# Obesity in Elderly Subjects

## In sheep's clothing perhaps, but still a wolf!

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Although the negative impact of high BMI on the risk of death from all-cause mortality is now well established, there is an apparent decline in the relative added risk of obesity with increasing age (1,2). This has led some experts to conclude that obesity should not necessarily be viewed as a disease in individuals older than 55 years. If such shift in the approach to adiposity during the latter phases of life is prematurely accepted, it may not only discourage attempted weight loss in older subjects, but also promote nutritional and lifestyle indulgence, which is presently difficult enough to overcome. It is the purpose of the present commentary to briefly outline the full spectrum of obesity-related hardships in the elderly. In our opinion, obesity-induced complications amount to real disease, which gravely affects quality of life and limits effective lifespan.

**OBESITY, HYPERTENSION, DIABETES, AND THE METABOLIC SYNDROME IN ADVANCED AGE** — The incidence of hypertension, diabetes, and the metabolic syndrome intensifies with age, and aging per se is closely linked to increased prevalence of most of the abnormalities contributing to the metabolic syndrome (3). The incidence of the metabolic syndrome rises with increasing BMI, and a broader waist circumference is more common in men older than 65 years than in younger age-groups (3). The occurrence of the metabolic syndrome reaches peak levels in the 6th decade for men and the 7th decade for women, and a decline is noted only in the 8th decade for men and for some women in different ethnic groups (3). As recently outlined by the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research, older age and obesity are two of the most powerful risk factors for uncontrolled hypertension (4), and high blood pressure, in turn, is a major determinant of mortality and stroke incidence, particularly in senior years. BMI and abdominal obesity are significantly and independently associated with an increase in the prevalence of type 2 diabetes and hypertension, and obesity contributes to the development of hypertension in diabetes in all ages, including old age (5). Hence, separation of abdominal adiposity from its closest sequels, i.e., the metabolic syndrome, hypertension, and diabetes, is somewhat artificial, especially later in life. Adiposity strongly influences these risk factors, which, with the passage of time, may directly dominate the occurrence of complications. The strongest support for such a sequence of events is the fact that attempted weight loss is associated with lower all-cause mortality, regardless of age (6).

**OBESITY AND MORTALITY IN OLDER SUBJECTS** — Despite claims that obesity is not harmful in older individuals, several large-scale studies, such as the 10-year follow-up of the National Institutes of Health–AARP cohort (1), indicated that both overweight and obesity, at all ages and in both sexes, particularly in those individuals who had never smoked and who had no history of disease, are linked to increased mortality (1,2,7). Although the relative escalation in risk associated with a high BMI may decline with advancing age, the absolute rise in mortality rates associated with a high BMI is still much greater in elderly subjects, simply due to increased death rates in this age range (2). This relationship may no longer exist for the very old, in whom mortality rates may be driven by malignancy or aging of the cardiovascular tree that evolved throughout life. In this extreme age range, body weight most likely reflects both overall health status and the process of aging-induced weight loss. However, this cannot be extrapolated to the older population at large or viewed as evidence that high BMI is generally beneficial in the 6th to the 8th decades of life.

The true impact of overweight and obesity on mortality may be obscured by confounding factors. For example, reverse causation induced by preexisting chronic disease and inadequate control for smoking status can mask the effect of obesity through the excessive death risk caused by these low BMI–associated conditions. In some distinct diseases of the elderly, such as Alzheimer's disease (8) or Parkinsonism (9), weight loss may precede the time of diagnosis by years, thus causing further false overrepresentation of morbidity and mortality in the low weight range.

Finally, cumulative attrition of the most vulnerable fraction of the obese population brought about by premature mortality of those subjects who do not survive the late-midlife years leaves only the most biologically advantaged obese survivors for "nonbiased" epidemiological analysis of obesity in advanced years. If one accepts that obesity increases mortality in younger years, attempted comparison between age-matched obese and lean humans in the older age inevitably leads to the study of two highly unequal cohorts of which only one has been subjected to the Darwinian process of obesity-related attrition.

**HEALTH ADVANTAGES OF OLDER OBESE SUBJECTS: RESILIENT BONES AND THE "OBESITY PARADOX"** — Reexamination of the impact of obesity on

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health in older individuals disclosed two potential benefits of weight excess: decreased osteoporosis and better survival of obese subjects with certain health hazards, known as the "obesity paradox." Obesity, linked to increased bone mineral density, is thus far uncontested, as is the fact that this also translates into a lower rate of hip fractures in elderly obese subjects (10). The latter may reflect not only greater bone resilience, but also improved cushioning by adipose tissue during falls. An important emerging exception to this general protective effect of obesity on bone is the recent finding that although men and women with the metabolic syndrome do indeed enjoy better total hip and femoral neck bone mineral density in a cross-sectional analysis, these associations do not translate to improved clinical outcome. In fact, incident clinical fractures were 2.6 times more likely to occur in subjects with the metabolic syndrome compared with participants without the metabolic syndrome after an average follow-up of 2 years (11).

The "obesity paradox" refers to the unexpected findings that obese subjects seem to fare better than, or at least as well as, their normal- or low-weight counterparts in terms of mortality rates in the context of conditions, such as coronary artery disease in hypertensive subjects, congestive heart failure, chronic kidney disease, hemodialysis, postcoronary revascularization, and some instances of non-ST segment elevation in myocardial infarction (12,13). Currently, it is unclear whether or not all these different situations that share some common, yet unidentified, underlying mechanism are related to obesity itself, or rather reflect nutritional status or reserve, and/or possibly coexisting medical therapy. It remains uncertain how older age interacts with these protective effects of excess adiposity. Additionally, obesity is not a general "savior" in acute medical conditions. Hence, this interesting and potentially critical phenomenon remains presently enigmatic, requiring case- and age-specific in-depth examination. As an example of this effect, some 20 years ago, obesity in the elderly was actually linked to the twofold increase of postmyocardial infarction and in-hospital mortality in subjects >65 years (14). Has the obese phenotype been changed by the environment, or chronic medical therapy, or rather, have advances in the quality of critical care preferentially affected the obese?

## OBESITY AND CARDIOVASCULAR DISEASE IN THE ELDERLY

— The cardiometabolic complications of obesity have been generally linked to central adiposity, but in many reports, obesity is quantified in terms of BMI alone, rather than waist circumference, which may potentially mask the association of abdominal fat and cardiovascular disease and events. Nevertheless, a body of evidence indicates that obese older subjects are more prone to cardiovascular morbidity. In the Health Professionals' Follow-up Study, men aged 65 years or older, with a waist-to-hip ratio of ≥0.98, had a 2.76-fold increased risk for coronary heart disease (CHD), even after adjustment for BMI and other cardiac risk factors (15). In the Physicians' Health Study (a randomized trial of aspirin and β-carotene among 22,071 apparently healthy U.S. male physicians, aged 40–84 years at baseline), abdominal adiposity, whether measured by waist-to-hip ratio or waist circumference, was associated with a modest elevation in the risk of CHD in both middle-aged and older men. Of particular note in this study is the finding that age did not significantly modify the relationship between either measure of abdominal adiposity and risk of CHD (16). In a Chinese cohort of 67,334 women, aged 40–70 years, who had no prior history of CHD, stroke, or cancer at recruitment into the study, in the course of a mean follow-up of 2.5 years (168,164 person-years), waist-to-hip ratio was positively associated with the risk of CHD in both younger and older women, while other anthropometrics, including BMI, were related to CHD risk primarily among younger women (17). In a prospective study of 516 Brazilian women, aged 60–84 years, who were followed up for an average period of 6.6 years, the presence of the metabolic syndrome and high waist-to-hip ratio was associated with increased cumulative risk (odds ratio 1.66 and 1.72, respectively) of stroke, myocardial infarction, evidence of coronary artery disease, or cardiovascular death (18). In the Epidemiologic Follow-Up Study of the First National Health and Nutrition Examination Survey (NHANES I), 1,259 Caucasian women aged 65–74 years with BMI ≥29 kg/m$^2$ showed 50% increased risk of CHD in the course of a mean follow-up period of 14 years, which was 2.5-fold higher than in women with BMI of 23–24 kg/m$^2$ (19). A Swedish study of 70-year-old subjects, initially free from CHD, found that the 15-year risk-adjusted incidence of CHD was increased by larger waist circumference and BMI in males but not in females (20). In a U.S. cohort of 4,968 older (≥65 years) men and women from the Cardiovascular Health Study followed up for 9 years, the risks of myocardial infarction or stroke did not differ in the overweight range of 25–29.99 kg/m$^2$, thus suggesting that a BMI cutoff point of 25 kg/m$^2$ may be overly restrictive for the elderly (21). Overall, these data support an association between adiposity, particularly central adiposity, as assessed by anthropometric measurements, and increased propensity for cardiovascular disease, predominantly CHD.

## OBESITY AND THE INCIDENCE OF STROKE IN OLDER SUBJECTS

— Association between obesity and stroke in advanced age has been inconsistent and may be sex-related. The Canadian Cardiovascular Health study did not find obesity to be a predisposing factor for stroke in older subjects (21). Conversely, the Honolulu Heart Program, which over a 22-year period prospectively followed up a cohort of 1,163 nonsmoking men aged 55–68 years, found that the rate of thromboembolic stroke rose significantly with increasing levels of BMI (22). In subjects from the Framingham Offspring Study aged 50–81 years, the 10-year population attributable risk of stroke was greater for the metabolic syndrome than for diabetes, particularly in women (27 vs. 5%), owing to its greater prevalence of the metabolic syndrome in the general population (23). Obesity did not affect stroke rates in Korean men (24). A Spanish stroke registry of 2,000 consecutive stroke patients identified obesity as one significant predictor of stroke in women (mean age 75 years), but not in men (25). A similar identification of obesity as a risk factor for atherothrombotic brain infarction in older female but not male subjects was also reported by Aronow et al. (26). In a post hoc analysis of the Systolic Hypertension in the Elderly (SHEP) trial, the lowest BMI quintile was associated with increased occurrence of stroke rather than obesity (27), but after introduction of control of multiple confounders, the relation of BMI to death or stroke rate in the placebo group became insignificant. Overall, we interpret this mixed outcome of the attempt to clarify whether obesity is a contributor to the etiology of stroke in the elderly as a simple reflection of the

dominant roles of hypertension, including obesity-related hypertension, as well as adiposity-related diabetes in this setting.

## OBESITY MAY BE A PREDISPOSING FACTOR FOR REDUCED COGNITIVE SKILLS AND ALZHEIMER'S DISEASE

— In the otherwise healthy older population, the combination of an expansive waist circumference or BMI, with high systolic or diastolic blood pressure, was linked to a modest decrease in performance on tests of motor speed, manual dexterity, and executive function (28). The Framingham Heart Study comprising male participants (age range 55–88 years) followed up over a period of 18 years revealed that obesity had an adverse effect on cognitive performance (29). In a Swedish cohort of nondemented adults who were followed up from age 70 to 88 years, high body mass was linked to increased propensity for dementia (30). The association appeared to be so profound that the risk for Alzheimer's disease increased by 36% for every BMI unit at the age of 70 years. In population studies, such linkage is subject to the confounding effect of the natural history of Alzheimer's disease often characterized by weight loss, which precedes the diagnosis of this condition (8). A recent meta-analysis of the literature suggested the existence of a significant U-shaped association between BMI and Alzheimer's disease. The pooled effects of obesity on incident Alzheimer's disease and vascular dementia revealed a 1.80- and 1.73-fold increase in risk, which was particularly evident in studies with long follow-up (>10 years) and young baseline age (<60 years). Of particular note was the finding in all the studies reviewed that weight gain and large waist circumference, or skinfold thickness, increased the risk of dementia (31).

## OBESITY, MOBILITY, AND PHYSICAL INDEPENDENCE IN OLDER SUBJECTS

— Low levels of spontaneous physical activity is a major predictor of adipose tissue accumulation in humans, and total body movement, most of which is related to ambulation, is negatively correlated with fat mass (32).

Physical inactivity, in turn, has rapid profound effects on skeletal muscle metabolism. Unlike the common association of obesity with increased lean body mass and muscle volume in young adults, obese older individuals often develop sarcopenia, reflected by reduction in lean body mass. Impaired mobility in older obese individuals is therefore hardly surprising. A recent study of 2,982 subjects, aged 70–79 years, followed up for 6.5 years, revealed that high adiposity increased the risk of new-onset mobility limitation by 40–50% (33). A cross-sectional study of 92 monozygotic and 104 dizygotic community-living pairs of twin sisters (aged 63–76 years) reared together found an inverse association between adiposity and mobility that was mostly due to the effect of shared genes (34). Larger waist circumference was a powerful predictor of new-onset disability 2 years later, associated with a 2.17-fold increase in the adjusted risk of mobility disability and a 4.77-fold higher adjusted risk of agility disability for men in the highest quintile compared with those in the lowest quintile (35).

## OBESITY AND FRAILTY IN OLDER AGE

— Obesity clearly exacerbates the age-related decline in physical function and causes frailty in older individuals. Frailty in older obese individuals may be related to the insulin resistance and inflammation that often accompany obesity (36). This is reflected by self-reported impairment in activities of daily living in the older obese individual, limitations in mobility and decreased physical performance (as detailed in the former segment), increased risk for functional decline, and a higher rate of nursing home admissions (35,37–39). Of particular significance in establishing a cause-and-effect relationship between obesity and frailty is the recent report that weight loss and exercise can ameliorate frailty in older obese adults (40).

## OBESITY AND DEGENERATIVE OSTEOARTHRITIS IN ADVANCED SENIOR YEARS

— Increased body mass has a negative impact on weight-bearing joints, and knee osteoarthritis is particularly common in obese men (58%) and women (68%) by the age of ≥65 years (41). The physical limitation caused by this condition is widely appreciated, but less attention is paid to the inevitable impact on pain and chronic overconsumption of analgesics that often underlie the development of drug-resistant hypertension and incipient nephropathy.

## SEXUAL DYSFUNCTION AND OBESITY IN OLDER SUBJECTS

— A recent study indicated that central obesity, assessed by several anthropometric indicators, is associated with the presence of erectile dysfunction in men >60 years, but not in younger men (42). Although age appeared to be the major determinant of erectile dysfunction in NHANES, obesity had an independent contributory effect, increasing the odds ratio for impotence by 1.6 (43). In a cross-sectional analysis of men >50 years of age in the U.S. Health Professionals' Study, obesity independent of other confounding factors increased the risk of erectile dysfunction by 30% (44).

## URINARY INCONTINENCE IN OLDER OBESE SUBJECTS

— Obesity is a recognized contributing factor to urinary incontinence in older women and men (45). Although the precise underlying mechanism(s) is unclear, the apparent excessive weight and pressure applied on the bladder by the increased intra-abdominal fat mass appears to be a reasonable contributor to this complication.

## OBESITY AND RENAL DISEASE IN OLDER SUBJECTS

— The prevalence of renal failure increases with age, and obesity is a significant risk factor for end-stage renal disease (46). Compiled data from 57 prospective studies clearly links obesity to mortality of kidney disease, such that death of renal disease increased progressively with BMI (47). Although age-specific trends were not provided, hazard ratio in this analysis was based on subjects up to the age of 79 years. A recent report indicated that increased waist-to-hip ratio was a significant and independent predictor of chronic renal disease in elderly Taiwanese (48). In a cross-sectional study in African Americans, increasing age and waist circumference were associated with increased chronic kidney disease (49). Collectively, this information suggests that obesity, particularly abdominal adiposity, imparts a negative effect on renal disease in the older population.

## CONCLUSIONS

— Obesity per se continues to contribute to mortality in advanced years. However, even if mortality is conceded to be unrelated to obesity at an older age, the unaffected risk of death remains, at best, an imperfect descriptive

measure of a disease spread over multiple years of life. Obese, or overweight, older subjects with such presumed unimpaired longevity are nevertheless more likely to have hypertension and diabetes; develop coronary artery disease and possibly stroke; experience erectile dysfunction; suffer from accelerated loss of cognitive function, incontinence, frailty, osteoarthritis, and functional disability; and are dependent on others. The clustering of so many well-defined ailments resulting from, or associated with, obesity, particularly in older subjects, is impressive enough to view obesity as a real primary disease that requires attention and medical care.

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