Sarcopenic Obesity in an ageing world. A narrative review regarding sarcopenic obesity in the elderly population

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Abstract

The population is ageing globally and along with the obesity pandemic, a new phenotype of sarcopenic obesity is recognized as a major health issue affecting the elderly. The two main components of this condition are obesity, mainly central adiposity, and sarcopenia which is characterized by low muscle mass, low strength and poor physical performance. Elderly individuals with sarcopenic obesity face greater health risks and exhibit poor physical performance, frailty, impaired quality of life and increased morbidity and mortality. The main interventions for the management of sarcopenic obesity are lifestyle changes, which include increased aerobic and resistance exercise, along with weight loss and balanced diets under specialist supervision. The purpose of this review is to summarize the definition, epidemiology and pathophysiology of the condition along with the ageing process mechanism analysis, diagnostic criteria and management guidelines. Further scientific research is required to better understand the pathophysiology of this phenotype, to give a precise definition and to design structured management protocols in order to enhance healthy ageing.

Key words: *elderly; ageing; obesity; sarcopenia; sarcopenic obesity*

INTRODUCTION

Ageing population

Life expectancy has been increasing globally in the last decades and the ageing population is increasing faster than other groups [1]. In the last 50 years, according to the World Health Organization (WHO), the proportion of people over 60 years has doubled from 11% to 22% [2].

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In Greece, according to Eurostat, it is estimated that the percentage of the elderly population is 21.3 %, which means that more than 1 out of five citizens is over 65 years old [3]. Life expectancy has increased to 83 years for women and 77.9 years for men, in Greece [4]. This life expectancy increase worldwide is attributed both to decreased mortality in young individuals in the developing countries, along with the increased life expectancy in the developed countries due to social, economic and scientific achievements [1, 5].

However, along with the increase in life expectancy, there is an increase in the prevalence of complex medical problems and conditions such as sarcopenia, reduced mobility, obesity, cognitive impairment and psychological issues that affect the quality of life of older people,

and have a great impact on health systems [5]. In this context, a great issue arises; if the additional years of life are spent in good health [1, 6].

Problems in the ageing man

Growing old comes both with physiological changes and increased risk of chronic disease. There are changes in vision, hearing, cognition, body composition and movement. Further, there is an increased risk of chronic diseases like heart disease, respiratory disease, dementia, stroke and cancer [1]. The above conditions can result in complex states like sarcopenia and frailty, which may compromise the elderly's quality of life [7]. Frailty is a clinical state which refers to the decline of physiological reserve and function of multiple systems of the organism and leads to increased vulnerability [8]. Frailty phenotype sometimes overlaps with sarcopenia, however sarcopenia precedes frailty [9]. Sarcopenia is one of the main bodily changes that affect the general wellbeing of the elderly and will be further analyzed on this article. It describes the loss of muscle mass along with reduced strength and impaired physical function. Sarcopenia and frailty are considered as major geriatric issues that affect general wellbeing and global functioning leading to increased hospital admissions and deaths in the elderly [10].

Review aim

Two of the major health-related concerns worldwide, mainly in developed countries, are ageing and obesity. The purpose of this review is to address ageing-related body changes, sarcopenia, obesity and the pathophysiology and complications arising from the combination of these conditions. In addition, we will propose interventions to preserve physical function and good quality of life for the elderly, in order to accomplish WHO target, adding health to years and living the rest of their lives in the best possible health conditions.

BODY CHANGES IN OLD PEOPLE: OBESITY AND SARCOPENIA

One of the recently noticed phenotypes of the ageing population is sarcopenic obesity. This is a combination of two body conditions observed at the elderly population, sarcopenia and obesity. In this section, we will review the definitions and the diagnostic approach to evaluate sarcopenia and obesity.

Obesity epidemic and ageing

A major issue that negatively affects the aging population and complicates the age- related frailty status, is the increasing prevalence of obesity. Obesity has become a pandemic, and according to WHO, in the last decade more than 1.9 billion adults worldwide are overweight, and 650 million of them are obese [11]. The Center for Disease Control (CDC) in the USA, in a more detailed estimation, has reported that in 2016 the prevalence of obesity for the population aged>60 years was 41% compared to 23.7% almost 20 years earlier [12]. It is evident that the obesity pandemic is rapidly expanding in the elderly population. The physical body changes due to ageing which become more complicated by obesity, lead to poor physical performance, impaired mobility, reduced strength and increased morbidity and mortality [13, 14]. Moreover, they are related to insulin resistance, metabolic syndrome and cardiometabolic disease risk factors more strongly than sarcopenia or obesity alone [15, 16].

Obesity is defined as the medical condition where extra fat accumulates in the body to an extent that it may have a negative effect on general health. It is related to increased caloric intake, decreased energy expenditure and often a genetic background [17, 18]. Changes in hormones regulating metabolism, changes in catabolism and disturbed gastric absorption may also affect body composition, especially in the elderly [19]. Obesity is estimated by the Body Mass Index (BMI), which is calculated by dividing the weight of a person in kilograms by the square of his height in meters (kg/m2). BMI classification is presented in table 1. Central obesity is evaluated by the waist to hip ratio (WHR). This is calculated by dividing the waist by the hip circumference. WHR>1 for men and >0.85 for women indicates increased abdominal fat accumulation and higher health risk [11, 18]. BMI may not be the most accurate way to evaluate obesity in the elderly, as it underestimates central adiposity. According to a recent systematic review, WHR is considered a better index for evaluating the risk of cardiovascular disease,

Table 1. *Weight classification according to Body Mass Index (BMI)*

Classification	BMI
Underweight	<18.5
Normal weight	18.5-24.9
Overweight	25-29.9
Obese class I	30-34.9
Obese class II	35-39.9
Obese class III	>40

metabolic syndrome and diabetes compared to BMI [20]. This is possibly related to the body changes observed in the elderly. With aging, body composition gradually changes: fat mass (FM) increases, while the fat-free mass (FFM), which contains the skeletal mass (SM), the bone mass (BM) and the total body water, decreases [21, 22]. Regarding fat tissue, there is a decrease in subcutaneous fat mass with increased intra-abdominal fat deposition [21, 22]. Thus, the combination of BMI and WHR is considered a more reliable marker to assess body composition and evaluate potential health risks in the elderly [23].

Sarcopenia in the elderly

One of the major physiological changes observed in the process of ageing is the loss of muscle mass and muscle strength and the impairment of physical performance. In a recent consensus, the European Working Group on Sarcopenia in older people has defined sarcopenia as the syndrome of "progressive and generalized loss of skeletal muscle mass (SMM) and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death" [24]. However, there are various definitions and sets of diagnostic criteria used in the studies. The most commonly used diagnostic criteria for sarcopenia are low muscle mass (MM), low muscle strength or low physical performance (two out of three criteria need to be met) [24].

There is a wide range of techniques to measure muscle mass, muscle strength and physical performance. The MM volume can be assessed by body imaging techniques, including computed tomography scan (CT) and magnetic resonance imaging (MRI) which are the gold standard, and alternatively with dual- energy X-Ray absorptiometry (DEXA). Bioimpendance analysis has also been proposed as an alternative to DEXA [25, 24]. Anthropometric techniques can be used in clinical practice but are less precise. MM can be clinically assessed by the measurement of mid upper arm and cuff circumference, and also skinfold thickness, but these are affected by body weight. Usually, low MM is defined as an outcome of two standard deviations below the general population mean, measured by the aforementioned techniques. [24, 26]. Muscle strength assessment is mainly measured by hand grip strength and knee flexion/ extension. Hand grip strength is a clinical marker of mobility and correlates well with leg strength which is assessed by a hand dynamometer. The procedure involves squeezing of a handle for 3-5 sec with a cutoff point of 30 kg for men and 20 kg for women [27]. Finally, physical performance, the third sarcopenia criterion, is usually assessed by gait speed, usual estimated by the time needed to walk a 4-meter distance with a cut-off point of <0.8 m/s, or with the short physical performance battery and the timed get up and go test [24]. During the short performance battery, various tests are used such as the ability to stand at various positions, to rise from a chair and walk a specific distance back and forth for 5 times [24, 28].

The epidemiology of sarcopenia is a challenge due to the wide variation of MM loss among individuals and the multiple definitions and assessment tools used. It has been extensively studied in recent years, reporting a prevalence of 5% to 13% in the early-old age (60- 70 years) and up to 50% in the oldest-old age (>80 years old) [29]. According to the report of the International Sarcopenia Initiative Team, the prevalence in the community is estimated to range between 1-29%, in long term care populations between 14% to 33% and in hospitalized populations around 10% [30]. A recent review regarding the epidemiology of sarcopenia showed that the decline of muscle strength and physical performance is more rapid than that of MM [31]. MM reaches its peak between 20 and 30 years, with a modest decrease from 30 to 50 years, and finally an additional decrease of 30% from 50 to 80 years of age [32]. The decline rate is rather similar between males and females, even though men generally have more MM and strength than women. In addition, ethnic differences, nutrition, environmental factors and general health status influence sarcopenia progression and prevalence.

The mechanisms leading to sarcopenia are multiple, with varying contributions over time. A previous status of decreased mobility and poor nutrition significantly promotes the degradation of muscle cell mass [33]. Furthermore, the age-related decrease in hormonal factors like testosterone and IGF-1 leads to decreased protein synthesis, decreased myoblast stimulation and disinhibition of myostatin [34, 35]. Finally, other mechanisms like apoptosis, autophagy, mitochondrial dysfunction and genetic influence impair muscle mass and function [33-36]. At last, the regular use of medications like corticosteroids, statins, glinides and sulphonylouria has been associated with the development of muscle wasting [37, 38].

Sarcopenia is a major issue for the elderly, as it contributes to poor quality of life, impaired mobility, physical frailty, functional impairment and increased death rate [30]. It has a great impact on morbidity, mortality, chronic disability, and is associated with high healthcare costs [24].

SARCOPENIC OBESITY

Definition, criteria and epidemiology

Sarcopenic obesity (SO) is a prevalent clinical condition of the geriatric population, and is associated with impaired physical function and poor general health status. There is a great research interest on SO, however, there is no clear definition according to recent literature reviews. It refers to a phenotype of increased body fat deposition, decreased lean MM and impaired muscle function [39, 40]. Its prevalence is difficult to be assessed, as there is a great variation in definition and diagnostic criteria used in relevant studies. It is estimated that the average prevalence is 5-10% in older adults, equal between males and females and higher in individuals over 80 years old [41].

The diagnostic criteria for SO include a combination of the criteria for obesity and sarcopenia. Although, the definition of obesity is more consistent, the definition of sarcopenia is more heterogenous, challenging SO diagnosis. A practical way to assess SO in clinical practice is the assessment and quantification of the two parameters. For obesity high BMI or high waist circumference (WC) or fat mass (FM), while for sarcopenia low MM and slow walking distance or weak hand grip test [41]. However, the great variability of tests complicates the clinical approach. A recent review has focused on the variation in definitions and assessment techniques of SO used in multiple studies [42, 43]. The more frequently used are presented in table 2 [42, 43]. SO is a clinical phenotype resulting from the interaction of high FM and low SMM, and not from the co- existence of two distinct entities, obesity and sarcopenia; therefore both conditions need to be assessed. The gold standard methods for body composition assessment are CT and MRI scan, though they are expensive and not easily accessible. DEXA is a highly recommended technique as it is more affordable and diagnostically accurate [42].

Pathophysiology

It is not clear whether obesity and sarcopenia co-exist as unique identities or share common pathogenic mechanisms. Sarcopenia, an age-related condition, synergistically worsens obesity-associated health outcomes in the elderly and vice versa.

Age-related changes

Aging itself is related both to loss of SMM, impaired function of the fat tissue and redistribution of FM. As mentioned above, MM follows a decline after the 4th decade of life, reaching to a decrease of up to 30% between 50 and 80 years of age [32, 44]. Furthermore, FM tends to increase until 70 years of age, when fat loss is initiated [45]. Apart from the changes in MM and FM volume, there is a redistribution of FM to ectopic areas like the liver and the skeletal mass with metabolically harmful results [46]. Lastly, age-related loss of spinal motor neurons contributes further to the reduction in muscle mass and muscle activity. These changes in body composition

Table 2. *Sarcopenia and Obesity Assessment Tools*

Sarcopenia Assessment	Obesity Assessment
Muscle Mass	• Body Mass Index (BMI)
• Appendicular Skeletal Mass (ASM)/ Weight (W)	• Fat Mass (FM)
• ASM/ Height 2 (H)	• Waist Circumference (WS)
• Fat Free Mass Index (FFMI)	• Visceral Fat Area (VFA)
• Muscle mass (MM)	
• Total Muscle Mass (TMM)	
• Calf cross sectional area	
• Thigh muscle cross sectional area	
• Appendicular Lean Mass (ALM)	
• ALM/BMI ratio	
Muscle strength and performance	
• Gait speed (GS)	
• Hand grip strength (HGS)	

lead to a decline of the resting metabolic rate and along with the decreased physical activity, they cause a decrease in total energy expenditure and an increase in body fat mass. Resting metabolic rate is a main factor of energy homeostasis at basal state, crucial to maintaining cellular function [47]. Another component of energy balance which is reduced up to 20% with age is thermogenesis, which is activated after caloric intake, increasing caloric expenditure. The sedentary lifestyle of the elderly, along with the changes in MM volume, the decreased resting metabolic rate and adaptive thermogenesis, directly affect energy balance leading to the development of metabolic complications in the elderly [47, 48]. Energy balance is also impaired in the elderly population due to decreased food consumption. Ageing is related to impaired orexigenic mechanisms and impaired diet habits. There is an increase in anorexigenic hormones like cholecystokinin (CKK) and peptide tyrosine tyrosine (PYY) and a decrease in gherlin [49]. Also, due to economic and social reasons, protein consumption is low while fat and salt intake is high, further affecting total body composition.

Hormonal Changes

Elderly body composition is related to sex specific hormonal changes, insulin resistance, increased cortisol levels, reduced growth hormone levels and impaired thyroid hormone responsiveness. Low menopausal estrogen levels contribute to an increase in body FM with a shift to the central body, along with a decrease in MM, as they attenuate skeletal mass inflammation which is one of the main pathogenic mechanisms for sarcopenia [50]. In elderly men over 80 years of age, testosterone deficiency is observed at a percentage exceeding 50%, which may also negatively affect body composition, favoring a SO phenotype [51, 52]. Furthermore, aging in both sexes is connected with a decrease in GH and IGF-1 production, along with an increase in cortisol levels. These changes are linked to the accumulation of visceral fat and the induction of inflammation [52-54].

Inflammation Status

Both aging and obesity are related to increased circulating pro inflammatory cytokines like tumor necrosis factor a (TNF-a), interleukin 1 and 6 (IL-1, Il-6), which are mainly released by adipocytes and immune cells in the adipose tissue [50]. This leads to increased risk of lipotoxicity, inflammation and impaired muscle protein synthesis. This low-level inflammation favors insulin resistance, which is enhanced by the age-related central fat distribution and muscle catabolism. Impaired insulin sensitivity promotes further MM loss and FM gain [55, 56]. Inflammatory factors directly affect skeletal MM, inducing muscle protein catabolism and myocyte apoptosis through oxidative stress and inflammation [50, 55, 56]. This condition promotes sarcopenia and further fat accumulation in the skeletal mass. Obesity itself activates macrophages, mast cells and T lymphocytes leading to increased secretion of leptin, GH and TNFa; thus exacerbating low-level inflammation and consequently inducing further muscle mass loss. This state of low-grade systemic inflammation initiates a vicious cycle of MM and FM inflammation, promoting both sarcopenia and obesity.

Clinical Consequences

There are recent studies on the possible effects of obesity and sarcopenia on disability, morbidity and mortality. A recent cohort study on elderly with SO compared groups of elderly with sarcopenia, obesity, SO and no sarcopenia or obesity regarding the prevalence of metabolic disease. It showed that elderly with SO were more likely to have cardiovascular disease risk factors, metabolic syndrome and insulin resistance [57]. According to the Cardiovascular Health Study of 3366 elderly individuals, SO was related with modestly increased cardiovascular disease risk compared to sarcopenia and obesity alone [58]. Similarly, another study by Chung et al. (2013) on an elderly population, showed a metabolic syndrome prevalence of 60.9% in SO subjects compared to 48.6% in obese non-sarcopenic subjects and 29.2% in sarcopenic non-obese individuals [59]. Several other studies have shown that SO is related to higher risk of hypertension, dyslipidaemia, insulin resistance and DM [60-62]. However, the link between SO and cardiovascular disease (CVD) risk has not been extensively studied, with weak evidence for the synergistic effect of obesity and sarcopenia on CVD risk. It seems that SO elderly has an increased risk of CVD mortality, equal however to elderly with either sarcopenia or obesity [63].

Patients with SO have a greater risk of postural instability and knee and hip osteoarthritis compared to patients with obesity or sarcopenia alone. A small increase in falls is also observed, which is related to dynapenic obesity-meaning obesity with low muscle strength as opposed to obesity with reduced MM [62-64]. General physical ability, self-perceived physical performance and daily instrumental use are also negatively affected in SO [67, 68]. Sarcopenia and obesity, either solely or in combination,

are negatively associated with cognitive function, and are also linked to poor general quality of life [69, 70]. A synergistic effect of increased body weight and sarcopenia on the risk of depression and impaired overall psychological health, has also been reported [71]. SO is associated with gastric cancer according to recent studies, though further investigation is required in the field [72, 73].

Finally, a few prospective studies have shown an association of SO with increased mortality risk. In a recent population study, the British Regional Heart Study, sarcopenic obesity was linked to a greater risk of CVD- mortality and all- cause mortality [74]. Another meta-analysis of recent prospective cohort studies, has also reported an increase of up to 24% of the risk for all-cause mortality in SO compared to non-SO subjects [75].

Management

The cornerstone in SO prevention and management is early lifestyle interventions, even before the syndrome develops. In order to accomplish WHO targets for the elderly to maintain physical function, good health status and better quality of life, measures need to be taken. Sedentary lifestyle and unhealthy eating habits lead to increased quantity and poor quality of food and pose a greater heath threat than aging itself. The main interventions studied are physical activity and proper nutritional management (eg weight loss, nutritional supplements and vitamins).

Most recent studies on physical activity have focused either on obesity or sarcopenia alone, while few have dealt with SO. The main suggestion derived from most of them is aerobic exercise of 150 min/week and twice a week exercise for strength, balance and flexibility [76]. Aerobic exercise has a positive cardiorespiratory impact and reduces mortality risk, while resistance exercise improves physical strength and muscle mass [77]. The combination of weight loss with exercise has a better outcome on physical function than each one alone. A recent study focused on the effect of three types of exercise interventions- aerobic, strength or both, in obese, elderly patients and showed that the combination of both exercise types provided the greatest benefits [78]. Each exercise program should be individualized according to the health expert consultation in order to minimize injury risk and maximize adherence.

Nutritional interventions to lose weight need to be guided by a dietician and a multidisciplinary team including a physician, a personal trainer, and possibly other specialties like physiotherapist and occupational therapist, while the elderly patient needs to be closely monitored. Most weight loss trials restrict about 500 to 1000 calories a day aiming at a weight loss of 0.5 kg/ week [79]. A weight loss program should however aim to optimize muscle anabolism and prevent reduction of muscle mass. Strict diets with energy deficit lead to decreased muscle protein synthesis and increased proteolysis. A recent study on a weight loss program with high protein intake combined with resistance exercise in SO patients, showed significant weight loss and improved muscle strength [80]. The PROT-Age group gives a general advice for about 1gr/kg of protein, adjusted to the individual needs with caution in patients with renal failure. However, even 25 to 30grs of protein per day have proved to improve frailty [81, 82]. The combination of caloric restriction and exercise, which includes both aerobic and resistance training seems to be the best intervention to manage SO, as it can lead to weight loss, increase of the MM volume and improved physical performance. Weight loss needs to be guided with caution, as a strict caloric restriction without proper combination with exercise may lead to loss of MM, osteopenia and worsening of the physical performance status [83, 84]. A holistic approach for the treatment of obesity is fundamental and a multidimensional approach is required [85].

Studies on vitamin D supplementation in the elderly for the improvement of physical function are contradictory. There are reports which show that vitamin D supplementation in elderly patients with vitamin deficiency improves physical performance [86], though others report an improvement in MM but not in muscle strength and physical performance [50, 87].

Other SO interventions include whole body vibration therapy, bariatric surgery for obesity with careful selection of patients, administration of testosterone with conflicting data, selective androgen receptor modulators and anamorelin a ghrelin analogue with inconclusive evidence, and vitamin K and myostatin, which are still under investigation [54].

CONCLUSION

Sarcopenic obesity is an emerging clinical condition, particularly disabling for the elderly population. It poses an increasing prevalence, which can be attributed to population aging, sedentary lifestyle and the obesity pandemic, thus constituting a scientific priority.

The main problem for research today arises from the inconsistency in the definition and the clinical criteria for SO used in relevant studies. There is a great need of

scientific societies to come to an agreement regarding the use of a universal definition and new standardized protocols for diagnosis and clinical management of SO. It is fundamental to deepen our knowledge, with further studies on SO pathophysiology and effective evidence-based therapies to improve physical function and reduce the risk of disability, morbidity and mortality in elderly patients.

Efforts should also be focused on raising physicians' awareness, especially at a primary care level, in order to monitor the population, provide early diagnosis and introduce preventative healthy lifestyle awareness programs.

Health authorities need to take urgent measures to promote healthy ageing with good physical function, reduced morbidity and mortality, reduced institutionalization rates, decreased healthcare costs and most of all better quality of life for the elderly and their caregivers.

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