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Dietary patterns and their relationships to sarcopenia in Portuguese patients with gastrointestinal cancer: An exploratory study

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Objectives: The purpose of this exploratory study was to identify the main dietary patterns of a Portuguese population of patients with gastrointestinal cancer and to analyze their association with sarcopenia.
Methods: This was a prospective study with a consecutive sample of 100 patients with gastrointestinal cancer enrolled at diagnosis. Dietary intake was assessed with a semiquantitative Food Frequency Questionnaire, and dietary patterns were obtained with principal component analysis. Nutritional assessment was done using the Patient-Generated Subjective Global Assessment, and body composition was evaluated with anthropometric measures and computed tomography image processing obtained at the third lumbar vertebrae. Sex and body mass index specific cutoffs were used to define sarcopenia.
Results: Four major patterns were identified: high-fat dairy products, fried snacks, and processed meat diet; legumes, vegetables, and fruit diet; fat and fish diet; and alcohol, cereal, and animal protein diet. On simple logistic regression, the occurrence of sarcopenia in participants in the second tertile (odds ratio [OR] 0.30; 95% confidence interval [CI] 0.10–0.83; $P = 0.02$) and third tertile (OR 0.24; 95% CI 0.08–0.69; $P = 0.01$) of adherence to the high-fat and fish diet was reduced compared with the first tertile. On multiple logistic regression, the second tertile (OR 0.38, 95% CI 0.11–1.19; $P = 0.10$) of the fat and fish dietary pattern maintained a trend toward a reduction of the odds of sarcopenia compared with the first tertile, independently of calorie intake, age, disease location, and stage.
Conclusions: The fat and fish dietary pattern was associated with lower odds of sarcopenia in this population of patients with gastrointestinal cancer.

Introduction

Cancer cachexia is a highly prevalent multifactorial syndrome characterized by ongoing muscle loss, with or without fat loss [1]. Sarcopenia (severe muscle depletion) is a key feature of cancer cachexia and affects 26% to 78.7% of gastrointestinal (GI) cancer patients [2,3]. Sex and body mass index (BMI) specific cutoffs for computed tomography (CT)–derived skeletal muscle index have been previously reported to define sarcopenia [4]. It is well established that sarcopenia is associated with a worse outcome, and recent research has focused on feasibility and effects of diet and exercise on body composition [5–9], but scientific evidence is still lacking.

Previous studies have reported the following: 1) cancer patients are able to maintain protein synthesis provided they receive a higher amount and type of protein or amino acids [10,11]; 2) ω-3 polyunsaturated fatty acids may be linked to skeletal muscle maintenance

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[12]; and 3) cancer patients maintain a capacity for muscle anabolism even until advanced stages [13], suggesting an opportunity for nutritional status optimization through dietary intervention.

Given the known effects of single nutrients on skeletal muscle and that dietary patterns may actually be more relevant than single nutrient intake, because of an expected synergistic effect of foodstuffs consumed, we hypothesized that dietary patterns could be linked to the odds of cancer-related sarcopenia.

Materials and methods

Study population

The study protocol was approved by the Scientific and Ethics Committee of Hospital Beatriz Ângelo in Loures, Portugal. From October 2014 to December 2015 a total of 100 outpatients age 18 or older, with a recent diagnosis of GI cancer and untreated, were consecutively enrolled in this prospective study. Informed consent was obtained. Clinical data were prospectively collected from electronic charts; however, the present study reports on baseline data. Data were coded to maintain pseudo-anonymity. Variables concerning disease location were categorized as hepatic-biliary-pancreatic cancer or upper (esophagus, gastric) and lower (colorectal cancer) GI. Disease stage was dichotomized in stages I, II, and III versus stage IV disease for non-metastatic and metastatic disease, respectively.

Performance status was assessed with the Eastern Cooperative Oncology Group Performance Status scale [14] and quality of life with the European Organization for Research and Treatment of Cancer Version 3.0 questionnaire [15]. Physical activity was assessed with the International Physical Activity Questionnaire [16], previously validated for the Portuguese population.

Body weight was measured with a digital scale (SECA) and height with a stadiometer. BMI was calculated and BMI classification was done according to the following categories: <20.0, underweight; 20.0 to 24.9, normal weight; 25.0 to 29.9, overweight; and 30.0 kg/m^2, obese. Patient-generated Subjective Global Assessment (SGA) assessment [17,18] was conducted by a single experienced dietitian (S.V.), and patients were classified as well nourished (SGA A), moderately malnourished or suspected of being malnourished (SGA B), or severely malnourished (SGA C).

Because CT imaging is part of the clinical staging of GI cancer patients, CT images were used for body composition analysis. CT methods are highly precise to quantify specific tissues and to predict whole-body composition [16]. Images were selected by radiologists at the third lumbar vertebra (L3) using a portal venous phase and were processed with specific software that performed an automatic segmentation of tissue cross-sectional areas, with manual corrections by the radiologist. Segmentation of tissue cross-sectional areas was conducted according to the following Hounsfield unit thresholds: −29 to 150 for skeletal muscle, −190 to −30 for subcutaneous and intramuscular adipose tissue, and −50 to −150 for visceral adipose tissue. Cross-sectional skeletal muscle, visceral fat, and subcutaneous fat were recorded in centimeters squared and mean muscle radiation attenuation in Hounsfield units. Skeletal Muscle Index (cm^2 / height^2) was calculated. Sex-specific cutoffs for Skeletal Muscle Index and muscle radiation attenuation as defined by Martin et al. [4] were used to define sarcopenia and low muscle radiation attenuation because there are no published cutoffs for the Portuguese population.

Dietary intake

Dietary intake was assessed with a semiquantitative food frequency questionnaire developed for the Portuguese population [19,20]. This questionnaire includes 86 commonly eaten food or drinks, and participants were asked to estimate the amount and frequency of intake of each food and drink according to frequency and amount. Conversion of foodstuffs to nutrients was conducted with Food Processor Plus software (ESHA Research, Salem, OR, USA) adapted to Portuguese commonly eaten food and drinks. This questionnaire was filled out during the interview with the dietitian.

Statistical analysis

Data analysis was performed with SPSS Version 20 (IBM Corp., Armonk, NY) and R Version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria), and statistical significance was set at $P \leq 0.05$.

Shapiro-Wilk's test was used to test for the adjustment of continuous variables to the normal distribution and differences in means were analyzed by *t* test or Mann-Whitney *U* test as appropriate. The association between categorical variables was tested with χ^2 test. Analysis of covariance was conducted to test for differences in mean dietary intakes while adjusting for BMI.

A total of 86 food items were categorized in 23 food groups (Table 1) according to their nutritional composition similarity. Principal component analysis (PCA) with varimax rotation was performed as previously described [21,22]. The suitability of the data for PCA was analyzed with Kaiser-Meyer-Olkin and Bartlett's test of sphericity. The Kaiser-Meyer-Olkin, a measure of sampling adequacy for PCA, was 0.61, which is greater than the established cutoff of 0.5, indicating that PCA could be performed [23]. Barlett's test, which tests the null hypothesis that the correlation matrix is an identity matrix, was statistically significant (<0.001), thereby indicating that variables are correlated and PCA is appropriate. The decision to retrieve dietary patterns was based on an eigenvalue >1, visual scree plot analysis, and interpretability [23]. Food groups were considered as relevant to a dietary pattern if the loading coefficient was >0.3 [24]. The score of each participant to each specific dietary pattern was computed with SPSS during PCA analysis, which was converted to percentiles and categorized in tertiles.

Table 1
Food groupings for dietary pattern analysis

Food group	Examples
Processed meat	Sausage, bacon, ham
Animal protein	Eggs, chicken, turkey, rabbit, pork, cow, liver, cow's tongue
Fish	Sardines, cod fish, tuna, squid, octopus, shrimp
Low-fat dairy products	Skim milk, low-fat milk, low-fat yogurt
High-fat dairy products	Whole milk, desserts, ice cream
Vegetables	Cabbage, broccoli, cauliflower, green beans, carrots, onions, turnip, tomato
Fresh fruits	Pear, apple, orange, banana, kiwi, strawberry, cherries, peach, fig
Low sugar drinks	Tea, coffee
High sugar drinks	Commercial fruit juice, cola, commercial iced tea
Alcohol drinks	Beer, wine, whiskey
Legume	Chickpea, kidney bean, black-eyed beans
Potato	
Cereal derived	Whole-grain bread, pasta, rice, cereals
Nuts	
Olive oil	Olive oil, olives
Sugar	
High-fat snacks	Cookies, chocolates
Processed fruit	Jam, marmalade, canned fruit
Margarine	
Butter	
Plant oil	
Portuguese fried snacks	Fried codfish cakes, croquettes, *rissois*
Soup	
Fast food	Pizza, french fries, hamburger, ketchup

Simple logistic regression was used to relate each variable with sarcopenia. For continuous variables, linearity of the logit in the predictor was assessed using a cubic spline and Wald's test of linearity [25]. Because for age linearity was not clear on cubic spline graphs (*P* value of Wald's test of linearity was 0.15), this variable was categorized as younger than 70 years and 70 years or older. Only variables with $P \leq 0.25$ or considered clinically relevant were selected for multiple logistic regression. Two multiple logistic regression models were adjusted without automatic stepwise variable selection because with this method, important variables, such as calorie intake and disease location, were discarded. Multicollinearity was also analyzed through the observation of variance inflation factors. Receiver operating characteristic (ROC) curves were computed and the respective area under the curve (AUC) was calculated to assess accuracy of both models. The positive predictive value and the negative predictive value were also given.

Because assumptions of analysis of variance failed—namely, homogeneity of variances (tested with Levene's test) or adjustment of the dependent variable to a normal distribution within each tertile (graphical analysis of P-P plots of studentized residuals)—a Kruskal-Wallis test was used to test for differences between the means of continuous variables and tertiles of adhesion to the fat and fish diet. Post hoc multiple comparisons were conducted with pairwise analysis.

Results

Characteristics of the studied population

Table 2 presents demographic characteristics of the studied population. A total of 32% of patients presented with sarcopenia. Sarcopenic patients were older and had a more advanced disease stage, worse performance status, and lower mean BMI. Regarding BMI categories, both normal weight and overweight had the highest percentage of sarcopenic patients. In respect to dietary intake we found that sarcopenic patients had a significantly lower total calorie, protein, and fat daily intake, whereas no difference was

Table 2
General characteristics of participants

Variables	Total (n = 100)	Sarcopenic (n = 32)	Nonsarcopenic (n = 68)	P	OR	95% CI	P
Age	69.49 ± 11.15	69.92 ± 10.64	67.53 ± 10.9	0.003	1.05	1.01– 1.10	0.01
Age categorized							
<70 (y)	50 (50%)	10 (31.2%)	40 (58.8%)	0.010	1.00		
≥70 (y)	50 (50%)	22 (68.8%)	28 (41.2%)		3.14	1.31–7.912	0.01
Sex							
Female	34 (34%)	11 (34.4%)	23 (33.8%)	0.957	1.00		
Male	66 (66%)	21 (65.6%)	45 (66.2%)		0.97	0.40–2.41	0.95
Disease location							
Upper GI	37 (37%)	9 (28.1%)	28 (41.2%)	0.276	1.00		
Lower GI	54 (54%)	21 (65.6%)	33 (48.5%)		1.97	0.79– 5.19	0.15
Hepatic-biliary-pancreatic	9 (9%)	2 (6.2%)	7 (10.3%)		0.88	0.11– 4.53	0.89
Disease stage							
Nonmetastatic	76 (76.0)	20 (62.5%)	56 (82.4%)	0.03	1.00		
Metastatic	24 (24.0)	12 (37.5%)	12 (17.6%)		2.80	1.08–7.32	0.03
High GI obstruction*							
No	74 (74%)	26 (81.2%)	48 (70.6%)	0.26	1.00		
Yes	26 (26%)	6 (18.8%)	20 (29.4%)		0.55	0.18– 1.48	0.26
Smoking habits							
No	82 (82%)	27 (84.4%)	55 (80.9%)	0.67	1.00		
Yes	18 (18%)	5 (15.6%)	13 (19.1%)		0.78	0.23–2.31	0.67
Performance status							
0	35 (35.4%)	11 (34.4%)	24 (35.8%)	0.06	1.00		
1	37 (37.4%)	8 (25.0%)	29 (43.3%)		0.60	0.20– 1.72	0.34
2	15 (15.2%)	5 (15.6%)	10 (14.9%)		1.09	0.28–3.89	0.89
3	11 (11.1%)	7 (21.9%)	4 (6.0%)		4.36†	1.12–19.41	0.04
4	1 (1.0%)	1 (3.1%)	0 (0%)				
Quality of life							
Function	52.50 ± 24.24	54.39 ± 23.94	51.5 ± 24.78	0.592	1.00	0.98– 1.02	0.58
Symptoms	33.56 ± 23.07	35.88 ± 22.09	32.42 ± 23.62	0.314	1.00	0.98– 1.02	0.48
Global score	47.91 ± 21.76	44.79 ± 25.64	49.47 ± 19.57	0.367	0.98	0.97–1.00	0.31
Patient-generated Subjective Global Assessment							
Well nourished	27 (27%)	7 (21.9%)	20 (29.4%)	0.579	1.00		
Severely Malnourished	34 (34%)	13(40.6%)	21 (30.9%)		1.26	0.43– 3.95	0.66
Moderately Malnourished	39 (39%)	12 (37.5%)	27 (39.7%)		1.76	0.59–5.55	0.31
Physical activity							
Low physical activity	60 (60%)	22 (68.8%)	38 (55.9%)	0.220	1.00		
Moderate physical activity	40 (40%)	10 (31.2%)	30 (44.1%)		0.57	0.22–1.37	0.22
Body mass index (kg/m^2)	26.08 ± 5.4	24.2 ± 3.7	26.9 ± 5.9	0.03	0.89	0.81–0.97	0.02
Body mass index							
Low weight	6 (6%)	2 (6.2%)	4 (5.9%)	0.005	1.00		
Normal weight	42 (42%)	13 (40.6%)	29 (42.6%)		0.89	0.15– 7.05	0.90
Overweight	31 (31%)	16 (50.0%)	15 (22.1%)		2.13	0.36– 17.05	0.41
Obesity	21 (21%)	1 (3.1%)	20 (29.4%)		0.10	0.004–1.27	0.09
Dietary intake							
Calorie intake (kcal/d)	2782.3 ± 889.0	2451.6 ± 803.1	2937.9 ± 890.2	0.013	0.99	0.998–0.999	0.01
Calorie intake (kcal/kg)	41.1 ± 14.6	37.3 ± 12.6	43.0 ± 15.1	0.07	0.97	0.93– 1.00	0.07
Protein(g/d)	105.5 ± 33.3	93.9 ± 34.2	111.0 ± 31.7	0.01	0.98	0.96– 0.99	0.02
Protein (g/kg)	1.56 ± 0.6	1.42 ± 0.5	1.63 ± 0.6	0.08	0.51	0.21– 1.09	0.09
Carbohydrates (g/d)	290.3 ± 106.9	277.7 ± 103.5	296.2 ± 108.8	0.261	0.99	0.99– 1.00	0.42
Carbohydrates (g/kg)	4.3 ± 1.7	4.2 ± 1.5	4.37 ± 1.5	0.674	0.94	0.72–1.20	0.63
Fat (g/d)	125.7 ± 49.25	103.1 ± 44.64	136.3 ± 48.0	0.001	0.98	0.97– 0.99	0.003
Fat (g/kg)	1.9 ± 0.8	1.6 ± 0.7	2.0 ± 0.8	0.01	0.47	0.24– 0.85	0.02
High-fat dairy products, fried snacks, and processed meat diet							
First tertile	33 (33%)	9 (28.1%)	24 (35.3%)	0.12	1.00		
Second tertile	33(33%)	15 (46.9%)	18 (26.5%)		2.22	0.80–6.39	0.12
Third tertile	34 (34%)	8 (25.0%)	16 (38.2%)		0.82	0.26–2.48	0.72
Legumes, vegetables, and fruit diet							
First tertile	33 (33%)	13 (40.6%)	20 (29.4%)	0.53	1.00		
Second tertile	33(33%)	9 (28.1%)	24 (35.3%)		0.57	0.19–1.61	0.29
Third tertile	34 (34%)	10 (31.2%)	24 (35.3%)		0.64	0.22–1.76	0.39
High-fat and fish diet							
First tertile	33 (33%)	17 (53.1%)	16 (23.5%)	0.01	1.00		
Second tertile	33(33%)	8 (25.0%)	25 (36.8%)		0.30	0.10–0.83	0.02
Third tertile	34 (34%)	7 (21.9%)	27 (39.7%)		0.24	0.07–0.69	0.01
Alcohol, cereal, and animal protein diet							
First tertile	33 (33%)	11 (34.4%)	22 (32.4%)	0.92	1.00		
Second tertile	33(33%)	11 (34.4%)	22 (32.4%)		1.00	0.35–2.80	1.00
Third tertile	34 (34%)	10 (31.2%)	24 (35.3%)		0.83	0.29–2.35	0.73

CI, confidence interval; GI, gastrointestinal; OR, odds ratio
Results expressed as mean ± standard deviation or number (percentage)
ORs and 95% CIs from simple logistics regression with sarcopenia as dependent variable
*Performance status categories 3 and 4 were merged to allow 95% CI determination.
†Patients classified as having GI obstruction presented endoscopic documentation of high GI stenosis and clinical manifestations of stenosis such as dysphagia for solid foods, regurgitation, or vomiting.

Table 3
Factor loading matrix for main dietary patterns

Variables	High-fat dairy products, fried snacks, and processed meat diet	Legumes, vegetables, and fruit diet	Fat and fish diet	Alcohol, cereal, and animal protein diet
High-fat dairy products	0.877			
Portuguese fried snacks	0.846			
Processed meat	0.791			
Nuts (with and without salt)	0.346			
Legumes		0.828		
Vegetables		0.805		
Potatoes		0.464		
Soup		0.424		
Fresh fruit		0.319		
Olive oil			0.751	
Butter			0.728	
High-fat snacks			0.381	
Fish			0.344	
Alcoholic drinks				0.776
Cereal-derived products				0.627
Fast food				0.551
Animal protein				0.424
% of variance explained	12.2	9.4	7.8	7.8

Values <0.30 were excluded for simplicity

found for carbohydrate intake. After adjusting for BMI, differences in calorie ($P = 0.013$), protein ($P = 0.013$), and fat ($P = 0.002$) remained statistically significant, whereas differences in carbohydrate ($P = 0.454$) intake remained non-significant.

Dietary patterns

Four major patterns were identified with PCA: high-fat dairy products, fried snacks, and processed meat diet; legumes, vegetables, and fruit diet; fat and fish diet; and alcohol, cereal, and animal protein diet. These patterns explained 37.2% of the overall variance. The first pattern was defined with food stuffs such as high-fat dairy products, fried Portuguese snacks, processed meat, and nuts (with or without salt), which presented high loadings (>0.3). The second pattern had high loadings for legumes, vegetables, potatoes, soup, and fresh fruit. The third pattern had high loadings for olive oil, butter, high-fat snacks (cookies and chocolates), and fish. The fourth pattern had high loadings for alcoholic drinks, cereal-derived products, fast food, and animal protein. Table 1 shows food groupings for dietary pattern analysis and Table 3 summarizes the results from PCA.

Dietary patterns and sarcopenia

Simple logistic regression was performed to explore which variables are associated with sarcopenia. The results of this analysis are presented in Table 2. This analysis indicated that patients with higher odds of sarcopenia were older, had worse performance status, and had more advanced disease stage, whereas calorie intake was associated with lower odds of sarcopenia. Regarding dietary patterns, patients in the second and third tertiles of adhesion to the fat and fish pattern presented significantly lower odds of sarcopenia. No association was found with other patterns.

Because the fat and fish diet was the only pattern with a significant association with sarcopenia, multiple logistic regressions focused on this pattern. Table 4 reports on the results from multiple logistic regressions. Interpretation of the variables was done considering that the participants had the same values on all variables, except for the one being compared. In model I we adjusted for age, fat and fish pattern, and calorie intake. According to this analysis the odds of sarcopenia were almost three times greater in patients with age ≥70 compared with patients with age <70. The odds of sarcopenia were reduced in 67% in patients in the second tertile and 68% in the third tertile, compared with the first tertile of adhesion to the fat and fish diet, independently of calorie intake.

Table 4
Models I and II for sarcopenia as dependente variable obtained with multiple logistic regression

	Model I			Model II		
Variables	OR	95% CI	*P*	OR	95% CI	*P*
Disease location	Not included					
Upper GI				1.00		
Lower GI				1.75	0.62–5.13	0.28
Hepatic-biliary-pancreatic				0.58	0.06–3.69	0.59
Disease stage	Not included					
Non-metastatic				1.00		
Metastatic				3.4	1.13–10.87	0.03
Age						
<70	1.00			1.00		
≥70	2.83	1.09– 7.71	0.03	3.2	1.17–9.23	0.03
Fat and fish diet						
First tertile	1.00			1.00		
Second tertile	0.33	0.10– 0.98	0.05	0.38	0.11–1.19	0.10
Third tertile	0.32	0.08–1.18	0.08	0.45	0.11–1.84	0.26
Calories	0.99	0.99–1.00	0.38	0.99	0.99–1.00	0.37

CI, confidence interval; GI, gastrointestinal; OR, odds ratio

Model II further adjusts for clinical variables—namely, disease location, disease stage, age, and calorie intake. Again the odds of sarcopenia was three times higher in patients age ≥70, compared with patients age <70. Besides age, disease stage was the only clinical variable associated with sarcopenia because the odds of sarcopenia were three times greater in patients with metastatic disease compared with non-metastatic patients. Lastly, a trend was found for a reduction of 62% of the odds of sarcopenia for patients in the second tertile of the fat and fish diet compared with the first tertile of adhesion to the fat and fish diet.

The AUC obtained through ROC curve analysis was 0.727 and 0.767 for model I and model II, respectively (Fig. 1). These AUCs indicate a fair discriminatory ability of both models in the prediction of sarcopenia. ROC curves are presented in Figure 1. Sensitivity was 59.4%, specificity was 76.5%, positive predictive value was 20%, and negative predictive value was 45.7% for model I. Sensitivity

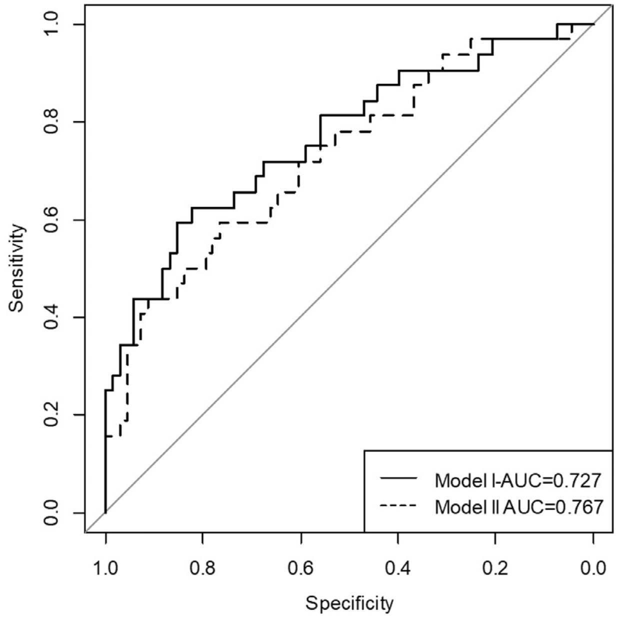

Fig. 1. Receiver operating characteristic curve analysis for models I and II. AUC, area under the curve.

was 62.5%, specificity was 82.4%, positive predictive value was 17.6%, and negative predictive value was 37.5% for model II.

Participant's characteristics according to compliance to fat and fish pattern

Table 5 shows the studied population characteristics across tertiles of adhesion to the fat and fish pattern. According to this analysis, patients did not differ in respect to clinical and anthropometric characteristics and body composition, except for the proportion of sarcopenic patients. Patients with a lower adhesion to the fat and fish pattern had a higher proportion of sarcopenia.

Regarding dietary intake, patients in the second tertile were characterized as having a similar calorie and protein intake normalized by body weight and carbohydrate intake as patients in the first tertile. The main difference was a higher lipid intake, but not as high as identified for the third tertile and the highest monounsaturated + polyunsaturated fat/saturated fat ratio. Also, patients in the second tertile had an energy intake predominantly >30 kcal/kg and a high lipid intake (only one patient had a lipid intake <30% of total calorie intake), and a higher proportion of patients were within the European Society of Parenteral and Enteral Nutrition recommendations of protein intake.

Discussion

To our knowledge this is the first study examining the relationship between dietary patterns and sarcopenia in a population of GI cancer patients. We identified four dietary patterns, but only the fat and fish diet was associated with a lower odds of sarcopenia.

After the seminal paper of Martin et al. [4], several other studies have clearly found that alteration in body composition—namely, sarcopenia—in cancer patients is a very important prognostic marker [26], with a high discriminant power regarding long-term survival [4]. However, the most effective way of tackling these alterations with the aim of improving final outcome is less clear.

Four main dietary patterns were identified in this prospective study: high-fat dairy products, fried snacks, and processed meat pattern; legumes, vegetables, and fruit pattern; fat and fish pattern; and alcohol, cereal, and animal protein pattern. Total variance of dietary intake was mostly explained by a dietary pattern characterized by the first pattern, and no explicit Mediterranean dietary pattern (MDP) was found.

Although in the 1960s Portugal was known to have an MDP [27], according to the results of the National Portuguese Report of Dietary Intake and Exercise, MDP is becoming less predominant and only 12% of the Portuguese population are highly compliant with the MDP [28]. This shift in the dietary intake paradigm supports the findings in our study, in which MDP was not explicit, but still foods from MDP were found.

In our study the fat and fish pattern was the only pattern exhibiting a protective effect in regard to sarcopenia. This pattern correlated highly with olive oil, which is a source of monounsaturated fatty acids (MUFA); butter and high-fat snacks, which are sources of saturated fatty acids; and fish, which provides both protein and polyunsaturated ω-3 fatty acids and was associated with calorie intake. Interestingly, a trend was found for reduced odds of sarcopenia for patients in the second tertile of the fat and fish dietary compared with the first tertile, independently of calorie intake, age, disease location, and stage. Patients in the second tertile had a higher percentage of compliance to the target supply of 1.2 to 2 g protein/kg/day, a fat intake higher than general recommendations but also a higher monounsaturated + polyunsaturated fat (PUFA)/saturated fat ratio. In other words, this pattern consisted of a nutrient- and energy-dense diet that may be protective of muscle loss. It is worth pointing out that high-fat snacks such as cookies and chocolate also contributed to this association. We hypothesized that these foodstuffs, if consumed within a dietary pattern with healthy fat sources, may facilitate an adequate calorie intake and a balanced overall lipid intake (MUFA + PUFA/saturated fat) depending on the amounts consumed. In our study, patients in the second tertile of the fat and fish diet presented the highest mean MUFA + PUFA/saturated fat ratio.

There is some evidence that in cancer patients lipid oxidation may be normal or increased [29], and according to our results, a higher fat intake may be needed to reduce the odds of sarcopenia. Most studies have focused on the effect of PUFA intake in cancer cachexianamely, ω-3 PUFAs, which have been found to have a beneficial effect in the treatment of age-related sarcopenia [30] and cancer-associated muscle wasting [10,31,32]. Eicosapentaenoic acid (EPA) is thought to improve anabolism by increasing protein synthesis and muscle sensitivity to insulin, but it has also been found to inhibit muscle degradation by down-regulation of acute phase response and by decreasing the expression of proteasome subunits [33].

It has been hypothesized that oleic acid may also be important for muscle health. Data from an animal model of muscular dystrophy (Mdx mice) suggest that high MUFA may assist muscle in coping with this pathologic condition. In Mdx mice, high oleic acid intake was associated with reduced serum creatine kinase compared with high PUFA intake [30]. Conflicting results have been reported regarding MUFA effect on cancer cells [34,35].

Still, studies concerning the relationship of dietary patterns and cancer-related sarcopenia are lacking. A cross-sectional study in Iranian community-dwelling elderly adults, which addressed the association between dietary patterns and sarcopenia, found that a higher adherence to a dietary pattern consistent with the Mediterranean diet (higher consumption of olive oil, fruits, vegetables, fish, and nuts) was associated with a lower odds of age-related sarcopenia [21], which is in line with our results. In a recent systematic review, the authors conclude that there is some cross-sectional evidence of an association between diet quality and the odds of sarcopenia [36].

Table 5
Fat and fish diet and participants' clinical characteristics, anthropometric measures, body composition, and dietary intake

Variables	Fat and fish diet First tertile(n = 33)	Second tertile(n = 33)	Third tertile(n = 34)	P
Age				
<70	15 (30.0)	17 (34.0)	18 (36.0)	0.810
≥70	18 (36.0)	16 (32.0)	16 (32.0)	
Sex				
Female	14 (41.2)	9 (26.5)	11 (32.4)	0.417
Male	19 (28.8)	24 (36.4)	23 (34.8)	
Disease location				
Upper GI	11 (23.9)	18 (39.1)	17 (37.0)	0.190
Lower GI	22 (40.7)	15 (27.8)	17 (31.5)	
Disease stage				
<IV	22 (28.9)	24 (31.6)	30 (39.5)	0.102
IV	11 (45.8)	9 (37.5)	4 (16.7)	
Physical activity				
Low	30 (33.7)	27 (30.3)	32 (36.0)	0.250
Moderate	3 (27.3)	6 (54.5)	2 (18.2)	
Anthropometric measures				
Weight loss	5.29 ± 9.4	3.82 ± 6.2	2.00 ± 7.8	0.292
BMI	25.7 ± 5.6	26.3 ± 4.5	26.2 ± 6.2	0.866
Arm circumference	27.5 ± 3.7	28.2 ± 3.7	28.0 ± 3.67	0.707
Triceps skinfold	19.1 ± 9.9	18.61 ± 7.3	20.1 ± 9.1	0.793
Waist circumference	96.7 ± 12.7	97.8 ± 12.8	96.1 ± 15.9	0.880
Body composition				
Skeletal mass area				
Female	104.3 ± 15.4	106.3 ± 16.7	108.9 ± 21.7	0.918
Male	136.0 ± 30.2	148.82 ± 28.5	145.03 ± 23.4	0.353
Skeletal mass index				
Female	43.4 ± 8.1	45.5 ± 6.3	44.5 ± 7.2	0.684
Male	47.9 ± 10.3	52.2 ± 9.3	51.5 ± 9.6	0.264
Sarcopenia	17 (17%)	8 (8%)	7 (7%)	0.013
Muscle attenuation	28.8 ± 9.8	29.5 ± 8.5	31.2 ± 8.7	0.528
Low muscle attenuation	29 (29%)	30 (30%)	29 (29%)	0.779
Visceral fat area	165.3 ± 112.1	200.5 ± 89.4	158.1 ± 126.6	0.100
Subcutaneous fat area	149.5 ± 91.4	159.7 ± 67.2	178.9 ± 126.2	0.648
Total fat area	314.81 ± 174.9	360.2 ± 137.7	337.1 ± 214.1	0.445
Dietary intake				
Calories (kcal/kg)	35.4 ± 17.1	38.5 ± 10.2	49.3 ± 12.0*	<0.001
Calorie intake (<25 kcal/kg)	11 (33.3%)	2 (6.1%)	0(0%)	<0.001
Calorie intake (>30 kcal/kg)	17 (51.5%)	28(84.8%)	34 (100%)	
Protein (g/kg)	1.4 ± 0.6	1.6 ± 0.4	1.8 ± 0.6†	0.012
Protein intake (1.2–2 g/kg)	14 (42.4%)	22 (66.7%)	20 (58.8%)	0.003
Carbohydrates (g/d)	274.0 ± 116.4	267.3 ± 82.3	328.4 ± 111.0†	0.023
Lipids (g/d)	84.6 ± 42.1*	122.0 ± 28.3*	169.0 ± 33.8*	<0.001
Lipids (% total calorie daily intake)	33.7 ± 8.3*	41.4 ± 6.4	45.9 ± 8.3	<0.001
Lipid intake <30% of total calorie daily intake	12 (85.7%)	1 (7.1%)	1 (7.1%)	<0.001
saturated ratio/saturated ratio	2.0 ± 0.6*	2.5 ± 0.6	2.3 ± 0.3	0.003
Monounsaturated + polyunsaturated/saturated ratio	2.6 ± 0.7*	3.0 ± 0.7*	2.8 ± 0.6*	<0.001

BMI, body mass index; GI, gastrointestinal
*Significantly different from the other groups.
†Pairwise significant difference between the lowest and highest tertile.

Lastly, several limitations must be considered in our study. Because of logistic and budget limitations, we performed an exploratory study, with a consecutive convenience sample. We used a food frequency questionnaire, which is susceptible to under- or overestimation bias but has been validated for the Portuguese population and is useful in dietary patterns determination [37].

In conclusion, the fat and fish pattern was associated with lower odds of sarcopenia in this Portuguese population of patients with GI cancer. We consider that our study has contributed as a first step in unraveling the association between dietary patterns and sarcopenia.

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