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Factors Associated with Poor Muscle Mass and Strength in A Community-Dwelling Elderly Population: A Cross-Sectional Study

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Abstract

Background: The pathophysiology of muscle wasting in the elderly is multifactorial and not fully understood.

Objective: To assess the main factors associated with poor muscle mass and strength in an elderly population and to assess differences by sex.

Methodology: An observational cross-sectional study of community-dwelling adults aged 75 years and older. Muscle mass was assessed by bio impedance analysis and muscle strength by handheld dynamometer. Main study factors included physical exercise, nutritional status, co-morbidities, anabolic and catabolic hormones (ghrelin, insulin-like growth factor1, testosterone, insulin and cortisol), and inflammatory markers (interleukin-6, C-reactive protein). Other study variables included sociodemographic characteristics, chronic medication, functional capacity, a complete blood count and basic biochemical analyses.

Results: A total of 324 persons were recruited: 170 men and 154 women, mean age 80.1 years. Muscle mass was independently associated with age, physical activity, obesity, gastro-duodenal ulcer and interleukin-6 levels in men and with physical activity, obesity, insulin-like growth factor 1 levels and fiber intake in women. In men, muscle strength was independently associated with previous falls, number of medications, dyspepsia and good nutrition and, in women, with age, physical activity, arthritis, diabetes, number of medications and cortisol levels.

Conclusions: Physical activity and obesity are the main factors associated with muscle mass in community-dwelling elderly men and women. Sex differences identified in certain biomarkers associated with loss of muscle mass and strength would suggest a more important role for inflammation in men and for anabolic/catabolic imbalances in women.

Keywords: Muscle wasting; Muscle mass; Muscle strength; Risk factors; Elderly; Sex differences

Introduction

A progressive loss of muscle mass occurs from approximately 40 years of age. This loss has been estimated at about 8% per decade until the age of 70 years, after which the loss increases to 15% per decade [1]. Loss of muscle mass accompanied by loss of muscle strength or function is known as sarcopenia [2], a devastating geriatric syndrome leading to frailty, functional decline, disability, falls and even death [3,4]. Muscle mass and function, the main components of the frailty phenotype proposed by Fried [5], are a main determinant of physical performance and quality of life. The pathophysiology of muscle wasting in the older population is multifactorial and not completely understood [6]. Poor physical exercise and poor nutritional status are considered to be the main risk factors for sarcopenia. Other factors such as an imbalance between anabolic and catabolic hormones [7], metabolic disorders and insulin resistance [8] and chronic pro-inflammatory states have been associated with muscle wasting [9]. However, the specific role of each of these factors in the development of sarcopenia is not well known. Moreover, gender differences exist not only in body composition, muscle mass and strength but also in the prevalence of frailty and disability [10]. Older women are more prone to experiencing accelerated functional decline, and although they live longer than men they usually have a poorer quality of life [11]. These data would suggest that the pathophysiology of sarcopenia and frailty and the role of the above-mentioned risk factors may differ in men and women. A profound knowledge of the mechanisms involved in muscle wasting and sarcopenia is essential to the design of effective preventive measures to reduce both incidence and consequences. We hypothesize that low physical activity, obesity, inflammation and hormonal misbalances are associated with low muscle mass and strength. The aim of this study was to assess the main factors associated with poor muscle mass and strength in a community-dwelling elderly population and to assess differences by sex.

Methods

Study design and population

An observational cross-sectional study was performed of community-dwelling adults aged 75 years and older. A sample was randomly selected from the database of 3 primary care centres in the municipalities of Mataró and Argentona (Barcelona, Spain). Individuals were excluded if they had active malignancy, dementia or serious mental illness, had a life expectancy of less than 6 months, were in a palliative care programme or were institutionalized. Persons who fulfilled all selection criteria and who signed the informed consent form were recruited from January to July 2014. The local ethics committee approved the study protocol (code 64/13). Details of the study design have been previously published [12].

Data collection

The main outcome measures considered were muscle mass and muscle strength. Muscle mass and body composition were assessed by bioimpedance analysis (Bioelectrical Impedance Analyser, EFG3 Electofluidgraph, Akern SRL), which determines fat mass, lean mass and muscle mass in both kilogrammes and as a percentage of total body weight. Fat distribution was assessed by triceps skinfold, waist and hip circumferences and waist-hip circumference ratio. Used as a measure of muscle strength was hand grip, assessed by a handheld dynamometer in terms of kilogrammes (JAMA model). Of 3 measurements made for each participant the highest value was used for this study. The main study factors were as follows: (a) physical exercise, assessed by the International Physical Activity Questionnaire and daily hours walked outdoors (www.ipaq.ki.se) [13]; (b) nutritional status, assessed by anthropometric measurements (weight, height, body mass index), recent weight loss and the short-form Mini Nutritional Assessment questionnaire; (c) comorbidities (arthrosis, diabetes, ischaemic heart disease, heart failure, stroke, chronic obstructive pulmonary disease, chronic kidney failure, chronic liver disease, Parkinson disease, depression, etc); (d) anabolic hormone levels, namely, fasting plasma levels of total ghrelin, insulin-like growth factor 1 (IGF-1), testosterone and insulin determined using validated commercial kits; (e) inflammatory markers, namely, fasting plasma levels of interleukin-6 (IL-6) and C-reactive protein, determined using validated commercial kits; and (f) frailty phenotype, whereby participants were classified as robust, pre-frail or frail if they fulfilled 0, 1-2 or ≥3, respectively, of the following five Fried criteria: unintentional weight loss, exhaustion, low physical activity, slow walking speed and poor grip strength [5]. Other study variables included sociodemographic characteristics (age, sex, education level); chronic medication; appetite and satiety assessed by means of a visual analogue scale; functional capacity assessed by the Barthel index, timed up-and-go test, single-leg stance test, falls and gait speed; and, finally, a complete blood count and basic blood biochemical analyses for glucose, creatinine, albumin and lipid profile. Information on co-morbidities and medication was obtained from electronic medical records for the patients and all other information was obtained directly from the patient by trained healthcare professionals.

Statistical analysis

Muscle mass as a percentage of total body weight was used as the main muscle mass indicator and hand grip in kg was used as a measure of muscle strength. The linear regression coefficient (β) and its 95% confidence interval (CI)were used to measure the relationship between risk factors and both muscle mass and muscle strength. All the variables first underwent bivariate analysis (simple linear regression); only variables significantly associated with muscle mass or muscle strength (for $p<0.05$) were used to fit a multivariate model (one for muscle mass and another for muscle strength). When multicollinearity was detected the most generic variable was selected. All analyses were performed separately for men and women. A p-value <0.05 was considered statistically significant.

Results

A total of 324 persons were recruited, 170 men and 154 women, with a mean age of 80.1 years (range 75-93 years). Main co-morbidities, for which participants were taking a mean of 6 medications, were arterial hypertension (70%), osteoarthritis (52.4%), dyslipidaemia (50.9%), diabetes (24.2%), ischaemic heart disease (21.5%) and depression (19.6%). Muscle mass and muscle strength were significantly correlated in both men and women (rs=0.18, p=0.019 and rs=0.18, p=0.026, respectively). Muscle mass/muscle strength associations with socio-demographic and clinical variables, with functional and nutritional indicators, and with analytical biomarkers stratified by sex are shown in Tables 1-3, respectively. These tables indicate that age, number of comorbidities and medications, diabetes, chronic liver diseases, dyspepsia, functional capacity, previous falls, nutritional status, physical activity and IL-6 levels are associated with muscle strength in both men and women. In men, muscle strength was also related with weight, hunger, gastroduodenal ulcer and anaemia, while in women, muscle strength was related with arthritis, depression, dyslipidaemia, fibre intake and cortisol and magnesium levels. Regarding muscle mass, this was related with number of medications, obesity, physical activity, fibre intake and testosterone and IL-6 levels in both sexes. In men, it was also associated with age, certain chronic diseases (arthritis, gastroduodenal ulcer and dyspepsia), previous falls and haemoglobin

	Men				Women			
	% MM β	p	MS, kg β	p	% MM β	p	MS, kg β	p
Age (years)	- 0.46	<0.001	-0.34	0.013	-0.02	0.842	-0.37	<0.001
Loneliness	-1.09	0.304	0.34	0.814	-0.69	0.312	0.46	0.530
≥ Secondary education	0.22	0.782	1.92	0.081	1.60	0.097	1.96	0.060
Never smoked	0.39	0.610	0.21	0.845	0.79	0.479	-0.78	0.521
Alcohol (gr/day)	0.03	0.546	0.004	0.933	-0.05	0,725	0.11	0.213
No. medications	-0.26	0.023	-0.44	0.005	-0.25	0.016	-0.52	<0.001
No. comorbidities	-0.38	0.055	-0.95	<0.001	-0.31	0.084	-0.88	<0.001
Arthritis	-1.82	0.009	-1.60	0.099	-1.07	0.132	-2.81	<0.001
Ischaemic heart disease	-1.06	0.172	-1.56	0.142	-1.34	0.148	-0.64	0.525
Peripheral vasculopathy	-0.23	0.830	0.43	0.776	-1.45	0.079	0.14	0.874
Stroke	-0.46	0.684	-1.68	0.286	-0.27	0.806	-1.96	0.104
Dementia	3.64	0.251	-2.12	0.628	-0.32	0.939	1.51	0.735
Cancer	-1.20	0.596	-2.40	0.440	0.70	0.812	-5.57	0.077
Chronic bronchitis	-1.66	0.070	-2.09	0.100	-0.14	0.897	-0.91	0.440
Asthma	0.82	0.555	-0.98	0.610	-0.20	0.858	-0.48	0.691
Diabetes	-0.55	0.497	-3.53	0.001	-0.91	0.237	-1.89	0.022
Gastroduodenal ulcer	-3.72	0.014	-4.56	0.029	-1.42	0.270	-0.64	0.647
Gastroesophageal reflux	-0.79	0.603	-1.70	0.397	-1.61	0.077	-0.84	0.395
Chronic liver disease	-1.18	0.492	-4.87	0.039	0.69	0.867	-10.6	0.017
Chronic kidney failure	1.79	0.195	-1.30	0.482	2.74	0.051	1.12	0.463

Dyspepsia	-3.18	0.048	-9.43	<0.001	-0.44	0.666	-3.33	0.002
Arterial hypertension	-0.91	0.219	-0.28	0.784	-0.59	0.432	-1.31	0.102
Gout-hyperuricaemia	1.20	0.147	-0.35	0.751	0.69	0.538	-2.70	0.024
Dyslipidaemia	0.27	0.709	-0.81	0.395	-0.21	0.757	-1.46	0.046
Urinary incontinence	-2.76	0.012	-3.55	0.019	-2.35	<0.001	-1.68	0.023
Faecal incontinence	-1.78	0.492	-4.83	0.174	-0.33	0.849	-1.73	0.348
Sleep disorders	-0.12	0.883	-2.20	0.041	-0.50	0.452	-1.73	0.015
Previous falls	-2.25	0.119	-8.45	<0.001	-1.32	0.091	-4.06	<0.001
Depression	-0.15	0.918	-0.18	0.929	-0.73	0.321	-2.26	0.004

Table 1: Association of sociodemographic and clinical variables with muscle mass (MM, %) and muscle strength (MS, hand grip in kg) by sex. Simple linear regression analysis results.

	Men				Women			
	% MM β	p	MS, kg β	p	% MM β	p	MS, kg β	p
Weight (kg)	-0.13	<0.001	0.14	0.005	-0.24	<0.001	0.02	0.509
Weight loss (kg)	-3.02	0.100	-12.0	<0.001	-3.29	0.019	-0.75	0.606
Body mass index ≥ 30	-2.29	0.007	0.46	0.695	-3.75	<0.001	-0.20	0.784
Tricipital skinfold (cm)	-0.42	<0.001	0.04	0.769	-0.27	<0.001	-0.05	0.329
Waist/hip ratio[1]	-2.04	0.025	-1.61	0.203	-0.80	0.283	-0.28	0.727
Total MNA-sf[2]	1.37	0.009	2.99	<0.001	0.20	0.494	0.78	0.013
Wellnourished[2]	-0.51	0.872	7.25	0.091	0.42	0.710	1.06	0.376
Outdoor life	-0.56	0.725	6.56	0.002	2.27	0.008	5.46	<0.001
Hours walked/day	0.03	0.003	0.01	0.448	0.01	0.295	0.03	0.021
Falls in last 3 months	-3.36	0.046	-5.69	0.014	-1.61	0.136	-3.09	0.007
Unable to use stairs	-9.60	0.002	-16.0	<0.001	-2.09	0.079	-3.56	0.005
Physical activity[3]	1.64	<0.001	1.63	<0.001	0.95	0.005	2.06	<0.001
Poor physical activity[3]	-4.28	<0.001	-5.72	<0.001	-0.97	0.161	-4.19	<0.001
Gait speed (m/s)	4.88	0.001	9.93	<0.001	5.48	<0.001	10.6	<0.001
Timed up-and-go test(s)	-0.50	< 0.001	-1.00	<0.001	-0.33	0.002	-0.69	<0.001
Single-leg stance test (5 s)	2.48	0.004	4.34	<0.001	1.81	0.007	2.76	<0.001
Barthel index score	0.28	< 0.001	0.60	<0.001	0.15	0.001	0.31	<0.001
Frailty (Fried criteria)	-1.91	0.001	-7.45	<0.001	-2.00	<0.001	-3.97	<0.001
Peakflow[4]	0.95	0.198	4.46	<0.001	1.32	0.053	3.62	<0.001
Energy intake[5]	2.5	0.822	-0.20	0.186	0.08	0.444	0.15	0.177
Fat intake[5]	3.4	0.895	-0.49	0.164	0.05	0.816	0.36	0.130
Protein intake[5]	-1.1	0.830	-1.2	0.095	0.13	0.784	0.29	0.585
Carbohydrate intake[5]	0.3	0.896	-0.18	0.549	0.27	0.188	0.15	0.490
Fibre intake[6]	15.5	0.010	2.7	0.741	10.6	0.049	5.51	0.344
Protein ratio[7]	2.1	0.107	-4.7	0.009	4.3	<0.001	-0.16	0.881

[1]Waist/hip ratio >1 for men and >0.9 for women, [2]Mini Nutritional Assessment-short form;well nourished >11, [3]Physical activity in metabolic equivalents (METs <500, 500-1000, 1000-1500, >1500). Poor physical activity <600 METs, [4]Peak flow >percentile 20, [5]Nutritional intake: x100 kcal/day, [6] x100g/day, [7]Ingested protein as a ratio of recommended protein intake

Table 2: Association of nutritional, dietary and functional variables with muscle mass (MM, %) and muscle strength (MS, hand grip in kg) by sex. Simple linear regression analysis results.

levels, while in women it was associated with malnutrition, insulin resistance and IGF-1 and magnesium levels.

Table 4 lists the variables that are independently associated with muscle mass and muscle strength in both men and women. The multivariate analysis showed that previous falls, IL-6 levels, number of medications, dyspepsia and malnutrition were independently associated with muscle strength in men, and that age, physical activity, arthritis, number of medications and cortisol levels were independently associated with muscle strength in women. Regarding muscle mass, the multivariate analysis showed an independent effect in men of age, physical activity, obesity, gastroduodenal ulcer and IL-6 levels and an independent effect in women of physical activity, obesity, haemoglobin levels<10, IGF-1 levels and fibre intake.

Discussion

Results show that, in both sexes, muscle mass was mainly associated with obesity and physical exercise, whereas muscle strength was mainly associated with comorbidities and number of medications. However, the results also disclose some differences between the sexes in terms of the factors associated with muscle mass and strength. In men, muscle mass was also associated with age and certain inflammatory biomarkers such as IL-6 levels, while in women it was associated with severe anaemia and anabolic hormones such as IGF-1 levels. The results also pointed to sex differences regarding muscle strength, associated with nutritional indicators and IL-6 in men and with age, physical exercise and cortisol levels in women.

Ageing is associated with a progressive decline in muscle mass,

	Men				Women			
	% MM β	p	MS, kg β	p	% MM β	p	MS, kg β	p
Haemoglobin (g/dL)	0.61	0.029	0.32	0.401	-0.26	0.386	0.27	0.413
Anaemia	-1.10	0.287	-2.79	0.043	0.04	0.968	-0.79	0.396
Albumin (mg/dL)	2.89	0.049	1.57	0.415	2.43	0.068	0.53	0.712
Albumin ≥ 3.8 mg/dL	1.46	0.743	-2.76	0.639	-0.69	0.776	1.91	0.461
Total cholesterol (mg/dL)	0.01	0.571	-0.01	0.416	-0.004	0.697	0.02	0.089
Total Cholesterol ≥ 160 mg/dL	-0.76	0.344	-0.44	0.678	-0.49	0.643	1.49	0.180
Glucose (mg/dL)	0.01	0.416	-0.01	0.606	-0.03	0.069	-0.03	0.037
Glucose ≥ 115 mg/dL	0.35	0.644	-0.30	0.766	-0.99	0.192	-1.58	0.054
Insulin (mcUl/mL)	0.01	0.210	0.01	0.210	0.05	0.005	0.05	0.005
Insulin resistance[1]	-0.16	0.156	-0.30	0.840	-0.29	0.033	-0.26	0.079
Total ghrelin (pg/mL)	-3.7×10^{-4}	0.611	-7.5×10^{-5}	0.938	0.001	0.200	4.6×10^{-5}	0.921
Total ghrelin categorized[2]	-0.78	0.289	-0.63	0.520	1.45	0.080	0.38	0.667
IGF-1 (ng/mL)	0.01	0.081	-0.01	0.459	0.02	0.014	0.01	0.334
IGF-1 ≥ 54 ng/mL	0.74	0.644	-1.05	0.624	-0.06	0.970	0.28	0.864
Testosterone (ng/mL)	0.51	0.007	0.07	0.792	1.80	0.033	0.50	0.580
Testosterone categorized[3]	2.01	0.185	1.67	0.409	-6.74	0.103	-5.53	0.216
Cortisol (µg/dL)	-0.07	0.346	-0.14	0.156	-0.06	0.364	-0.17	0.016
Cortisol >14.5 µg/dL	-1.47	0.057	-1.13	0.273	-0.97	0.221	-2.48	0.003
TNF-a (pg/mL)	-0.21	0.281	-0.04	0.893	0.21	0.159	0.09	0.628
TNF-a categorized[4]	-1.78	0.048	-1.23	0.321	0.38	0.697	0.87	0.460
IL-6 (pg/mL)	-0.004	0.895	-0.04	0.273	-0.05	0.443	-0.04	0.642
IL-6 categorized5	-2.42	<0.001	-2.42	0.008	-2.05	0.007	-1.46	0.078
CRP (mg/dl)	-1.48	0.290	-0.87	0.634	0.12	0.757	-0.03	0.953
CRP ≥ 0.8 mg/dL	-1.91	0.352	2.46	0.357	0.25	0.867	-2.12	0.191
Vitamin D (ng/mL)	-0.01	0.740	0.001	0.976	0.03	0.301	-0.003	0.924
Calcium (mg/dL)	-0.17	0.740	-0.38	0.574	0.65	0.415	-1.42	0.084
Magnesium (mg/dL)	-1.83	0.261	-0.74	0.730	4.89	0.003	3.41	0.049
Zinc (mcg/dL)	-0.003	0.902	0.02	0.631	-0.02	0.358	-0.02	0.426
Selenium (mcg/L)	0.03	0.096	0.05	0.073	0.01	0.786	0.02	0.492
Vitamin A (mg/L)	2.39	0.084	1.38	0.453	-1.23	0.411	0.98	0.546
Vitamin E (mcg/mL)	0.02	0.683	-0.01	0.878	-0.02	0.727	0.00	0.996

CRP: C-reactive protein; IGF-1: insulin-like growth factor 1; IL-6: interleukin 6; TNF-a: tumour necrosis factor alpha; [1] As per Homeostatic Model Assessment (HOMA), [2] Total ghrelin (pg/mL) ≥900 for men and ≥1000 for women, [3] Testosterone (ng/mL) <1.93 for men and <0.029 for women, [4] TNF-a(pg/mL) >8.5 for men and >7.7 for women, [5] IL-6 (pg/mL) >3 for men and>2.4 for women

Table 3: Biomarkers associated with muscle mass (MM, %) and muscle strength (MS, hand grip in kg) by sex. Simple linear regression analysis results.

muscle strength and aerobic capacity, which all contribute to reduced mobility and impaired functionality and quality of life. Loss of muscle mass and strength with age is a complex and multifactorial process. Decreased physical activity, malnourishment, chronic diseases, insulin resistance, chronic inflammation and imbalances in anabolic/catabolic hormones have all been suggested as possible reasons for muscle wasting [14]. Moreover, some evidence suggests that men and women differ in terms of risk factors associated with the decline in grip strength in old age [15]. Our results point to physical activity as one of the main factors associated with greater muscle mass and strength in both sexes, corroborating most scientific evidence indicating the benefits of physical activity on muscle mass and function [16]. Although the optimal combination of aerobic, resistance and endurance exercises remains unclear, clinicians should encourage older adults to participate in physical exercise programmes, since these have been shown to be the most efficient method to counteract age-related changes in muscle mass and strength [17], as well as the only strategy that consistently improves sarcopenia and physical function in older adults [18]. Although some studies suggest that the benefits of exercise training are enhanced when combined with dietary supplements and nutritional interventions in the older population, the existing evidence is inconsistent [19]. Adequate calorie, protein and vitamin intake is essential to preserve muscle mass and strength during the ageing process [20]. Approximately 1.5 g protein/kg of body weight/day is recommended for the older population, considering potential anabolic resistance; however, maximum protein intake without adverse effects is not known, so recommendations must be individualized [21]. A meta-analysis of 15 controlled trials revealed that protein or essential amino acid supplementation did not significantly increase the effects of resistance exercise training on muscle mass, strength and functionality [22]. Our study reveals a weak independent association between nutritional status and strength and only in men. These findings may be explained by the fact that the study sample had good baseline nutritional and functional status.

Our results point to an independent negative relationship between IL-6 levels and muscle mass and strength in men but not in women. A chronic low-grade inflammatory state in the elderly has been referred to as inflammageing. An increased concentration of pro-inflammatory cytokines leads to increased protein degradation and reduced protein synthesis and has, furthermore, been associated with increased muscle wasting, strength loss and functional impairment [23]. The present study

Men					
% muscle mass (1)			Muscle strength (kg) (2)		
	β	p		β	p
Age	-0.43	<0.001	Previous falls	-4.63	0.023
Body mass index ≥30	-1.93	0.017	Well nourished	8.79	0.018
Physical activity	0.76	0.030	No. medications	-0.38	0.010
Gastroduodenal ulcer	-3.02	0.033	Dyspepsia	-6.76	0.003
IL-6	-1.30	0.046	IL-6	-1.61	0.070
Women					
% muscle mass (3)			Muscle strength(kg) (4)		
	β	p		β	p
Body mass index ≥30	-3.67	<0.001	Age	-0.28	0.002
Physical activity	0.69	0.027	Physical activity	1.17	0.002
Fibre intake	1.21	0.012	No. medications	-0.29	0.009
IGF-1	0.022	0.003	Arthritis	-2.18	0.001
			Diabetes	-1.56	0.037
			Cortisol	-0.14	0.028

Table 4: Factors associated with muscle mass (MM, %) and muscle strength (MS, hand grip in kg) by sex. Multivariate analysis results. Variables included in the model (stepwise): (1) Age, body mass index, physical activity in metabolic equivalents (METs<500, 500-1000, 1000-1500, >1500), gastroduodenal ulcer, interleukin-6 (IL-6, pg/mL; >3 for men and >2.4 for women), number of medications, arthritis, chronic bronchitis, dyspepsia, waist/hip ratio (>1 for men and >0.9 for women), albumin, haemoglobin, insulin-like growth factor 1 (IGF-1), testosterone, vitamin A, fibre intake (x100 g/day). (2) Previous falls, well nourished (>11 in the Mini Nutritional Assessment-short form), number of medications, dyspepsia, IL-6, age, education level, arthritis, diabetes, gastroduodenal ulcer, chronic liver disease, physical activity, anaemia, selenium, sleep disorders. (3) Body mass index, physical activity, fibre intake (x100 g/day), IGF-1, education level, number of medications, peripheral vasculopathy, gastro-esophageal reflux, chronic kidney failure, previous falls, albumin, insulin resistance (Homeostatic Model Assessment -HOMA-), total ghrelin (pg/mL, ≥900 for men and ≥1000 for women), testosterone, IL-6, magnesium. (4) Age, physical activity, number of medications, arthritis, diabetes, cortisol levels(µg/dL), education level, chronic liver disease, dyspepsia, dyslipidaemia, depression, insulin resistance, IL-6, calcium, magnesium.

shows that, in women, muscle mass is associated with decreased IGF-1 levels, and muscle strength with increased cortisol levels, suggesting an imbalance between anabolic and catabolic hormones. These results corroborate those reported by Tay et al. in another cross-sectional study in community dwelling older adults, which showed lower IGF-1 levels in sarcopenic women in comparison to non-sarcopenic women [24]. However, this anabolic/catabolic imbalance seems to be less relevant in men, who may be protected by higher testosterone levels. Obesity was independently associated with muscle mass in both sexes. This result is only to be expected, given the trade-off between muscle mass and fat mass, but also because obesity is related to insulin resistance, higher levels of cytokine release, fat infiltration of muscle and poor physical activity, all of which favor muscle wasting and atrophy.

Comorbidities and number of medications were also independent factors associated with hand grip. The effect of arthritis and musculoskeletal diseases, which are more frequent in older women because of menopause-related osteoporosis, is possibly due to limited physical activity secondary to pain. A high prevalence of pain in elderly subjects and its relationship with arthritis and weakness has been reported elsewhere [25,26]. Pain may lead to low physical activity and immobility, and, consequently, to muscle atrophy and loss of muscle strength. Diabetes and insulin resistance also have an impact on skeletal muscle [27,28]. Insulin is an anabolic signal that stimulates muscle protein synthesis and improves the bio-energetic capacity of skeletal muscle. There is evidence suggesting that insulin resistance reduces protein synthesis and increases protein degradation, thereby enhancing frailty [29]. Our study indicates that insulin resistance has an independent effect on muscle strength in women but not in men. Somewhat surprising is the relationship between dyspepsia and muscle strength, especially in men; whereas our results point to a strong relationship between dyspepsia and frailty, even in the multivariate analysis [12], we were unable to locate any other study reporting similar results. Tze Pin Ng [30] reported more gastrointestinal problems in frail subjects in a bivariate analysis, although this effect disappeared in a multivariate analysis. Gastric ageing with less acid secretion, together with lower gastric motility and slower emptying, may favor a sensation of fullness, dyspepsia, bacterial overgrowth and changes in the microbiota that, in turn, may cause chronic gastrointestinal inflammation [31]. Further studies are necessary to understand the relationship between dyspepsia and muscle wasting.

The number of medications, obviously related to the number of comorbidities, has been identified as an indicator of frailty [12,30]. However, our multivariate analysis showed that the number of medications had an independent effect on muscle strength; this would suggest that some medications may have an effect on muscle, as has also been suggested by a review on this topic [32]. Again, further studies are needed to explore in more detail the potential impact of certain medications on muscle wasting.

The main limitation of the present study is its cross-sectional design, which does not allow causal relationships to be established between the studied factors and muscle mass or muscle strength, only associations between variables. Exposure to risk factors for muscle strength decline in old age may occur years before in early adulthood. Another limitation of this study is the relatively small sample size, which does not allow detection of statistically significant associations between muscle mass/muscle strength and other clinical or sociodemographic characteristics.

To sum up, physical activity and obesity are the main factors associated with muscle mass in community-dwelling elderly subjects. These clearly modifiable risk factors need to be addressed, specifically in strong tailored recommendations by healthcare professionals regarding physical activity. Co-morbidities and the number of medications are associated with muscle strength, so good control of baseline diseases and periodic evaluation of prescribed medication may play a role in preventing muscle wasting and frailty. On the other hand, the sex differences in some biomarkers reflecting a loss of muscle mass and strength suggest that, in men, chronic inflammation and, in women, anabolic/catabolic imbalances may play more important roles. Further research is needed to explore the role played by these factors in muscle mass and function and to establish whether their modulation might be effective in preventing muscle wasting.

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