

Hormonal and lifestyle determinants of appendicular skeletal muscle mass in men: the MINOS study¹⁻³

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ABSTRACT

Background: Aging-related sarcopenia is characterized by a loss of muscle mass and strength and increased fatigability. However, studies of its determinants in elderly men are scarce.

Objective: We investigated risk factors for sarcopenia in a large cohort of men.

Design: We analyzed 845 men aged 45–85 y who belonged to the MINOS cohort. Lifestyle factors (physical activity, tobacco smoking, alcohol intake, caffeine intake) were evaluated by using a standardized questionnaire. Appendicular skeletal muscle mass (ASM) was estimated by using dual-energy X-ray absorptiometry. The relative appendicular skeletal muscle mass index (RASM) was calculated as ASM/body height^{2.3}. Apparent free testosterone concentration (AFTC) and free testosterone index (FTI) were calculated on the basis of concentrations of total testosterone and sex hormone-binding globulin.

Results: RASM decreased with age ($r = -0.29$, $P < 0.0001$). Current smokers had lower RASM than did subjects who never smoked (-3.2% ; $P < 0.003$). RASM increased with the intensity of physical activity at work (P for trend < 0.001). Men who participated in regular exercise during leisure time had 2.2% higher RASM than did those who did not ($P < 0.03$). Men whose values for AFTC, FTI, or 25-hydroxycholecalciferol [25(OH)D] were >2 SDs below the mean for young men had significantly lower RASM than did men with higher values. Men with sarcopenia, defined as the lowest quartile of RASM in the studied cohort (<6.32 kg/m^{2.3}), were significantly older than men with normal RASM, weighed significantly less, smoked more, and spent significantly less time on leisure-time activities. Sarcopenic men also had lower values for testosterone, AFTC, FTI, and 25(OH)D.

Conclusion: In elderly men, low physical activity, tobacco smoking, thinness, low testosterone (AFTC and FTI), and decreased 25(OH)D concentrations are risk factors for sarcopenia. *Am J Clin Nutr* 2004;80:496–503.

KEY WORDS Sarcopenia, appendicular skeletal muscle mass, physical activity, tobacco smoking, testosterone, 25-hydroxycholecalciferol, men

INTRODUCTION

Increased life expectancy over the past decades has resulted in an increased prevalence of age-related disorders, such as cardiovascular diseases, osteoporosis, and dementia. Similarly, sarcopenia is an aging-related condition characterized by loss of muscle mass, loss of muscle strength, and increased fatigability (1, 2). Sarcopenia may contribute to decreased physical performance

and deterioration in quality of life, and assistance with daily living activities may be required (3, 4).

Several experimental, clinical, and intervention studies on aging-related sarcopenia have been published in recent years. Experimental studies have focused on the pathophysiologic and molecular mechanisms of the age-related loss of muscle mass and strength as the preferential atrophy of fast-twitch (type II) fibers, the reduction in the synthesis rates of myosin heavy chain and mitochondrial proteins, and the reduction in the number of excitable motor units (5–7). Clinical studies have confirmed an age-related decrease in the mass and strength of different groups of muscles in the elderly (8–11) and have shown that, in elderly men, the decrease in muscle strength outweighs the decrease in muscle mass (11–13). Intervention studies have shown the role of exercise and hormone replacement therapy in increasing muscle mass and strength in elderly men (14–16).

In contrast, there are few epidemiologic studies of the risk factors for sarcopenia in elderly men. Most such studies were performed in small groups of elderly men or in mixed cohorts of men and women; in addition, few risk factors were analyzed in these studies, and the statistical models that were used only partially adjusted for confounding variables (17, 18). However, the evaluation of risk factors for sarcopenia in elderly men may be useful for identifying adequate interventions aimed at maintaining muscle mass and strength in elderly men. Thus, the purpose of the present study was to analyze lifestyle and hormonal factors associated with low appendicular skeletal muscle mass (ASM) in a large group of Frenchmen aged 45–85 y who belonged to the MINOS cohort.

SUBJECTS AND METHODS

Description of the cohort

The MINOS study, which was initiated in 1995, is a prospective study of osteoporosis and its determinants in men (19). The

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study is the result of a joint collaboration between the Institut National de la Santé et de la Recherche Médicale (INSERM) and the Société de Secours Minière de Bourgogne (SSMB) of Montceau les Mines, France, a town 130 km northwest of Lyon in the Saône et Loire region. The town has a population of 21 000 inhabitants, including 7150 men aged >19 y. SSMB is one of the region's largest health insurance companies. This analysis was carried out in 840 men aged 45–85 y. All the men who consented to participate completed an epidemiologic questionnaire covering demographic and behavioral information and provided a detailed medical record of conditions that could influence bone mass and metabolism (19). The study was performed in accord with the Helsinki Declaration of 1975 as revised in 1983.

Evaluation of lifestyle factors

Tobacco smoking and intakes of alcohol and caffeine were evaluated by using a standardized questionnaire. Smoking habits were evaluated in 3 groups: current smokers, former smokers, and never smokers. Alcohol intake was evaluated by adding up the current average weekly intakes of wine, beer, and spirits, and all the data for the sum of the collected values were divided into quartiles: first quartile, 0–48 g/wk; second quartile, 48.1–224 g/wk; third quartile, 224.1–448 g/wk; and fourth quartile, >448 g/wk. Caffeine intake was defined as the total amount of cups of coffee, cups of tea, and glasses of cola drunk per week; the data for the total values were then divided into quartiles: first quartile, 0–7 cups (and glasses)/wk; second quartile, 7.1–14 cups/wk; third quartile, 14.1–21 cups/wk; fourth quartile, >21 cups/wk.

Current and past physical activity at work was evaluated according to a self-reported 4-level scale (low, medium, hard, and very hard). Current physical activity during leisure time was evaluated by using a standardized questionnaire. Weekly individual activity was calculated on the basis of the overall amount of time spent walking, gardening, and participating in leisure sport activity. An annual average assessment of seasonal activities (gardening and certain kinds of exercise) was also made and expressed as h/wk. Physical activity was evaluated in 4 groups according to the entire time spent per week on different activities: <10, 10–19.99, 20–30, and >30 h/wk. Past and current leisure sport activity was evaluated as periods of regular training for any sport. We evaluated the period of sport training in years, but we did not take into account the intensity of training (number of hours per week or number of months per year).

Measurement of appendicular skeletal muscle mass

Whole-body and regional body composition were estimated by using dual-energy X-ray absorptiometry (DXA) with a Hologic 1000W device (Hologic, Bedford, MA) as described previously (20). The software provides values for the masses of lean soft tissue, fat, and bone mineral for the whole body and specific regions. For analysis of tissue composition, a step phantom consisting of 6 fields of acrylic and aluminum of varying thickness with known absorptive properties is scanned with the patient and serves as an external standard. ASM calculation was based on the sum of lean soft tissue in both the right and left arms and legs. The limbs were isolated from the trunk by using DXA regional computer-generated lines with manual adjustment. With the use of specific anatomic landmarks, the legs and arms were defined according to this method as the soft tissue extending from a line drawn through and perpendicular to the axis of the femoral neck

and angled with the pelvic brim to the phalange tips and as the soft tissue extending from the center of the arm socket to the phalange tips, respectively. Relative appendicular skeletal muscle mass index (RASM) was calculated as ASM/body height^{2.3}. ASM is determined by 3 dimensions of the body (height, width, and depth), and this exponential allows one to obtain a measure of muscle mass that is independent of body height, in contrast to the previously used variable ASM/body height² (18, 21).

Hormones

Serum total 17 β -estradiol and total testosterone concentrations were measured with the use of tritiated radioimmunoassays after diethylether extraction (22). For testosterone, the limit of detection was 0.06 nmol/L, and the interassay CV was 10% for a concentration of 1 nmol/L and 7.8% for a concentration of 6 nmol/L. For 17 β -estradiol, the limit of detection was 11 pmol/L, and the interassay CV was 9.4% for a concentration of 169 pmol/L and 6.2% for a concentration of 510 pmol/L. Sex hormone-binding globulin (SHBG) was measured by using an immunoradiometric assay (¹²⁵I SBP Coatria; Bio-Mérieux, Marcy l'Etoile, France) with an interassay CV of 4.1% for a concentration of 16 nmol/L and 5.3% for a concentration of 100 nmol/L. The limit of detection was 0.5 nmol/L. Apparent free testosterone concentration (AFTC) was calculated as described previously by Vermeulen et al (23) on the basis of the measured concentrations of total testosterone and SHBG with adjustment for the constant albumin concentration of 43 g/L. The association constants of testosterone are 10⁹ L/mol for SHBG and 3.6 \times 10⁴ L/mol for albumin. Free testosterone index (FTI) was calculated as total testosterone/SHBG and expressed as nmol/nmol. Normal reference values for AFTC and FTI were established in 150 healthy, nonsmoking, nonobese men aged 19–40 y after exclusion of outlying values (24). Serum androstenedione concentrations were measured with the use of a tritiated radioimmunoassay after diethylether extraction (22). The interassay CV was 6% for a concentration of 1.96 nmol/L and 8.3% for a concentration of 3.98 nmol/L. Serum 25-hydroxycholecalciferol [25(OH)D] concentrations were measured with the use of a radioimmunoassay (Incstar Corp, Stillwater, MN) that excludes any interference from lipids (25). The intraassay and interassay CVs were 5% and 11%, respectively. The detection limit was 3 ng/mL. Serum parathyroid hormone concentrations were measured with the use of an immunochemoluminometric assay (Magic Lite, Ciba Corning Diagnostic, Medfield, MA) (25). The intraassay and interassay CVs were 5% and 7%, respectively. The detection limit was 0.2 pmol/L.

Statistical analyses

All calculations were performed by using SAS version 8.2 software (SAS Institute Inc, Cary, NC). Pearson's simple correlation coefficients were calculated for continuous variables. The selection of the breakpoint in the correlation between RASM and age comprised 2 parts. First, we evaluated the arithmetic means in 5-y groups, and then we systematically analyzed all possible breakpoints between 45 and 75 y of age by using least-squares regression analysis; the model with the highest coefficient of determination (r^2) was chosen. Differences between the men with sarcopenia (lowest quartile of RASM) and those with normal RASM values (3 upper quartiles) were tested for statistical significance, first with Student's *t* test and then with analysis of



covariance adjusted for multiple covariates. Comparisons of ASM and RASM for classes of different risk factors investigated in our study were performed by using analysis of covariance adjusted for confounding factors. First, we evaluated the comparisons by using analysis of variance to identify the significant determinants of low RASM. Then, these variables were included in the analysis of covariance models with adjustment for multiple covariates to identify the independent determinants. A given analysis was adjusted for other determinants that entered into the model as significant variables. For instance, comparisons according to AFTC were adjusted for age, weight, tobacco smoking, 25(OH)D concentrations, and physical activity both at work and during leisure time. Comparisons according to 25(OH)D concentrations were adjusted for age, weight, tobacco smoking, AFTC, and physical activity both at work and during leisure time. No interaction between the independent variables was significant. Post hoc comparisons were performed by using Tukey's test.

RESULTS

Descriptive analysis

The study was performed in 845 men aged 45–85 y (**Table 1**). Their professions required physical activity ranging from low (clerks) to very high (coal miners). At the time the study was carried out, many of the subjects had already retired, which accounts for the high level of physical activity during leisure time. Their alcohol intake consisted of intakes of wine (92%), spirits (5%), and other alcoholic beverages (3%). Coffee intake made up ≈95% of caffeine intake. Two thirds of the men were either current or former smokers.

RASM decreased with age ($r = -0.29$, $P < 0.0001$), mainly after the age of 60 y (**Figure 1**). Skeletal muscle mass of upper and lower limbs decreased with age ($r = -0.42$ and -0.34 , respectively; both $P < 0.0001$). Body height decreased with age ($r = -0.25$, $P < 0.0001$); however, even after adjustment for body height, skeletal muscle mass of upper and lower limbs decreased with age ($r = -0.35$ and -0.24 , respectively; both $P < 0.0001$). After adjustment for age, RASM was correlated with weight, lean mass, and fat mass ($r = 0.54$, 0.61 , and 0.37 , respectively; all $P < 0.0001$).

Lifestyle factors: tobacco, alcohol, and caffeine

Mean (\pm SD) daily tobacco consumption was 13 ± 9 cigarettes. The median value was 10 cigarettes/d, and only 10% of smokers smoked >20 cigarettes/d. The average duration of smoking was 37 ± 11 y in the current smokers and 25 ± 12 y in the former smokers. After adjustment for confounding variables, the current smokers had lower RASM values than did the subjects who had never smoked (-3.2% ; $P < 0.003$). In 526 current and former smokers, those who smoked >15 packet-years (median) had slightly lower RASM values than did the men who smoked less (-1.8% ; $P < 0.03$).

The average alcohol intake was 37.1 g/d (median: 33.5 g/d). The adjusted association between RASM and quartiles of alcohol intake was not significant (partial $F = 1.14$, $P = 0.28$). The average daily caffeine intake was 2.43 cups/d (median: 2 cups/d). The adjusted association between RASM and quartiles of caffeine intake was not significant (partial $F = 0.21$, $P = 0.89$).

TABLE 1

Descriptive characteristics of men aged 45–85 y who belonged to the MINOS cohort¹

Variable	Value
Age (y)	64 \pm 8 ²
Body weight (kg)	80 \pm 13
Body height (cm)	169 \pm 6
BMI (kg/m ²)	28.0 \pm 3.7
Lean mass	
(kg)	54.5 \pm 6.8
(%)	68.5 \pm 6.2
ASM (kg)	23.01 \pm 3.28
Upper limbs	6.72 \pm 1.08
Lower limbs	16.16 \pm 2.28
RASM (kg/m ^{2.3})	6.84 \pm 0.77
Fat mass	
(kg)	22.0 \pm 7.7
(%)	27.2 \pm 6.1
Smokers (%)	
Current	13
Former	55
Never	32
Alcohol intake (g/wk)	269 \pm 250
Coffee, tea, and cola intake (cups/wk)	17 \pm 13
Leisure-time physical activity (h/wk)	21 \pm 13
Duration of sport activity (y)	9 \pm 14
Testosterone (nmol/L)	17.73 \pm 6.96
AFTC (pmol/L)	203 \pm 79
FTI	0.24 \pm 0.10
17 β -Estradiol (pmol/L)	113 \pm 29
Androstenedione (nmol/L)	1.67 \pm 0.60
SHBG (nmol/L)	84 \pm 44
25(OH)D (ng/mL)	27 \pm 11
PTH (pg/mL)	40 \pm 18

¹ $n = 845$. ASM, appendicular skeletal muscle mass; RASM, relative appendicular skeletal muscle mass index; AFTC, apparent free testosterone concentration; FTI, free testosterone index; SHBG, sex hormone-binding globulin; 25(OH)D, 25-hydroxycholecalciferol; PTH, parathyroid hormone.

² $\bar{x} \pm$ SD (all such values).

Lifestyle factors: physical activity

Current and past physical activity at work was evaluated by using a self-reported 4-level scale. After adjustment for confounding variables, RASM increased with the intensity of physical activity at work (test for trend, $F = 6.04$, $P < 0.001$) (**Figure 2A**). The difference in RASM between the activity levels was due to a difference in the muscle mass of upper limbs (partial $F = 8.41$, $P < 0.0001$) but not in the muscle mass of lower limbs (partial $F = 2.04$, $P = 0.11$). In the men whose jobs required very high physical activity, muscle mass of upper limbs was 5.9% ($P < 0.0001$) higher than that in the men whose jobs required low physical activity.

The association between RASM and current physical activity during leisure time (walking, gardening, tinkering, and sport activity during leisure time) was evaluated after adjustment for confounding variables, including sport activity before recruitment. RASM was positively correlated with physical activity during leisure time ($r = 0.15$, $P < 0.0001$). RASM values were 5.2% ($P < 0.0001$) higher in the men who participated in leisure-time physical activity for >30 h/wk than in the men who spent <10 h/wk on leisure-time physical activity (**Figure 2B**). The difference in muscle mass between the men who had the highest

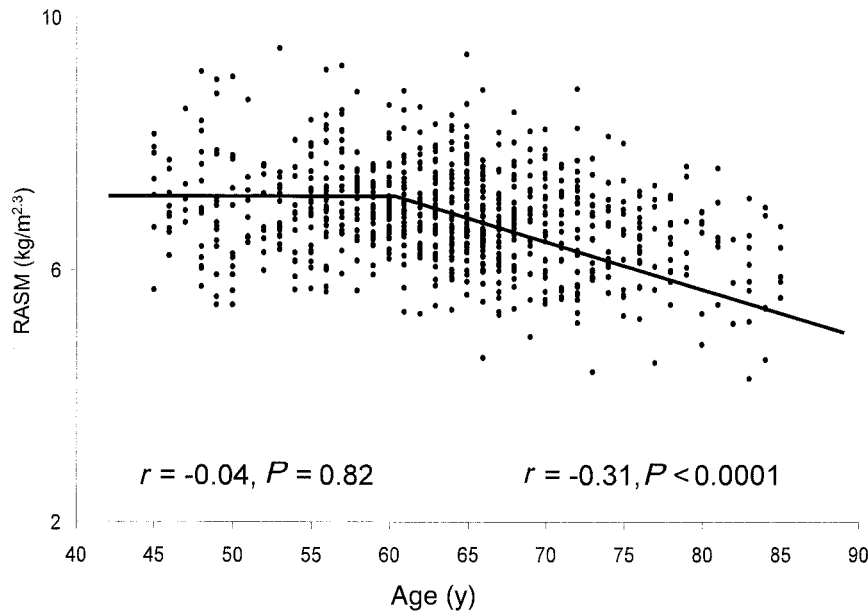


FIGURE 1. Relative appendicular skeletal muscle mass index (RASM) according to age in 845 men aged 45–85 y who belonged to the MINOS cohort.

and lowest levels of physical activity during leisure time was greater at the upper limbs (4.9%; $P < 0.0001$) than at the lower limbs (3.0%; $P < 0.003$), which is consistent with the fact that gardening and tinkering constituted 62% of current leisure-time physical activity.

The 107 men who participated in regular leisure-time exercise at the time of the study had RASM values that were 2.2% higher than those of the men who did not exercise ($P < 0.03$). The difference in skeletal muscle mass between the 2 groups was marginally higher at the lower limbs (2.9%; $P = 0.001$) than at the upper limbs (2.5%; $P < 0.03$), probably because the most frequent sport was bicycling.

When the association between RASM and current nonsport leisure-time physical activity (walking, gardening, and tinkering) was evaluated separately, the results were similar to those for

overall physical activity during leisure time. RASM was positively correlated with current nonsport leisure-time physical activity ($r = 0.14$, $P < 0.001$). RASM values were 3.7% ($P < 0.0001$) higher in the men in the highest quartile of leisure-time physical activity (>29 h/wk) than in the men in the lowest quartile (<14 h/wk). The difference in the muscle mass between the highest and the lowest quartiles was higher at the upper limbs (3.8%; $P < 0.001$) than at the lower limbs (2.3%; $P < 0.01$).

Hormonal factors

After adjustment for confounding variables, AFTC and FTI remained significant determinants of RASM (partial $F = 6.03$, $P < 0.001$ and partial $F = 5.67$, $P < 0.001$, respectively) (**Figure 3**). RASM values were significantly lower in the men who had AFTC or FTI values >2 SDs below the respective means in

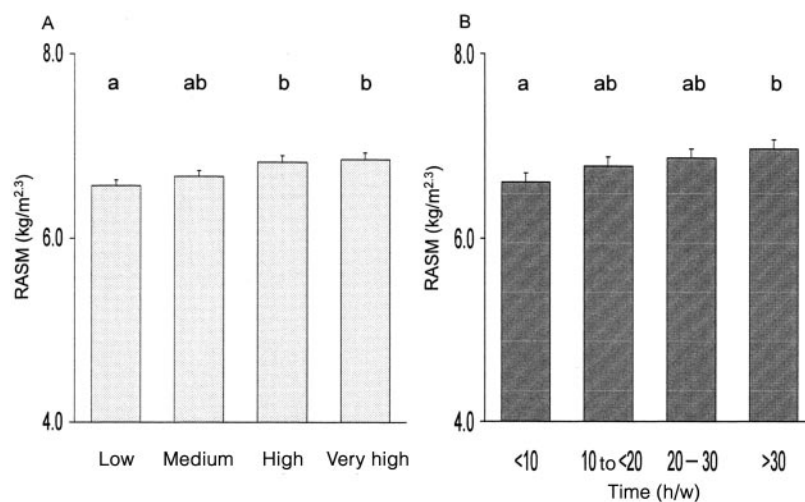


FIGURE 2. Adjusted mean (\pm SEM) values for relative appendicular skeletal muscle mass index (RASM) according to level of physical activity at work (A) or current time spent per week on leisure-time physical activity (B) in 845 men aged 45–85 y who belonged to the MINOS cohort. After adjustment for confounding variables, P for trend < 0.001 (both panels). Bars with different letters are significantly different, $P < 0.05$ (ANCOVA and Tukey's test).



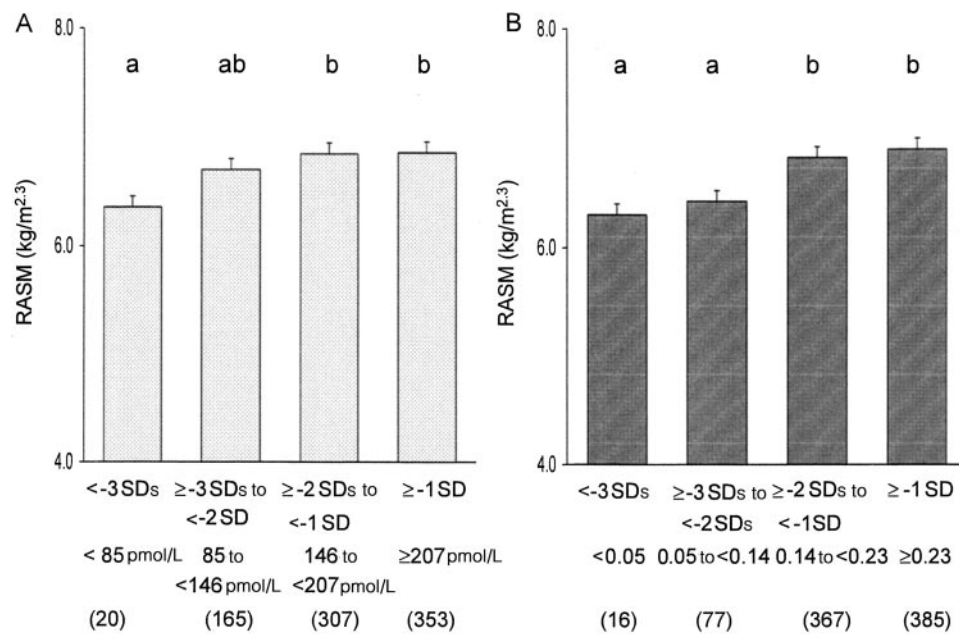


FIGURE 3. Adjusted mean (\pm SEM) values for relative appendicular skeletal muscle mass index (RASM) according to apparent free testosterone concentration (A) and free testosterone index (B) expressed in SDs from the respective mean values in young healthy men. $n = 845$, $P < 0.001$ (both panels). Bars with different letters are significantly different, $P < 0.05$ (ANCOVA and Tukey's test). n values in parentheses.

young men than in those who did not, and this was especially true in the men who had AFTC or FTI values >3 SDs below the respective means. Neither total testosterone nor total 17β -estradiol were determinants of RASM ($P > 0.2$). Androstenedione and SHBG were not associated with RASM ($P > 0.2$).

After adjustment for confounding variables, $25(\text{OH})\text{D}$ was a significant determinant of RASM (partial $F = 2.84$, $P < 0.04$) (Figure 4). RASM values were significantly lower in the men

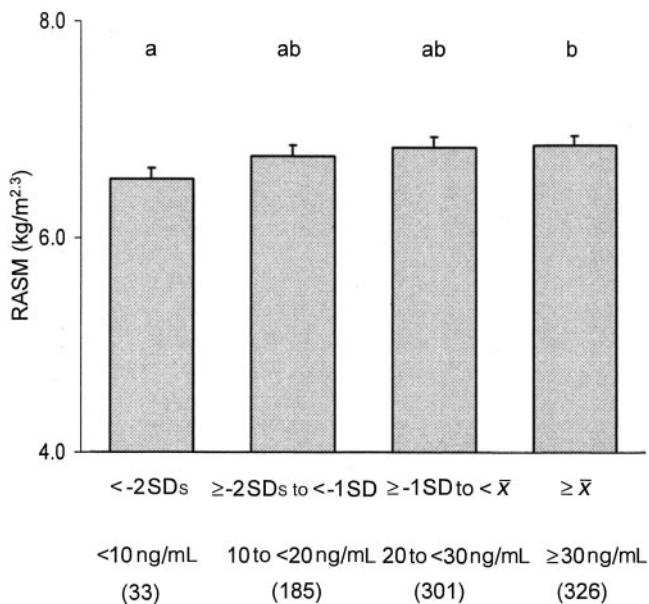


FIGURE 4. Adjusted mean (\pm SEM) values for relative appendicular skeletal muscle mass index (RASM) according to 25 -hydroxycholecalciferol concentration expressed in SDs from the mean value in young healthy men. $n = 845$, $P < 0.04$. Bars with different letters are significantly different, $P < 0.05$ (ANCOVA and Tukey's test). n values in parentheses.

who had a $25(\text{OH})\text{D}$ concentration <10 ng/mL (25 nmol/L), which corresponded to 2 SDs below the mean in young men, than in those who had a concentration ≥ 30 ng/mL. Parathyroid hormone was not a significant determinant of RASM in this cohort of men ($P = 0.66$).

Characteristics of men with sarcopenia

Sarcopenia was defined as the lowest quartile of RASM in the studied cohort (<6.32 kg/m^{2.3}). In comparison with the men in the 3 upper quartiles of RASM, the men with sarcopenia were significantly older (Table 2). The men with sarcopenia also had significantly lower body weight due to significantly lower lean mass and fat mass. In contrast, the percentages of lean mass and fat mass did not differ significantly between the 2 groups. The men with sarcopenia were significantly more likely than the men with normal RASM values to be current or former smokers (74% compared with 66%; $P = 0.03$). The men with sarcopenia also had significantly lower levels of current leisure-time physical activity. After adjustment for confounding variables, the men with sarcopenia had significantly lower AFTC values than did the men with normal RASM values. In contrast, concentrations of total testosterone, 17β -estradiol, androstenedione, $25(\text{OH})\text{D}$, and parathyroid hormone did not differ significantly between the 2 groups.

DISCUSSION

Our results show that, in elderly men, low physical activity, tobacco smoking, thinness, low concentrations of the free fraction of testosterone, and possibly decreased $25(\text{OH})\text{D}$ concentrations are risk factors for sarcopenia (low muscle mass). Several methods have been suggested to assess ASM, and their results are correlated; however, there is no gold standard (20, 26–28). Each method has specific limitations: high cost and assumption of constant density of skeletal muscle for magnetic

TABLE 2

Comparison of anthropometric, lifestyle, densitometric, and hormonal variables between men with sarcopenia defined as a relative appendicular skeletal muscle mass index (RASM) in the lowest quartile (<6.32 kg/m^{2.3}) and men with normal RASM values (>6.32 kg/m^{2.3})¹

Variable	Low RASM (<6.32 kg/m ^{2.3})	Normal RASM (≥ 6.32 kg/m ^{2.3})
Age (y)	67 \pm 9 ^{2,3}	63 \pm 8
Body weight (kg)	71 \pm 10 ³	83 \pm 12
Body height (cm)	169 \pm 7	169 \pm 6
BMI (kg/m ²)	25.0 \pm 2.6 ³	28.9 \pm 3.5
Lean mass		
(kg)	48.8 \pm 5.6 ³	56.3 \pm 6.0
(%)	68.6 \pm 6.5	68.5 \pm 6.1
Fat mass		
(kg)	19.1 \pm 6.4 ³	22.9 \pm 7.6
(%)	26.6 \pm 6.6	27.3 \pm 5.9
Smokers (%)		
Current	17 ⁴	12
Former	57	54
Never	26	34
Alcohol intake (g/wk)	247 \pm 236	277 \pm 256
Coffee, tea, and cola intake (cups/wk)	15 \pm 11	17 \pm 14
Leisure-time physical activity (h/wk)	18 \pm 11 ³	22 \pm 13
Duration of sport activity (y)	10 \pm 16	10 \pm 13
Testosterone (nmol/L) ⁵	17.52 \pm 7.18	17.88 \pm 6.88
AFTC (nmol/L) ⁵	190 \pm 75 ⁶	208 \pm 80
FTI ⁵	0.22 \pm 0.11 ⁶	0.25 \pm 0.09
17 β -Estradiol (pmol/L) ⁵	110 \pm 29	113 \pm 29
Androstenedione (nmol/L) ⁵	1.64 \pm 0.63	1.68 \pm 0.60
SHBG (nmol/L) ⁵	87 \pm 45	82 \pm 41
25(OH)D (ng/mL) ⁵	27 \pm 11	28 \pm 11
PTH (pg/mL) ⁵	39 \pm 17	40 \pm 17

¹ AFTC, apparent free testosterone concentration; FTI, free testosterone index; SHBG, sex hormone-binding globulin; 25(OH)D, 25-hydroxycholecalciferol; PTH, parathyroid hormone.

² $\bar{x} \pm$ SD (all such values unless indicated otherwise).

³ Significantly different from the men with normal RASM values, $P < 0.0001$ (unpaired t test).

⁴ Nearly significantly different from the men with normal RASM values, $P = 0.05$ (unpaired t test).

⁵ $\bar{x} \pm$ SD adjusted for age, weight, tobacco smoking, and physical activity both at work and during leisure time.

⁶ Significantly different from the men with normal RASM values, $P < 0.01$ (ANCOVA).

resonance imaging, high radiation exposure and high cost for computerized axial tomography, inaccuracy and high cost for in vivo neutron activation analysis combined with whole-body potassium counting, high precision error and dependence on weight and height for bioelectrical impedance analysis, and combined assessment of both muscle and bone cross-sectional area for anthropometric measurements combined with appropriate calculations.

We assessed ASM as the lean mass of limbs measured by using whole-body DXA. The lean mass of limbs is composed of striated muscle, skin, and bone marrow. Thus, the values of RASM should be considered as approximate and not accurate. This method measures only the lean mass of the limbs, which constitutes $\approx 75\%$ of the entire muscle mass. The advantages of DXA include low irradiation dose and good precision. RASM was

stable until the age of 60 y and then decreased significantly with aging. A similar trend was described previously by researchers using the same technique (21). Hypogonadism is a risk factor for sarcopenia. In hypogonadal men, muscle mass is low and increases during testosterone replacement therapy (29–31). We observed low RASM values only in the men with the lowest values for the free fraction of testosterone (AFTC and FTI), whereas total testosterone was not predictive of decreased skeletal muscle mass. This finding confirms that free testosterone and bioavailable testosterone are better markers of androgenic status in elderly men than is total testosterone, which is in agreement with previous data (23, 32, 33).

Muscle mass and muscle strength should be distinguished. In young men, low testosterone secretion results in decreased muscle mass and strength, and testosterone replacement therapy increases muscle mass and restores muscle strength (29, 34–36). In contrast, in elderly hypogonadal men, the decrease in muscle strength outweighs the loss of muscle mass because the decrease in the mass of muscle contractile proteins is accompanied by age-related phenomena, such as decreased muscle perfusion, decreased activity of oxidative enzymes, and deterioration in neuromuscular coordination (2, 7, 37). Mechanisms of the age-related deterioration of muscle function that are independent of testosterone secretion are not reversible under testosterone treatment. Thus, testosterone therapy in elderly men increases the mass of contractile proteins but not necessarily muscle strength (15, 38–41).

We found decreased RASM values in the men with the lowest 25(OH)D concentrations. Low ASM can be the direct consequence of the effect of vitamin D deficiency on protein metabolism in muscle cells (11). However, low muscle mass and vitamin D deficiency may be parallel consequences of poor health status and nutritional deficits. No significant association between 25(OH)D concentrations and ASM was found in 2 small groups of elderly men (42, 43). In contrast, several (44–47), although not all (43, 48), studies showed positive correlations of 25(OH)D concentrations with muscle strength, physical performance, and the aging-related loss of muscle strength in the elderly. Several mechanisms, including disorders in the intracellular transport of calcium and phosphorus, atrophy of type II muscle fibers, and reduced nerve conduction velocity (49, 50), may contribute to this association.


Physical exercise is a factor that is well known for increasing muscle mass. However, most studies concern the effect of strenuous, vigorous exercise performed in a very standardized way. These studies are often performed in young professional sportsmen, in selected highly motivated groups of elderly persons, or in patients with various conditions who have low muscle mass due either to the disease itself or to treatment. Fewer data concern the effects of physical activity at work or during leisure time (mild physical exercise, gardening, and housework) on muscle mass (18). Our data suggest that this type of physical activity can also have a positive effect on muscle mass in elderly men.

Younger men may have greater muscle mass and higher levels of physical activity than do older men. However, the age-adjusted association between current physical activity and muscle mass in the present study was also significant. One could argue that, at the same age, men who are healthier have higher levels of physical activity and greater muscle mass than do those who are less healthy. We evaluated the effect of comorbidity on

muscle mass; however, this effect was not significant (data not shown) even when we pooled men with different pathologic conditions that could influence muscle mass, ie, neurologic disorders and gastrointestinal diseases. Thus, regular physical activity has a significant positive effect on muscle mass in elderly men independently of age and general health status.

In the present study, current smokers had slightly lower RASM values than did the subjects who had never smoked, and among the smokers, RASM values were lower in those who smoked more. In several studies, smoking was associated with lower lean mass and low muscle mass and strength (18, 51, 52). In other studies, differences in lean mass between smokers and nonsmokers were not significant, but the groups were small and comparisons were not adjusted for confounding variables (53–55). Smokers often have lower body mass indexes (mainly due to lower fat mass), lower levels of current and past leisure-time physical activity, hormonal disorders, and nutritional deficits. Therefore, the data regarding smokers should be interpreted cautiously.

Our study had several limitations. Our cohort comprised mainly low-to-middle-class men and may not be representative of the French population. The evaluation of lifestyle factors was based on a self-reported questionnaire, and answers may have been subjective. With regard to certain lifestyle factors, we evaluated only the current status, which may have differed from previous habits; for example, the retired men tended to spend more time on gardening and drank less wine than did the men who had not retired. For seasonal activities, it is difficult to calculate the real yearly average time spent per week on these activities. Answers concerning past activities, eg, duration of sport activity or tobacco smoking, could have been influenced by recall bias.

Another limitation was the accuracy of the evaluation of ASM. DXA measures the lean mass of limbs, which comprises skeletal muscle, connective tissue, and water. However, connective tissue replaces atrophied muscle fibers, and the fraction of water in fat-free mass increases with aging due to a disproportionate decrease in protein mass (39). Thus, DXA underestimates the aging-related decrease in skeletal muscle mass. DXA measures lean mass but does not distinguish between different age-related structural and molecular modifications (decrease in the mass of type II fibers compared with decrease in the mass of type I fibers, decrease in the mass of structural proteins compared with decrease in enzymatic activity, and neuropathic changes in the fibers that innervate skeletal muscle). In conclusion, despite certain methodologic limitations, the present study indicates that low physical activity, tobacco smoking, thinness, low concentrations of the free fraction of testosterone, and decreased 25(OH)D concentrations increase the risk of aging-related sarcopenia in men. 

PS was in charge of recruiting participants into the MINOS cohort, performed all the statistical analyses, and wrote the manuscript. FD was responsible for quality control of bone densitometric analyses and for the training of DXA technicians. FM is a physician employed by the SSMB in Montceau les Mines, France; was the local coordinator of this study; and was responsible for the collaboration between the INSERM Unit 403 and the authorities of the SSMB. PDD is the head of the INSERM Unit 403 and is the principal investigator of the MINOS study. None of the authors had any conflicts of interest.

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