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Leptin concentration and risk of impaired physical function in older adults: the Seniors-ENRICA cohort

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Abstract

Background: leptin resistance, which may develop during the ageing process, stimulates the production of pro-inflammatory cytokines and insulin resistance that could impair the muscle function. However, the role of leptin on physical functioning among older adults has not yet been elucidated.
Objective: to examine the association between serum leptin levels and physical function impairment in older adults.
Design and setting: prospective study of 1,556 individuals 60 years and older from the Seniors-ENRICA cohort, who were free of physical function limitation at baseline.
Main outcome measure: serum leptin was measured in 2008–10, and incident functional limitation was assessed through 2012. Self-reported limitations in agility and mobility were assessed with the Rosow and Breslau scale, limitation in the lower extremity function was measured with the Short Physical Performance Battery, and impairment in the overall physical performance with the physical component summary of the SF-12.
Results: after adjustment for potential confounders and compared to individuals in the lowest quartile of leptin concentration, those in the highest quartile showed increased risk of impaired physical function; the odds ratio (95% confidence interval) and *P*-trend was: 1.95 (1.11–3.43), $P = 0.006$ for self-reported impaired mobility; 1.76 (1.08–2.87), $P = 0.02$ for self-reported impaired agility; 1.48 (1.02–2.15), $P = 0.04$ for limitation in the lower extremity function; and 1.97 (1.20–3.22), $P = 0.01$, for decreased overall physical performance. These associations were only modestly explained by C-reactive protein and insulin resistance. Moreover, the associations held across groups with varying health status and were independent of estimated total body fat.

Conclusions: higher leptin concentration was associated with increased risk of impaired physical function. Preserving metabolic function during the old age could help delaying physical function decline.

Keywords: *older people, mobility limitation, physical fitness, leptin, biological markers, prospective studies*

Introduction

Life expectancy has rapidly increased in the last decades, but healthy life expectancy has grown more slowly [1, 2]. Healthy ageing is a process, which enables older people to take an active part in society and to enjoy an independent and high quality of life [3]. A well-known threat to healthy ageing is the impairment of physical functioning. Unfortunately, the understanding of the biological factors that lead to impaired physical function in the old age is still limited [4].

There is evidence of the detrimental effect of obesity on physical function in older adults [5–9]. In other studies, underweight has also been associated with functional decline [10]. A plausible explanation is that adiposity, in addition to body weight, has a pivotal role on physical functioning [11]. In fact, older adults with sarcopenia or obesity are at higher risk of impaired physical function [12] probably because fat infiltrated in the muscle induces oxidative stress and chronic inflammation, which at the same time decreases skeletal muscle mass and strength [13, 14]. Furthermore, other long-term effects of adiposity, such as insulin resistance, could also have an impact on physical function [15]. However, the association between sarcopenic obesity and impairment in physical functioning has only been modestly explained by C-reactive protein (CRP) and insulin sensitivity [12], suggesting that other metabolic factors could be involved, such as adipokines.

Leptin is the first adipokine discovered and one of the best characterised. It is mainly secreted by the white adipocyte tissue and it acts predominantly through the central nervous system, contributing to the regulation of appetite and several neuroendocrine pathways, like glucose homeostasis [16]. But leptin has also peripheral effects, some of which are associated with the production of pro-inflammatory cytokines and insulin resistance [17]. Obese subjects can develop a state of central leptin resistance followed by increased serum leptin levels. In this state, the peripheral effects of leptin could prevail over its central action [18]. It has been suggested that leptin resistance could develop with the ageing process [13]. In fact, one prospective study among middle-aged women has recently found that higher leptin concentration predicts impairments in mobility [19]. Nevertheless, its role on physical functioning among older adults has not yet been elucidated, specially whether or not is mediated by inflammation or insulin resistance. Thus, we hypothesise that the increase in serum leptin levels associated with ageing could lead to functional limitations. Thus, the aim of this study was to examine the prospective association between serum leptin levels and the incident impairment of physical function among older adults.

Methods

Study design and participants

Baseline data for this prospective study were obtained from the ENRICA cohort, which was established in 2008–10 and involved 12,948 individuals representative of the non-institutionalized adult population of Spain [20]. At baseline, information on socio-demographic characteristics, lifestyle, health status and morbidity was collected through a telephone interview. In two subsequent home visits, trained research staff also obtained dietary information, conducted a physical examination and obtained blood` and urine samples for several biochemical and hormonal determinations. In 2012, we performed a second wave of data collection among the participants aged 60 and older (n = 2,614), which comprise the Senior-ENRICA cohort; given that 95 (3.6%) individuals passed away during the follow-up period, updated information was obtained only for the remaining 2,519 subjects. The Clinical Research Ethics Committee of the *'La Paz'* University Hospital approved the study protocol. All study participants gave written informed consent.

Study variables

Leptin and other biomarkers

Baseline serum leptin concentration (ng/ml) was determined by enzyme-linked immunoassay (Diagnostics Biochem Canada) using a BEST2000 robot. The sensitivity of this test was 0.5 ng/dl, and the coefficients of variation intra- and inter-assay were 7.5% and 9.6%, respectively. We also measured levels of insulin resistance and inflammation because they could be associated with leptin concentration. The homeostatic model assessment for insulin resistance index (HOMA-IR) was calculated by multiplying glucose by insulin and dividing by 405. Glucose (mg/dl) was measured by the glucose oxidase method, and insulin (μU/ml) by immunoradiometric assay. Finally, CRP (mg/l) was determined by latex-enhanced nephelometry. The coefficients of variation intra- and inter-assay were < 4% and <4% for glucose, 5.2% and 6.9% for insulin and 3.2% and 5.9% for CRP, respectively.

Physical function

We considered three basic domains of physical function: self-reported agility and mobility and an objective measure of lower extremity function, as well as a measure of overall self-reported physical performance. Limitation in self-reported agility was defined by answering '*a lot*' to the following question from the Rosow and Breslau scale [21]: '*On an average day with your current health, would you be limited in bending and kneeling?*'; whose categories of response were '*yes, a lot*', '*yes, a little*' and '*not at all*'. In the same way, limitation in self-reported mobility was defined by answering '*a lot*' to any of the following questions from the Rosow and Breslau scale [21]: '*On an average day with your current health, would you be limited in the following activities: (i) picking up or carrying a shopping bag?; (ii) climbing one flight of stairs? and (iii) walking several city blocks (a few hundred metres)?*'. Limitation in the lower extremity function was assessed using the Short Physical Performance Battery (SPPB). The SPPB combines the results of three measurements: the gait speed across 2.44 m, balance using three hierarchical tandem tests and the ability to rise from a chair five times consecutively [22]. The score with the sum of these three components ranges from 0 to 12 (highest level of function). Participants were considered to have limited function when they scored ≤9 points in the SPPB; of note is that this test was only measured in 2012. Lastly, limitation in self-reported overall physical performance was deemed to exist when the score of the physical component summary (PCS) of the 12-Item Short-Form Health Survey (SF-12) decreased at least 10 points from baseline to follow-up. We used this cut-off point because a 10-point lower score has been associated with severe adverse health outcomes [23, 24]. Moreover, in medical practice, a 10-point change in individual patients is considered as a clinically relevant alarm signal [25].

Other variables

We also collected data on several potential confounders of the study association. These included socio-demographic variables and health behaviours such as age, sex, educational level, tobacco smoking, alcohol intake, time spent watching TV and physical activity during leisure time (using the EPIC-Spain validated questionnaire) [26]. Additionally, we considered two dietary variables derived from a validated diet history [27]: adherence to the Mediterranean diet, according to the Trichopoulou index [28] and total energy intake. Regarding adiposity, we estimated the percentage of body fat using the CUN-BAE equation, which is based on sex, age, weight and height [29]. Finally, we obtained information on morbidity. Blood pressure was measured under standardized conditions, and hypertension was defined as having a systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg or being under drug treatment. Being diabetic was defined as having a medical diagnosis, fasting serum glucose ≥ 126 mg/dl or being treated with insulin or other hypoglycaemic agents. Individuals also reported whether they had been diagnosed with cardiovascular disease, chronic obstructive pulmonary disease, cancer at any site, osteomuscular disease (including osteoarthritis, arthritis and hip fracture) or depression requiring pharmacological treatment. Moreover, cognitive function was measured using the Mini-Mental State Examination (MMSE), defining cognitive impairment as an MMSE score of <23 [30]. Finally, the Lawton–Brody index was used to ascertain limitations in instrumental activities of daily living (IADL) [31].

Data analysis

Of the sample comprising 2,519 individuals, we excluded 24 subjects with baseline medical diagnosis of dementia, Alzheimer or Parkinson disease. We excluded 658 participants who lacked data on mobility (n = 184), agility (n = 3), SPPB (n = 447) or PCS score (n = 24), 6 individuals without leptin determination and 54 with missing data on potential confounders. Additionally, we excluded the participants with basal limitations in physical functioning: 91 with self-reported impaired mobility, 75 with self-reported impaired agility and 55 with fatigue, as a proxy of overall limitation in physical functioning. Baseline fatigue was measured by asking respondents how much time during the past 4 weeks they felt tired; responses of '*all of the time*' or '*most of the time*' were considered positive [32]. Thus, the analyses were conducted with 1,556 individuals.

Logistic regression models were used to estimate the odds ratios (OR) and the 95% confidence interval (CI) of the association between the serum concentration of leptin and incident limitation in physical function. Given that leptin concentration did not follow a normal distribution, we used the log-transformed values. Participants were classified into sex-specific quartiles, because leptin concentration was significantly higher in women (30.9 ± 18.9 ng/dl) than in men (12.3 ± 9.5 ng/dl). Several regression models and sensitivity analyses were built (please see a detailed description in Appendix 1 on http://www.ageing.oxfordjournals.org/). Moreover, to summarise the study associations, we repeated all the analyses using an increment of one standard deviation (SD) of leptin concentration as the independent variable. We tested if the main results varied with sex by using interaction terms. Since the results were similar in each sex and the interactions did not reach statistical significance, the results are reported for the total study sample. Statistical analyses were performed with the STATA software (version 13.0; Stata Corp., College Station). A two-tailed $P < 0.05$ was considered statistically significant.

Results

During a mean follow-up period of 3.5 years, the incidence of limitations in mobility was 12.5%, in agility 20.4% and in overall physical performance 16.7%. Furthermore, 54.8% of the individuals had impaired lower extremity function at the end of the follow-up. Table 1 shows the socio-demographic, behavioural and clinical characteristics of the

Table 1. Participants' characteristics at baseline according to physical function impairment (N = 1,556)

	Self-reported impaired mobility		Self-reported impaired agility		SPPB score ≤ 9 points		10-point decrease in PCS	
	No	Yes	No	Yes	No	Yes	No	Yes
Participants, *n*	1,361	195	1,239	317	703	853	1,296	260
Leptin, ng/ml	19.6 (15.7)	32.2 (24.1)***	18.9 (15.3)	30.1 (22.1)***	20.4 (16.7)	25.1 (20.5)***	18.1 (14.4)	23.8 (19.2)***
Age, y	67.7 (5.8)	70.1 (6.4)***	67.6 (5.8)	69.7 (6.4)***	66.3 (5.2)	69.4 (6.2)***	67.8 (5.8)	68.9 (6.4)**
Men, %	55.7	28.7***	57.6	31.6***	59.7	46.2***	53.2	48.1
Primary education, %	47.8	65.1***	45.2	68.5***	42.1	56.4***	48.1	59.2**
Current smoker, %	12.5	11.8**	12.8	11.0**	13.8	11.3	12.7	10.8
Heavy drinker, %	9.3	5.1**	9.2	7.3*	11.2	6.8***	9.0	7.7
Physical activity, MET-h/wk	23.5 (15.6)	18.8 (13.6)***	24.0 (15.8)	18.5 (13.1)***	24.8 (15.8)	21.3 (15.0)***	23.1 (15.6)	21.7 (14.5)
TV watching, h/wk	16.9 (10.4)	20.2 (11.4)***	16.5 (10.1)	20.3 (11.9)***	16.3 (10.3)	18.1 (10.9)**	17.0 (10.3)	18.8 (12.2)*
Trichopoulou index score	4.6 (1.5)	4.3 (1.6)*	4.6 (1.5)	4.4 (1.6)*	4.7 (1.5)	4.4 (1.5)***	4.6 (1.5)	4.5 (1.6)
Energy intake, kcal/d	2,121 (769)	1,892 (538)***	2,131 (784)	1,943 (564)***	2,165 (826)	2,032 (671)**	2,100 (750)	2,054 (735)
Estimated body fat, %	35.7 (6.7)	40.6 (4.5)***	35.2 (6.5)	40.7 (7.0)***	35.0 (6.4)	37.4 (7.2)***	36.1 (6.9)	37.7 (6.9)**
Morbidity, %								
Diabetes	13.3	19.0*	13.0	18.0*	9.5	17.7***	13.9	16.6
Hypertension	63.9	66.2	63.8	65.9	61.6	66.4	63.4	68.1
Cardiovascular disease	3.2	7.2**	3.2	5.7*	3.1	4.1	3.6	4.2
Chronic lung disease	6.3	11.8**	5.7	12.3***	5.4	8.3*	6.2	11.2**
Cancer	1.6	2.1	1.5	2.2	1.4	1.9	1.5	2.3
Osteomuscular disease	39.5	71.8***	36.5	71.0***	36.9	48.9***	41.6	53.1**
Depression	5.7	12.3**	5.0	12.6***	4.6	8.2**	5.6	11.5**
Incident morbidity during follow-up, %	24.0	36.4***	23.6	33.1**	21.9	28.5**	28.5**	35.0***
IADL disability, %	6.2	14.9***	5.6	13.9***	4.8	9.2**	6.9	8.9
MMSE score	28.3 (1.9)	27.1 (2.6)***	28.3 (1.8)	27.4 (2.5)***	28.4 (1.6)	27.9 (2.3)***	28.2 (1.9)	27.8 (2.3)**
CRP[a], mg/l	0.17 (1.03)	0.21 (1.10)*	0.17 (1,03)	0.22 (1.07)***	0.16 (1.04)	0.19 (1.04)**	0.17 (1.03)	0.20 (1.08)*
HOMA-IR	2.3 (0.1)	3.1 (0.3)***	2.3 (2.1)	2.9 (2.7)***	2.4 (2.3)	2.4 (1.6)	2.3 (2.1)	2.6 (2.3)*

For continuous variables, the mean (SD) is reported.
MET; Metabolic equivalent.
*P < 0.05; **P < 0.01; ***P < 0.001.
[a]Geometric mean (standard error of the geometric mean).

participants at baseline, according to categories of functional impairment. With regards to leptin, the mean ± SD of serum concentration was 21.2±17.5 ng/ml, and it was significantly higher among subjects with any incident functional impairment.

Compared to individuals in the lowest quartile of leptin concentration, those in the highest quartile showed increased risk of impaired physical function; in Model 3, the ORs (95% CI) and P-trend were: 1.95 (1.11–3.43), P = 0.006 for self-reported impaired mobility, 1.76 (1.08–2.87), P = 0.02 for self-reported impaired agility, 1.48 (1.02–2.15), P = 0.04 for lower extremity function and 1.97 (1.20–3.22), P = 0.01 for decreased overall physical performance (Table 2). The additional adjustment for CRP and HOMA-IR only modestly reduced the association found. Moreover, analyses using the increment of one SD of leptin instead of the quartiles of the concentration gave similar statistically significant results (Table 2). Additional adjustment for the length of the follow-up did not materially change the results (data not shown).

Table 3 shows the association between leptin concentration and impairment in physical function among subgroups of participants with better health status. Per each increment of one SD of leptin concentration, we observed a higher incidence of limitations in all the domains, especially in self-reported impaired mobility, with a range of 55–62% of risk increment, followed by a 22–41% for impaired overall physical performance, 21–38% for self-reported impaired agility and 10–18% for impaired lower extremity function. In stratified analyses, the association between leptin concentration and the impairment of physical function was statistically significant only among individuals with less physical activity, more hours watching TV and higher percentage body fat (please see Appendix 2 on http://www.ageing.oxfordjournals.org/). Nevertheless, the study association did not significantly vary across the strata (P for interaction > 0.08 in all cases).

Discussion

In this prospective study of community-dwelling older adults, higher serum leptin concentration was associated with greater risk of impairment in mobility, agility, lower extremity function and overall physical performance. These associations were observed in groups with varying health behaviours and status and were independent of the estimated body fat, which suggests that the impact of leptin on physical function is not totally explained by adiposity.

Several studies have found that body composition plays a role in the age-associated decline of physical function and the occurrence of frailty in older adults [5–10, 14]. This

Table 2. ORs (95% CI) for the association between sex-specific quartiles of serum concentration of leptin[a] and physical function impairment during a 3.5-year follow-up (N = 1,556)

	Leptin concentration					Per one SD increase of leptin
	Quartile 1 (n = 394)	Quartile 2 (n = 388)	Quartile 3 (n = 391)	Quartile 4 (n = 383)	P-trend	
Self-reported impaired mobility						
Cases	39	37	45	74		
Model 1[b]	1.00	0.98 (0.61–1.60)	1.20 (0.76–1.91)	2.18 (1.42–3.34)	<0.001	1.48 (1.30–1.70)
Model 2[c]	1.00	0.84 (0.50–1.42)	1.07 (0.65–1.76)	1.82 (1.13–2.93)	0.004	1.42 (1.22–1.66)
Model 3[d]	1.00	0.88 (0.51–1.51)	1.12 (0.65–1.92)	1.95 (1.11–3.43)	0.006	1.55 (1.30–1.85)
Model 4[e]	1.00	0.82 (0.47–1.43)	1.01 (0.57–1.80)	1.69 (0.92–3.13)	0.03	1.53 (1.27–1.85)
Self-reported impaired agility						
Cases	53	69	79	116		
Model 1[b]	1.00	1.45 (0.97–2.16)	1.68 (1.14–2.49)	2.87 (1.97–4.18)	<0.001	1.44 (1.28–1.62)
Model 2[c]	1.00	1.32 (0.85–2.04)	1.57 (1.02–2.40)	2.36 (1.55–3.59)	<0.001	1.32 (1.16–1.61)
Model 3[d]	1.00	1.14 (0.73–1.80)	1.28 (0.80–2.02)	1.76 (1.08–2.87)	0.02	1.21 (1.04–1.42)
Model 4[e]	1.00	1.14 (0.71–1.81)	1.24 (0.76–2.03)	1.62 (0.95–2.76)	0.06	1.17 (1.00–1.39)
SPPB score ≤ 9 points						
Cases	201	202	204	246		
Model 1[b]	1.00	1.08 (0.80–1.46)	1.03 (0.77–1.38)	1.67 (1.24–2.26)	0.001	1.22 (1.09–1.27)
Model 2[c]	1.00	1.02 (0.75–1.38)	0.95 (0.69–1.27)	1.36 (0.99–1.27)	0.05	1.13 (1.01–1.27)
Model 3[d]	1.00	1.05 (0.77–1.44)	1.00 (0.71–1.38)	1.48 (1.02–2.15)	0.04	1.18 (1.03–1.35)
Model 4[e]	1.00	1.04 (0.75–1.43)	1.00 (0.70–1.43)	1.48 (0.98–2.23)	0.11	1.18 (1.02–1.38)
10-point decrease in PCS[e]						
Cases	46	66	68	80		
Model 1[b]	1.00	1.63 (1.08–2.46)	1.71 (1.13–2.57)	2.18 (1.46–3.26)	0.001	1.29 (1.14–1.46)
Model 2[c]	1.00	1.51 (0.98–2.32)	1.62 (1.06–2.48)	1.92 (1.25–2.94)	0.004	1.23 (1.08–1.41)
Model 3[d]	1.00	1.53 (0.98–2.37)	1.64 (1.04–2.57)	1.97 (1.20–3.22)	0.01	1.25 (1.07–1.46)
Model 4[e]	1.00	1.68 (1.06–2.64)	1.82 (1.12–2.94)	2.12 (1.24–3.62)	0.02	1.25 (1.06–1.48)

[a]Sex-specific quartile cut-off points for leptin levels were 5.5, 9.8 and 16.6 ng/ml in men and 18.0, 29.1 and 39.5 ng/ml in women.
[b]Model 1: logistic regression model adjusted for sex and age (years).
[c]Model 2: Model 1 additionally adjusted for educational level (≤primary, secondary, university), smoking behaviour (never, former, current), alcohol consumption (none, moderate, heavy drinker), leisure-time physical activity (quartiles of MET-h/wk), TV watching (tertiles of h/d), Mediterranean diet score (tertiles), energy intake (quartiles of Kcal/d), diabetes, hypertension, cardiovascular disease, cancer, chronic lung disease, osteomuscular disease, depression, incident chronic disease during follow-up and MMSE score (quartiles).
[d]Model 3: Model 2 additionally adjusted for percentage body fat (quartiles).
[e]Model 4: Model 3 additionally adjusted for CRP (quartiles) and HOMA-IR (quartiles).
[e]Additionally adjusted for basal PCS.

Table 3. ORs (95% CI)[a] of physical function impairment during a 3.5-year follow-up per one SD increase of serum concentration of leptin among subgroups of participants with better health status

	Self-reported impaired mobility	Self-reported impaired agility	SPPB score ≤ 9 points	10-point decrease in PCS[b]
No basal diabetes (n = 1,338)				
Cases	158	260	222	702
OR (95 % CI)	1.55 (1.27–1.89)	1.27 (1.07–1.51)	1.24 (1.04–1.47)	1.18 (1.02–1.37)
No basal osteomuscular disease (n = 879)				
Cases	55	92	122	436
OR (95 % CI)	1.62 (1.20–2.21)	1.38 (1.06–1.78)	1.41 (1.11–1.78)	1.10 (0.92–1.32)
No basal IADL disability (n = 1,443)				
Cases	166	273	237	774
Model 2	1.56 (1.29–1.89)	1.23 (1.05–1.45)	1.22 (1.04–1.44)	1.16 (1.01–1.34)
No incident cognitive impairment (n = 1,524)				
Cases	183	299	249	825
OR (95 % CI)	1.55 (1.29–1.85)	1.21 (1.03–1.42)	1.23 (1.04–1.43)	1.18 (1.03–1.36)
No incident morbidity (n = 1,159)				
Cases	124	212	169	610
OR (95 % CI)	1.60 (1.26–2.03)	1.21 (1.00–1.47)	1.24 (1.01–1.52)	1.17 (1.01–1.38)

[a]Analyses adjusted as Model 2 in Table 2.
[b]Additionally adjusted for basal PCS.

could be due to several closely related mechanisms. First, a sedentary lifestyle may contribute to muscle weakness and atrophy, with muscle being progressively infiltrated by fat tissue. In turn, impaired physical function may lead to greater sedentariness. Moreover, excess adiposity induces inflammation and metabolic dysfunction, which also contribute to reduce muscle quality. These factors could partially explain the clustering of various body phenotypes, such as obesity and sarcopenia, which leads to sarcopenic obesity [12]. However, there is evidence that weight loss in older adults predicts disability [33], especially among those who were obese at entering old age [34].

Leptin contributes to energy balance mostly by reducing food intake and increasing energy expenditure, and it also has a role in vascular function and in the regulation of serum glucose and insulin [35, 36]. However, in obese and older people, high leptin levels may reflect a state of resistance in which vascular function and insulin sensitivity are altered. Moreover, given that leptin concentration reflects the metabolic activity of body fat, the mechanisms for the association between leptin and functional limitations could also entail an increased energy demand due to excess body fat and the subsequent metabolic dysfunction. In addition, leptin is a pro-inflammatory adipokine. Thus, given that higher leptin is associated with higher risk of cardiovascular disease and diabetes [37, 38], which are both linked to impaired physical function, we adjusted the analyses for cardiovascular disease and diabetes. The fact that the results held after adjustment and that they were also observed among individuals free of these diseases suggests that other mechanisms may account for the leptin-functional impairment association. Moreover, our results also held after adjustment for CRP and HOMA-IR, which were used as a non-specific proxy of the inflammation process and insulin resistance, respectively. Both conditions have often been related to functional impairment, but our findings suggest that leptin could be a prior step of the causal pathway.

Our results concur with those of Karvonen-Gutierrez *et al.* [19] showing that leptin concentration predicts poorer physical functioning. These are the first investigations to report an association between leptin and physical function, thought their study was conducted among middle-aged women and ours among older men and women. Specifically, in the study of Karvonen-Gutierrez *et al.* [19], leptin was prospectively associated with longer stair climb, sit-to-rise and 2-pound lift times, and shorter reach distance. Contrary to our findings, Karvonen-Gutierrez *et al.* did not observe an association between leptin and worse results in the walking test or leg strength; although leptin has deleterious effects on muscle [39], a lack of an association in their study might be due to including younger individuals. Our results are of particular importance for the older population because they showed an association of leptin with lower extremity performance, which is a good predictor of disability, hospitalisation and mortality [22].

Our study has several strengths, including the relatively large sample size and the fact that most variables, including leptin and the components of physical functioning, were ascertained using standardized and validated methods. Also, the analyses were adjusted for a good number of well-measured confounders, and the results were robust in several sensitivity analyses. The main limitation was the lack of measurement of the soluble receptor of leptin, which has shown a stronger relation than leptin with some health outcomes. Also, we did not measure other adipokines of potential interest, such as adiponectin [19]; however, we attempted to partially account for this limitation by adjusting the analyses for our estimation of subjects' body fat, as a proxy for adipokines secretion, although the use of an objective measure of percentage body fat would have been desirable. We also lacked data about lean mass, which would have allowed us to characterise those individuals with sarcopenic obesity. Another limitation was the use of self-reported information as a proxy for mobility, agility and overall physical performance; however, we combined it with an objective assessment of lower extremity function, to achieve a more complete measurement of impaired physical function. Moreover, functional impairment was evaluated at the end of the follow-up so that temporality and development of impairments during the interval period could not be fully ascertained. Finally, as in most observational studies, certain residual confounding cannot be ruled out despite adjustment for many variables.

Conclusion

In conclusion, in community-dwelling older men and women, we found a significant association between higher leptin concentration and an increased risk of impaired physical function, which was independent of the estimated body fat. The mechanisms of this association should be elucidated, but preserving metabolic function during the old age could help to delay physical function decline and subsequent disability.

Key points

- Leptin is mainly secreted by the white adipocyte tissue and contributes to the regulation of energy balance by promoting satiati.
- Higher leptin concentration increases the risk of impaired physical function in community-dwelling older men and women.
- The association between higher leptin concentration and impaired physical function is independent of body fat.
- Preserving metabolic function during the old age could help to delay disability.

Supplementary data

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Conflicts of interest

The authors have nothing to disclose.

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Blood pressure and all-cause mortality: a prospective study of nursing home residents

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Abstract

Aim: to explore the natural course of blood pressure development and its relation to mortality in a nursing home cohort.
Methods: a cohort of 406 nursing home residents in south east Sweden was followed prospectively for 30 months. Participants were divided into four groups based on systolic blood pressure (SBP) at baseline. Data were analysed using a Cox regression model with all-cause mortality as the outcome measurement; paired Student *t*-tests were used to evaluate blood pressure development over time.
Results: during follow-up, 174 (43%) people died. Participants with SBP < 120 mmHg had a hazard ratio for mortality of 1.56 (95% confidence interval, 1.08–2.27) compared with those with SBP 120–139 mmHg, adjusted for age and sex. Risk of malnutrition or present malnutrition was most common in participants with SBP < 120 mmHg; risk of malnutrition or present malnutrition estimated using the Mini Nutritional Assessment was found in 78 (71%). The levels of SBP decreased over time independent of changes in anti-hypertensive medication.
Conclusions: in this cohort of nursing home residents, low SBP was associated with increased all-cause mortality. SBP decreased over time; this was not associated with altered anti-hypertensive treatment. The clinical implication from this study is that there is a need for systematic drug reviews in elderly persons in nursing homes, paying special attention to those with low SBP.

Keywords: *older people, prospective study, nursing home, hypertension, hypotension, all-cause mortality*