://doi.org/10.1016/S2213-8587(17)30191-2
18. Jastreboff AM, Kotz CM, Kahan S et al (2019) Obesity as a disease: the Obesity Society 2018 Position Statement. Obesity 27(1):7–9. https://doi.org/10.1002/oby.22378
19. Di Angelantonio E, Bhupathiraju SHN, Wormser D et al (2016) Global BMI Mortality Collaboration. Body-mass index and all-cause mortality: individual- participant-data meta-analysis of 239 prospective studies in four continents. Lancet 388(10046):776–786. https://doi.org/10.1016/s0140-6736(16)30175-1
20. Morgan Stanley (2015) Sustainable economics. the bitter aftertaste of sugar. In: MORGAN STANLEY RESEARCH, March 18, 2015
21. Livingston EH (2018) Reimagining obesity in 2018. A JAMA theme issue on obesity. JAMA 319(3):238–240. https://doi.org/10.1001/jama.2017.21779
22. McAuley PA, Kokkinos PF, Oliveira RB et al (2010) Obesity paradox and cardiorespiratory fitness in 12,417 male veterans aged 40 to 70 years. Mayo Clin Proc 85(2):115–121. https://doi.org/10.4065/mcp.2009.0562
23. Childers DK, Allison DB (2010) The 'Obesity Paradox:' a parsimonious explanation for relations among obesity, mortality rate, and aging? Int J Obes (Lond) 34:1231–1238
24. Andres R, Elahi D, Tobin JD et al (1985) Impact of age on weight goals. Ann Intern Med 103:1030–1033
25. Bender R, Jockel KH, Trautner C et al (1999) Effect of age on excess mortality in obesity. JAMA 281:1498–1504
26. Kalinkovich A, Livshits G (2016) Sarcopenic obesity or obese sarcopenia: a cross talk between age-associated adipose tissue and skeletal muscle inflammation as a main mechanism of the pathogenesis. J Funct Foods 33:244–250. https://doi.org/10.1016/j.arr.2016.09.008
27. Shao A, Campbell WW, Chen O et al (2017) The emerging global phenomenon of sarcopenic obesity: Role of functional foods; a conference report. J Funct Foods 33:244–250. https://doi.org/10.1016/j.jff.2017.03.048 (**1756**)
28. Kim JH, Lim S, Choi SH et al (2014) Sarcopenia: an independent predictor of mortality in community-dwelling older Korean men. J Gerontol A Biol Sci Med Sci 69:1244–1252
29. Johnson Stoklossa CA, Sharma AM, Forhan M et al (2017) Prevalence of sarcopenic obesity in adults with class II/III obesity using different diagnostic criteria. J Nutr Metab. https://doi.org/10.1155/2017/7307618
30. Cruz-Jentoft AJ (2019) Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 48:16–31. https://doi.org/10.1093/ageing/afy169
31. Bowman K, Atkins JL, Delgado J et al (2017) Central adiposity and the overweight risk paradox in aging: follow-up of 130,473 UK Biobank participants. Am J Clin Nutr 106(1):130–135. https://doi.org/10.3945/ajcn.116.147157
32. Chapman IM (2010) Obesity Paradox during aging. Interdiscip Top Gerontol 37:20–36. https://doi.org/10.1159/000319992
33. Mathus-Vliegen E (2012) Obesity and the elderly. J Clin Gastroenterol 46(7):533–544. https://doi.org/10.1097/MCG.0b013e31825692ce
34. Zamboni M, Mazzali G, Zoico E et al (2005) Health consequences of obesity in the elderly: a review of four unresolved questions. Int J Obes (Lond) 29:1011–1029. https://doi.org/10.1038/sj.ijo.0803005
35. Das SR, Alexander KP, Chen AY et al (2011) Impact of body weight and extreme obesity on the presentation, treatment, and in-hospital outcomes of 50,149 patients with ST-segment elevation myocardial infarction: results From the NCDR (National Cardiovascular Data Registry). J Am Coll Cardiol 58(25):2642–2650. https://doi.org/10.1016/j.jacc.2011.09.030
36. Romero-Corral A, Montori VM, Somers VK et al (2006) Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. Lancet 368(9536):666–678
37. Masters RK, Powers DA, Link BG (2013) Link obesity and US mortality risk over the adult life course. Am J Epidemiol 177(5):431–442. https://doi.org/10.1093/aje/kws325
38. Alam I, Ng TP, Larbi A (2012) Does inflammation determine whether obesity is metabolically healthy or unhealthy? The aging perspective. Mediators Inflamm ID 456456:1–14
39. Hainer V, Aldhoon-Hainerova I (2013) Obesity paradox does exist. Diabetes Care 36(2):S276–S281
40. Rios-Diaz AJ, Lin E, Williams K et al (2017) The obesity paradox in patients with severe soft tissue infections. Am J Surg 214(3):385–389. https://doi.org/10.1016/j.amjsurg.2016.05.006
41. Curtis JP, Selter JG, Wang Y et al (2005) The obesity paradox: body mass index and outcomes in patients with heart failure. Arch Int Med 165(1):55–61
42. Kalantar-Zadeh K, Anker SD, Coats AJ et al (2005) Obesity paradox as a component of reverse epidemiology in heart failure. Arch Intern Med 165(15):1797 **(author reply 1797-8)**

43. Tankó LB, Christiansen C (2005) Can the obesity paradox be explained by the protective effects of peripheral adiposity? Arch Intern Med 165(15):1796–1797 **(author reply 1797-8)**
44. Gielen S, Sandri M (2012) The obesity paradox—a scientific artifact? Int J Cardiol 162(3):140–142. https://doi.org/10.1016/j.ijcard.2012.01.089
45. Strulov Shachar S, Williams GR (2017) The obesity paradox in cancer-moving beyond BMI. Cancer Epidemiol Biomark Prev 26:13–16
46. Despres JP (2011) Excess visceral adipose tissue/ectopic fat the missing link in the obesity paradox? J Am Coll Cardiol 57(19):1887–1889. https://doi.org/10.1016/j.jacc.2010.10.063
47. Flegal KM, Kit BK, Orpana H, Graubard BI (2013) Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA 309(1):71–82. https://doi.org/10.1001/jama.2012.113905
48. Willett WC, Hu FB, Thun M (2013) Overweight, obesity, and all-causes mortality. JAMA 309(16):1679
49. Malik VS, Willett WC, Hu FB (2013) Global obesity: trends, risk factors and policy implications. Nat Rev Endocrinol 9(1):13–27
50. Coutinho T, Goel K, Corrêa de Sá D et al (2011) Central obesity and survival in subjects with coronary artery disease: a systematic review of the literature and collaborative analysis with individual subject data. J Am Coll Cardiol 57(19):1877–1886. https://doi.org/10.1016/j.jacc.2010.11.058
51. De Schutter A, Kachur S, Lavie CJ et al (2016) The impact of inflammation on the obesity paradox in coronary heart disease. Int J Obes 40:1730–1735
52. Batsis JA, Mackenzie TA, Emeny RT et al (2017) Low lean mass with and without obesity, and mortality: results from the 1999-2004 National Health and Nutrition Ex- amination Survey. J Gerontol A Biol Sci Med Sci 72:1445–1451
53. Sandbakk SB, Nauman J, Lavie CJ et al (2017) Combined Association of cardiorespiratory fitness and body fatness with cardiometabolic risk factors in older Norwegian adults: the generation 100 study. Mayo Clin Proc Innov Qual Out 1(1):67–77. https://doi.org/10.1016/j.mayocpiqo.2017.05.001
54. Lee DC, Sui X, Artero EG et al (2011) Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular disease mortality in men: the Aerobics Center Longitudinal Study. Circulation 124:2483–2490
55. Jahangir E, De Schutter A, Lavie CJ (2014) Low weight and over weight in older adults: risk and clinical management. Prog Cardiovasc Dis 57(2):127–133
56. Hickner J (2017) Is obesity a disease? J Fam Pract 66(10):596. https://www.mdedge.com/jfponline/article/148105/obesity/obesity-disease. Accessed 28 Jan 2018
57. Harrison P (2018) Obesity is a disease, not a choice, experts advise. https://www.medscape.com/viewarticle/896444. Accessed 28 Jan 2018
58. Bosello O, Donataccio MP, Cuzzolaro M (2016) Obesity or obesities? Controversies on the association between body mass index and premature mortality. Eat Weight Disord. https://doi.org/10.1007/s40519-016-0278-4
59. Antonopoulos A, Tousoulis D (2017) The molecular mechanisms of obesity paradox. Cardiovasc Res 113:1074–1086. https://doi.org/10.1093/cvr/cvx106 **(SPOTLIGHT REVIEW)**
60. McAuley PA, Beavers KM (2014) Contribution of cardiorespiratory fitness to the obesity paradox. Progr Cardiovasc Dis 56(4):434–440. https://doi.org/10.1016/j.pcad.2013.09.006 **(Epub 2013 Oct 11)**
61. Park Y, Peterson LL, Colditz GA (2018) The plausibility of obesity paradox in cancer-point. Cancer Res 78(8):1898–1903
62. Caan BJ, Cespedes Feliciano EM, Kroenke CH (2018) The importance of body composition in explaining the overweight paradox in cancer-counterpoint. Cancer Res 78(8):1906–1912
63. Wang Z, Aguilar EG, Luna J et al (2019) Paradoxical effects of obesity on T cell function during tumor progression and PD-1 checkpoint blockade. Nat Med 25(1):141–151. https://doi.org/10.1038/s41591-018-0221-525
64. Harris T, Cook EF, Garrison et al (1988) body mass index and mortality among nonsmoking older persons. The Framingham Heart Study. JAMA 259(10):1520–1524. https://doi.org/10.1001/jama.1988.03720100038035
65. Shenki SD, Harrison JK, Wilkinson T et al (2017) Systematic reviews: guidance relevant for studies of older people. Age Ageing 46:722–728. https://doi.org/10.1093/ageing/afx105)
66. Oesch L, Tatlisumak T, Arnold M, Sarikaya H (2017) Obesity paradox in stroke—myth or reality? A systematic review. PLoS One 12(3):e0171334. https://doi.org/10.1371/journal.pone.0171334
67. Trestini I, Carbognin L, Bonaiuto C et al (2018) The obesity paradox in cancer: clinical insights and perspectives. Eat Weight Disord 23(2):185–193. https://doi.org/10.1007/s40519-018-0489-y
68. Spelta F, Fratta Pasini AM, Cazzoletti L, Ferrari M (2018) Body weight and mortality in COPD: focus on the obesity paradox. Eat Weight Disord 23(1):15–22. https://doi.org/10.1007/s40519-017-0456-z
69. Global BMI Mortality Collaboration (2016) Body mass index and all-cause mortality: individual participant-data meta-analysis of 239 prospective studies in four continents. Lancet 388:776–786
70. Lechi A (2017) The obesity paradox: is it really a paradox? Hypertension. Eat Weight Disord 22:43. https://rdcu.be/bop1D
71. Fassio A, Idolazzi L, Rossini M et al (2018) The obesity paradox and osteoporosis. Eat Weight Disord 23:293. https://rdcu.be/boqaL. Accessed 15 Apr 2019
72. Gilardini L, Zambon A, Soranna D et al (2018) Predictors of the transition from metabolically healthy obesity to unhealthy obesity. Eat Weight Disord 23:739. https://rdcu.be/boqbA. Accessed 15 Apr 2019
73. Bosello O, Donataccio MP (2013) Obesity paradox. Eat Weight Disord 18(4):447–448. https://doi.org/10.1007/s40519-013-0080-5