Original Article

Association between protein intake and indicators of muscle strength and mass in gastrointestinal and accessory organs of digestion cancer outpatients: a preliminary and cross-sectional study from a single center

Associação entre ingestão proteica e indicadores de força e massa muscular em pacientes ambulatoriais com câncer gastrointestinal e de órgãos acessórios da digestão: estudo preliminar e transversal de um único centro

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ABSTRACT
Introduction: Cancer patients have metabolic and physiological changes that contribute to loss of muscle mass and function. However, adequate protein ingestion before bed combined with lunch is effective on muscle mass and strength in cancer patients. This study aimed i) to identify the distribution of protein in meals throughout the day, and ii) to verify the association between protein intake and indicators of muscle mass and function in gastrointestinal and accessory organs of digestion cancer patients. **Methods:** A cross-sectional study enrolled a total of 115 gastrointestinal and accessory organs of digestion cancer outpatients. Body weight, height, body mass index (BMI), calf circumference, arm circumference, adductor pollicis muscle thickness (APMT), gait speed and handgrip strength (HGS), were collected. The cut-off point used to classify the adequate consumption of protein was set at 30g at the last meal before bed combined with lunch. Differences between groups were tested using the T Student or Chi-Square tests. Logistic regression analyses were done to assess the association between pre-sleep protein and indicators of muscle mass and function. **Results:** Of the 115 patients, 26% had protein intake ≥ 30g at the last meal before bed and lunch (n = 30; 58.5 ± 11.7 years) and 74% had pre-sleep protein intake < 30g (n = 85; 61.9 ± 13.1 years). Association between the ≥30g protein intake and HGS in the crude model (OR: 1.07 95%CI [1.01-1.12], p= 0.005), as well as adjusting for age, sex, treatment type, physical activity, alcohol use, smoking habit, daily protein intake (g/kg), and daily calorie (kcal/d) (OR: 1.12 95%CI [1.0-1.26], p = 0.03) was found. **Conclusion:** In gastrointestinal and accessory organs of digestion cancer outpatients, ≥30 g protein intake at the last meal before bed combined with lunch was positively associated with muscle strength.

RESUMO
Introdução: Pacientes com câncer apresentam alterações metabólicas e fisiológicas que contribuem para a perda de massa e função muscular. No entanto, a ingestão adequada de proteínas antes de dormir combinada com o almoço é eficaz na massa e força muscular em pacientes com câncer. Este estudo teve como objetivo i) identificar a distribuição de proteína nas refeições ao longo do dia e ii) verificar a associação entre a ingestão proteica e indicadores de massa e função muscular em pacientes com câncer gastrintestinal e de órgãos acessórios da digestão. **Método:** Estudo transversal recrutou um total de 115 pacientes ambulatoriais com câncer gastrintestinal e de órgãos acessórios da digestão. Foram coletados peso corporal, altura, índice de massa corpórea (IMC), circunferência da panturrilha, circunferência do braço, espessura do músculo adutor do polegar (EMAP), velocidade da marcha e força de preensão palmar (FPP). O ponto de corte utilizado para classificar o consumo adequado de proteína foi fixado em 30g na última refeição antes de dormir combinada ao almoço. As diferenças entre os grupos foram testadas com os testes t de Student ou Qui-Quadrado. Análises de regressão logística foram feitas para avaliar a associação entre proteína pré-sono e indicadores de massa e função muscular. **Resultados:** Dos 115 pacientes, 26% tiveram ingestão proteica ≥ 30g na última refeição antes de dormir e almoço (n = 30; 58,5 ± 11,7 anos) e 74% tiveram ingestão proteica pré-sono < 30g (n = 85; 61,9 ± 13,1 anos). Foi encontrada associação entre a ingestão de proteína ≥30g e FPM no modelo bruto (OR: 1,07 IC95% [1,01-1,12], p= 0,005), bem como ajuste para idade, sexo, tipo de tratamento, atividade física, uso de álcool, hábito de fumar, ingestão diária de proteínas (g/kg) e calorias diárias (kcal/d) (OR: 1,12 IC 95% [1,0–1,26], p = 0,03). **Conclusão:** Em pacientes ambulatoriais com câncer gastrointestinal e de órgãos acessórios da digestão, a ingestão ≥30 g de proteína na última refeição antes de dormir combinada com o almoço foi positivamente associada à força muscular.

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INTRODUCTION

Cancer is a multifactorial disease that promotes physiological, metabolic, hormonal and inflammatory changes in the body that trigger the loss of muscle mass and function, characterizing the condition of sarcopenia and/or cachexia, which is intensified with physical inactivity, aggressive treatment and age advanced[1,2]. Therefore, it is important to defined strategies that mitigate muscle mass and strength loss, in order to improve the mobility and quality of life of the patient[3-5].

It is known that there are strategies that collaborate to prevent loss of muscle mass and function, preventing severe catabolism, responsible for promoting stress to the body, increasing inflammation, and improving the patient's prognosis. Among these strategies, there is the adequacy of protein consumption[6-9]. However, there is no evidence to prove that the recommendations in the references and consensus that define the daily amount ingested are sufficient to obtain these results, as well as when protein consumption should be boosted[10].

Protein intake have an important role in muscle anabolism. ESPEN's recommendations for cancer patients is that protein intake should be between 1 g to 1.5 g/kg/day[11,12]. However, if timing of ingestion of protein and quantity infer to consequences sarcopenia-related markers is not fully elucidated.

Although, there are studies showing in elderly people that 30g of protein per meal had positive impact on muscle mass loss[13-15], there was no study in cancer patients that evaluated the pre-sleep protein intake and its effects on muscle-related indicators.

Therefore, this study aimed to identify the distribution of proteins in meals throughout the day and to verify the association between the adequate proteins at the last before bed combined with lunch and indicators of muscle mass and strength in patients with gastrointestinal and accessory organs of digestion cancer.

METHODS

Design of Study and Patients

A cross-sectional study was conducted with 115 patients under outpatient in a Public hospital at the Federal University of Goiás for medical treatment and nutritional counseling. This study was approved by the Research Ethical Committee under the number 2.132.915 and all patients agreed to participate in the study signed the consent form in accordance with resolution number 466/12 of the National Health Council. Inclusion criteria were patients of both sexes, with diagnosis of gastrointestinal cancer and accessory organs of digestion cancer, such as the liver, gallbladder and pancreas cancer, age ≥18 years and under medical treatments.

The Figure 1 presents the flowchart of the study.

Data Collection

Body weight and height were measured using a digital scale (Filizola®, São Paulo, Brazil). Body mass index (BMI) (kg/m^2) was calculated using body mass and height. Calf (cm) and arm (mm) circumferences were measured using a flexible tape. Calf circumference was measured at the level of the widest circumference of calf while the participants were standing. Arm circumference was measured at the middle point between the acromion and the olecranon process of

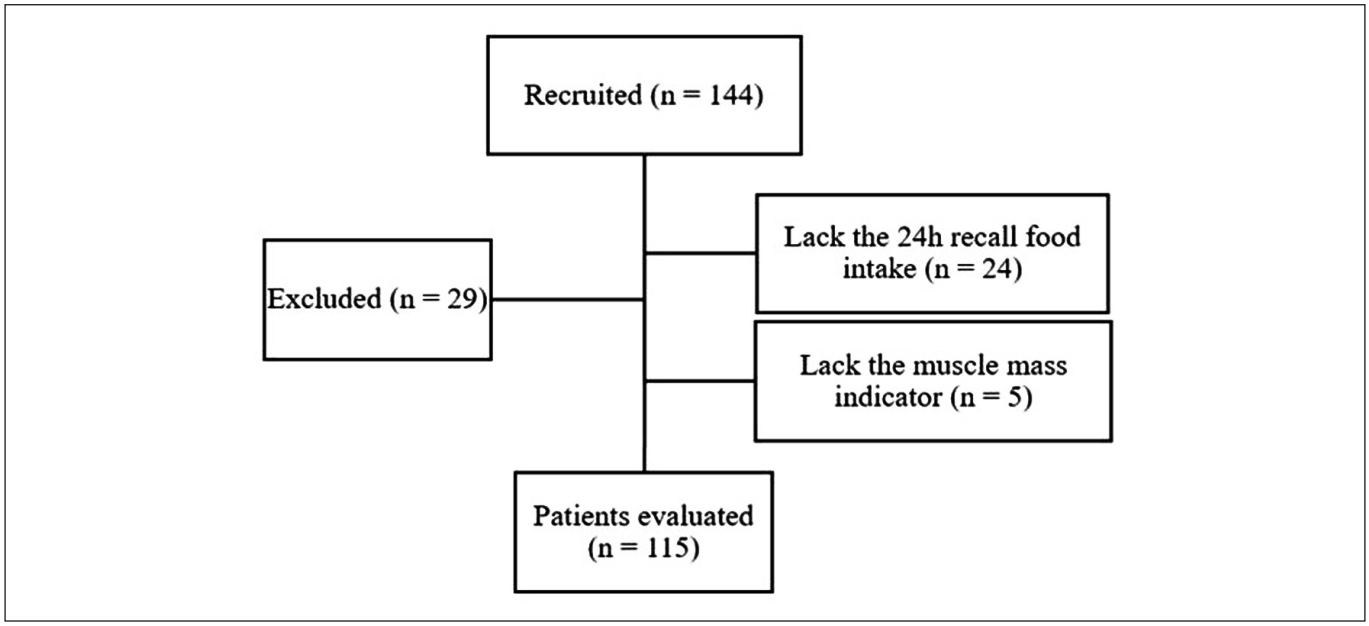

Figure 1 - *Flowchart of the study.*

the non-dominant arm. All measurements were conducted by a trained staff. Gait speed was obtained after instructing patients to walk at their normal speed for four meters in a straight line and the time required to complete the walk was divided by the distance (m/s), being performed twice and considered the fastest walking time, including start-stop time. The handgrip strength (HGS) was obtained by means of a digital dynamometer (Camry®, China). The measurement was made on the patient's dominant hand and three repetitions were performed and the average among them[16,17]. Adductor pollicis muscle thickness (APMT) was measured with a Lange® caliper, the procedure was done on the non-dominant hand, the average of three measurements was considered[18,19].

Food Intake

The dietary intake was evaluated by a 24-h dietary food recall. This tool assessed all the food and beverages consumed by patients on the day before the consultation with nutritionist. The food consumption there were varied, some consumed an exclusive oral diet, others an exclusive enteral diet, others having an association of oral and enteral nutrition diet, and those who received an oral diet were sometimes supplemented with oral nutritional therapy. The calculus of total calories and proteins was analyzed by means of a specialized software (Dietpro® - version 5.8, Viçosa, MG, Brazil) using the American Food Composition Table (USDA)[20,21]. Additionally, protein intakes per meal were analyzed. Food intake was compiled in four meals: i) in the morning, consisted of breakfast and morning snack; ii) lunch; iii) in the afternoon, consisted of snack; and iv) last meal before bed, consisted of dinner and evening meals, since not all patients had the habit of consuming evening meals. To classify the protein intake, we adopted the cut-off point of ≥30g (if dinner and/or evening meals) as adequate protein at the last meal before bed. In this case, those with adequate protein intake also ingested a high protein ingestion at the lunch[13,15].

Statistical Analyses

The normality of the data was verified using the Shapiro-Wilk test and the MedCalc® software (Belgium, version 11.1.1.0) was used for all analyses. To compare non-parametric variables, the Mann-Whitney U test was used and the Student's t test was used for parametric variables and for categorical variables was used the Chi-Square test. Logistic regression analyses were performed to assess the association between protein intake at the last meal before bed combined with lunch and indicators of muscle mass and strength. We used the crude model-without adjust and model 1-adjusted for age, sex, oncological treatment, physical activity, alcohol use, smoking habit, daily protein intake (g/kg), and daily calorie (kcal/d). The level of statistical significance was set at 5% ($p < 0.05$).

RESULTS

The characteristics of the patients are described in Table 1. We found that 26% of cancer patients had ≥30g protein intake at the last meal (pre-sleep). Consuming ≥30 protein at the last meal before bed combined with lunch had ingested more calories and protein than the <30g protein pre-sleep group (Table 1). In addition, ≥30g protein group ingested higher protein in the lunch and at the last meal before bed than the < 30g protein pre-sleep group (Figures 2 and 3).

Table 1 – Characteristics of patients.

Variables	Protein < 30 g (n=85)	Protein ≥30 (n=30)	p
Age (years) #	61.9 ± 13.1	58.5 ± 11.7	0.20
Sex (n=115)†			0.38
Female	36	10	
Male	49	20	
Alcohol use (n=113)†			0.85
Yes	7	2	
No	78	26	
Smoking habit (n=113)†			0.27
Yes	13	2	
No	72	26	
Current physical activity (n=111)†			0.10
Yes	8	6	
No	75	2	
Treatment type†			
Chemotherapy (n=107)			0.67
Yes	57	20	
No	21	9	
Radiotherapy (n=103)			0.07
Yes	13	9	
No	63	18	
Surgery (n=104)			0.42
Yes	63	25	
No	13	3	
Body mass index (kg/m²)#	20.83 ± 4.87	22.3 ± 4.43	0.15
Calf circumference (cm)#	31.1 ± 5.4	33.3 ± 4.1	0.03*
Arm circumference (cm)#	24.53 ± 5.16	26.09 ± 4.51	0.13
Adductor pollicis muscle thickness (mm)#	8.4 ± 3.4	8.2 ± 4.6	0.88
Handgrip strength (kg)#	22.06 ± 9.17	28.46 ± 9.83	0.002*
Calories (kcal/d)#	1214.7 ± 471.0	2037.6 ± 681.6	<0.0001*
Protein (g/kg)#	0.94 ± 0.64	1.63 ± 0.88	<0.0001*

t Student´s test, †Chi-square.
*p<0.05 was considered as significant.

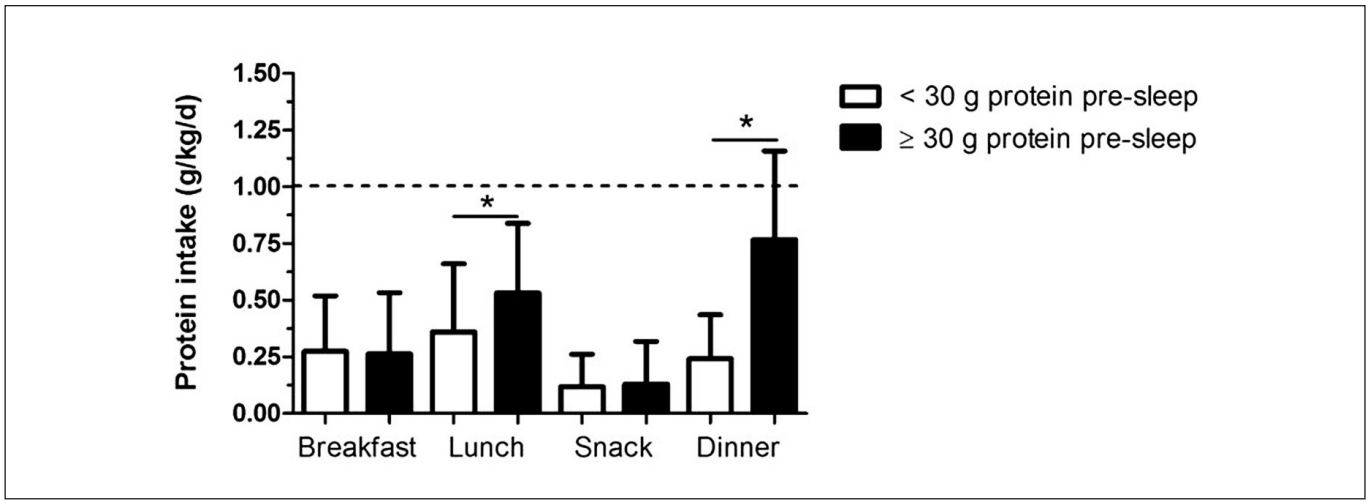

Figure 2 - *Protein (g/kg/d) consumption by meals.*

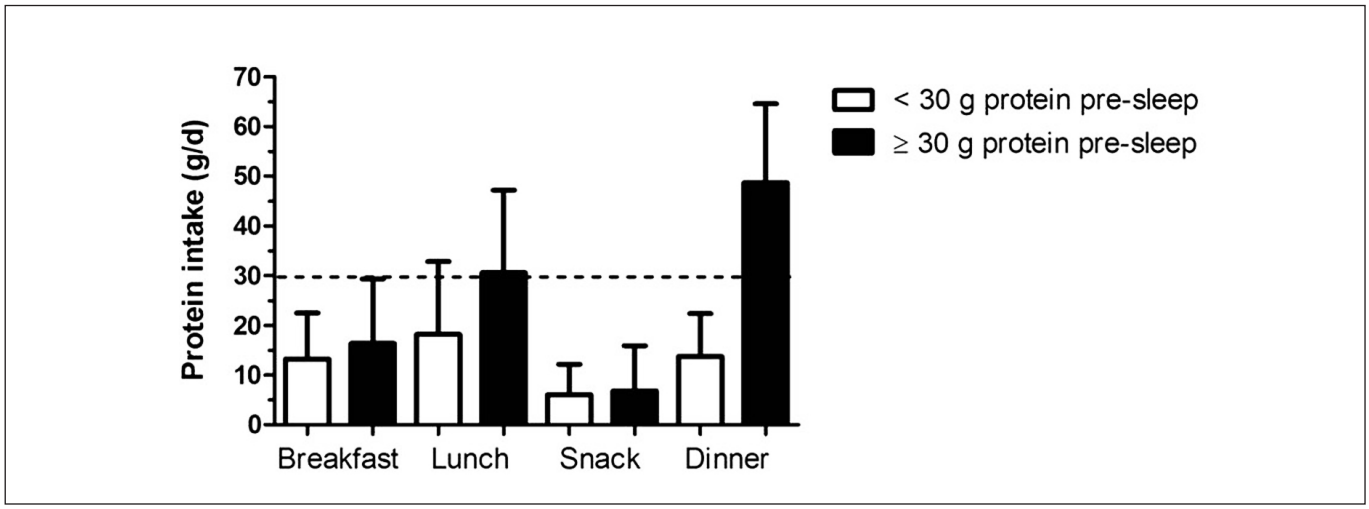

Figure 3 - *Protein (g/d) consumption by meals.*

There was no difference between group for sex, alcohol consumption, smoking, physical activity, treatment type, BMI, and arm circumference. However, ≥30g protein group had higher calf circumference and HGS when compared to <30 protein group (≥30g: 33.3 ± 4.1 vs. <30g: 31.1 ± 5.4 cm, p = 0.03), and (≥30g: 28.4 ± 9.8 vs. 22.06 ± 9.17 kg, p = 0.002) (Table 1).

The logistic regression analyses showed an association between ≥30g protein intake at the last meal before bed combined with lunch and HGS in the crude model (OR: 1.07 95%CI [1.01-1.12], p= 0.005), as well as adjusting for age, sex, treatment type, physical activity, alcohol use, smoking habit, daily protein intake (g/kg), and daily calorie (kcal/d) (Model 1) (OR: 1.12 95%CI [1.0-1.26], p = 0.03) (Table 2). However, no difference was found with indicators of muscle mass (arm circumference, calf circumference, APTM, and gait speed) (Table 2).

Table 2 – Logistic regression between the last meal containing ≥ 30g protein intake and indicators of muscle mass and function.

Variables	Crude OR (95% CI)	Model I OR (95%CI)
Arm circumference	1.06 (0.97-1.16)	1.14 (0.94-1.39)
P value	0.16	0.15
Calf circumference	1.08 (0.99-1.20)	1.13 (0.94-1.35)
P value	0.07	0.18
Adductor pollicis muscle thickness	0.98 (0.88-1.11)	0.84 (0.68-1.03)
P value	0.86	0.11
Handgrip strength	1.07 (1.01-1.12)	1.12 (1.00-1.26)
P value	0.005*	0.03*
Gait speed	2.10 (0.34-11.83)	1.12 (0.07-18.22)
P value	0.43	0.93

Model 1: adjusted for age, sex, surgery, chemotherapy, radiotherapy, physical activity, alcohol use, smoking habit, protein intake (g/kg) and calorie (kcal/d).
*p<0.05 was considered as significant.

DISCUSSION

To our knowledge, this is the first study to examine the relationship between protein intake at the last meal before bed combined with lunch and indicators of muscle strength in gastrointestinal and accessory organs of digestion cancer outpatients. We found that 26% of cancer patients ingested ≥30g of protein at the last meal before bed combined with lunch.

The first aim of the study was to identify the distribution of protein in meals throughout the day, we consider this amount is similar according to studies that consumption of 20-40 g of protein before bed has positive effects on muscle protein synthesis (MPS)[22-24]. However, our study found positive associations between pre-sleep protein intake and muscle strength, indicating a potential protective effect of pre-sleep protein on cancer-induced muscle strength loss.

Considering that there are no studies that relate muscle strength with pre-sleep protein intake and that with an increase in muscle mass there is an increase in strength, Hayashi et al.[13] evaluated the protein intake of elderly individuals and found that the intake of ≥20 g or ≥30 g of protein and that those who consumed at least 2 meals or those rich in protein had a better distribution of protein consumption were associated with muscle mass in the elderly. Similarly, Loenneke et al.[15] assessed the frequency of high-protein meals that adults consumed at least 30g of protein in one diet and found that meals containing 30 to 45g of protein leads to greater association with lean body mass and leg strength. In accordance with this idea study, Buckner et al.[23] evaluated the association between the consumption of protein in the afternoon and at night in different amounts (15, 20, 25 and 30 g) in relation to lean mass and leg muscle strength and found that those who consumed 20g, 25g and 30g of protein at night had greater lean mass, and in relation to strength, only those who consumed 30g of protein had greater leg extensor muscle strength.

In contrast to our study, Trommelen et al.[25] evaluated the impact of 30g of casein protein and 2 grams of leucine pre-sleep on myofibrillar protein synthesis rates during overnight post-exercise recovery in healthy young people, and this protein bedtime did not increase muscle protein synthesis rates. However, unlike our study, this study was carried out in healthy young people and after resistance exercise.

In our study, there was an association between pre-sleep protein intake and increased muscle strength, some studies have suggested that pre-sleep protein has been shown to be effective in increasing muscle protein synthesis, inducing a positive net protein balance muscle overnight, being effectively digested and absorbed and thus increasing the availability of plasma amino acids leading to skeletal muscle hypertrophy[22-27].

It is important to consider this study's limitations. First, is the small sample size. Second, includes the cross-sectional design, rendering a conclusion on temporality not possible. In addition, the data collection was done in a single hospital. Major strengths of this investigation include that we used methods of easy and fast application, and of low cost, that may in the future help in the early detection of comorbidities and nutritional status in hospitalized patients. Also is a limitation that the calf and arm circumferences may not be very sensitive measures for muscle mass like dual-energy X-ray absorptiometry (DEXA) and bioimpedance (BIA), but they were used because are easy-to-apply and low-cost tools.

CONCLUSIONS

In conclusion, we found that in gastrointestinal and accessory organs of digestion cancer outpatients who ingest ≥30 g protein at the last meal before bed combined with lunch had association with muscle strength. Furthermore, we know that the daily calorie and protein intake is necessary for cancer patients, but it appears that not only consuming the daily calorie and protein is important but measuring it by meal as well. However, large cross-sectional studies, prospective and clinical trials are crucial to test the hypothesis if protein (in particular the last meal combined or not with lunch) for cancer patients is essential to attenuate the muscle strength loss during oncological treatment.

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