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Original article

Exploring the dietary protein intake and skeletal muscle during first-line anti-neoplastic treatment in patients with non-small cell lung cancer

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SUMMARY

Background: Loss of skeletal muscle mass is the corner stone of cancer cachexia, but no effective therapies are yet identified. The optimal protein quantity and pattern to support muscle mass maintenance in cancer patients is unknown. The *aim* of the current exploratory study was to observe the pattern and quantity of dietary protein intake as well as the prevalence of muscle wasting in patients with inoperable non-small cell lung cancer (NSCLC) undergoing primary anti-neoplastic treatment. The secondary aim was to assess the potential contributory factors associated with maintenance of muscle mass.
Method: A longitudinal observational study was conducted in patients with NSCLC undergoing first line of anti-neoplastic treatment. Nutrient intake was assessed by repeated 24-h recalls and skeletal muscle by routine thoraco-abdominal CT scans at baseline and after three cycles of treatment. Descriptive analyses, paired samples t-test, binomial logistic and linear regression analyses were performed.
Results: Out of 186 consecutively screened patients, 62 were included and 52 patients were available for analysis. Protein intake increased from baseline to follow up, but were lower in muscle wasters (1.0 g/kg/d) than in muscle maintainers (1.4 g/kg/d). The majority of the meals contributed less than 20 g of protein and less than 10% of the meals contributed at least 40 g of protein. Significant loss of skeletal muscle area was observed in 26 out of 52 patients. A higher protein intake (OR 18.7, $p = 0.01$), energy intake (OR 1.1, $p = 0.04$) and stable body weight (OR 1.2, $p = 0.03$) were associated with muscle maintenance in the univariate regression, whereas age, sex, cachexia, tumour stage, treatment adherence and response did not. In the multivariate regression, a trend was seen for protein intake (OR 35.2, $p = 0.08$) and body weight (OR 1.2, $p = 0.06$).
Conclusion: Muscle wasting occurred frequently and early during primary anti-neoplastic treatment. Protein intake seems important for maintaining skeletal muscle. Validated dietary methods in cancer patients must be identified and the optimal protein quantity and intake pattern to support muscle maintenance should be explored in future trials.

1. Introduction

Low muscle mass has received much attention in the recent years. The negative impact of low muscle mass in cancer patients is well documented and includes increased toxicity from anti-neoplastic treatment, decreased QOL, physical impairment as well as increased risk of death [1–4]. Low muscle mass is the hallmark of cancer cachexia, which is defined as a multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment [5]. The negative energy and protein balance that

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characterizes cachexia is believed to be driven by reduced food intake and/or abnormal metabolism [5]. Nevertheless, the relative contribution of each factor remains undetermined [6].

A disrupted muscle protein turnover has been identified in cancer patients, with reports of a higher protein turnover as a result of blunted muscle protein stimuli and/or exaggerated muscle protein breakdown [7]. An anabolic muscle response to high protein quantities and certain essential amino acids has been shown [8–11]. However, the available literature in relation to habitual protein intake and muscle mass is limited and no studies to date have assessed the pattern of dietary protein intake.

The *aim* of this study was to describe the quantity and distribution of dietary protein intake as well as the rate of skeletal muscle wasting during the first line three cycles of anti-neoplastic treatment in patients with non-small cell lung cancer (NSCLC). The secondary aim was to explore the contribution of demographic, clinical and nutritional factors associated with maintenance of skeletal muscle.

2. Materials and methods

All patients newly diagnosed with NSCLC referred to the Oncology Department, Aalborg University Hospital, were consecutively screened from February to December 2017. If eligible to the study criteria, patients were invited to participate in the prospective observational study.

Patients were eligible if histopathologically or cytologically verified with NSCLC, inoperable tumour, candidates for, but naïve to systemic anti-neoplastic treatment, performance status $\leq$2 (Eastern Cooperative Oncology Group), age >18 and provided oral and written consent. Patients with an excessive alcohol abuse were excluded. Patients were observed from the first cycle until the clinical follow up after three cycles of anti-neoplastic treatment in the outpatient setting.

According to the national guidelines, the standard first-line of anti-neoplastic treatment consisted of palliative platinum-based combination chemotherapy or immunotherapy every three weeks [12]. Curative-intended platinum-based combination chemotherapy was given concurrent with external radiotherapy with 66 Gray/33 fractions 5 days a week starting from the 2nd cycle of chemotherapy [13]. Treatment delay, dose reduction or stop of treatments were registered. Standard supportive and antiemetic care included prednisolone (50 mg daily for three days), ondansetrone (8 mg BID for one day), metoclopramide (10 mg TID for three days) and lorazepam (1 mg TID for one day) for patients receiving chemotherapy. Patients treated with immunotherapy received ondansetrone (8 mg BID for one day) and metoclopramide (10 mg TID for one day). Patients did not receive physical training or dietetic counselling as part of the standard of care, but if hospitalized and severely malnourished, enteral or parenteral nutrition could be initiated.

Dietary intake was assessed at the 1st and 2nd cycle as well as at the clinical follow up after three cycles of anti-neoplastic treatment. A 24-h dietary recall was conducted using a previously described three-step procedure [14]. In short, the dietary interviews were performed face-to-face by clinical dietitians or health care professionals trained for this study. The nutrient intake were quantified by an online nutritional database (VITAKOST® 2006–2018, Denmark). All food, beverages and oral nutritional support were sorted into the corresponding main meals (breakfast, lunch and dinner) or snack times (morning, afternoon and evening snack). The description of the protein meal quantity was presented as absolute (g) and relative (g/kg body weight) protein intake per meal.

Skeletal muscle was estimated from routine thoraco-abdominal diagnostic computed tomography (CT) scans taken approximately 2–3 weeks prior to the 1st cycle (baseline) and approximately 2 weeks prior to the clinical follow up after three cycles of treatment. The skeletal muscle cross-sectional area (cm^2) and total fat area (cm^2) were quantified from CT images at the 3rd lumbar vertebra (L3) using a semi-automatic software (VikingSlice, Denmark, 2018) [15]. Skeletal muscle area was identified by using standard Hounsfield Unit (HU) threshold of −29 to +150 HU and fat area by HU of −190 to −30 [16]. Two observers (a radiologist and an oncologist) identified systematically the L3 vertebrae and selected the CT image at the middle of the 3rd vertebrae for analysis. They reviewed and manually edited areas misclassified by the algorithm and delineated intramuscular fat. The quantification of lean body mass and fat mass was performed automatically by VikingSlice software using algorithms proposed by Mourtzakis et al. [17]. Absolute changes in skeletal muscle and fat area (cm^2) were calculated from CT scans at baseline and the clinical follow up. The skeletal muscle was normalised for stature (cm^2/m^2). The minimal detectable change of muscle and fat area is approximately 3 cm^2 [17,18]. Maintenance of skeletal muscle area was defined as ±5.9 cm^2, while significant loss or gain of skeletal muscle was defined as $\geq$6 cm^2 in either direction [18,19].

Demographic and clinical data, including C-reactive protein (CRP) and serum albumin, were obtained from patient charts. The inflammation-based prognostic score, a modified version of the Glasgow Prognostic Score (mGPS), was calculated as described by Proctor et al. [20]. The cachexia criteria were based on the criteria described by Fearon et al. [5], whereas pre-cachexia was defined as any weight loss $\leq$5% and presence of anorexia (patient-reported). Treatment response was based on clinical and thoraco-abdominal CT evaluation after three cycles of anti-neoplastic treatment. Nutrition impact symptoms (NIS) were assessed by the symptom assessment in the Patient Generated-Subjective Global Assessment short form [21].

All study data were collected and managed using REDCap electronic data capture tools hosted at Aalborg University Hospital [22]. Data were handled in accordance with Danish legislation and Good Clinical Practise. The study protocol was approved by the North Jutland Ethics Board (N-20160018) and conducted according to the Declaration of Helsinki. Written consent was obtained from the patients prior to inclusion.

2.1. Statistical analysis

Demographic and descriptive nutrient intake data were summarized by means and standard deviations, median and range, or absolute numbers. Changes in the nutrient intake between visits were assessed by Friedman's test. Differences in the relative protein intake (g protein/kg body weight) between the visits were further analysed by paired samples t-test. Inter-observer reliability of the skeletal muscle estimates were assessed by comparing the results from the two independent investigators using the two-way random effects model intra-class correlation coefficient (ICC). Absolute differences in body composition features were assessed by paired samples t-test. To explore contributing factors of maintenance or gain of skeletal muscle (dependent variable), univariate logistic regressions were conducted using age, gender, tumour stage, type of treatment, cachexia, mGPS, performance status, energy and protein intake, weight loss, treatment response and adherence, NIS and number of days between CT scans as independent variables. Statistically significant contributing factors identified by the univariate logistic regression were included in a multivariate logistic regression analysis. Lastly, a linear regression analysis of change in skeletal muscle (dependent variable) and the relative protein intake (independent variable) were applied to explore the role of dietary protein on skeletal muscle. Differences were considered

statistically significant when $p < 0.05$. IBM SPSS® Statistics (version 25.0, IBM, US, 2017) was used.

3. Results

In all, 186 patients were screened, of which approximately 120 patients were eligible and 62 patients accepted study inclusion. Eight patients died during the study and two patients withdrew consent; hence, 52 patients were eligible analysis.

The patient characteristics at baseline are presented in Table 1. The majority had disseminated disease and received palliative anti-neoplastic treatment. The presence of inflammation (defined as mGPS 1–2) and pre-cachexia/cachexia was observed in approximately half of the patients. The four patients with tumour stage I-IIb were medically inoperable due to poor lung capacity (n = 3) or deeming an operation as too invasive (n = 1).

3.1. Dietary protein intake

The details of the nutrient intake can be seen in Table 2. The energy intake remained unchanged, but the relative protein intake (g/kg body weight) tended to increase during the study (1.15–1.32, $p = 0.05$). The protein intake was statistically significantly higher at the clinical follow up compared to the 2nd cycle of anti-neoplastic treatment (1.14–1.32, $p = 0.01$), but not between the 1st and the 2nd cycle. Dinner was the meal that contributed the highest protein quantity throughout the study; on average, dinner contributed >30 g protein or >0.4 g protein/kg body weight. On the other hand, the majority of breakfast and lunch meals were low in protein (<20 g or <0.3 g/kg) (Fig. 1). Snacks contributed minimally to the total protein intake, with a mean protein contribution ranging from 1.3 to 7.4 g protein/snack and 0.05–0.11 g protein/kg/snack (data not shown). However, wide ranges of protein intake and protein meal quantity were observed.

Table 1
Baseline patient characteristics.

Characteristics	n = 62
Sex	
Male	36
Female	26
Age, median (range)	67.5 (49–80)
NSCLC stage[a]	
I-IIb[b]	4
IIIa-IIIc	17
IV	41
Anti-neoplastic treatment	
Palliative chemotherapy	35
Palliative immunotherapy	13
Curative-intended chemo-radiation	14
Comorbidities	
COPD	18
Arthritis	3
Inflammatory bowel disease	1
Diabetes mellitus	2
mGPS[c]	
0	30
1	8
2	23
Nutritional status	
Cachectic	22
Pre-cachectic	11
Non-cachectic	29
Weight (kg), mean ± SD	68.8 ± 13.9
BMI (kg/m^2), mean ± SD	24.0 ± 3.7

COPD: Chronic obstructive pulmonary disease; mGPS: modified Glasgow Prognostic Score (0: CRP ≤10 mg/L; 1: CRP >10 mg/L and serum albumin ≥35 mg/L; 2: CRP >10 mg/L and serum albumin <35 mg/L); NSCLC: non-small cell lung cancer.
[a] TNM stage (UICC 8th ed.).
[b] Patients were medically or surgically inoperable.
[c] C-reactive protein (CRP) was missing for one patient at baseline; hence, mGPS was undetermined in this patient.

3.2. Change in skeletal muscle from baseline to clinical follow up after three cycles of anti-neoplastic treatment

The inter-rater variance in skeletal muscle estimates between the two observers was minimal, as determined by ICC of 0.98 (95% CI: 0.98–0.99). The skeletal muscle, skeletal muscle index and lean body mass were significantly reduced from baseline to the clinical follow up ($p < 0.001$), while body weight, fat area and fat mass remained unchanged (Table 3). The mean changes (95% confidence intervals) were: skeletal muscle mass −7.6 cm^2 (−4.4 to −10.8 cm^2, $p < 0.001$), skeletal muscle index −2.6 cm^2/m^2 (−1.6 to −3.7 cm^2/m^2, $p < 0.001$), and lean body mass −2.3 kg (−1.3 to −3.2 kg, $p < 0.001$). Skeletal muscle remained unchanged (±5.9 cm^2) in 24 patients, two patients gained skeletal muscle (≥6.0 cm^2) and 26 patients lost skeletal muscle (≤6 cm^2) (Fig. 2). Amongst patients with loss of skeletal muscle, the body weight remained stable (±4.9%) in 23 patients, two patients lost ≥ 5% of body weight whereas one patient gained ≥ 5% during the trial.

3.3. Exploring contributing factors for maintaining skeletal muscle

Protein intake, energy intake and body weight stability were statistically significant associated with an increased likelihood of maintaining skeletal muscle mass (Table 4). None of these three factors reached statistical significance in the multivariate model ($p > 0.05$), although a trend could be seen for weight loss ($p = 0.06$) and protein intake ($p = 0.08$). None of the demographic and clinical factors were statistically associated with maintenance of skeletal muscle mass. The relative protein intake predicted a change in skeletal muscle, $F(1,50) = 4.6$, $p = 0.04$, and accounted for 8.4% of the explained variability of the change in skeletal muscle. The regression equation was: predicted change in skeletal muscle area (cm^2) = −18.833 + 9.135 × (relative protein intake).

4. Discussion

To our knowledge, this is the first study to observe the dietary protein pattern during primary anti-neoplastic treatment in NSCLC patients. The protein intake increased during the treatment trajectory although the energy intake remained unchanged. The majority of the meals contributed small amounts of protein. Depletion of skeletal muscle, but not of body weight occurred during the average time span of 16 weeks. Half of the patients experienced a significant loss of skeletal muscle. Neither demographic characteristics, nor clinical features such as disease stage, type of treatment, cachexia, inflammatory score (mGPS), nutrition impact symptoms, treatment adherence or response were associated with change in skeletal muscle. However, a higher protein and energy intake as well as body weight stability may increase the likelihood of maintaining skeletal muscle.

One of the potential contributing factors identified was protein intake. Although no previous trials have elucidated the role of dietary protein in skeletal muscle, the current findings suggest that approximately 8% of the variance of the skeletal muscle was explained by the dietary protein intake. This finding is similar to the results of a large cohort study of cachectic cancer patients in which energy and protein intake explained 3–11% of the variance of weight change [23]. The protein intake in the patients with muscle loss was on average 1.0 g/kg body weight/d compared to 1.4 g/kg body weight/d in muscle maintainers. Although the European Society of Clinical Nutrition (ESPEN) recommend a protein

Table 2
Longitudinal descriptive presentation of nutrient intake and protein meal quantity.

	1st cycle	2nd cycle	Clinical follow up	P value
Nutrient intake				
Energy intake (kcal)	1984 ± 770	2084 ± 787	2216 ± 718	0.18
Relative energy intake (kcal/kg bw/d)	30.4 ± 12.4	31.7 ± 12.1	34.2 ± 12.7	0.10
Protein intake (g/d)	77.5 ± 33.8	76.4 ± 24.6	87.9 ± 29.3	0.29
Relative protein intake (g/kg bw)	1.14 ± 0.47	1.14 ± 0.35	1.32 ± 0.46	0.21*
Main courses				
Absolute intake (g protein)				
Breakfast	12.8 ± 9.1	13.8 ± 11.2	14.3 ± 10.1	
Lunch	16.1 ± 11.4	17.9 ± 11.9	18.5 ± 14.2	
Dinner	30.6 ± 21.4	31.4 ± 17.1	34.6 ± 18.1	
Relative intake (g protein/kg bw)				
Breakfast	0.18 ± 0.13	0.20 ± 0.15	0.21 ± 0.14	
Lunch	0.24 ± 0.17	0.26 ± 16.8	0.28 ± 0.23	
Dinner	0.45 ± 0.28	0.46 ± 0.25	0.51 ± 0.25	

Values are presented as the mean ± SD. kg bw: kilograms of body weight. Changes in nutrient intake over time was analysed by Friedman's test. * Additional paired samples t-test were conducted for the relative protein intake between visits and a tendency of increased intake in the relative protein intake were observed from the 1st cycle to the clinical follow up ($p = 0.05$), significant difference in the relative protein intake from the 2nd cycle to the clinical follow up ($p = 0.01$), but no difference between the 1st and 2nd cycle of anti-neoplastic treatment ($p = 0.70$).

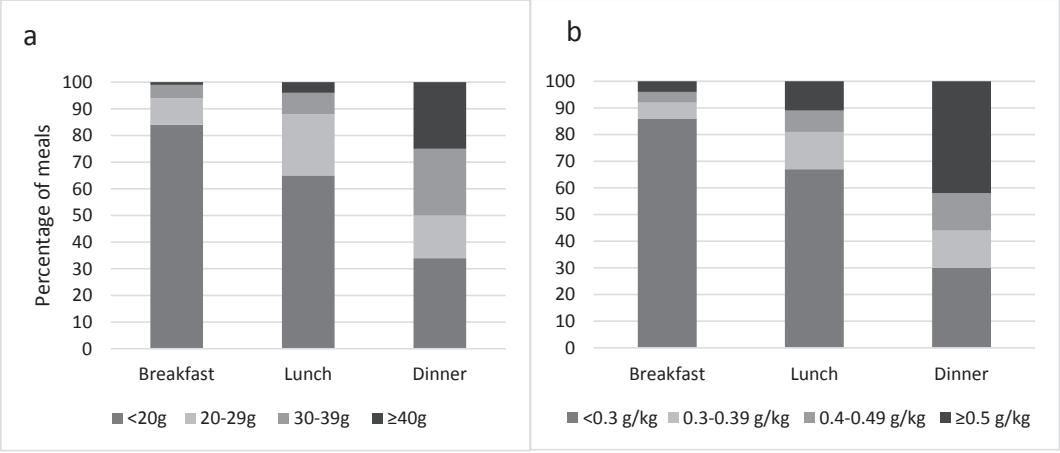

Fig. 1. Absolute (a) and relative (b) protein meal quantity, expressed as percentage of meals.

Table 3
Change in body composition features from baseline and after three cycles of anti-neoplastic treatment (n = 52).

	Baseline	After three cycles of anti-neoplastic treatment	P value
Skeletal muscle area at L3 (cm^2)	135.3 ± 32.2	127.7 ± 28.1	<0.001
Skeletal muscle index (cm^2/m^2)	47.4 ± 9.0	44.7 ± 7.8	<0.001
Lean body mass (kg)	46.6 ± 9.7	44.4 ± 8.4	<0.001
Total fat area at L3 (cm^2)	297.8 ± 157	295.3 ± 161	0.784
Fat mass (kg)	23.7 ± 6.6	23.6 ± 6.8	0.784
Body weight (kg)	69.6 ± 14.9	69.1 ± 15.2	0.231

Data are presented as the mean ± SD. Skeletal muscle index as squared cm of muscle mass at L3 divided by squared body height. Lean body mass (kg) was automatically quantified as 0.30 × skeletal muscle (cm^2) + 6.06 and fat mass (kg) as 0.042 × fat tissue (cm^2) + 11.2 [17].

intake in the range of 1.0–2.0, the target intake is at least 1.2 g of protein/kg body weight [24]. Previous small studies have found inconsistent results on muscle mass when protein intake was in the range of 1.0–1.2 g/kg body weight/d [25,26]. One of the largest RCT in lung cancer patients, found a significantly difference in lean body mass after an 8-week intervention, $p = 0.01$ [27]. The intervention group reached a protein intake of approximately 1.5 g of protein/kg body weight/d whereas to the control group had a protein intake of approximately 1.0 g/kg body weight/d [27]. Taken together, it seems a protein intake below 1.2 g/kg body weight/d may not be sufficient to maintain skeletal muscle in patients with lung cancer.

There are no current recommendations regarding protein meal quantity. Nevertheless, a blunted anabolic response to protein has been implicated in cancer patients in acute kinetic studies [7]. The blunted anabolic response to amino acids has previously shown to be overcome by a supplementation of high amino acid quantity or by using certain essential amino acids [8,10]. Deutz et al. [10] found an increased muscle protein synthesis to oral nutritional support (ONS) containing 40 g of protein including 10% free leucine but not to an ONS containing 24 g of protein [10]. If muscle protein synthesis respond to high, but not to low protein quantities, it is not unlikely that the lack of muscle gain in the current study may be a result of the shortfall of high protein meals.

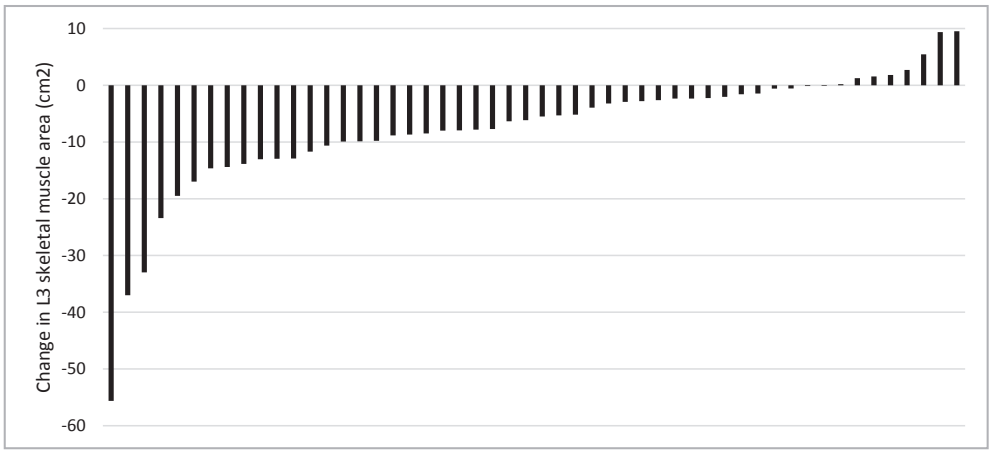

Fig. 2. Absolute changes in skeletal muscle at L3 (cm^2) assessed by thoraco-abdominal CT scans of the individual patients from diagnosis to the clinical follow up after three cycles of anti-neoplastic treatment (n = 52).

Table 4
Logistic regression analysis of demographics, nutrient and clinical factors associated with maintenance of skeletal muscle mass.

	Muscle wasters (n = 26)	Muscle maintainers (n = 26)	B	S.E	Wald	Univariate		Multivariate	
						OR (95% CI)	P-value	OR (95% CI)	P-value
Baseline factors									
Age (years), mean ± SD	66.0 ± 7.7	65.8 ± 8.4	−0.001	0.036	0.001	1.0 (0.9–1.1)	0.971		
Male sex, n (%)	17 (65)	14 (54)	0.482	0.570	0.715	1.6 (0.5–5.0)	0.398		
Metastatic disease, n (%)	17 (65)	15 (58)	0.326	0.572	0.324	1.3 (0.5–4.2)	0.569		
Palliative treatment, n (%)	19 (73)	18 (69)	0.188	0.613	0.094	1.4 (0.5–4.3)	0.569		
Baseline cachexia, n (%)	7 (27)	8 (31)	0.188	0.613	0.094	1.2 (0.4–4.0)	0.760		
mGPS, mean ± SD	0.85 ± 1.0	0.64 ± 1.0	−0.098	0.304	0.104	0.9 (0.5–1.6)	0.748		
PS 0	13	11				Reference			
PS 1	6	6	0.251	0.766	0.108	1.3 (0.3–5.8)	0.743		
PS 2	7	9	−0.167	0.708	0.056	0.8 (0.2–3.4)	0.813		
Longitudinal factors									
Energy intake, mean ± SD	28.8 ± 9.8	35.7 ± 9.2	0.068	0.033	4.350	1.1 (1.0–1.1)	0.037	1.0 (0.9–1.1)	0.706
Protein intake, mean ± SD	1.0 ± 0.6	1.4 ± 0.3	2.929	1.055	7.707	18.7 (2.4–148.0)	0.006	35.2 (0.7–1805.1)	0.076
Body weight, mean % ± SD	−2.1 ± 4.5	0.7 ± 2.6	0.216	0.097	4.947	1.2 (1.0–1.5)	0.026	1.2 (1.0–1.4)	0.060
Treatment response, n (%)	18 (69)	23 (88)	−1.226	0.747	2.697	0.3 (0.1–1.3)	0.101		
Treatment adherence, n (%)	15 (58)	20 (77)	−0.894	0.612	2.135	0.4 (0.1–1.4)	0.114		
NIS, mean ± SD	0.9 ± 1.3	1.1 ± 1.8	0.100	0.171	0.344	1.1 (0.8–1.5)	0.557		
Days between CT scans, mean ± SD	109 ± 38	116 ± 33	0.004	0.938	0.217	1.0 (1.0–1.0)	0.626		

CT: computed tomography; mGPS: modified Glasgow Prognostic Score (inflammatory score); NIS: nutrition impact symptoms; PS: performance status. The energy and protein intake are presented as relative values (kcal/kg body weight and g/kg body weight). Treatment adherence includes dose reductions, treatment delays and unplanned treatment termination. Treatment response was based on radiologic and clinical evaluation after three cycles of anti-neoplastic treatment. NIS includes loss of appetite, nausea, vomiting, dyspnoea amongst others.

Moving from kinetic studies to body composition, few have assessed protein intake in relation to skeletal muscle mass. All trials were small and have been conducted with ONS in addition to regular feeding. The results are inconsistent. The addition of 14–16 g protein once or twice per day were found to increase lean body mass in some [27–30], but without effect in others [31,32]. However, none provided details on the total protein meal quantity. Thus, the optimal number, the frequency and the minimal threshold of protein meal quantity to support skeletal muscle remain unknown.

A stable body weight increased the likelihood of maintaining skeletal muscle. Monitoring cancer related weight loss is therefore important; but, weight loss alone was not sufficient to identify patients with loss of skeletal muscle. Indeed, in all but two patients with loss of skeletal muscle maintained, body weight remained ±4.9%. Thus, patients with muscle wasting may therefore go undetected if identification relies on weight loss alone.

None of the baseline characteristics (age, sex, cachexia, performance status, tumour stage, inflammatory status, treatment) were associated with change in skeletal muscle mass, which corresponds to previous findings [18]. Likewise, tumour response, treatment adherence, nutrition impact symptoms and days between CT scans were not associated with change in skeletal muscle. This analysis was exploratory in nature; thus, contributing factors of skeletal muscle must be confirmed by studies in a larger sample size of NSCLC patients.

4.1. Strength and limitations

Despite the use of broad inclusion criteria, a surprisingly high percentage of the screened NSCLC patients were not eligible or declined participation. One third of the screened patients had a performance status of 3 and 4 whereas approximately one third of the patients were distressed by the severity of the disease. This situation is unlikely to change in the near future. To raise the inclusion rate, consecutive cohort studies should be conducted in a multicentre setting.

Another limitation was to obtain valid nutrient information in cancer patients undergoing anti-neoplastic treatment which is challenging. Although repeated 24-h recalls are regarded as valid in epidemiologic studies of healthy populations, no validation studies have been conducted in cancer outpatients. Nutrition impact symptoms are frequent in patients undergoing anti-neoplastic treatment, with a mean duration of 11 days post treatment [33]. Conducting dietary assessment on treatment days may thus not be representative of the actual intake in-between the cycles. Therefore, the number of days and intervals between the dietary assessments needed to provide valid nutrient information are unknown.

The advantage of the chosen 24-h recall method is to minimize the patient burden and to ensure detailed information. To minimize recall bias, the patients were prompted to increase the recall accuracy. All patients were included consecutively. Likewise, all data was systematically collected by clinical dietitians and health care professionals trained for this study. The patient cohort was relatively homogenous and the prospective study design enabled observation of the protein intake which otherwise remain unexplored in cancer patients. Low food intake is regarded a key feature in patients with cancer cachexia, but its role remain undetermined [6].

This study adds new knowledge worth exploring further. Future trials should therefore seek to unveil the role of dietary intake, especially the quantity and pattern of protein intake. For dietitians providing nutritional care, details of the nutrient quantity and protein pattern will determine how patients are counselled. Today, dietary counselling is based on different strategies to achieve sufficient quantities of nutrients, without any particular targets for meal protein quantity or timing.

In conclusion, the protein intake increased during the trial and seems important for maintaining skeletal muscle. However, few high protein meals and wide ranges of protein intake were observed. Wasting of skeletal muscle occurred frequently and early during primary anti-neoplastic treatment in patients with NSCLC. Muscle wasting should be diagnosed with CT scans as it may be undetected by monitoring body weight alone. Validating dietary methods to uncover the protein intake in patients undergoing anti-neoplastic treatment are necessary. The optimal protein quantity and pattern to support muscle maintenance or anabolism should be identified in future trials.

Statement of authorship

All authors contributed to the design of the study. RT and NAJ were responsible for data acquisition. RT, NAJ and AMD analysed the data. UF, MB and RT interpreted the results. RT drafted the manuscript. HHR, MH, AC, NAJ, MB and UF critically revised the manuscript for intellectual content. All authors revised and approved the final version of the manuscript as well as agreed to be accountable for all aspects of the work related to the accuracy and integrity of any part of the work.

Conflict of interest statement

HHR received an unrestricted research grant from Fresenius Kabi. RT, NAJ, AC, MH, MB, AMD and UF have no conflicts of interest to declare.

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