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ANOREXIA IS INDEPENDENTLY ASSOCIATED WITH DECREASED MUSCLE MASS AND STRENGTH IN COMMUNITY DWELLING OLDER ADULTS

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Abstract: *Objectives:* We aimed to investigate the association between anorexia and sarcopenia in community dwelling older adults. *Method:* Anorexia was assessed by Simplified Nutritional Appetite Questionnaire (SNAQ) and sarcopenia defined by EWSGOP criteria. Study participants consisted of 442 patients from Turkish validation study of the SNAQ. Study is designed as cross-sectional in community dwelling outpatients. *Measurements:* Muscle mass was determined by using bioimpedance analysis. Skeletal muscle mass index (SMMI) was calculated as SMM (kg)/height (m)^2. Muscle strength was evaluated by hand grip strength (HGS) with Jamar hydraulic hand dynamometer. Gait speed (GS) was assessed by usual 4 meters speed. Depression and quality of life were assessed by using Geriatric Depression Scale (GDS) and Euro-Quality of Life-5D(EQ-5D). Univariate analysis and multivariate regression analysis were run to evaluate the association between poor appetite and components of sarcopenia. *Results:* Prevalences of low HGS, low gait speed and sarcopenia were higher in group with poor appetite ($p=0.001$, $p<0.0001$, $p=0.036$, respectively). Depression and constipation were more prevalent in participants with poor appetite ($p<0.0001$, $p=0.033$, respectively). SNAQ was correlated with SMMI and EQ-5D. Regression analysis showed that lower muscle mass, lower SMMI, and lower HGS were independently associated with poor appetite after adjustment for confounders. Neither gait speed nor diagnosis of sarcopenia was associated with poor appetite in regression analysis models. *Conclusion:* We observed poor appetite has independent association with lower skeletal muscle mass and decreased muscle strength. Prospective studies are needed to evaluate exact relationship between poor appetite and sarcopenia.

Key words: SNAQ, appetite, sarcopenia, muscle mass, muscle strength.

Introduction

Anorexia of ageing is a notable problem with prevalence up to 30% in community-dwelling older adults (1, 2). It has been reported with multiple negative outcomes such as malnutrition, frailty, and mortality (3).The Simplified Nutritional Appetite Questionnaire (SNAQ) is one of the recommended tools for screening poor appetite in older adults (4). Recently, Turkish version of the SNAQ has been validated by our group (5) and gave 21.5% prevalance of poor appetite for our outpatient older adults.

Sarcopenia is a well-known geriatric syndrome resulted in age-related disability. It is defined as age-related decline in muscle mass and function (6, 7). Inadequate food intake often results in reduced physical activity and declining muscle mass and strength in older adults (8). However, association between loss of appetite and sarcopenia has not been established precisely. Previous cross-sectional studies showed conflicting results due to different sarcopenia assessment methods presumably (9-13). There has been different consensus definitions for sarcopenia organized by different groups which all share the presence of low muscle mass together with low muscle function (6, 7, 14-16). The consensus report of European Working Group on Sarcopenia in Older People (EWGSOP) consensus is one of the widely depicted such definition for sarcopenia (6). EWGSOP recommends the presence of both low muscle mass and low muscle function (strength or performance) for the diagnosis of sarcopenia (6). Regarding assessment of low muscle mass, EWGSOP recommends to use skeletal muscle mass index, which is calculated as skeletal muscle mass/height^2. EWGSOP also recommends the use of normative data of the study population rather than other predictive reference populations. Both SMMI and hand grip strength cut-off points according to the EWGSOP definition were reported in Turkish population previously (17).

In this study, we aimed to investigate the association between poor appetite assessed by SNAQ and sarcopenia defined by EWSGOP criteria by using national Turkish population cut-off points as being the first one in the literature.

Methods

Study participants consisted of patients from Turkish validation study of the SNAQ (5). Those are 442 community dwelling older adults admitted to Istanbul Medical School Geriatrics outpatient clinic between 2013-2016. Number of medicines and number chronic diseases were noted. Poor appetite prevalence was assessed by using the SNAQ with cut point of <=14 through previous validation study.

Assessment of Sarcopenia

Body weight and muscle mass were calculated with bioimpedance analysis (BIA) (Tanita BC 532 model). The EWGSOP remarked BIA as one of the most feasible, valid,

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Table 1
Associations between poor appetite assessed by SNAQ and sarcopenia, depression, and constipation

	Poor appetite(n=95) N(%) or median(min-max)	Normal appetite(n=347) N(%) or median(min-max)	P-value	Total population N(%) or median(min-max)
Low muscle mass	6(6.8%)	10(3%)	0.09	
Low HGS	53(64.6%)	144(44.9%)	0.001*	197/403(48.9%)
Low gait speed	50(60.2%)	29(38.9%)	<0.0001*	179/415(43.1%)
Sarcopenia	5(6%)	6(1.8%)	0.036*	11/408(2.7%)
Depresssion	44(50%)	85(25.5%)	<0.0001*	123/421(30.6%)
Constipation	38(40.4%)	100(28.9%)	0.033*	138/440(31.5%)
Number of medicines(n=422)	6 (0-20)	6 (0-16)	0.5	6 (0-20)
Number of chronic diseases(n=422)	5 (0-11)	4 (0-10)	0.068	4 (0-11)

SNAQ: Simplified Nutritional Appetite Questionnaire,HGS: Hand grip strength; *significant p values

and reliable method of measuring muscle mass in daily practice. Fat free mass (FFM) was measured by BIA and then the skeletal muscle mass (SMM) was calculated using the following formula: SMM (kg)= 0.566 * FFM (kg) (18). As EWGSOP recommends, skeletal muscle mass index (SMMI) was calculated as SMM (kg)/height (m)^2 (19).Participants with low muscle mass (low MM) were defined according to the national population cut-off points: If SMMI<7.4 kg/m^2 and <9.2 kg/m^2 for females and males, respectively (17).

Muscle strength was evaluated by hand grip strength (HGS) with Jamar hydraulic hand dynamometer using validated protocol (20, 21). Maximum HGS was measured for 3 times from bilateral hands. Resting intervals of at least 30 seconds were allowed. Low HGS was defined according to the national data (<22 kg and <32 kg for females and males, respectively) (17).

Physical performance was assessed by usual 4 meters speed. Poor physical performance was defined as if gait speed ≤0.8 m/s. All of the measurements were made by the same geriatric physiotherapist qualified on these measurements previously.

Diagnosis of sarcopenia was determined by the presence of low muscle mass plus the documentation of either low hand grip strength or poor physical performance (6).

Assessment of other possible associated factors with poor appetite: depression and quality of life

Depression was evaluated by Geriatric Depression Scale short form (GDS-SF) (22). GDS scores >=5 points reflect higher possibility of depression. Quality of life was assessed by Euro-Quality-of Life-5D-3L (EQ-5D) scale (23) which consists of 2 parts: The first part is EQ-5D descriptive system which is scored between 5-15 points and higher test scores state poor quality-of-life. The second part is EQ-visual analogue scale (EQ VAS) with a grade ranging from 0 (the worst possible health status) to 100 (the best possible health status).

The study was conducted according to guidelines in the Declaration of Helsinki. Informed consent was obtained for all participants. The study was approved from the Istanbul University, Istanbul Medical School local ethic committee.

Statistical analysis

Data were analyzed by IBM SPSS Statistics version 21 for Windows (SPSS Inc, Chicago, Ill, USA). Descriptive statistics are given as means ± standard deviations, median and interquartile range or percentages as appropriate. Chi-square test was run to compare categorical variables. Groups with/without poor appetite were compared with independent sample t-test or Mann Whitney U test as necessary. Spearman's correlation was used to determine the relationship between SNAQ score and SMMI, HGS, gait speed, number of medicines, number of chronic disease, GDS-SF, EQ-5D, and EQ VAS. Correlation results were interpreted as follows: values between 0.0-0.24 as weak, 0.25-0.49 as moderate, 0.50- 0.74 as substantial, and 0.75- 1.00 as almost perfect. After univariate analysis, multicollinearity was checked among the parameters significantly related to poor appetite. Then binary logistic regression analysis was run. A p-value of <0.05 was accepted as statistically significant.

Results

442 participants with full-filled SNAQ forms were included. 305 were female and 137 were male, with a mean age of 77.1 ± 6.8 years. According to the SNAQ, the prevalence of poor appetite was 21.5% (n=95). Median number of medicines was 6 (0-20, min-max). Median number of chronic diseases was 4 (0-11, min-max). Mean SMMI was 10.28±1.2 kg/m^2. HGS median value was 24 kg (8-58 kg, min-max; mean 25±8.2 kg). Gait speed median value was 0.85m/s (0.14-1.59 m/s, min-max; mean 0.82±0.26 m/s).

3.8% of study population had low MM, 48.9% had decreased HGS, 43.1% had decreased gait speed. 30.6% of participants had depression according to GDS-SF [Mean GDS-SF score is 4.1±3.6, median GDS-SF score is 3 (0-15, min-max)].The

Table 2
Correlations between SNAQ and SMMI, HGS, gait speed, number of medicines, number of chronic disease, GDS-SF, EQ-5D, EQ VAS and age

	SMMI	HGS	Gait speed	NoM	NoD	GDS-SF	EQ-5D	EQ VAS	Age
r-value	0.243	0.250	0.235	-0.027	-0,092	-0.323	-0.264	0.233	-0.111
p-value	<0.0001	<0.0001	<0.0001	>0,05	0,059	<0.0001	<0.0001	0.002	0.019

SNAQ: Simplified Nutritional Appetite Questionnaire, SMMI:Skeletal muscle mass index,HGS: Hand grip strength, NoM: Number of drug, NoD: Number of chronic disease,GDS-SF: Geriatric Depression Scale Short Form, EQ-5D:EQ-5D descriptive system, EQ VAS:EQ-visual analogue scale

Table 3
Results of multivariate regression analysis:Association between poor appetite and low SMMI and low HGS after adjustment for confounders

	Model 1	Model 2	Model 3	Model4	Model5
	Odds ratios [95 % confidence interval]				
Age	1.055 [0.998-1.116]	1.026 [0.969-1.086]	1.056[0.993-1.122]	1.059[1.003-1.118]***	1.060[1.003-1.119]
Gender	0.700 [0.254-1.930]	1.123 [0.342-3.685]	0.403 [0.145-1.126]	0.339[0.114-1.009]	0.254[0.078-0.825]
Constipation	0.562 [0.228-1.512]	0.538[0.228-1.268]	0.563[0.236-1.342]	0.564[0.234-1.357]	0.514[0.210-1.258]
Depression	0.599 [0.238-1.512]	0.750 [0.306-1.839]	0.729[0.295-1.798]	0.601[0.242-1.493]	0.550[0.219-1.383]
EQ-5D	1.031 [0.842-1.262]	0.941 [0.762-1.163]	1.053[0.814-1.362]	1.002[0.815-1.234]	0.983[0.798-1.211]
SMMI	0.583 [0.408-0.834]*				
HGS		0.900 [0.828-0.978]**			
Gait speed			0.966[0.097-9.628]		
Diagnosis of Sarcopenia				0.160[0.019-1.365]	
Low MM					0.70[0.009-0.529]^

EQ-5D:EQ-5D descriptive system, SMMI:Skeletal muscle mass index,HGS: Hand grip strength, MM: Muscle mass; *p=0.06; **p=0.013, ***p=0.037, ^p=0.01

mean scores of EQ-5D and EQ VAS were 7.6±2.1 and 64.3% ±19.6%, respectively. Constipation rate was 31.5% (Table 1).

Associated factors with poor appetite

Results of univariate analysis

Univariate analysis between poor appetite and low MM, low HGS, low gait speed, diagnosis of sarcopenia, depression, constipation, number of medicines, and number of chronic diseases are shown in Table 1. Prevalences of low HGS, low gait speed and sarcopenia were higher in group with poor appetite (p=0.001, p<0.0001, p=0.036, respectively). Depression and constipation were more prevalent in participants with poor appetite (p<0.0001, p=0.033, respectively).Median number of medicines and chronic diseases were not statistically different between groups. The Spearman's correlation was run to assess correlation between the SNAQ and SMMI, HGS, gait speed, number of medicines, number chronic diseases, GDS-SF, EQ-5D, and EQ VAS (Table 2). The SNAQ score was statistically significantly weakly correlated with SMMI, HGS, gait speed (r=0.243, r=0.250, r=0.235, respectively. p<0.0001 for all). EQ-5D was moderately; EQ VAS was weakly correlated with SNAQ (r=-0.264, p<0.0001; r=0.233, p=0.002, respectively).There was statistically significant moderate correlation between SNAQ and GDS-SF (r= -0.323, P<0.0001).There was no correlation between SNAQ and number of medicines and number of chronic diseases.

Increased age (p=0.019) (Table 2) and female gender (female 25.2%, male 13.1%, p=0.004) were documented as associated factors with poor appetite.

Results of multivariate regression analysis

Factors those were associated with poor appettite in univariate analysis (p<0.05) were used as independent factors in regression analysis. Poor appetite was dependent factor while age, gender, presence of constipation, depression, EQ-5D and components of sarcopenia were independent factors. Each components of sarcopenia [SMMI, HGS, gait speed] and diagnosis of sarcopenia were added individually and consecutively in 4 different regression models (Table 3). Although low MM did not show statistically significant association with poor appetite in univariate analysis, it was included in the model because of its clinical relevance. Multivariate regression analysis showed that lower SMMI, lower HGS, and low MM were independently associated with poor appetite after adjustment for confounders. Age was an independent factor in only model 4 (Table 3). Neither gait speed

nor diagnosis of sarcopenia was associated with poor appetite in regression analysis models.

Discussion

In this cross sectional study, we documented that poor appetite assessed by SNAQ was independently associated with low MM, lower SMMI and lower HGS in community dwelling older adults. Also, in univariate analysis, low gait speed, diagnosis of sarcopenia, depression, lower quality of life, and constipation were associated with poor appetite. In multivariate regression analysis, gait speed was not associated with poor appetite. Most probably because of this, diagnosis of sarcopenia was not independently associated with poor appetite in multivariate regression analysis. There was no association between SNAQ and number of medicines and number of chronic diseases.

Previous cross sectional studies gave conflicting results about relationship between poor appetite and components of sarcopenia (9-13). To our knowledge there is no prospective study investigating the relationship between poor appetite and sarcopenia. Among previous cross sectional studies only one study assessed sarcopenia according to the EWSGOP's recommendation including low muscle mass and low muscle function (i.e. low gait speed and/or low muscle strength).This ilSIRENTE study by Landi et al. included 354 community dwelling older adults reported association between anorexia of aging and sarcopenia (9). Usual gait speed and muscle strength were assessed by 4-m course and HGS like our study protocol and they assessed low muscle strength by their national cut-off values similar to our study. However, differently they did not calculate muscle mass via BIA. Instead, they measured mid-arm muscle circumference to assess low muscle mass. They defined anorexia by asking the presence of loss of appetite and/or lower food intake instead of use any formal assessment tool. Similar with our results, gait speed and HGS were lower in their anorexic subjects. They did not perform univariate analysis between mid-arm muscle circumference and anorexia. Finally they found that anorexia is independently associated with sarcopenia in multivariate regression models. However their regression analysis had somewhat difference compared to ours. They performed multivariate regression analysis to find associated factors with "sarcopenia" which were dependent factor in their analysis. We run regression analysis with anorexia as a dependent factor while sarcopenia as an independent factor to predict factors associated with anorexia. Different result may depend on this different regression model. On the other hand, anthropometric measures are vulnerable to error and are not recommended for routine use instead of exact muscle mass measurements by BIA or DXA in the diagnosis of sarcopenia (6). Hence, to our knowledge our study is the first study investigating relationship between poor appetite and sarcopenia defined by EWSGOP criteria.

None of remain studies below assessed three components of sarcopenia together. Among remain studies investigating association of poor appetite and sarcopenia component, a study investigated the association between poor appetite assessed by a different tool [The Council on Nutrition Appetite Questionnaire (CNAQ)] and body composition and HGS in 112 community dwelling older adults >=60 years (10). Similar with our result, authors reported that CNAQ was associated with HGS. Unlike our study, they did not calculate SMM or SMMI. Instead they use "muscle mass (kg)" determined by BIA. Mean muscle mass (kg) was lower in group with anorexia. But these associations with anorexia were disappeared in regression analyses after adjustment for confounders.

In Japanese validation study of SNAQ, similar with our study, authors observed that SNAQ score was correlated with parameters of physical performance including gait speed,chair stands time, and Timed Up and Go test in 84 community dwelling older adults (11). SNAQ was correlated with HGS (r=0.19, p=0.08) but this was not statistically significant. However, in this study regression analysis was not performed.

Similar with our study, Dent et al. reported that SNAQ score was correlated with HGS in hospitalized adults >=70 years old (12) and Pilgrim et al. (13) observed poor appetite assessed by SNAQ at hospital admission was associated with several clinical characteristics including lower grip strength in inpatient female older adults in univariate analysis.

Our study has some strengths and drawbacks. First one is the use of national cut-off values for sarcopenia which EWSGOP recommends, in a study group with larger sample size. Three components of sarcopenia –muscle mass, muscle strength, gait speed- were assessed all. Measurements of body composition, muscle strength, and gait speed were done by the same qualified geriatric physiotherapist that makes the inter-assessor variability minimum. We evaluated various possible associated factors taking into account the results of our recent study with poor appetite then run multivariate regression analysis adjusting for various confounders to investigate independent relationship between poor appetite and components of sarcopenia. On the other hand, because of cross sectional design we could not provide definite information about cause-and-effect relationship.

In conclusion, we reported poor appetite has independent association with lower skeletal muscle mass and decreased muscle strength. Prospective studies are needed to remark definite information regarding the relation.

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Ethical standard: The authors declare that the study procedures comply with current ethical standards for research involving human participants in Turkey. The study protocol had been approved by the ethical committee of Istanbul University, Istanbul Medical School.

Author contributions: This study was designed by all authors. Data were obtained by BI and CK. Statistical analysis was performed by BI, GB and TE. BI, GB and MAK prepared the manuscript. All authors read and approved the final manuscript.

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