Skeletal muscle mass and body fat in relation to successful ageing of older adults: the multi-national MEDIS study


1Parc Sanitari Sant Joan de Déu, Fundació Sant Joan de Déu, CIBERSAM, Universitat de Barcelona, Barcelona, Spain; 2Department of Nutrition and Dietetics, School of Health Science and Education, Harokopio University, Athens, Greece; 3Health Center of Aeropolis, General Hospital of Sparta, Aeropolis, Greece; 4University of Malta, Nutrition, Family and Consumer Studies Office, Msida, Republic of Malta; 5Department of Life Sciences and Biotechnology, University of Ferrara, Ferrara, Italy; 6Clinic of Social and Family Medicine, School of Medicine, University of Crete, Heraklion, Greece; 7Health Center of Kalloni, General Hospital of Mitilini, Mitilini, Greece; 8Research Group on Community Nutrition and Oxidative Stress, Universitat de les Illes Balears & CIBERobn, Guillem Colom Bldg, Campus, E-07122 Palma de Mallorca, Spain

Address for Correspondence

Prof. Demosthenes B. Panagiotakos
46 Paleon Polemiston St., Glyfada, 166 74, Attica, Greece
Tel. +30210-9603116 & Fax. +30210-9600719
E-mail: dbpanag@hua.gr
Abstract

**Background:** The determinants that promote successful ageing still remain unknown. The aim of the present work was to evaluate the role of skeletal muscle mass and body fat percentage (BF%), in the level of successful ageing. **Methods:** during 2005-2011, 2663 older (aged 65-100 years) from 21 Mediterranean islands and the rural Mani region (Peloponnesus) of Greece were voluntarily enrolled in the study. Appendicular skeletal muscle mass (ASM), skeletal muscle mass index (SMI) and BF% were calculated using population formulas. Dietary habits, energy intake, expenditure and energy balance were derived throughout standard procedures. A successful ageing index ranging from 0 to 10 was used. **Results:** The mean ASM mass was 24±6.0 kg, the SMI was 0.84±0.21 and the BF% was 44%. Females had lower SMI and higher BF% in comparison with males, respectively [(SMI: 0.66±0.09 vs. 1.03±0.11; BF%: 51% vs. 34%, (p<0.001)]. High successful agers had better rates in ASM (p=0.01), SMI (p<0.001) and BF% (p<0.001), compared with the medium and low successful ones. Changes in SMI [b-coefficient (95% CI):2.14 (1.57 to 2.71)] were positively associated with successful ageing, while changes in BF% [b-coefficient (95% CI): -0.04 (-0.05 to -0.03)] were inversely associated with successful ageing. Results from sensitivity analysis showed that the effects of variations on body composition were consistent, less pronounced in the positive energy balance group and more pronounced among the oldest old. **Conclusions:** Body composition changes seem to be associated with lower quality of life in the older adults, as measured through successful ageing.

**Keywords:** Successful ageing; appendicular skeletal muscle mass; body fat; energy balance; older adults
Introduction

It is well known that ageing is associated with various physiological changes. Changes in body composition and especially in muscle mass tissue as well as in the body fat are associated with advanced age [1]. It has been reported that the muscle mass loss is almost 2% for the middle aged populations while for the octogenarians this muscle tissue loss is around 50% in comparison with younger populations [2]. Skeletal muscle mass consists almost the half of body mass and has an important role in mobility as well as in various body’s metabolic functions [3,4]. Taking into account its aforementioned role, any decline in the skeletal muscle mass has an inverse effect on human health. Muscle mass decline has been related with various disability patterns, with mental health disorders (i.e. cognitive problems) as well as with increased mortality [3,4,5]. The decline in muscle mass is often replaced by increase in the body fat mass [1]. Moreover it has been reported that not only the muscle mass loss but also the increase in body fat has been related with various co-morbidities, for the older adults. It is well known that high body fat (i.e. central obesity, excess waist circumference) is associated with various metabolic disorders such as, diabetes mellitus, hypertension, metabolic syndrome, cardiovascular diseases (CVDs), cancer and low quality of life [6].

Determinants that promote successful ageing still remain not well understood and appreciated. Clearly the process of ageing is quite complex and is associated with a variety of factors, not only with physical health. Successful ageing is a concept which is considered as low probability of disease and disability, high cognitive and physical capacity, active participation throughout various social activities and represents the
aforementioned complexity in the ageing process [7,8]. A variety of factors have been associated with successful ageing such as high waist circumference, alcohol consumption as well as various co-morbidities [8]. However until now, the role of skeletal muscle mass and BF% in the level of successful ageing has never been explored in the past.

Given the complexity of ageing pathway, the association of skeletal muscle mass and body fat with elder’s health and with the ageing process, together with the lack of data among Mediterranean populations, the aim of the present work was to evaluate the role of skeletal muscle mass and BF%, in the level of successful ageing of a random sample of older adults living in the Mediterranean basin and who participated in the MEDIS (MEDiterranean ISlands) study. Specifically, it was hypothesized that those with higher skeletal muscle mass and lower body fat percentage would be more likely to have higher successful ageing levels compared to those individuals with lower skeletal muscle mass and higher body fat percentage. Additionally, the older Mediterranean’s had rarely been studied in the past; a fact that makes this survey of major importance, as it included islands (i.e., Corfu and Crete, known from the historical Seven Countries Study and Ikaria, known from the Blue Zones) where others have previously reported determinants of healthy ageing and long-living [9].

Methods

The MEDIS study sample

During 2005-2011, a population-based, multi-national, convenience sampling was performed to voluntarily enroll \( n = 2512 \) older people from 21 Mediterranean islands: Republic of Cyprus (n=300), Malta (n=250), Sardinia (n=60), Sicily (n=50), Mallorca
and Menorca (n=111) and the Greek islands of Lesvos (n=142), Samothrace (n=100), Cephalonia (n=115), Crete (n=131), Corfu (n=149), Limnos (n=150), Ikaria (n=76), Syros (n=151), Naxos (n=145), Zakynthos (n=103), Salamina (n=147), Kassos (n=52), Rhodes and Karpathos (n=149), Tinos (n=129), as well as n=300 older adults from the rural region of Mani (a southern Greek peninsula). The sampling scheme anticipated a target sample size of 300 older people from Cyprus and Malta and at least 100 from each of the other islands; according to an a-priori power analysis, a sample of 2500 participants is adequate to test two-sided hypotheses of odds ratios equal to 1.20 achieving statistical power >80%. According to the study's protocol, individuals were not eligible for inclusion if they resided in assisted-living centers, had a clinical history of cardiovascular disease (CVD) or cancer, or had lived away from the island for a considerable period of time during their lives (i.e., >5 years); these exclusion criteria were applied because the study aimed to assess lifestyle habits that were not subject to modifications due to existing chronic health conditions or by environmental factors, other than living milieu. A group of health scientists (physicians, dietitians and nurses) with experience in field investigation collected all the required information using a quantitative questionnaire and standard procedures.

The study followed the ethical considerations provided by the World Medical Association (52nd WMA General Assembly, Edinburgh, Scotland, October 2000). The Institutional Ethics Board of Harokopio University approved the design and procedures of the study (reference No. 16/19-12-2006). Participants were informed about the aims and procedures of the study and gave their consent prior to being interviewed.

Evaluation of clinical and anthropometric characteristics
All the measurements taken in the different study centres were standardized and the questionnaires were translated in all the cohorts’ languages following the World Health Organization (WHO) translation guidelines for tools assessment [10]. Weight, height and waist circumference were measured using a standard protocol; body mass index (BMI) was calculated as the ratio of weight by height squared (kg/m^2). Overweight was defined as BMI between 25 and 29.9 Kg/m^2 and obesity was defined as BMI > 29.9 Kg/m^2. Moreover, waist circumference (WC) in cm was measured in the middle between the 12th rib and the iliac crest and hip circumference in cm was measured around the buttocks. Muscle mass was calculated throughout the appendicular skeletal muscle mass (ASM) based on the equation proposed by Lee et al [11]. Specifically, the equation was:

\[
\text{ASM} = (0.244 \times \text{weight}) + (7.8 \times \text{height}) + (6.6 \times \text{gender}) - (0.098 \times \text{age}) + (\text{race} - 3.3) 
\]

This indicator was further adjusted by BMI to create a skeletal muscle mass index (SMI) as the proportion of ASM/BMI [12]. The percentage of body fat (BF%) was calculated based on a sex specific equation using the waist circumference measurements [13]. Specifically for the males the equation was: \( BF\% = (0.567 \times WC) + (0.101 \times age) - 31.8 \) while for the females was: \( BF\% = (0.439 \times WC) + (0.221 \times age) - 9.4 \). Diabetes mellitus (type 2) was determined by fasting plasma glucose tests and was analyzed in accordance with the American Diabetes Association diagnostic criteria (glycated haemoglobin A1C≥6.5 or fasting blood glucose levels greater than 125 mg/dl or 2-h plasma glucose > 200 mg/dl during an oral glucose tolerance test-OGTT- or a random plasma glucose > 200 mg/dl, or by a prior diagnosis of diabetes). Participants who had blood pressure levels ≥140/90 mmHg or used antihypertensive medications were classified as hypertensive. Fasting blood lipid levels (HDL-, LDL-cholesterol and triglycerides) were also recorded and
hypercholesterolemia was defined as total serum cholesterol levels >200 mg/dL or the use of lipid-lowering agents according to the NCEP ATPIII guidelines [14].

**Evaluation of socio-demographic, dietary habits and other lifestyle characteristics of the participants**

Basic socio-demographic characteristics, such as age, gender, years of school, financial status and lifestyle characteristics, such as smoking habits and physical activity status, were recorded. Regarding financial status, the participants were asked to report their mean income during the previous three years using a four-point scale (low, inadequate to cover daily expenses = 1, medium, trying hard to cover daily expenses = 2, good, adequate to cover daily expenses = 3, very good, very adequate to cover daily expenses = 4); this scale was decided upon because of the variety of the populations studied, as well as the common difficulty of accessing exact financial data. The participants that were in the upper category were classified as participants with high financial status while all the others were classified as low and medium financial status (high vs. low-medium financial status).

Physical activity was evaluated in MET-minutes per week, using the shortened, translated in all the cohort’s languages and validated in Greek version of the self-reported International Physical Activity Questionnaire (IPAQ) [15]. As minimally active or “health-enhancing physical activity (HEPA) active” were classified individuals who reported at least 3 MET-minutes per week. Furthermore, the weekly frequency of physical activity was recorded. Dietary habits were assessed through a semi-quantitative, validated and reproducible food-frequency questionnaire [16]. To evaluate the level of adherence to the Mediterranean diet, the MedDietScore (theoretical range 0-55) was used
Higher values for this diet score indicate greater adherence to the Mediterranean diet. Energy intake was evaluated through the quantification of the portions of foods and beverages consumed, using food composition tables [18, 19]. Total daily energy expenditure (TEE) was estimated using the Schofield prediction equations, adopted by the 2004 FAO/WHO/UNU report [20], using age, weight and self-reported physical activity level (PAL) information (i.e. frequency and kind of physical activities as well as the duration of the activity). Moreover, the energy balance was calculated throughout the equation: Energy Balance = Energy intake – Total energy expenditure. Negative energy balance was considered when energy balance was < 0, while positive energy balance was considered when energy balance was > 0 [21]. Furthermore, consumption of various alcoholic beverages (i.e., wine, beer, whiskey, vodka, and the traditional ouzo, tsipouro and retsina) was measured in terms of wineglasses per day, adjusted for ethanol intake (i.e., one 100 ml glass was considered to have 12% ethanol) and classified for the present analyses, into 0 for no alcohol consumption and 1 for alcohol consumption of at least 1 glass/week. A similar dichotomized coding followed for the tea and coffee consumption.

Current smokers were defined as smokers at the time of the interview. Former smokers were defined as those who had previously smoked, but had not done so for a year or more. The remaining participants were defined as occasional or non-current smokers. Symptoms of depression during the previous month were assessed using the validated and locally adopted version of the shortened, self-report Geriatric Depression Scale (GDS) (range 0-20) [22]. Moreover, in order to evaluate the older adult’s social participation, the weekly frequency of their social activities with their family, their friends as well as their yearly frequency of excursions were recorded.
Further details about the MEDIS study protocol may be found elsewhere [23].

**Evaluated outcomes**

Following the multi-dimensional approach of successful ageing already reported by several experts [24,25] as well as the MEDIS study group [8, 26, 27], 10 components (i.e., education as measured in years if school, financial status, physical activity status as classified using the IPAQ, body mass index, psychological level as measured using the GDS score, participation in social activities with friends, with family, yearly excursions, burden of CVD risk factors and dietary habits as evaluated using the MedDietScore) were incorporated for the measurement of successful ageing. The composed successful ageing index was represented as the cumulative score of the 10 components (theoretical range 0-10); specifically, individual ratings (from 0 to 1) in each of the 10 components were assigned, according to their positive or negative (i.e. reverse scoring) influence on successful ageing [8, 26, 27]. Furthermore, the tertiles of the successful ageing index, i.e. 1.91/10, 1.92.-3.08/10 and >3.09/10 were used as cutoffs to classify participants as low, moderate or high successful agers.

**Statistical analysis**

Continuous variables are presented as mean ± standard deviation (SD) and categorical variables as frequencies. Comparisons of continuous variables between groups of study were performed using the independent samples t-test and the Analysis of Variance (for the normally distributed variables), or the Mann-Whitney U-test and the Kruskall-Wallis test (for the skewed variables). Associations between categorical variables were tested using the chi-square test. Spearman rho coefficient was applied to evaluate the correlation between continuous or ordinal variables, BF% and SMI. Linear
regression models were applied in order to evaluate the association between various socio-demographic, bio-clinical, nutritional factors (independent variables), the SMI, the BF% and the level of successful ageing (dependent outcome). Colinearity was tested using the Variance Inflation Factor criterion (VIF; values >4 suggested colinearity between independent variables and one of them was excluded from the model). The assumption of homoscedasity was tested by plotting the scatter plot of standardised residuals over the predicted score values. Results from linear regression models are presented as b-coefficients and their 95% Confidence Intervals (CI). All reported p-values were based on two-sided tests. SPSS software (version 20) was used for all calculations (IBM Statistics, Greece).

Results

In the entire sample, the mean ASM mass was 24±6.0 kg, the mean SMI was 0.84±0.21 and the mean BF% was 44%. The females had lower SMI and higher BF% comparing with the males, respectively (SMI: 0.66±0.09 vs. 1.03±0.11, p<0.001; BF%: 51 vs. 34, p<0.001). Comparing participants living in rural and urban areas, there was no significant difference in the SMI and in the BF%. When the 6 geographical areas of the participants were taken into account (i.e., Aegean, Ionian islands, Crete, Cyprus, west Mediterranean islands and South Peloponnesus), the inhabitants of Crete had the highest percentage of body fat (i.e., 46%), followed by Aegean islands (i.e., 45%) and Cyprus (i.e., 44%) while the participants living in South Peloponnesus had the lowest ones (i.e., 42%) (p<0.001). Demographic, behavioral, clinical, anthropometric and lifestyle characteristics of the sample, by age group (<80 vs. >80 years old), are summarized in Table 1. Compared
with younger older adults, the octogenarians were rural residents \((p<0.001)\), had lower financial status \((p=0.01)\), were less physically active \((p=0.004)\) and ever smokers \((p=0.02)\), had lower prevalence of hypercholesterolemia \((p<0.001)\), lower rates of appendicular skeletal muscle mass \((\text{kg}) \ (p<0.001)\) and lower SMI rates \((\text{ASM kg/BMI}) \ (p<0.001)\), lower BMI levels \((p<0.001)\), lower education status \((p<0.001)\) and lower adherence to the Mediterranean diet \((p=0.009)\), while the most of them were living alone \((p<0.001)\). Moreover, no differences were observed between both age \((<80 \text{ vs. } >80 \text{ years old})\) with regards to BF%, the prevalence of hypertension, diabetes, and the level of successful ageing.

[Table 1]

In **Table 2** factors associated with the level of successful ageing among older Mediterranean individuals, are presented. Specifically, compared with low successful agers, the medium and high ones were not living alone \((p<0.001)\), were greater ever smokers \((p<0.001)\), had higher alcohol consumption \((p<0.001)\), while they had higher appendicular skeletal muscle mass \((\text{kg}) \ (p=0.01)\), higher rates of the SMI \((\text{ASM kg/BMI}) \ (p<0.001)\), lower BF% \((p<0.001)\) and lower waist circumference \((p<0.001)\).

[Table 2]

After adjusting for age, urban residence, sex, living alone, smoking habits, alcohol consumption, coffee, tea consumption, adherence to the Mediterranean diet, physical activity, hypertension, hypercholesterolemia and diabetes mellitus, it was found that the level of SMI \((\text{ASM kg/BMI})\) was positively associated with the successful ageing levels \([b\text{-coefficient (95\% CI): } 2.14 \ (1.57 \text{ to } 2.71)]\) while the BF% \([-0.04 \ (-0.05 \text{ to } -0.03)]\) was inversely associated. When the analysis was stratified by age group (**models 2 and 3 of**
Table 3), in the oldest old, the increase in the SMI (ASM kg/BMI) had a greater impact in
the level of successful ageing than in the group of the “younger” older participants [Older
adults < 80yrs: 1.95 (1.29 to 2.60); Older adults ≥ 80yrs: 2.3 (1.29 to 3.35)]. Moreover,
the BF% was inversely related with the successful ageing score (p<0.001) in both the age
groups [i.e. b-coefficient (95% CI) for <80yrs vs. b (95% CI) for ≥ 80yrs)] (Table 3). In
addition when the analysis was stratified by gender, in males, the increase in the SMI
(ASM kg/BMI) had a greater impact in their successful ageing score than in female
individuals [Males: 2.5 (1.76 to 3.33); Females: 1.9 (1.03 to 2.77)]. Moreover the BF%
was inversely related with the level of successful ageing in both the genders [Males: -
0.04 (-0.05 to -0.02); Females: -0.05 (-0.06 to -0.04)].

Due to the high relation among under-nutrition with skeletal muscle mass and
ageing status, the analysis was repeated separately for energy balance (positive energy
balance vs. negative energy balance) and a consistent relationship was reported between
the SMI (ASM kg/BMI) and level of successful ageing. Specifically, in the positive
energy balance group, an increase in the SMI (ASM kg/BMI) was associated with a less
pronounced increase in the level of successful ageing, than in the negative energy balance
group [Positive energy balance: 1.50 (0.39 to 2.61); negative energy balance: 2.54 (1.79
to 3.29)]. Also a consistent inverse association between the BF% and the successful
ageing score was reported (p ≤ 0.001).

Concerning the macronutrients consumption, an inverse correlation was observed
between carbohydrates (CHO) intake as an expression of daily energy intake (CHO/EI)
and the level of SMI (ASM kg/BMI) (rho=-0.07, p<0.006) and a positive correlation was
observed between protein (PRO) intake as an expression of daily energy intake (PRO/EI)
and SMI (ASM kg/BMI) (rho=0.11, $p<0.001$). There was reported no correlation between dietary fat (FAT) intake as an expression of daily energy intake (FAT/EI) and SMI (ASM kg/BMI) (rho= 0.04, $p=0.07$), as well as among all the macronutrients intake (CHO, FAT and PRO) and the BF% ($p$ for all $< 0.08$) (*data shown only in text*).

**Discussion**

In the present work it was revealed that skeletal muscle mass levels was positively associated with the successful ageing score of the older adults, irrespective of age, urban residence, sex, living alone, smoking habits, alcohol, and coffee and tea consumption. In addition, an inverse association among the BF% and the older adult’s successful ageing level was reported. The aforementioned confirms the study’s main hypothesis that higher skeletal muscle mass levels and lower BF% is related with better successful ageing among the older adults. The by-energy-balance group analysis reported that the later findings remained consistent among the positive and negative energy balance grouped participants. However, the changes in the SMI had greater effect among those in the group of the high energy intake. Moreover it was reported that the greater the alterations in the SMI, the greater the effect in the successful ageing level of the oldest old, in comparison with the younger participants. All of the aforementioned relationships, especially among elderly Mediterranean populations, have rarely been studied.

Despite the lack of previous findings regarding skeletal muscle mass and successful ageing among older populations, a number of studies have previously reported the role of skeletal muscle tissue on human health [3, 28]. Also in the literature it is reported that the oldest old facing greater declines in their muscle tissue [2]. *Specifically,*
Baumgartner et al., in the New Mexico Elder Health Survey reported that advanced age (>75 years old) was related to 3.28 and 2.28 higher odds of sarcopenia in males and females, respectively [2]. The later was also confirmed from the applied data analysis where the population ≥80 years old had lower rates in ASM and in the SMI. Within our unadjusted data analysis the greater the level of successful ageing the lower was the decline of skeletal muscle mass as well as the increase BF%. According to several researchers, the excess decrease in skeletal muscle mass was associated with higher disability and mortality rates as well as with various co-morbidities [3, 28]. In parallel the excess body fat, it is well known that is related with higher morbidity and mortality rates among the populations of various ages.[29]. In recent well documented multi-country study it was reported that sarcopenic obesity (a combination of low muscle mass with excess BF%) was associated with greater levels of disability [b-coefficient 3.01 (95%CI 1.14-4.88)] [30]. Also, throughout the unadjusted analysis, the older adults ever smoked had high degree of successful ageing. The later contradictory finding may have been altered due to the cross-sectional nature of the study, the potential survival bias, and/or lifestyle modifications due to doctor’s consultations (probably older participants have modified their smoking habits not only because of age, but also because of known co-morbidities).

It has been reported that the process of muscle mass decline is multi-dynamic and is related with advanced age, various chronic diseases, endocrinal changes, inflammation and nutritional deficiencies [31]. The linear regression analysis confirmed the aforementioned and a positive association among the SMI and the level of a successful ageing was reported. Additionally, the stratified linear regression analysis by energy
balance group (i.e., positive vs. negative) was performed. According to the applied analysis, changes on SMI and on BF% were consistently related with the level of successful ageing among the energy balance groups. However, the aforementioned relationship between the SMI and the successful ageing level was less pronounced in the high energy balance group, a fact that indicates the possible interfering role of over-nutrition [32]. The maintenance of energy balance is a very complex procedure in the older adults and especially in the oldest old [33]. As has been reported in the literature, throughout the ageing process the decline in skeletal muscle tissue often is replaced from fat mass [34]. This process could be accelerated throughout the positive energy balance in relation with the low metabolic rate and the high physical inactivity of the elders [35]. Additionally well documented studies had proposed the role of macronutrients intake on skeletal muscle protein turnover [36]. Recently various studies were referred to positive balance between muscle protein synthesis and degradation after protein and amino acids dietary intake in the older adults [37, 38]. These findings, in combination with observations that were used in the present analysis (i.e., PRO/EI positively correlated with SMI and CHO/EI was inversely correlated with SMI), may explain the complex interrelations between the energy imbalance (positive or negative), dietary intake (macronutrients consumption), changes in body composition (i.e., SMI and BF) and successful ageing of older adults.

Taking into account the analysis by age group (i.e., older adults < 80 yrs vs. older adults > 80 yrs) the association between SMI, BF% and successful ageing were more pronounced among the oldest old individuals. Based on longitudinal data, BF% increases with age and appears a peak among the ages of 60 and 75 [39, 40], while, muscle mass
declines progressively for the age of 30s and over and is more accelerated after the age of 60 years [41]. Moreover, the relation between SMI and successful ageing was more prominent among males. According to several researchers, the aforementioned associations could be the result of specific biological and physiological pathways related to advanced age [1, 30] and to the well known gender-health paradox [42]. In contrast, BF% increase is related with declines in the physical activity that appeared in the older population as well as with the interfering factor of positive energy balance [43]. Previous results of the MEDIS study have shown that physical activity in comparison with sedentary life was related with almost 2 kg/m² (p<0.001) decrease in the BMI levels of the older participants [44]. Moreover Tyrovolas et al., in a multi-country alder adults study reported that low levels of physical activity compared to high levels were associated with higher odds for sarcopenia [OR 1.36 (95%CI 1.11-1.67)] and sarcopenic obesity [OR 1.80 (95%CI 1.23-2.64)] [45]. However, muscle mass loss is associated with testosterone and growth hormone declines due to the advanced age. Furthermore, in the older adults, the late response of the muscles on the insulin had been related with muscle mass declines. Moreover it had been reported that inflammation markers such as TNF-α, IL-6, and C - reactive protein, are negatively related with skeletal muscle tissue, while hormones such as adiponectin and leptin are reported to be also associated with muscle mass loss throughout a complex bio-molecular signaling [1]. These bio-physiological pathways could possibly explain the association of SMI and BF% with successful ageing as well as them different effect on the advanced age and for the population on energy imbalance. The progressive muscle mass loss in the older adults, if accompanied with muscle strength and gait speed decline could lead to sarcopenia [46], a condition related
with various health risk factors [47] and with high healthcare expenditures for the state [48]. These associations raise some concerns about the need for early measures (i.e., physical exercise and nutritional and health interventions and education etc.) in order to promote healthy and successful ageing throughout the prevention of body composition changes (i.e., muscle mass loss and increase of body fat %).

**Strengths and limitations**

The present study has several strengths. It is the first study that tried to evaluate the association of body composition parameters (i.e., skeletal muscle tissue and BF%), and the level of successful ageing of a large sample of ‘healthy’, independently-living older people in the Mediterranean basin. Among limitations, the fact that this is a cross-sectional study limits the potential for aetiological conclusions. Estimation of successful ageing among elders is a difficult task [8, 26, 27]. The calculation of BF% and ASM was based on equations that may under- or over-estimate the actual body composition rates. However, these formulas have been previously validated and present good agreement with the classical methods of bioelectrical impedance measurements and dual-energy X-ray absorptiometry (DXA) measurements [11, 13, 49]; recently large epidemiologic studies have used these formulas for the calculation of skeletal mass and body fat in diverse populations [45, 30]. Another limitation is that the data analysis was not adjusted for menopause medication since the survey did not include a detailed medication intake assessment. Finally, the cumulative successful ageing index that was used here by simply adding the presence of the common determinants of the individuals may not accurately estimate the successful ageing status of these individuals.

**Conclusion**
The present work investigated the role of body composition changes (BF% and SMI) on the successful ageing level of older Mediterranean people. It is of major interest nowadays to study the body composition transition of older people in order to understand the dynamics and the transforming nature of ageing. In the present study the successful agers had the better rates on ASM, SMI and BF%. Data analysis of the MEDIS study also revealed that major changes in body composition, like, the increase in the SMI and the BF%, might depict some of the major determinants of the successful ageing. Moreover the body composition changes were consistent among different sub-groups however the impact on successful ageing level was differentiated. Further exploration is needed in order to understand how these body composition factors interrelated and which are most important in the process of successful ageing. Taking into account the increased risk for the sarcopenia and sarcopenic obesity after the progressive loss of muscle mass tissue and the increase of fat mass [2], the prevention of skeletal muscle mass and body fat present an important goal for the public health authorities in order to maintain older population’s healthy and successful ageing.

Funding

The Study was funded by Research grants from the Hellenic Heart Foundation, and therefore we would also like to thank Prof. Pavlos Toutouzas, Director of the Foundation. Stefano Tyrovola’s work was supported by the Foundation for Education and European Culture (IPEP), the Sara Borrell postdoctoral programme (reference no. CD15/00019 from the Instituto de Salud Carlos III (ISCIII - Spain) and the Fondos Europeo de Desarrollo Regional (FEDER). Josep A. Tur was funded by grants PI11/01791, CIBERobn CB12/03/30038, and CAIB/EU 35/2001.
Acknowledgements

We are particularly grateful to the men and women from the islands of Malta, Sardinia, Sicily, Mallorca, Menorca, Cyprus, Lesvos, Samothraki, Crete, Corfu, Lemnos, Zakynthos, Cephalonia, Naxos, Syros, Ikaria, Salamina, Kassos, Rhodes, Karpathos, Tinos and the rural area of Mani, who participated in this research. We also wish to express our gratitude to: M. Tornaritis, A. Polystipioti, M. Economou, (field investigators from Cyprus), K. Gelastopoulou, I. Vlachou (field investigator from Lesvos), I. Tsiligianni, M. Antonopoulou, N. Tsakountakis, K. Makri (field investigators from Crete), E. Niforatou, V. Alpentzou, M. Voutsadaki, M. Galiatsatos (field investigators from Cephalonia), K. Voutsa, E. Lioliou, M. Miheli (field investigator from Corfu), Tyrovolas S, G. Pounis, A. Katsarou, E. Papavenetio, E. Apostolidou, G. Papavassiliou, P. Stravopodis (field investigators from Zakynthos), E. Touloukis, V. Bountziouka, A. Aggelopoulou, K. Kaldaridou, E. Qira, (field investigators from Syros and Naxos), D. Tyrovolas (field investigators from Kassos), I. Protopappa (field investigator from Ikaria), C. Prekas, O. Blaserou, K.D. Balafouti (field investigators from Salamina), S. Ioakeimidi (field investigator from Rhodes and Karpathos), A. Mariolis (field investigator from Mani), S. Piscopo (field investigator from Malta), J.A. Tur (field investigator from Mallorca and Menorca), G. Valacchi, B. Nanou (field investigators from Sardinia and Sicily) for their substantial assistance in the enrolment of the participants.

Conflict of Interest Statement

Conflicts of interest: none
References


Table 1. Demographic, anthropometric, behavioral, clinical and lifestyle characteristics of the Multi-national MEDIS sample, by age group

<table>
<thead>
<tr>
<th></th>
<th>Older adults &lt; 80yrs (n=1925)</th>
<th>Older adults &gt; 80yrs (n=613)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex (%)</td>
<td>48</td>
<td>55</td>
<td>0.005</td>
</tr>
<tr>
<td>Urban residence (%)</td>
<td>64</td>
<td>52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.7±4.8</td>
<td>27.3±4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education (years of school)</td>
<td>7.8±4.0</td>
<td>5.8±3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High financial status (%)</td>
<td>20</td>
<td>15</td>
<td>0.01</td>
</tr>
<tr>
<td>Living alone (%)</td>
<td>23</td>
<td>34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ever smoking (%)</td>
<td>36</td>
<td>31</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical activity (%)</td>
<td>44</td>
<td>37</td>
<td>0.004</td>
</tr>
<tr>
<td>MedDietScore (0-55)</td>
<td>32±4.8</td>
<td>31±5.2</td>
<td>0.009</td>
</tr>
<tr>
<td>Alcohol consumption (%)</td>
<td>49</td>
<td>46</td>
<td>0.15</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>62</td>
<td>64</td>
<td>0.43</td>
</tr>
<tr>
<td>Diabetes Mellitus (%)</td>
<td>23</td>
<td>21</td>
<td>0.18</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>52</td>
<td>39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASM (kg)</td>
<td>24.3±5.9</td>
<td>22.1±5.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SMI (ASM/BMI)</td>
<td>0.86±0.2</td>
<td>0.82±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>43.8</td>
<td>44</td>
<td>0.55</td>
</tr>
<tr>
<td>Successful ageing (0-10)</td>
<td>2.6±1.3</td>
<td>2.5±1.2</td>
<td>0.36</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI: Body mass index (kg/m²); ASM: Appendicular skeletal muscle mass; SMI: Skeletal muscle mass index

P-values derived from Student’s t-test for normally distributed continuous data, chi-square test for categorical data and Mann-Whitney U-test for not-normally distributed continuous data.
Table 2: Demographic, anthropometric, and lifestyle characteristics of the Multi-national MEDIS sample, by successful ageing group.

<table>
<thead>
<tr>
<th></th>
<th>Degree of successful ageing</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low (n=886)</td>
<td>Medium (n=826)</td>
</tr>
<tr>
<td>Age</td>
<td>75±7.1</td>
<td>74±7.6</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>36</td>
<td>53</td>
</tr>
<tr>
<td>Urban residence (%)</td>
<td>62</td>
<td>56</td>
</tr>
<tr>
<td>Living alone (%)</td>
<td>31</td>
<td>24</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>106±12</td>
<td>98±14</td>
</tr>
<tr>
<td>ASM (kg)</td>
<td>23±5.7</td>
<td>24±6.0</td>
</tr>
<tr>
<td>SMI (ASM/BMI)</td>
<td>0.77±0.18</td>
<td>0.86±0.21</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>48</td>
<td>41</td>
</tr>
<tr>
<td>Ever smoking (%)</td>
<td>24</td>
<td>37</td>
</tr>
<tr>
<td>Alcohol consumption (%)</td>
<td>34</td>
<td>49</td>
</tr>
<tr>
<td>Coffee consumption (%)</td>
<td>82</td>
<td>81</td>
</tr>
<tr>
<td>Tea consumption (%)</td>
<td>41</td>
<td>41</td>
</tr>
</tbody>
</table>

**Abbreviations:** ASM: Appendicular skeletal muscle mass; SMI: Skeletal muscle mass index.

P-values derived through one-way ANOVA for continuous variables (using the Bonferroni correction for the between groups comparisons) and the chi-square test for the categorical ones.
Table 3: Association of skeletal muscle mass and body fat with successful ageing.

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=864</td>
<td>(&lt; 80yrs, n=656)</td>
<td>(≥ 80yrs, n=208)</td>
</tr>
<tr>
<td>SMI (ASM/BMI)</td>
<td>2.14 (1.57; 2.71)</td>
<td>1.95 (1.29; 2.60)</td>
<td>2.3 (1.29 to 3.35)</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>-0.04 (-0.05; -0.03)</td>
<td>-0.05 (-0.06; -0.04)</td>
<td>-0.03 (-0.05; -0.02)</td>
</tr>
</tbody>
</table>

Model 1, 2 and 3 adjusted for age, urban residence, sex, living alone, smoking habits, alcohol consumption, coffee and tea consumption, adherence to the Mediterranean diet, physical activity, hypertension, hypercholesterolemia and diabetes mellitus.

**Abbreviations:** ASM: Appendicular skeletal muscle mass; SMI: Skeletal muscle mass index