Time-restricted feeding and lower-extremity functioning in community-dwelling older adults

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Research

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Abstract

Background: Time-restricted feeding, a specific form of intermittent fasting, has been associated with several possible health benefits including improved body composition, blood lipid levels and extended lifespan. However, it is unknown if time-restricted feeding confers a protective effect on the physical function of older adults. The aim of this study was to assess time-restricted feeding in association with performance-based lower-extremity function (LEF) in a large population of community-dwelling older adults.

Methods: Cross-sectional study among 1,226 individuals ≥64 years from the Seniors-ENRICA-II cohort. In 2016-2017, habitual diet was assessed through a validated diet history. Fasting time was classified into the following categories: ≤9, 10-11, and ≥12hours/day, the latter being considered time-restricted feeding. Performance-based LEF was assessed with the Short Physical Performance Battery (SPPB).

Results: After adjusting for potential confounders, a longer fasting period was associated with a higher likelihood of impaired LEF [odds ratio (OR) and 95% confidence intervals (CI) for the second and third categories: 2.27 (1.56-3.33); and 2.70 (1.80-4.04), respectively, considering the ≤9 hours/day fasting group as the reference category; p-trend <0.001]. When assessing each SPPB subtest separately, fasting time showed a significant association with balance impairment (OR for highest vs. lowest fasting time: 2.48; 95% CI: 1.51-4.08; p-trend= 0.001) and difficulty to rise from a chair (OR for highest vs. lowest fasting time: 1.47; 95% CI: 1.05-2.06; p-trend= 0.01).

Conclusions: Time-restricted feeding was associated with a higher likelihood of impaired LEF, balance impairment, and difficulty to rise from a chair in older adults. These results need to be confirmed in further longitudinal studies.

Trial registration: ClinicalTrials.gov NCT03541135. Registered 30 May 2018, retrospectively registered.

Introduction

Several types of intermittent fasting have emerged as an alternative to caloric restriction and to a prolonged period of fasting because this diet strategy is relatively easy to maintain [1] and there is some evidence from studies in animals and humans that it might improve overall health [2] and body composition [3], protects against cardiometabolic risk factors [4, 5], and extends life span [6]. A specific type of intermittent fasting is time-restricted feeding (TRF), in which the daily eating period is limited to 12 hours or less per day. Studies in humans have shown that TRF is associated with weight loss [7], fat mass decrease [8], metabolic disease risk reduction [4], and improvement in glycemic response [9].

Several physiological mechanisms might explain how intermittent fasting can affect metabolic pathways [10]. Generally, after 12 hours of food deprivation, the hepatocytes glycogen stores are depleted and the liver shifts from glucose storage to gluconeogenesis and produces ketone bodies from fatty acids, such as β-hydroxybutyrate and acetoacetate, to satisfy the energy requirements of brain cells and to preserve muscle mass and muscle function [2, 11, 12]. Thus, individuals engaging in intermittent fasting might maintain or even enhance their physical function [13-15]. Although the relatively short duration of fasting in TRF may not lead to ketosis, it can trigger other processes such as autophagy, where damaged macromolecules and organelles can be cleared to preserve normal cell function [16]. Moreover, intermittent fasting may have an impact on the circadian rhythm that regulates metabolism, energetics, and sleep-wake cycles [17, 18].

Yet, evidence about the effects of intermittent fasting in free-living populations is scarce. Specifically, the impact of TRF on physical function in older adults is unknown. In this population, TRF may pose individuals at higher risk of malnutrition, because although the need of energy intake is substantially reduced with age, macronutrient needs are similar or even greater than in younger adults, in order to prevent sarcopenia and frailty [19]. We hypothesized that TRF could be related to functional impairment in older adults. Therefore, the aim of this study was to assess TRF in association with performance-based lower-extremity function (LEF) in a large population of community-dwelling older adults.

Methods

Study design and participants

We performed a cross-sectional analysis of data obtained from the Seniors-ENRICA-II (Study on Nutrition and Cardiovascular Risk in Spain) cohort, among 3,273 community-dwelling individuals aged 64 years or older residing in the city of Madrid and four surrounding towns: Alcalá de Henares, Alcorcón, Getafe, and Torrejón de Ardoz. This cohort followed the same design as the Seniors-ENRICA I [20]. The study participants were selected by random sampling sex- and district-stratified among all individuals with a national healthcare card between 2015 and 2017. Given that all people residing in Spain is entitled to free healthcare, the list of card holders closely approximates the entire resident population of Madrid. Information was collected by trained staff in three stages: 1) a computer-assisted telephone interview on socio-demographic data, lifestyle, health status, and morbidity; b) a first home visit to perform a physical examination and obtain biological samples (blood and urine); and c) a second home visit, conducted 7 days after the first one, to take a diet history and obtain other questionnaire data. At the end of the first home visit, an accelerometer was located on the wrist of participants and was returned during the second visit, seven days apart [21]. Study participants and their relatives gave written informed consent. The study was approved by the Clinical Research Ethics Committee of `La Paz´ University Hospital in Madrid (Spain).

Study variables

Diet

Trained interviewers obtained information on food consumption through a validated computerized dietary history, which was developed from the one used in the EPIC-Spain cohort study [22]. The diet history included 880 foods along with 127 sets of photographs to help estimate the serving size. This instrument collects food consumption by occasions of intake, and accommodates habitual diet information to a 24-hour format, by asking participants to indicate the time in which they usually had their meals, including snacks. Fasting time was defined as the window (in hours) between the last food ingested before going to sleep and the first food consumed upon getting up in the morning. Participants were classified in three categories: those reporting a fasting time of ≤9 hours/day, those with fasting time between 10-11 hours/day, and those with fasting time ≥12hours/day, which can be considered TRF [12].

Nutrient intakes were estimated using standard food composition tables for the Spanish population [23]. The Mediterranean Diet Adherence Screener (MEDAS) score was also estimated for all participants in order to define the overall diet quality [24]. This score ranged from 0 to 14, and higher scores indicated greater adherence and thus higher diet quality. The validity of the diet history was evaluated by comparing results from this instrument with seven 24-h recalls over a one-year period among a subsample of participants; the observed correlations ranged between 0.27 and 0.71 across food groups and nutrients, which are in line with those for most instruments assessing self-reported diet in population studies [25].

Physical function

We assessed LEF with the Short Physical Performance Battery (SPPB), which includes three timed tasks: gait speed, standing balance, and ability to rise from a chair [26, 27]. Gait speed was calculated as the time that a participant walked at usual pace across 2.44 m, timed from a standing position. The standing balance test evaluated the time that participants could maintain three hierarchical tandem positions: side-by-side, semitandem, and tandem positions. The ability to rise from a chair was assessed by the time required to stand up and sit down from a chair five times consecutively as fast as possible and with their arms folded across their chest. Each test was scored from 0 to 4, and the total SPPB score was the sum of these three components (range 0-12); a higher score, indicates better physical performance. We used the standard cut-off of ≤9 to define impaired LEF (ILEF). In addition, balance impairment, difficulty to raise from a chair and slow gait were defined as a score of ≤3 in each scale [26].

Other variables

We obtained information on age, sex, education (primary, secondary, or university level), smoking status (never-, former- or current-smoker), sedentary behavior (hours/week spent watching TV), alcohol intake (g/day), sleep duration (hours/d), and energy intake (kcal/day). Physical activity (metabolic equivalent-hours per week) was assessed with the ActiGraph GT9X (ActiGraphInc, Pensacola, FL, USA) accelerometer, which was asked to be worn for seven consecutive days [21]. Weight and height were measured under standardized conditions, using electronic scales, and portable extendable stadiometers. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) and classified as <25, 25–29.9, or ≥30 kg/m^2. In addition, the following physician-diagnosed diseases were self-reported: osteomuscular disease, cardiovascular disease, diabetes, cancer, chronic lung disease, and depression requiring treatment. Cognitive function was assessed with the Mini-Mental State Examination (MMSE) [28].

Statistical analyses

We selected the 1,732 participants with information on timing of food consumption. Then, we excluded one participant with implausibly high or low energy intake (outside the range of 800-5000 kcal/day for men and 500-4000 kcal/day for women) and another without information on educational level. Additionally, we excluded 454 individuals without measurement of SPPB, and 50 without accelerometry. Thus, the analyses were conducted with 1,226 individuals.

Participants' characteristics were summarized as means ± SD for continuous variables and as percentages for categorical variables. Differences in characteristics across participants in the different fasting categories were tested by ANOVA for quantitative variables and by the chi-square test for categorical variables. Logistic regression was used to estimate the odds ratios (OR) and the 95% confidence interval (CI) for the association between different fasting categories and ILEF.

Several logistic models were built with sequential adjustment for potential confounders: the first one included sex, age, and energy intake; the second one was additionally adjusted for educational level, smoking status, sedentary behavior, alcohol intake (g/d), BMI, morbidity, sleep duration, protein intake, and MEDAS score; and the third model was also adjusted for physical activity since this variable could also be considered a potential mediator in the studied association. Additionally, we assessed the linear dose-response relationship (p for trend) by modeling fasting time as a continuous variable. The association between TRF and each SPPB component was also evaluated.

We replicated the analyses for the associations by strata of sex, BMI (<30, ≥ 30 kg/m^2), energy intake (above and below the median), total protein intake (above and below the median), diet quality (above and below the median), sleep time (above and below the median), and depression (no, yes) to assess the robustness of the results. The possible modifying effect of these variables on the studied association was assessed with the likelihood-ratio test. Finally, we examined the joint effect of fasting categories and physical activity on ILEF, by considering physical activity in tertiles and using as reference category the simultaneous condition of a fasting time of ≤ 9 hours/day and being in the highest tertile of physical activity. Lastly, in a sensitivity analysis, we examined the impact of cognitive function in the studied association by excluding participant with a score <23 in the MMSE. Statistical significance was set at two-tailed $p < 0.05$. Analyses were conducted using Stata (version 15.1; Stata Corp., College Station).

Results

Characteristics of study participants according to the three fasting time categories are presented in **Table 1**. Those with TRF (≥ 12 hours of fasting) were significantly older, more often women, never smokers, more likely to have a diagnosis of depression, and reported more hours of sleep, compared to those in the shortest fasting time category. In addition, total energy, and fat intake were lower in those with TRF.

Table 1. Baseline characteristics of the study participants by categories of fasting time (N= 1,226).

	≤9h fasting	10h –11h fasting	≥12 h fasting	p value[a]
n	578	388	260	
Age, y	70.8 ± 3.9	70.6 ± 3.7	71.7 ± 4.2	0.002
Sex, men %	54	53	42	0.005
Educational level, %				
≤ Primary	58	44	52	0.001
Secondary	17	22	20	
University	25	34	28	
Smoking status, %				
Current smoker	11	9	5	0.02
Former smoker	42	45	38	
Never smoker	47	46	57	
TV watching, h/wk	22.1 ± 10.3	20.9 ± 9.9	21.1 ± 10.0	0.16
Physical activity, MET-h/week	67.4 ± 34.4	66.7 ± 36.7	63.7 ± 35.8	0.37
BMI, kg/m^2, %				
<25	30.3	29.4	29.6	0.17
25-29.9	42.6	49.0	47.7	
≥30	27.1	21.6	22.7	
Diagnosed morbidity, %				
Osteomuscular disease[b]	45	40	43	0.33
Cardiovascular disease[c]	3	5	5	0.23
Diabetes	25	25	23	0.84
Cancer	3	2	4	0.18
Chronic lung disease	7	8	8	0.87
Depression	6	6	13	0.001

Sleep duration, h/d	6.8 ± 1.3	6.8 ± 1.2	7.1 ± 1.4	0.03
Energy, kcal/d	1930 ± 386	1842 ± 276	1828 ± 301	<0.001
Protein, g/d	93.7 ± 18.3	90.3 ± 16.2	88.7 ± 15.3	<0.001
Protein, g/kg/d	1.3 ± 0.3	1.2 ± 0.2	1.3 ± 0.3	0.05
Fat, g/d	73.3 ± 23.6	69.6 ± 18.9	68.7 ± 21.2	0.005
Carbohydrate, g/d	205.6 ± 42.2	194.4 ± 36.0	197.7 ± 33.2	<0.001
Alcohol intake, g/d	10.0 ± 14.2	10.5 ± 13.2	8.5 ± 11.6	0.18
MEDAS score	6.6 ± 1.6	6.5 ± 1.6	6.5 ± 1.7	0.63

Abbreviations: BMI, Body Mass Index; MEDAS, Mediterranean Diet Adherence Screener.

For continuous variables, mean and standard deviation are reported.

[a] ANOVA test was used for quantitative variables and the chi-square test for categorical variables.

[b] Osteo-arthritis, arthritis, and hip fracture.

[c] Ischemic heart disease, stroke, and heart failure.

In **Table 2,** a significant association between a longer fasting time and ILEF was found; in age-, sex- and energy intake-adjusted models, the ORs (95% CI) for 10-11 h and ≥12 hours/day of fasting were 2.06 (1.44-2.94), and 2.56 (1.76-3.73) respectively, using ≤9 hours as the reference category; p-trend <0.001. After additional adjustment for other potential confounders including physical activity, we obtained similar results [OR (95% CI): 2.27 (1.56-3.33); 2.70 (1.80-4.04), respectively; p-trend <0.001]. Fasting time also showed a significant association with balance impairment (OR for longest vs. shortest fasting time: 2.48; 95% CI: 1.51-4.08; p-trend= 0.001) and difficulty to rise from a chair (OR 1.47; 95% CI: 1.05-2.06; p-trend= 0.01). Slow gait speed was not associated with fasting.

Table 2. Odds ratios (95% confidence interval) for the association between fasting time categories and impaired lower-extremity function (ILEF), balance impairment, difficulty to rise from a chair, and slow gait (N=1,226).

	≤9h fasting	10-11h fasting	≥12 h fasting	p trend
n	578	388	260	
ILEF, n cases	74	84	76	
Model 1	1.00	2.06 (1.44-2.94)	2.56 (1.76-3.73)	<0.001
Model 2	1.00	2.25 (1.55-3.27)	2.77 (1.86-4.12)	<0.001
Model 3	1.00	2.27 (1.56-3.33)	2.70 (1.80-4.04)	<0.001
Balance impairment, n cases	41	30	43	
Model 1	1.00	1.21 (0.73-1.99)	2.39 (1.49-3.84)	<0.001
Model 2	1.00	1.20 (0.71-2.02)	2.60 (1.58-4.26)	<0.001
Model 3	1.00	1.18 (0.69-1.99)	2.48 (1.51-4.08)	0.001
Difficulty to raise from a chair, n cases	365	261	183	
Model 1	1.00	1.24 (0.94-1.63)	1.38 (1.00-1.90)	0.03
Model 2	1.00	1.34 (1.01-1.79)	1.47 (1.06-2.06)	0.01
Model 3	1.00	1.37 (1.03-1.82)	1.47 (1.05-2.06)	0.01
Slow gait, n cases	148	95	87	
Model 1	1.00	0.93 (0.69-1.26)	1.26 (0.91-1.74)	0.26
Model 2	1.00	0.91 (0.66-1.24)	1.28 (0.91-1.79)	0.25
Model 3	1.00	0.91 (0.67-1.24)	1.27 (0.90-1.78)	0.27

Model 1: OR (95% CI) adjusted for sex, age and energy intake (quintiles of kcal/day).

Model 2: OR (95% CI) additionally adjusted for educational level (≤primary, secondary, or university), smoking status (never, former, current smoker), sedentary behavior (tertiles of h/week watching TV), alcohol intake (quintiles of g/day), BMI (<25, 25-29.9, ≥30 kg/m^2), morbidity (osteomuscular disease, cardiovascular disease, cancer, diabetes, chronic lung disease, and depression), sleep duration (tertiles of hours/d), protein intake (quintiles of g/d), and for MEDAS score (tertiles).

Model 3: OR (95% CI) additionally adjusted for physical activity (tertiles of METs-h/week).

The association between different fasting categories and ILEF was assessed by strata of sex, BMI, energy intake, total protein intake, diet quality, sleep and depression, and is shown in **Table 3**. No significant differences were identified across the strata (p for interaction >0.05 in all cases). In addition, when fasting time and physical activity were considered simultaneously, ≥12 h fasting had double risk of ILEF than those with <9 h of fasting (OR: 1.50, 95% CI: 0.62-3.60 vs. OR: 1) among those with high levels of physical activity; in addition, the risk associated with ≥12 h fasting among those with the lowest levels of physical activity was three times higher than among those with ≤9 hours fasting with the same low level of physical activity (OR: 4.60, 95% CI: 1.42-14.84 vs. OR:1.55, 95% CI: 0.49-4.88) (p for interaction: <0.001) (Figure 1). Lastly, sensitivity analyses by excluding participants with impaired cognitive function yielded similar association than in the main tables (Additional table 1).

Table 3. Odds ratios (95% confidence interval)* for the association between fasting time categories and impaired lower-extremity function, by specific subgroups of older adults (N=1,226).

	≤9h fasting	10-11h fasting	≥12 h fasting	p trend	p for interaction
n	578	388	260		
Sex					
Men (n=627)	1.00	1.41 (0.77-2.59)	2.63 (1.34-5.17)	0.006	0.24
Women (n=599)	1.00	3.06 (1.75-5.34)	3.33 (1.86-5.97)	<0.001	
BMI					
< 30 kg/m^2 (n=926)	1.00	2.14 (1.32-3.46)	2.48 (1.47-4.18)	<0.001	0.70
≥ 30 kg/m^2 (n=300)	1.00	1.97 (0.95-4.08)	2.82 (1.30-6.10)	0.006	
Sleep duration					
< median (n=613)	1.00	1.87 (0.96-3.63)	3.13 (1.51-6.47)	0.002	0.89
≥ median (n=613)	1.00	2.36 (1.43-3.91)	2.67 (1.58-4.51)	<0.001	
Depression					
No (n=1,130)	1.00	2.24 (1.50-3.34)	2.92 (1.88-4.53)	<0.001	0.94
Yes (n=96)	1.00	2.35 (0.28-20.0)	4.28 (0.54-34.1)	0.17	
Energy intake					
< median (n=613)	1.00	3.29 (1.85-5.85)	3.28 (1.79-6.00)	<0.001	0.10
≥ median (n=613)	1.00	1.31 (0.74-2.32)	2.46 (1.32-4.59)	0.006	
Protein intake					
< median (n=613)	1.00	2.65 (1.51-4.64)	2.50 (1.38-4.50)	0.002	0.34
≥ median (n=613)	1.00	1.65 (0.91-2.99)	2.96 (1.57-5.57)	0.001	
MEDAS score					
< median (n=590)	1.00	2.84 (1.62-5.00)	3.58 (1.93-6.64)	<0.001	0.28
≥ median (n=636)	1.00	1.67 (0.94-2.96)	2.08 (1.14-3.80)	0.014	

Median sleep duration: 7 hours; median energy intake: 1833 kcal; median protein intake: 90.3g; median MEDAS score: 7.

*From logistic regression models adjusted for sex, age, educational level (≤primary, secondary, or university), smoking status (never, former, current smoker), sedentary behavior (hours/week watching TV), alcohol intake (quintiles of g/day), BMI (<25, 25-29.9, ≥30 kg/m²), morbidity (osteomuscular disease, cardiovascular disease, cancer, diabetes, chronic lung disease, and depression), sleep duration (tertiles of hours/d), energy intake (quintiles of kcal/day), protein intake (quintiles of g/d), and MEDAS score (tertiles), except for the stratification variable.

Discussion

In this cross-sectional study of community dwelling older adults, a fasting time of more than 12 hours per day was associated with a higher risk of ILEF, balance impairment, and difficulty to rise from a chair. These associations were robust across different strata, including sex, BMI, energy intake, total protein intake and diet quality. In addition, these results held on different levels of physical activity, which suggests that despite the beneficial effect of physical activity on function, fasting time has an independent association with this endpoint in older adults. Notwithstanding this, high physical activity could compensate for part of the excess frequency of ILEF associated with longer fasting.

Most of the evidence on the effects of intermittent fasting has been obtained in animal studies [4-6]. Human studies have been restricted to younger adults in experimental designs with extreme intermittent fasting, and a small number of participants [7-9]. To our knowledge this is the first study assessing intermittent fasting in association with ILEF. Our findings of an increased risk of balance impairment in participants on TRF are in line with previous publications in older adults who practiced Ramadan fasting [29, 30]. A study among 15 older men showed that fasting approximately 17 hours per day for four weeks had a detrimental effect on postural balance performance and in simple reaction time [29]. Another study compared the effects of Ramadan fasting on postural control between a group of 12 participants with a history of at least two spontaneous and unexpected falls during the previous year and a group of 12 non-fallers. Ramadan fasting had similar adverse effects on in postural control both groups, that could lead to balance dysfunction and mobility limitation in older adults [30]. Despite Ramadan fasting is a common variety of TRF, it is of note that fasting time is approximately 12 hours per day from dawn to sunset [17], which contrast with TRF in our study participants and with usual TRF diets. In our population, fasting time was not associated with the risk of slow gait. In a small clinical trial among ten overweight older adults who were asked to fast for 16 h per day during four weeks, slow gait, grip strength, quality of life were improved, although this may be driven by the weight loss that all participants experienced, which was the main target of the intervention [13].

It is well-known that the best approach to counteract physical function impairment is regular practice of physical activity [31-33]. In our study, although participants with a higher level of physical activity had a lower risk of ILEF than their less active counterparts, the augmented risk of ILEF associated with longer fasting was present at all physical activity levels. Adequate dietary protein intake is also strongly related to physical function. Protein has been associated with maintenance of physical function, muscle mass and bone mass density [34-38], and has shown to prevent frailty in older adults [39]. A previous study found that a higher intake of dietary animal-protein in combination with physical activity was associated with higher skeletal muscle mass and a lower likelihood of functional limitation development [40]. In our study, participants on TRF had lower intake of dietary protein and energy in comparison with participants with fasting time <9 hours/day; however, all participants in the 3 fasting groups had a protein intake above the current recommended dietary allowance (RDA), of 0.8 g protein/kg/d [41, 42]. Despite participants on TRF are meeting their adequate intake of proteins and are physically active, it is possible that it is not enough to halt the detrimental effects of TRF in older adults.

In our study, participants on TRF presented more depression than those who did not fast ≥12 hours. A recent study in community-dwelling older adults found a higher prevalence of depression in participants with poor appetite, in comparison to those with normal appetite. Also, they found an association between poor appetite and lower skeletal muscle mass, lower grip strength, and low muscle mass [43]. The involuntary loss of appetite that leads to reduced food intake is a common problem in older adults, usually known as anorexia of aging [44]. However, in our sensitivity analyses among participants with depression, we still found a detrimental association between TRF and physical function, therefore, this association in not totally mediated by the effect of depression on eating patterns.

A variety of intermittent fasting regimens such as TRF, periodic fasting, complete alternate-day fasting, modified fasting regimens, and religious fasting (e.g., Ramadan fasting) have been associated to health benefits, including improvements in glucose regulation, blood pressure, and heart rate [2, 11, 12, 16-18]. There are also evidence of a beneficial effect of these regimes on stress resistance pathways, including increased expression of antioxidant defenses, DNA repair, protein quality control, mitochondrial biogenesis and autophagy and down-regulation of inflammation [10]. However, intermittent fasting has been mostly studied as a practical approach to restrict energy intake for weight loss [13]. Thus, the extrapolation of the health benefits of common intermittent fasting to the general population is difficult. Specifically, among older adults, intermittent fasting may lead to malnutrition, cachexia, sarcopenia and frailty [45].

One of the strengths of this study was the assessment of fasting time through a validated diet history that collected habitual diet information in a 24-hour format. Another strength was the adjustment for many potential confounders, including sleep duration, energy intake, protein intake, comorbidities, and physical activity. Additionally, the use of an accelerometer is a more reliable way to assess physical activity than self-reported questionnaires, since it provides objective measures on 24-hour activity cycle. On the other hand, the main limitation of this study was the cross-sectional design, which does not allow for causal inference.

In conclusion, fasting time ≥12 h/d was associated with a higher frequency of ILEF, balance impairment, and difficulty to rise from a chair in older adults. These results suggest a detrimental effect of TRF in older adults. Further longitudinal studies of TRF in relation to ILEF would be valuable to understand if this is a causal association. Since TRF might increase the risk of malnutrition in the old population, this intermittent fasting regime does not seem to be considered an option to improve LEF in this subgroup of population.

Declarations

Ethics approval and consent to participate

The study was approved by the Clinical Research Ethics Committee of `La Paz´ University Hospital in Madrid (Spain). Study participants and their relatives gave written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from Universidad Autónoma de Madrid but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Universidad Autónoma de Madrid.

Competing interests

The authors declare that they have no competing interests.

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Authors´contributions

DBE, EAS and ELG designed the research; DBE and FFC performed the statistical analyses; DBE, EAS and ELG drafted the manuscript; ELG supervised the conduct of research and had primary responsibility for final content; all authors read and approved the final manuscript.

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Figures

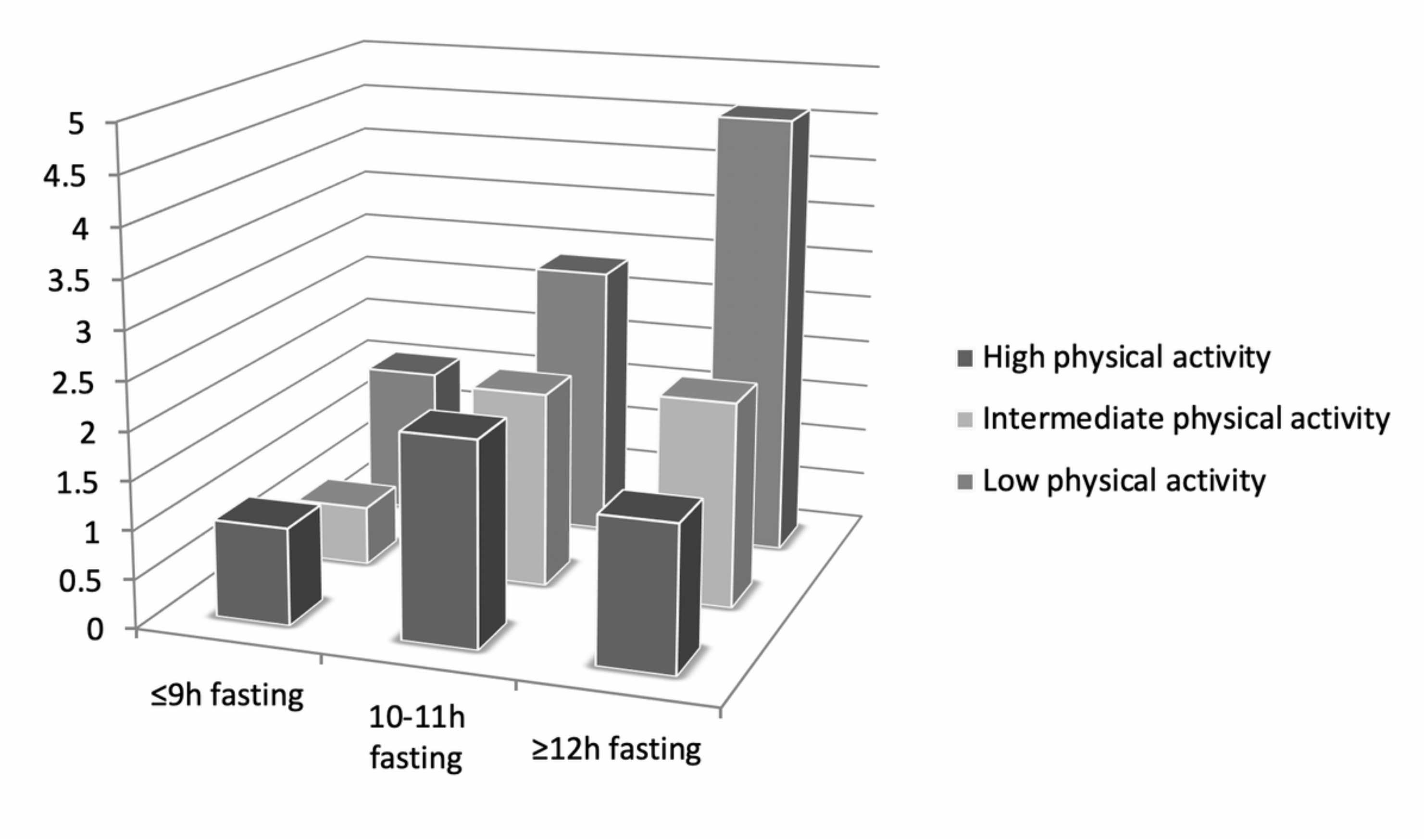

Figure 1

Odds ratios (95% confidence interval) for the joint association of fasting time and physical activity categories with impaired lower-extremity function. Adjusted for sex, age, educational level (≤primary, secondary, or university), smoking status (never, former, current smoker), sedentary behavior (hours/week watching TV), alcohol intake (quintiles of g/day), BMI (<25, 25-29.9, ≥30 kg/m²), morbidity (osteomuscular disease, cardiovascular disease, cancer, diabetes, chronic lung disease, and depression), sleep duration (tertiles of hours/d), energy intake (quintiles of kcal/day), protein intake (quintiles of g/d), and MEDAS score (tertiles). Cutoff points to define levels of physical activity were: ≤57.5 (low), 57.6-82.0 (intermediate) and ≥82.1 METs-h/week (high). Reference category included participants with ≤9 hours/d of fasting time and with high physical activity level

Supplementary Files

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