

OBESITY IN THE ELDERLY

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ABSTRACT

As the proportion of population above age 65 grows, so too increases the prevalence of those individuals who are obese. This phenomenon of an elderly population with obesity is the source of much research and debate with regards to treatment recommendations. It appears that older individuals on the extreme ends of the BMI spectrum, those who are underweight and those who are morbidly obese, have an increased risk of mortality. One major concern in the treatment of obese, elderly individuals is that many may have sarcopenic obesity which can be worsened with weight loss where some degree of lean body mass loss is inevitable. While various methods of weight loss may be recommended in some elderly who are obese, it is clear that any chosen method should be accompanied by a resistance training program in order to preserve muscle mass.

INTRODUCTION

The aging population in the U.S. is expected to more than double by 2050, increasing from 40.2 million to

88.5 million people (1). In tandem with this increase in elderly individuals is the high prevalence of those who are both elderly and obese. The significance of the increasing number of elderly individuals with obesity in terms of appropriate care and associated healthcare costs is the source of much debate.

PREVALENCE

Approximately 35% of adults in the U.S. aged 65 and over between 2007-2010 were obese as defined by body mass index (BMI, weight in kilograms over height in meters squared). In crude numbers this represents over 8 million adults aged 64-74 years and almost 5 million adults aged 75 and over (1). For individuals aged 75 and over there is a lower prevalence of obesity (27.8%) compared to those aged 65-74 years (40.8%) (1). A growing number of elderly are residing in nursing home (NH) facilities, and in line with this trend, researchers are examining the prevalence of obesity in NH facilities and its impact on healthcare utilization. Between 2000 and 2010, the prevalence of moderate to severe obesity in NHs increased from 14.7% to 23.9% (2). The rapid growth of the elderly

population, which can largely be attributed to the aging baby boomers, will mark a change in the population's composition in terms of sex ratios and ethnic diversity. Sex ratios of the population are projected to shift to include a larger share of elderly men (3). Moreover, the racial and ethnic make-up of this elderly cohort of patients is expected to develop to include more Hispanic individuals and a larger proportion of racial groups other than white. Between 2010 and 2050, the number of Hispanic people 65 years and older will increase from 2.9 to 17.5 million and the number of non-Hispanic individuals 65 years and older will increase from 37.4 to 71 million (3). These numbers of elderly individuals with obesity are also expected to increase as the population ages. Paradoxically, increased longevity does not necessarily translate to extra years spent in healthy living but may in fact result in more years spent in chronic poor health.

PATHOPHYSIOLOGY

Aging is accompanied by alterations in body composition. Fat free mass composed mostly of skeletal muscle declines by 40% between ages 20 and 70 years (4). Following age 70, both fat free mass and fat mass decrease together. With aging, there is also a redistribution of fat mass mainly in the visceral component but deposits are also observed in skeletal muscle and liver. The balance between energy intake and energy expenditure determines body fat mass. In the elderly, energy intake does not appear to increase significantly or may even decrease over time; therefore, decreased energy expenditure plays an important role in increasing fat mass with aging (4). After the age of 20, resting metabolic rate decreases by 2-3% per decade mainly due to a loss of fat free mass (4). In addition to a decrease in resting metabolic rate, physical activity declines and there is an increase in sedentary time, which accounts for approximately half the loss in total energy expenditure with aging (4).

The redistribution of body fat centrally leads to the production of pro-inflammatory cytokines (5). Pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF- α) and interleukin 6 (IL-6) lead to muscle loss and sarcopenia due to their catabolic effects (6). This loss of muscle mass leads to adverse outcomes such as decreased mobility and increased frailty.

Endocrinologic changes that occur with aging also play a role in the pathophysiology of obesity including a decrease in growth hormone, testosterone, and DHEA in addition to resistance to leptin and insulin.

HEALTHCARE OUTCOMES: THE POSITIVE AND THE NEGATIVE

Limitations To BMI Measurements

The American College of Cardiology and the American Heart Association define adults as overweight if BMI ≥ 25 kg/m² and obese as BMI ≥ 30 kg/m² regardless of age range. Accurately assessing obesity outcomes in the elderly can be a challenge given the drawbacks of defining obesity by BMI. Other methods have been utilized including hydrostatic densitometry (underwater weighing), dual-energy x-ray absorptiometry (DXA), and waist circumference. Given that BMI can either underestimate or overestimate body fat mass in the elderly and the fact fat deposition in the elderly tends to be accumulated intraabdominally, measurement of waist circumference may be a better way of assessment. Despite its drawbacks, most studies analyzing healthcare outcomes in the obese elderly have utilized BMI as an assessment tool.

The Obesity Paradox

According to existing studies and meta-analyses, a higher BMI can be protective in the elderly. In an analysis of 13 observational studies from 1966 to 1999

examining cardiovascular mortality in non-hospitalized subjects aged 65 and above, a U-shaped curve was observed with an increase in right curve only when BMI was above 31-32 kg/m² (7). A subsequent meta-analysis showed that BMI in overweight range did not confer an increased risk of mortality and a BMI in moderately obese range was only associated with a modest increase in mortality risk by 10% independent of gender, disease and smoking status (8). In a large, multi-ethnic study of community dwelling men and women aged 65 and above, the lowest hazard ratios (HRs) for mortality were seen in individuals with BMI 25 to less than 30 and BMI 30 to less than 35. HRs for mortality were increased when BMI was below 25 or higher than 35 (9). Similarly, in a large study of mortality in over 10,000 patients with type 2 diabetes

mellitus and a median age of 63 years followed for a median of 10.6 years, a lower mortality risk was observed in overweight (BMI ≥ 25 kg/m²) and a higher mortality risk in those who were underweight (BMI ≤ 18.5 kg/m²) or obese (BMI ≥ 30 kg/m²) (10). A subsequent systemic review and meta-analysis evaluating the association of BMI with all-cause and cardiovascular mortality in subjects with type 2 diabetes mellitus, showed a strong non-linear relationship between BMI and all-cause mortality in both men and women. The lowest risk was seen in those with BMI 31-35 kg/m² and 28-31 kg/m². Lower BMI values were associated with higher mortality in both sexes (11). Combining available data suggests that BMI < 25 and > 35 kg/m² is associated with higher mortality (41) (Figure 1).

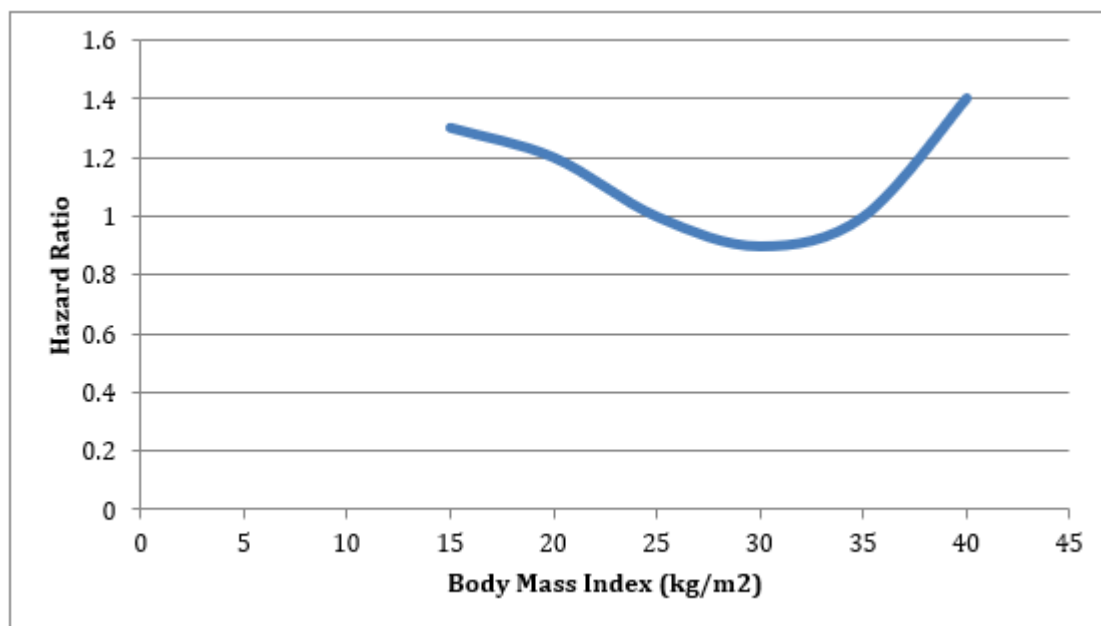


Figure 1. BMI and Mortality in Elderly

While there are positive effects of obesity including increased energy reserve and prevention of malnutrition, protection from bone mineral density loss and osteoporosis, and delay in cognitive decline, there are also potential biases which may account for the obesity paradox seen in the elderly. The survival effect is one such bias which postulates that the remaining

living elderly with obesity are more resistant to the complications of obesity compared to those who were perhaps more susceptible and therefore died earlier. Many studies are epidemiologic in design with the limitation of reverse causation where an overestimation of mortality risk can occur if unintentional weight loss due to an underlying disease

occurs prior to BMI measurements and are then compared to the BMI of healthy group. Finally, cohort effects can be seen as subjects in different environments practicing different lifestyles are compared to one another (12).

One of the most significant complications of obesity in the elderly is the metabolic syndrome. This clustering of risk factors including increased waist circumference, hypertension, dyslipidemia, and glucose intolerance increases the likelihood of diabetes and cardiovascular disease. Obesity can stress the joints leading to joint dysfunction and mobility impairment as well as lead to pulmonary dysfunction and obstructive sleep apnea. Certain cancers are associated with higher BMIs including breast, uterine, colon and leukemia.

Weight Loss

Numerous population-based studies have found that weight loss in older persons is associated with increased mortality (13, 42, 43, 44). This is also true in diabetes (14). Obviously, a part of this may be due to the disease itself causing weight loss, but a number of studies have used different approaches to control for this. The negative effects of weight loss are muscle loss (sarcopenia), the protective effect of fat (on hip fracture for example), lipolysis leading to accelerated atherosclerosis, and fat loss leading to release of fat-soluble toxins into circulation (15). Fat and protein loss can also lead to drug toxicity due to the alteration of the pharmacokinetics of medications that are either fat-soluble or protein-bound (15). The benefits of weight loss need to be weighed against the risks in older persons (Figure 2).

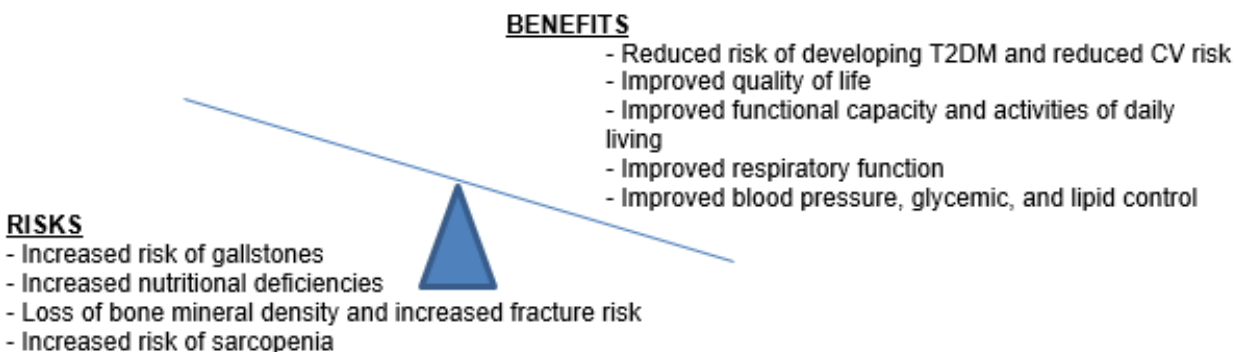


Figure 2. Risk and Benefits of Weight Loss in the Elderly

Sarcopenic Obesity

Diet-induced weight loss in both younger and elderly adults consist of 75% fat tissue loss and 25% is fat free mass loss (16, 17). Hypothetically, in the elderly with obesity the loss of lean body mass is buffered by the already increased muscle mass. This proved to be a falsely reassuring concept when sarcopenic obesity was first described in the early 2000s. Sarcopenia is defined as the loss of skeletal mass and function and leads to frailty, disability, and loss of independence in the elderly. Elderly individuals with obesity have the

unique difficulty in that although weight gain causes increased lean body mass and fat mass, the increased muscle mass is of poor quality. In a study by Villareal and colleagues, 52 obese elderly adults, 52 nonobese frail adults and 52 nonobese, nonfrail subjects matched for age and sex were compared. Elderly adults with obesity showed lower muscle quality compared with the other two groups in addition to reduced functional performance, aerobic capacity, strength, balance, and walking speed (18). In essence, the elderly with obesity cohort were sarcopenic and their increased adiposity proved

deleterious. Subsequent studies have continued to demonstrate that sarcopenic obesity is associated with and precedes the onset of instrumental activities of daily living (IADLs) disability in community dwelling elderly (19). However, elderly subjects who are obese with increased muscle mass have better outcomes compared to those with low muscle mass. Determining which individuals who are elderly and obese have sarcopenia is important clinically and can be accomplished inexpensively and easily by measuring

muscle strength via handgrip dynamometry or gait speed. The brief SARC-F questionnaire (Table 1) can also be used to identify obese individuals with poor muscle function (20). Another method for measuring and monitoring skeletal muscle mass is the use of creatine (*methyl-d₃*) creatine dilution. In this noninvasive test, an oral tracer dose of D3-creatine is given and then subsequently measured in a fasting morning urine sample. Creatine dilution is a better measure of functional muscle mass than DXA (21).

Table 1. SARC-F Questionnaire		
Component	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None = 0 Some = 1 A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0 Some = 1 A lot, use of aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0 Some = 1 A lot or unable without help = 2
Climb stairs	How much difficult do you have climbing a flight of 10 stairs?	None = 0 Some = 1 A lot or unable = 2
Falls	How many times have you fallen in the past year?	None = 0 1-3 falls = 1 4 or more falls = 2

Score: ≥ 4 predictive of sarcopenia

TREATMENT

Who Should Be Recommended For Weight Loss?

Select elderly individuals with obesity and BMI ≥ 30 kg/m² who either have metabolic derangements or functional impairment may be recommended for weight loss provided that muscle and bone loss can be avoided (22).

Lifestyle Changes: Dietary Changes & Physical Exercise

Weight loss can be achieved alone by a moderate caloric deficit of 500-1000 kcal/day which leads to 1-2 pounds lost per week and 8-10% over 6 months (4). However, dietary changes should be prescribed in conjunction with an exercise program consisting of aerobic, resistance and balance training to promote functionality and improve frailty (23). In a study of 107 frail elderly subjects with obesity randomized to control, diet group with 500-750 kcal deficit with 1 gm protein/kg/day, and a multi-component exercise and diet group, the combined exercise and diet group was more effective. The combined group had better

physical performance scores, functional status, and aerobic capacity. Subjects also lost less lean body mass and bone mineral density compared to the diet group (24). Additionally, lifestyle interventions can reduce disease burden. In the Diabetes Prevention Program, men and women ≥ 65 years with obesity were more likely to achieve 7% weight loss compared to their younger (age ≤ 45 years) counterparts with obesity, at 3 years, 63% and 27% respectively. For every kilogram lost through diet and physical activity, the incidence of T2DM was decreased by 16% over a 3-year period (25).

In order to prevent muscle catabolism, elderly individuals with obesity with or at risk for sarcopenic obesity should be counseled on a less restrictive caloric deficit of 200-500 kcal/day combined with a recommended protein intake of 1.0-1.5 gm/kg assuming normal renal function.

Pharmacotherapy

There is limited data on safety and efficacy of weight loss medications in the elderly as they have largely been excluded from clinical trials. The FDA has approved five medications for chronic weight management: Semaglutide, Liraglutide, Naltrexone/Bupropion, Phentermine/Topiramate, and Orlistat. Additionally, metformin has been studied as a weight loss medication in obese, non-diabetic subjects. There is also a study in progress of elderly Japanese patients with type 2 diabetes assessing the efficacy and safety of empagliflozin, a sodium-glucose cotransporter-2 inhibitor (SGLT2i), known to cause weight loss (EMPA-ELDERLY). In this population, the effects on skeletal muscle mass, muscle strength, and physical performance will be assessed in subjects age 65 and older with type 2 diabetes on Empagliflozin (26). Overall, drug interactions, affordability, efficacy, and safety are all potential drawbacks to pharmacotherapy for weight loss in the elderly. However, there are no studies of outcomes of

anorectic drugs used with exercise to protect muscle and bone.

SEMAGLUTIDE

The weekly injectable glucagon-like peptide (GLP-1) receptor agonist was approved in 2021 for chronic weight management in adult patients with BMI of 30 kg/m² or greater or 27 kg/m² or greater plus a weight-related comorbid condition (hypertension, type 2 diabetes or dyslipidemia) as an adjunct to reduced calorie diet and increased physical activity. In the clinical trials, 233 (8.8%) of patients were between 65 and 75 years and 23 (0.9%) were 75 years or older and no differences in safety or efficacy were observed (27).

LIRAGLUTIDE

Liraglutide, a daily injectable GLP-1 receptor agonist was approved at doses of 3mg daily for weight loss by the FDA in 2014 for chronic weight management. This incretin-based therapy appears to have a short-term effect on decreasing gastric emptying but a long lasting central anorectic effect leading to a mean weight loss of 5.8kg in clinical studies (28, 29). The concern surrounding any weight loss in the elderly is the loss of skeletal muscle mass and sarcopenia. In a small study of elderly subjects who were either overweight or obese with type 2 diabetes mellitus treated with liraglutide 3mg daily in addition to metformin, reductions in fat mass and android fat were observed with the beneficial effect of preserved muscle tropism (30). A multicenter randomized, double-blind, parallel-group study of subjects with type 2 diabetes mellitus aged 18-80 years evaluated the effects of Liraglutide (as monotherapy or in combination with metformin) at various doses approved for treatment of diabetes mellitus (0.6mg, 1.2mg, 1.8mg daily) compared to individuals treated with Glimepiride or placebo. Mean body weight was reduced from baseline in all liraglutide treatment arms

(up to 3.2 kg) and reduced fat tissue mass (1.0-2.4 kg) more than lean mass (1.5 kg) while glimepiride increased the mass of one or both tissue types (31). CT assessment also confirmed that reductions in fat tissue mass occurred in both abdominal subcutaneous and visceral fat compartments (31).

CONTRAVE

Contrave, the combination of naltrexone, an opioid antagonist, and bupropion, an aminoketone antidepressant, was FDA approved in 2014 for chronic weight management. Only 2% (62 of 3,239 subjects) in the Contrave clinical trials were over age 65 years and none older than 75 years (32). Data is lacking in terms of safety in older individuals, but given potential for neuropsychiatric disturbances, seizures, increased blood pressure and heart rate; extreme caution should be observed with this medication in the elderly.

QSYMIA

The combination of phentermine, a sympathomimetic amine anorectic, and topiramate extended release, an antiepileptic drug was FDA approved for chronic weight management in 2012. A small proportion of the subjects (254 total, 7%) studied in Qsymia clinical trials were aged 65 and older (33). While no differences in safety or effectiveness were observed, the adequate study numbers are also lacking. Given the side effect profile including risk of increased heart rate, acute myopia and secondary angle closure glaucoma, cognitive impairment and elevated creatinine, caution should be taken with starting this medication in elderly. Lower doses should be chosen and potential drug-drug interactions evaluated.

ORLISTAT

Orlistat acts as a pancreatic and gastric lipase inhibitor and leads to a 6.5-7.5 lb loss at one year. Its major

side effects include steatorrhea, flatulence, fecal incontinence and malabsorption of fat-soluble vitamins. It appears to be equally efficacious with similar tolerance in a both the younger and elderly population (34).

METFORMIN

Metformin, a biguanide antidiabetic medication developed in the 1950s, may be a safe option to achieve modest weight loss even in nondiabetic individuals. In a small study of middle-aged nondiabetic subjects with obesity, metformin 2500mg daily without further caloric restriction or increased physical activity requirement resulted in a mean weight loss of 5.8 +/- 7kg (5.6+/-6.5%) compared to untreated controls (35). It may therefore be an efficacious and cost-effective strategy in elderly persons pending further studies.

Bariatric Surgery

According to the NIH, bariatric surgery procedures including sleeve gastrectomy, laparoscopic adjustable gastric banding (LAGB), Roux-en-Y gastric bypass (RYGB), and biliopancreatic diversion with or without duodenal switch are potential options for individuals with obesity between ages 18 and 64 with BMI ≥ 40 kg/m² or BMI ≥ 35 kg/m² with additional co-morbidities. The American Diabetes Association has recommended lower BMI cutoffs of ≥ 30 kg/m² for select individuals with uncontrolled hyperglycemia despite medical therapy (36). A retrospective review at a major surgical center in the U.S., found that of the 393 older patients (age > 65 years) who underwent bariatric surgery, older subjects had a higher comorbid burden compared to younger patients but exhibited comparable complication rates to patients under the age of 65 (37). In a systematic review of over 8,000 patients aged 60 years and older who underwent bariatric surgery, outcomes (resolution of hypertension, diabetes, lipid disorders) and

complication rates were similar to a younger population, independent of type of procedure (38). While age should not necessarily be a barrier to recommending bariatric, this must be balanced against the limited existing data from pooled results of mostly small studies. Furthermore, bariatric surgery in the young and the elderly should always be coupled with resistance exercise.

Cryolipolysis

Cryolipolysis is FDA approved for treatment of focal fat deposits in the flanks, abdomen and thighs. In this procedure, fat cells are destroyed through a process of thermal reduction by which temperatures below normal but above freezing induce apoptosis-mediated cell death (39). Damaged adipocytes are then removed via an inflammatory response (39). This procedure has the advantage of being less invasive, does not require anesthesia with no downtime. In a retrospective review of a single surgery center with 528 subjects with age ranging from 18-79 years, the procedure was well tolerated with no adverse events

and only 3 cases of mild or moderate pain reported to resolve in 4 or fewer days (40). However, there are limitations regarding the evaluation of the literature on this procedure thus far, including short follow-up time (typically 2-3 months), variability in cooling intensity factor (CIF) applied, differences in the evaluation of efficacy, and differences in the duration of procedure.

CONCLUSION

The landscape of the population is certainly changing and is marked by two significant trends: an increasingly elderly population and an ongoing obesity epidemic. This will undoubtedly impact families, social structures, and healthcare costs. How to appropriately care for these individuals will be the subject of much debate and further research. Physicians will need to balance the potential danger of weight loss in older persons against the complications of obesity to decide on the best patient centered approach. One clear recommendation is that all weight loss regimens in the elderly need to be coupled with a comprehensive resistance exercise program.

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