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Original Research Article

Sarcopenia, Obesity, or Both. What is the dominant Variable of the Associated Risks of Sarcopenic Obesity?

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Abstract

Background and objective: Sarcopenic obesity (SO), obesity, and sarcopenia have been related to adverse events in older adults, raising the question about the role of each component in the risk associated with SO. The objective of this manuscript is to evaluate the role of sarcopenia, obesity, and its interaction in the risks (frailty, disability, mortality) associated with sarcopenic obesity.

Research Design and Methods: Data from the Toledo Study of Healthy Aging (TSHA) were used. This is a cohort-based study composed of community-dwelling adults ≥65 years. Obesity (Body Mass Index-BMI ≥30) and sarcopenia (the Foundation for the National Institutes of Health-FNIH criteria, standardized to our population) were assessed at baseline. Frailty, through the Frailty Phenotype (FP) and the Frailty Trait scale-5 (FTS5), and disability (Katz Index) were evaluated at baseline. Mortality, frailty, and disability were assessed at follow-up. Logistic (odds ratio, OR) and Cox (hazard ratio, HR) regression models were computed to assess the associations.

Results: A total of 1 538 (74.73 years, 45.51% men) individuals were included. Cross-sectionally, SO, sarcopenia, and obesity were significantly associated with the risk of frailty and disability. Longitudinally, Sarcopenia was associated with all the adverse events (ORs/HRs ranged from 1.41 to 4.14, *p*-value < .05); whereas SO [FP, OR (95% confidence interval—CI): 4.27 (2.05, 8.93); FTS5, OR (95% CI): 6.14 (3.58, 10.51), *p*-value < .001] and obesity [FP, OR (95% CI): 3.10 (1.95, 4.94), *p*-value < 0.001; FTS5, OR (95% CI): 2.26 (1.17, 4.35), *p*-value 0.015] was only associated with incident frailty. Sarcopenia added risk to obesity for frailty (FP and FTS5) whereas obesity only did for frailty (FTS5) in sarcopenic individuals. The interaction between sarcopenia and obesity was not associated with any outcome.

Discussion and Implications: Sarcopenia and obesity provide each other an additive risk for frailty, but not a multiplicative (ie, interaction) one, in sarcopenic obesity. Sarcopenia is the mean factor accounting for the associated risk.

Keywords: Disability, Frailty, Obesity, Sarcopenia, Sarcopenic obesity

Translational significance: According to our results, risks associated with sarcopenic obesity in community-dwelling older adults are accounted for by an additive effect by each one of its components (ie, sarcopenia and obesity), but without showing any evidence of a synergistic (with interaction term not significant) effect among them. Moreover, this additive effect is only shown for the case of frailty, but not for mortality or worsening disability. Sarcopenia, and not obesity, appears to be the most hazardous factor in these older adults with sarcopenic obesity.

Background

Functional independence is a key aspect of the management of older adults. In this population, various aging-related entities, such as sarcopenia, obesity, or frailty, threaten this independence (1). Sarcopenia is a progressive skeletal muscle disease (2), defined as the presence of low muscle mass and function (3). Sarcopenia is a highly prevalent disease in older adults (4,5), and these individuals are at increased risk for adverse events (such as falls, impairment in the quality of life (6), frailty (7), disability (8–10) and mortality (8,10)). Another highly prevalent entity that frequently accompanies sarcopenia is obesity (11). Obesity has been related to several

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adverse events in older populations, including frailty (12,13), mobility disability (14) or mortality (15). In fact, sarcopenic obesity (SO), or the presence of low muscle mass and function accompanied by excess adipose tissue (16–18), is present in 1 out of 10 older adults (19), and has been recognized as an own entity by several scientific societies (18).

However, it is unclear whether the coexistence between sarcopenia and obesity provides an additional or a multiplicative risk of adverse events that the presence of each of the conditions separately (20,21). Indeed, a recent systematic review has found that obesity worsens physical function whereas it improves the survival prognosis of older adults with sarcopenia (22). Likewise, SO is cross-sectionally associated with frailty in community-dwelling older adults (23–25), however, to the best of our knowledge, only one manuscript has evaluated this relationship at the longitudinal level. In the manuscript by Hirani et al. (26), sarcopenic obesity was defined as the presence of obesity (defined as body mass index, BMI ≥30) and sarcopenia (individuals with low muscle mass according to the cutoff point established by the Foundation for the National Institutes of Health, FNIH (27,28)), but no physical function variables, such as muscle strength and gait speed, were included.

Therefore, the aim of this manuscript is to evaluate the role of and their coexistence on the risks (frailty, disability, mortality) classically accepted to be associated with sarcopenic obesity to disentangle the portion of the risk attributable to each factor (sarcopenia and obesity) and its combination.

Method

Data were taken from the Toledo Study of Healthy Aging (TSHA) (29), a study approved by the Clinical Research Ethics Committee of the Toledo Hospital in Spain and fulfilled according to the ethical standards defined in the 1964 Declaration of Helsinki. Participants signed an informed consent form prior to recruitment.

Briefly, TSHA is a longitudinal cohort that includes rural and urban institutionalized and community-dwelling older adults older than 64. It was designed to identify aging phenotypes by studying clinical, genetical, and sociodemographic data and its association with lifestyle components such as nutrition, smoking and alcohol consumption, and physical activity (29).

For the purposes of the present study, data from the visits performed between 2011 and 2013 (considered at baseline, Supplementary Figure 1) and 2014–2017 (follow-up) waves were taken. The follow-up evaluation for frailty and disability was performed 2.99 (range 2.0–5.4) median years after the first one. For the case of mortality, this follow-up was extended until a median of 6.29 (range: 0.59–7.47) years. In addition, only community-dwelling participants were included in this study.

Primary Exposure Variables

Obesity

Obesity was defined as a body mass index (BMI) ≥30 kg/m^2 (30). Body weight and height were measured through a stadiometer and an analog medical scale and a stadiometer, respectively. BMI was estimated as body weight in kg (adjusted to the nearest 0.1) divided by height (adjusted to the nearest cm) in meter squared.

Sarcopenia

Sarcopenia was defined according to the Foundation for the National Institutes of Health (FNIH) (27,28), adapted to the TSHA (standardized FNIH [sFNIH]) (31). A participant suffers from sarcopenia when low Appendicular Lean Mass (ALM), low gait speed, and low grip strength criteria are met.

ALM was defined by the sum of the muscle mass present in the arms and the legs. Lean mass was measured by Dual-Energy X-ray Absorptiometry (DEXA; Hologic, Serie Discovery QDR, Bedford, MA, USA). DEXA scans were analyzed using the Physician's Viewer software (apex System Software, version 3.1.2: Bedford, USA). Low ALM criteria were met if participants presented an ALM/BMI < 0.65 in men and <0.54 in women.

Gait speed was measured using the 3-meter walking test at their usual pace, according to the standard protocol. The fastest of the 2 performances expressed in m/s was chosen. Low gait speed cutoff point was <0.8 m/s.

Handgrip strength was evaluated using a JAMAR Hydraulic Hand Dynamometer (Sammons Preston Rolyan, Bolingbrook, IL). The best of 3 trials using international standard procedures (32) was chosen, with at least a minute of resting between them. Grip strength cutoff points were <25.51 kg for men and <19.19 kg for women.

Sarcopenic Obesity

Sarcopenic Obesity was defined as the confluence of obesity and sarcopenia in the same participant. Both entities were measured at baseline.

Primary Negative Health Outcomes

Frailty status

Frailty status was assessed at baseline and at follow-up according to 2 established criteria: the Frailty Phenotype (FP) (33) and the Frailty Trait scale 5 (FTS5) (34).

Fried's Frailty Phenotype criteria (33) (weight loss, exhaustion, weakness, slowness, and low physical activity) were fitted to our population (29) (Supplementary Table 1). Frailty status was defined as robust or nonfrail (individuals who did not meet any criteria), prefrail (1 or 2 criteria met), and frail (≥3).

FTS5 domains' (gait speed, grip strength, physical activity, BMI, and balance) are displayed in Supplementary Table 2 (34). Each of the 5 domains scores from 0 (the lowest) to 10 (the highest), being 50 the highest score possible in this tool. Participants with a score higher than 25 were considered as frail.

Disability

Katz Index (35) was used to assess the ability to perform basic activities of daily living (BADL). Disability according to this test was measured at baseline and at follow-up. Worsening disability was defined as any worsening in any category of BADL.

Mortality

Vital status was ascertained by the Spanish National Death Index (Ministry of Health, Consumer Affairs and Social Welfare), hospital records, and phone contact during the study follow-up. Mortality median follow-up time was 6.29 (range: 0.59–7.47) years.

Table 1. Descriptive Characteristics of the Participants

Variable	All	Sarcopenia			Obesity			Sarcopenic obesity		
		Yes	No	*p*	Yes	No	*p*	Yes	No	*p*
N (%)	1538	348 (22.63)	1190 (77.37)		597 (38.32)	941 (61.18)		191 (12.42)	1347 (87.58)	
Age, mean (*SD*)	74.73 (5.73)	77.53 (5.57)	73.91 (5.52)	**<.001**	74.28 (5.09)	75.01 (6.09)	0.114	76.59 (5.00)	74.46 (5.78)	**<.001**
Gender, male (%)	700 (45.51)	60 (17.24)	640 (53.78)	**<.001**	210 (35.18)	490 (52.07)	**<.001**	27 (14.14)	673 (49.96)	**<.001**
Charlson Index, mean (*SD*)	1.18 (1.59)	1.52 (1.89)	1.08 (1.48)	**<.001**	1.18 (1.63)	1.18 (1.58)	0.783	1.52 (1.94)	1.13 (1.53)	**.005**
Frailty phenotype (FP)										
Robust, *n* (%)	1058 (68.79)	159 (45.69)	899 (75.55)	**<.001**	398 (66.67)	660 (70.14)	0.358	87 (45.55)	971 (72.09)	**<.001**
Prefrail, *n* (%)	436 (28.35)	164 (47.13)	272 (22.86)		181 (30.32)	255 (27.10)		90 (47.12)	346 (25.69)	
Frail, *n* (%)	44 (2.86)	25 (7.18)	19 (1.60)		18 (3.02)	26 (2.76)		14 (7.33)	30 (2.23)	
Frailty trait scale 5 (FTS5)										
No frail, *n* (%)	1377 (89.53)	125 (35.92)	36 (3.03)	**<.001**	97 (16.25)	64 (6.80)	**<.001**	111 (58.12)	1266 (93.99)	**<.001**
Frail, *n* (%)	161 (10.47)	223 (64.08)	1154 (96.97)		500 (83.75)	877 (93.20)		80 (41.88)	81 (6.01)	
Katz Index at baseline, mean (*SD*)	5.81 (0.52)	5.62 (0.74)	5.86 (0.42)	**<.001**	5.78 (0.51)	5.83 (0.52)	**.006**	5.64 (0.58)	5.83 (0.50)	**<.001**
Disabled at baseline, *n* (%)	241 (15.67)	100 (28.99)	141 (11.98)	**<.001**	113 (19.09)	128 (13.76)	**.006**	58 (30.37)	183 (13.59)	**<.001**
Longitudinal health events										
Incident frailty (FP), *n* (%)	45 (3.60)	26 (9.89)	19 (1.93)	**<.001**	23 (4.58)	22 (2.94)	0.127	16 (10.39)	29 (2.65)	**<.001**
Incident frailty (FTS5), *n* (%)	96 (8.19)	50 (26.74)	46 (4.67)	**<.001**	54 (12.39)	42 (5.71)	**<.001**	31 (32.29)	65 (6.04)	**<.001**
Worsening disability, *n* (%)	308 (23.62)	89 (30.38)	219 (21.66)	**.002**	134 (25.77)	174 (22.19)	0.137	44 (26.19)	264 (23.24)	.401
Death, *n* (%)	214 (13.91)	67 (19.25)	147 (12.35)	**.001**	70 (11.73)	144 (15.30)	**.048**	31 (16.23)	183 (13.59)	.323

Notes: Data are expressed as mean (SD) and frequency (%). In bold: *p*-value <.05. *N*: Number of the sample. FP: Frailty Phenotype. FTS5: Frailty Trait scale 5. *SD*: standard deviation.

Comorbidity

Comorbidity was assessed at baseline by the Charlson Comorbidity Index (36).

Statistical Analysis

Characteristics of the subjects at baseline were stratified according to the presence or absence of sarcopenia, obesity, and SO. Descriptive statistics were shown as mean (standard deviation, *SD*) and number (*N*, %). Differences between individuals with and without SO were tested using Mann–Whitney or Kruskal–Wallis and Chi-square test, respectively.

The association among SO, sarcopenia, obesity, and the interaction between sarcopenia and obesity with the outcomes were assessed using logistic regression models for frailty or disability (both prevalent and incident) and Cox proportional hazard models for death. To explore these associations, we used 4 nested models. Model 1 was the raw model. Model 2 added Age, Gender, and Charlson Index to model 1. Model 3 included only sarcopenia and obesity, and Model 4 added Age, Sex, and Charlson Index to Model 3.

When the interaction term was the variable of interest, Model 1 was adjusted by sarcopenia and obesity, and Model 2 added Age, Gender, and Charlson Index to Model 1.

Moreover, to assess the conditional effect of sarcopenia and obesity on each other, we estimated Models 1 and 2 just in those who met each condition.

Analyses were performed using the Statistical Package R version 4.1.2 for Windows (Vienna, Austria). The statistical significance level was set at *p*-value < .05.

Results

Study Population

The main characteristics of the 1 538 participants (700 men) are shown in Table 1. Participants presented a mean age of 74.73 ± 5.73. Of the whole sample, 348 and 597 met the sarcopenia and obesity criteria, respectively. One hundred ninety-one participants met the criteria for both sarcopenia and obesity.

SO rates were significantly higher in individuals with frailty, being sarcopenic obese 31.82% (FP) and 49.69% (FTS5) of those considered as frail (Supplementary Table 3). According to nonfrail participants, only 8% of the individuals met the SO criteria.

Cross-sectional associations

Participants with SO were more likely to meet criteria for frailty and disability, regardless of age, sex, or comorbidity [FTS5, odds ratio (OR) 9.09, 95% confidence interval (CI) = (6.04. 13.68), *p*-value < .001; FP OR (95% CI): 3.58 (1.73. 7.41), *p*-value < .001; disability OR (95% CI) 2.92 (1.42. 6.02), *p*-value.004]. We explored this

association with each entity (sarcopenia and obesity) in isolation (Supplementary Table 4). Sarcopenia was closely related to frailty (up to an OR of 10.25 with FTS5, *p*-value <.001) and disability [OR (95% CI): 1.64 (1.17, 2.30), *p*-value 0.004]. For its part, obesity was related to disability [OR (95% CI): 2.55 (1.69, 3.85), *p*-value <.001] and frailty when assessed with FTS5 [OR (95% CI) 1.54 (1.13, 2.09), *p*-value .006], but not with FP (*p*-value .527). Nevertheless, the interaction of meeting sarcopenia and obesity criteria did not an increase the likelihood of being frail or disabled cross-sectionally (Supplementary Table 5).

Longitudinal associations

Role of sarcopenic obesity

Association between SO and the incidence of adverse events is shown in Table 2. The presence of this condition was only longitudinally associated with the incidence of frailty [FP OR (95% CI): 6.14 (3.58, 10.51), *p*-value <.001; FTS OR (95% CI): 4.27 (2.05, 8.93), *p*-value <.001] but not with worsening disability 3 years after the baseline visit nor mortality on the almost 7 years of follow-up.

Role of sarcopenia and obesity

We evaluated the independent role of obesity and sarcopenia on the incidence of different negative health outcomes (Table 3). Obesity was shown to be a risk factor for developing frailty, especially when the scale chosen was the FTS5 [OR (95% CI): 2.65 (1.64, 4.29), *p*-value <.001]. In contrast, having a BMI ≥30 had a protective effect against death, although this effect was not maintained when age, sex, and comorbidity were considered.

In turn, individuals who met sarcopenia criteria had an increased risk of suffering any of the adverse events studied. This increased probability of adverse events ranged from OR 1.73 for worsening disability to OR 4.14 (*p*-value <.001) for incident frailty according to FTS5. In this sense, subjects with sarcopenia presented HR 1.41 for mortality (*p*-value 0.040).

Role of sarcopenia and obesity among each other (additional risk)

Given our results, we wanted to perform a sensitivity analysis evaluating the effect that obesity and sarcopenia had on each other. Within individuals with obesity, statistically significant differences were found in all variables (except for worsening disability) in the descriptives according to sarcopenia status (Supplementary Table 6). Alternatively, among individuals with sarcopenia, only the mean FTS5 score at baseline was significantly higher in those with obesity.

We evaluated whether these results were consistent adjusting for age, sex, and comorbidity. Cross-sectionally, sarcopenia increased the risk of disability or frailty by 7.9 to 10.76 in obese subjects, whereas obesity only increased the risk of frailty according to FTS5 (Table 4). Longitudinally, the presence of sarcopenia in those with obesity significantly increases the likelihood of incident frailty, regardless of the tool used [FP: 3.93 (2.06, 7.49), *p*-value <.001, FTS5: 4.75 (1.60, 14.15), *p*-value .005]. Likewise, those with a BMI ≥30 with sarcopenia were more likely to end up being frail according to the FTS5. Although no further results were significant, in the raw models, we found nonsignificant trends showing sarcopenia as a risk factor for death in the obese (*p*-value .061), and obesity as a protective factor for disability (*p* .072) and mortality (*p*-value 0.097) in older adults with sarcopenia.

Role of the interaction between sarcopenia and obesity

As in the cross-sectional analyses, the interaction between sarcopenia and obesity did not confer an increased likelihood of frailty, disability, or mortality (Table 5).

Discussion

This study evaluates the cross-sectional and longitudinal role of sarcopenic obesity, sarcopenia, obesity, and its interaction with some negative health events in community-dwelling older adults. According to our results, although there is an additive effect of sarcopenia and obesity in determining the risk of frailty in people with sarcopenic obesity, the interaction between obesity and sarcopenia, does not seem to confer a higher risk than that conferred by these 2 highly prevalent conditions separately. Moreover, although the presence of sarcopenia was related to all the events studied, obesity was only related to frailty and showed a marginal, nonsignificant protective effect for disability and mortality in people with sarcopenia.

Accordingly, once all the covariables are considered in the fully adjusted model, the presence of obesity only appears to confer an additional risk of incident frailty (as assessed by the FTS5) in community-dwelling older adults who meet the criteria for sarcopenia. Although not shocking, this finding is certainly striking. Some authors have already explored the relationship of BMI with different negative health events with mixed results (15,37,38), and a paradox may be found (39). In fact, some authors have proposed that the cutoff point of 30 may not accurately capture the negative health effects of obesity, especially those attributed to fat tissue, in older adults (15). In our population of community-dwellers, virtually 4 in 10 met the criteria for obesity. In a systematic review with

Table 2. Association Between Sarcopenic Obesity With Incident Negative Health Outcomes

Variable	Model 1			Model 2		
	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*
Incident frailty (FTS5) [a]	7.42 (4.52, 12.18)		**<.001**	6.14 (3.58, 10.51)		**<.001**
Incident frailty (FP) [b]	4.27 (2.26, 8.05)		**<.001**	4.27 (2.05, 8.93)		**<.001**
Worsening disability [c]	1.17 (0.81, 1.70)		.401	0.94 (0.63, 1.38)		.737
Death [d]		1.10 (0.75, 1.62)	.608		1.22 (0.82, 1.82)	.325

Notes: CI = confidence interval; FP = frailty phenotype; FTS5 = frailty trait scale 5; HR = hazard ratio; OR = odds ratio. Model 1: raw model. Model 2: adjusted by Age, Sex, and Charlson Index. In bold: *p*-value <.05.
[a]: *N* = 1172; [b]: *N* = 1250; [c]: *N* = 1304; [d]: *N* = 1538. In all the models, the reference category was composed of those individuals without sarcopenic obesity.

Table 3. Association Between Sarcopenia and Obesity With Incident Negative Health Outcomes

Variable	Bivariate Models						Multivariant Models					
	Model 1			Model 2			Model 3			Model 4		
	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*
Incident frailty (FTS5)[a]												
Sarcopenia[e]	7.45 (4.80, 11.55)		**<.001**	4.73 (2.94, 7.62)		**<.001**	6.83 (4.38, 10.64)		**<.001**	4.14 (2.56, 6.71)		**<.001**
Obesity[f]	2.34 (1.53, 3.56)		**<.001**	3.10 (1.95, 4.94)		**<.001**	1.89 (1.22, 2.95)		**.005**	2.65 (1.64, 4.29)		**<.001**
Incident frailty (FP)[b]												
Sarcopenia[e]	5.59 (3.04, 10.27)		**<.001**	3.95 (1.94, 8.04)		**<.001**	5.45 (2.92, 10.18)		**<.001**	3.51 (1.70, 7.25)		**.001**
Obesity[f]	1.58 (0.87, 2.88)		.13	2.26 (1.17, 4.35)		**.015**	1.11 (0.60, 2.07)		.733	1.84 (0.94, 3.60)		.077
Worsening disability[c]												
Sarcopenia[e]	2.99 (1.91, 4.68)		**<.001**	1.67 (1.01, 2.77)		**.045**	3.28 (2.07, 5.21)		**<.001**	1.73 (1.03, 2.90)		**.039**
Obesity[f]	0.84 (0.54, 1.33)		.462	0.98 (0.61, 1.60)		.945	0.66 (0.41, 1.06)		.087	0.88 (0.53, 1.45)		.607
Death[d]												
Sarcopenia[e]		1.48 (1.11, 1.98)	**.008**		1.38 (1.00, 1.90)	**.049**		1.61 (1.20, 2.17)	**.002**		1.41 (1.02, 1.94)	**.040**
Obesity[f]		0.74 (0.55, 0.98)	**.035**		0.95 (0.71, 1.27)	.737		0.67 (0.50, 0.90)	**.008**		0.90 (0.67, 1.22)	.504

Notes: CI = confidence interval; FP = frailty phenotype; FTS5 = frailty trait scale 5; HR = hazard ratio; OR = odds ratio. Model 1: raw model. Model 2: adjusted by age, sex, and Charlson Index. Model 3: adjusted by sarcopenia and obesity. Model 4: Model 3 + age, sex, and Charlson Index. In bold: $p < .05$.
[a]: $N = 1\,172$;
[b]: $N = 1\,250$;
[c]: $N = 1\,304$;
[d]: $N = 1\,538$;
[e]: ref. individuals without sarcopenia (independently of obesity status);
[f]: ref. individuals without obesity (independently of sarcopenia status).

Table 4. Association Between Sarcopenia (only in participants with obesity) and Obesity (only in those with sarcopenia) and Negative Health Outcomes

Variable	Sarcopenia (just in those with obesity)						Obesity (just in those with sarcopenia)					
	Model 1			Model 2			Model 1			Model 2		
	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*
Cross-sectional associations												
	Ref. obese without sarcopenia [a]			Ref. obese without sarcopenia [a]			Ref. sarcopenic without obesity [b]			Ref. sarcopenic without obesity [b]		
Prevalent frailty (FTS5)	16.49 (9.38, 29.00)		**<.001**	9.82 (5.38, 17.93)		**<.001**	1.79 (1.14, 2.81)		**.010**	2.48 (1.51, 4.09)		**<.001**
Prevalent frailty (FP)	7.95 (2.58, 24.49)		**<.001**	10.76 (2.99, 38.68)		**<.001**	1.05 (0.46, 2.38)		.907	1.44 (0.60, 3.47)		.413
Prevalent disability	7.97 (2.59, 24.57)		**<.001**	7.90 (2.21, 28.22)		**.001**	0.96 (0.43, 2.14)		.923	1.62 (0.67, 3.95)		.285
Longitudinal associations												
	Ref. obese without sarcopenia[c]			Ref. obese without sarcopenia[c]			Ref. sarcopenic without obesity[d]			Ref. sarcopenic without obesity[d]		
Incident frailty (FTS5)	6.57 (3.60, 12.00)		**<.001**	3.93 (2.06, 7.49)		**<.001**	1.81 (0.93, 3.50)		.080	2.34 (1.15, 4.79)		**.019**
	Ref. obese without sarcopenia[e]			Ref. obese without sarcopenia[e]			Ref. sarcopenic without obesity[f]			Ref. sarcopenic without obesity[f]		
Incident frailty (FP)	5.65 (2.27, 14.03)		**<.001**	4.75 (1.60, 14.15)		**.005**	1.15 (0.50, 2.64)		.745	2.01 (0.78, 5.17)		.148
	Ref. obese without sarcopenia[g]			Ref. obese without sarcopenia[g]			Ref. sarcopenic without obesity[h]			Ref. sarcopenic without obesity[h]		
Worsening disability	1.03 (0.68, 1.57)		.879	0.82 (0.51, 1.33)		.427	0.63 (0.38, 1.04)		.072	0.75 (0.44, 1.26)		.277
	Ref. obese without sarcopenia [a]			Ref. obese without sarcopenia [a]			Ref. sarcopenic without obesity[b]			Ref. sarcopenic without obesity [b]		
Death		1.57 (0.98, 2.52)	.061		1.51 (0.88, 2.58)	.135		0.67 (0.41, 1.08)	.097		0.91 (0.55, 1.51)	.724

Notes: CI = Confidence interval; FP = frailty phenotype; FTS5 = frailty trait scale 5; OR = odds ratio; HR = hazard ratio. Model 1: raw model. Model 2: Model 1 + age, sex, and Charlson Index. In bold: $p < .05$.
[a]: $N = 597$;
[b]: $N = 348$;
[c]: $N = 436$;
[d]: $N = 187$;
[e]: $N = 502$;
[f]: $N = 263$;
[g]: $N = 520$;
[h]: $N = 293$.

Table 5. Association Between Sarcopenia, Obesity, and Their Interaction With Incident Negative Health Outcomes

Variable	Model 1			Model 2		
	OR (95% CI)	HR (95% CI)	*p*	OR (95% CI)	HR (95% CI)	*p*
Incident frailty (FTS5)[a]						
Ref: individuals without sarcopenia or obesity	1		—	1		—
Sarcopenia	7.14 (3.71, 13.74)		**<.001**	3.83 (1.89, 7.79)		**<.001**
Obesity	1.96 (1.08, 3.55)		**.026**	2.50 (1.34, 4.66)		**.004**
Sarcopenia * obesity	0.92 (0.38, 2.24)		.856	1.15 (0.45, 2.93)		.769
Incident frailty (FP)[b]						
Ref: individuals without sarcopenia or obesity	1		—	1		—
Sarcopenia	5.28 (2.22, 12.54)		**<.001**	2.86 (1.08, 7.53)		**.034**
Obesity	1.07 (0.42, 2.75)		.884	1.46 (0.55, 3.92)		.451
Sarcopenia * obesity	1.07 (0.30, 3.76)		.916	1.54 (0.40, 5.87)		.527
Worsening disability [c]						
Ref: individuals without sarcopenia or obesity	1		—	1		—
Sarcopenia	3.42 (1.89, 6.17)		**<.001**	1.83 (0.96, 3.50)		.066
Obesity	0.68 (0.36, 1.31)		.253	0.90 (0.46, 1.77)		.757
Sarcopenia * obesity	0.93 (0.36, 2.39)		.883	0.95 (0.36, 2.53)		.918
Death [d]						
Ref: individuals without sarcopenia or obesity		1	—		1	—
Sarcopenia		1.63 (1.12, 2.38)	**.011**		1.37 (0.92, 2.05)	.122
Obesity		0.68 (0.47, 0.98)	**.040**		0.89 (0.61, 1.28)	.517
Sarcopenia * obesity		0.97 (0.53, 1.78)	.930		1.06 (0.58, 1.94)	.850

Notes: CI = confidence interval; FP = frailty phenotype; FTS5 = frailty trait scale 5; OR = odds ratio; HR = hazard ratio. Model 1: adjusted by sarcopenia, obesity, and the interaction between them. Model 2: Model 1 + age, sex, and Charlson Index. In all the models, the reference category was composed of those individuals without sarcopenic obesity. In bold: $p < .05$.
[a]: $N = 1\,172$;
[b]: $N = 1\,250$;
[c]: $N = 1\,304$;
[d]: $N = 1\,538$.

meta-analysis, Winter et al. found that the risk of death began to increase for BMI >33 (38). This cutoff point was later confirmed by Jiang et al. in another systematic review, in which the authors also observed that the risk of disability increased from a BMI >28 (40). Future studies are needed to assess whether different BMI cutoff points according to the presence of sarcopenia could ascribe an additional risk and whether these cutoff points could be different according to the event studied or even considering the presence of sarcopenia status.

In previous studies done in community-dwelling older adults the presence of sarcopenia according to the FNIH criteria increases the risk of death (41), as we found in our study. According to our results, the presence of obesity does not modify this increased risk of death. In fact, in models in which age, sex, and comorbidity were not considered, those categorized as obese had a significantly lower risk of mortality, even when sarcopenia was considered [HR (95% CI): 0.67 (0.50, 0.90), *p*-value .008]. In this regard, Batsis et al. (42) observed that the increased risk of death attributed to sarcopenic obesity occurred in women, but not in men. However, once mobility limitations were added to the model, this association became nonsignificant, a fact that reinforces our findings. On the contrary, in a recent study involving 141 adults over 18 years of age with pancreatitis, those who met the criteria for obesity and sarcopenia died to a greater extent after 1 year of follow-up than those who only met the criteria for sarcopenia (43).

To accurately interpret our results, it is important to consider that our definition of sarcopenia requires individuals to meet the criteria of low strength, low appendicular muscle mass, and low gait speed. In other definitions, such as those proposed by the European consensus, meeting all 3 criteria is referred to as severe sarcopenia (3). Some authors have included the domain of low gait speed in their definition of sarcopenia according to the FNIH algorithm (28,31,44), whereas others have not (45,46). In this sense, the conceptual definition of the Global Leadership Initiative in Sarcopenia (GLIS), considered that walking speed should not be included as a component of sarcopenia, despite the fact that 79.8% of the participants voted in favor (47). The inclusion of this domain could influence our results. However, presenting low gait speed according to the FNIH definition was not associated with neither worsening disability nor mortality in our population (10).

Our findings have important practical and clinical implications. First, our results suggest that assessment of sarcopenia appears necessary to evaluate the risk of adverse events in older adults. In the functional continuum, from robustness to disability, sarcopenia appears to play a central role as an important risk factor for developing frailty (7). Furthermore, in individuals with sarcopenia, the presence of obesity increases the risk of frailty. Interventions based on nutritional programs and physical exercise have been shown to be effective in both the prevention and treatment of obesity, sarcopenia, and frailty in older adults (48–52). According to our results, emphasizing those interventions that especially improve sarcopenia, such as strength exercise coupled with

sufficient caloric and protein intake, could be an optimal strategy in the management of older adults.

Among the strengths of our study are the inclusion of 2 frailty scales, the prior standardization of the frailty and sarcopenia criteria in our population, and the objective evaluation of muscle mass by DEXA. Regarding limitations, we should highlight the low prevalence of frailty according to the FP, which is lower in this study than in the entire TSHA study because some individuals could not attend the DEXA evaluation. In addition, our sample was composed of highly homogenous community-dwelling older adults from Spain and extrapolation to people in other conditions (eg, hospitalized), environments, race, or ethnicity should be carefully made.

Conclusions

Risks associated with sarcopenic obesity are accounted for by an additive effect of the risks conferred by each one of its components (i.e., sarcopenia and obesity), but without showing any evidence of a synergistic effect among them. Moreover, this additive effect is only shown for the case of frailty, but not for mortality or worsening disability. Sarcopenia, and not obesity, appears to be the most hazardous factor in these older adults with sarcopenic obesity.

Supplementary Material

Supplementary data are available at *Innovation in Aging* online.

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Conflict of Interest

None.

Data Availability

Our study uses secondary data that was not preregistered. Data will be available upon reasonable request after consultation with F. José García García and L. Rodríguez Mañas.

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