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Immunonutrition Associated with the Protein Module in the Nutritional Evolution of Lung Cancer Patients Undergoing Systemic Treatment: Case Report

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ABSTRACT

Background: Lung cancer patients are at high risk of malnutrition.

Methods: Case report of two elderly patients diagnosed with lung cancer were followed up during chemotherapy and/or immunotherapy. Patients used nutritional supplementation combined with immunonutrition and Whey Protein module alone during 4 treatment cycles. For nutritional and functional assessment, the following were used: Body Mass Index, percentage of weight loss, calf circumference, Patient Generated Subjective Global Assessment, muscle strength by dynamometer, SARC-F, Barthel Index, biochemical tests and food recall of 24 hours.

Results: During follow-up, patients were able to maintain adequate nutritional status, as well as functionality, and were not at risk for sarcopenia. Muscle strength varied, but not significantly.

Conclusion: Immunonutrition associated with the protein module appears to be beneficial in cancer patients during systemic treatment.

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Introduction

According to data from GLOBOCAN 2020, lung cancer ranks worldwide as the first most common type of cancer among men and the third among women, representing 2.2 million new cases (11.4% of total cancer cases), and first in mortality, with 1.79 million deaths (18% of total cancer deaths) [1].

Lung cancer patients have a high risk of malnutrition due to tumor hypercatabolism and treatment toxicity. It is estimated that 20% of cancer patients' deaths can be attributed to malnutrition and not to the malignancy itself; in addition, only 30% to 60% of cancer's patients receive adequate nutritional support, nutritional counseling and intervention [2].

The use of oral nutritional supplements contributes to an increase in caloric-protein intake, favoring the recovery of nutritional status. In this way, the patient improves their tolerance to the treatment, has a shorter hospital stay and, consequently, improves their quality of life. It is worth mentioning that nutritional supplements enriched with pharmaconutrients, such as arginine, nucleotides and omega-3, enable beneficial results of anticancer treatment, as it helps in weight recovery, with improvement in body composition, improves functional status and reduces levels of inflammatory markers [2].

The objective of this case report was to evaluate whether the specialized nutritional intervention associated with protein supplementation influenced the nutritional status, functionality and toxicity of treatments.

Material and Methods

Two patients aged over 60 years, diagnosed with metastatic or non-metastatic lung cancer, were followed up during chemotherapy and/or immunotherapy at a Cancer Center in the city of São Paulo. Patients were designated as patients 1 and 2 and followed for a period of 4 cycles of systemic treatment and all assessments were performed in each cycle.

Both patients consented to participate in the study by signing the consent form. The study was approved by the research ethics committee of the AC Camargo Cancer Center under the number RC98/21.

Nutritional intervention started in the interval between the first and second cycles of anticancer therapy. Patient 1 underwent the immunotherapy treatment regimen, with carboplatin, pemetrexed and pembrolizumab, and patient 2 underwent the carboplatin chemotherapy regimen with taxol.

Patients used nutritional supplementation combined with immunonutrition and whey protein alone during the 4 treatment cycles. The prescribing schedule considered the posology of 200 ml (twice/day) of an immunonutrional formula (Impact® containing 214 kcal/ 13 of protein/ 5.6g of lipids/ 0.6g of omega 3/ 2800mg of L-arginine/ 280 mg of nucleotides) and 13g (one time/day) of whey protein isolate (Nutren Just Protein® - 52 kcal and 13 g of protein) 5 days before each chemotherapy and/or immunotherapy cycle. During the intervals between each cycle (21 days), the patients used protein supplementation with 26g of whey protein isolate (Nutren Just Protein®) (Figure 1).

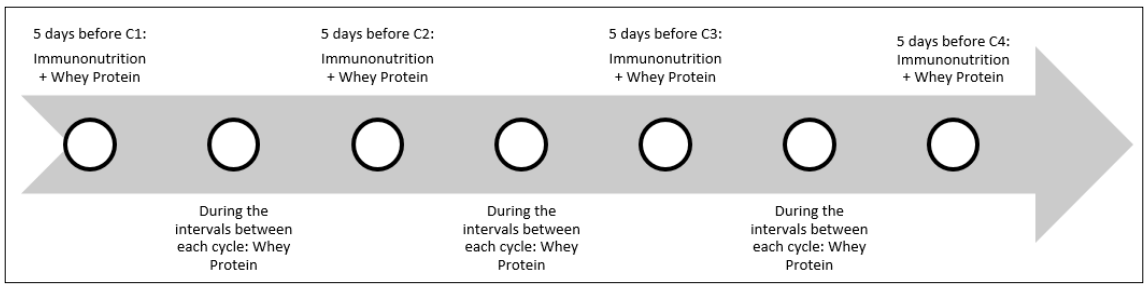

Figure 1: Nutritional supplement prescription

During the combined supplementation period, patients had an increase of 452 calories and 39 grams of protein per day in their food intake. In the period of protein supplementation, the increase was 104 calories and 26 grams of protein per day.

To assess the nutritional status, weight and height were measured to obtain the Body Mass Index (BMI) and weight loss percentage. BMI was calculated using the formula: BMI = weight / (height)². Weight was measured on a Filizola® scale, with the participant standing and barefoot. Height was measured with a Filizola® stadiometer with the participant standing, barefoot, heels together, arms at the sides, palms facing inwards and head erect with eyes fixed ahead. The reference value used for the classification of BMI was from the Pan American Health Organization, for they were both elderly [3]. The percentage of weight loss was calculated using the formula: initial weight – final weight/initial weight x 100. Values were classified according to Blackburn et al. [4].

Due to the profile of the patients, the measurement of calf circumference was used. The measurement was performed with the patient standing with the legs not contracted at about 20 cm away, measuring the largest point of the horizontal circumference of the calf with a TBW® inextensible measuring tape. The reference values used were those proposed for the Brazilian population [5].

Nutritional assessment was also performed through the Patient Generated Subjective Global Assessment (PG-SGA), where it was already possible to observe the presence or absence of adverse effects[6]. The PG-SGA was prioritized because it is a sensitive method for evaluating symptoms during cancer treatment, nutritional impact, physical capacity and food intake, being a tool of high sensitivity and specificity in oncology.

To assess muscle strength, the Handgrip Strength (HGS) method was used with a hydraulic dynamometer (Saehan®). Participants were seated in an armless chair, feet flat on the floor, with hips and knees positioned at approximately 90 degrees of flexion. The evaluated upper limb was placed along the body with the elbow at a 90° angle and the non-evaluated limb was relaxed on the thigh. The test was performed with the non-dominant hand for 3 times, and the participants were instructed to make a maximum contraction for 3 seconds in each test. There was a 30 second rest period between each test. As a final result, the average of these 3 results was calculated. The reference values used were those proposed by Cruz-Jentoft et al. [7].

Patients were also evaluated for sarcopenia, using the algorithm proposed by Cruz-Jentoft et al [7], starting with the SARC-F screening. The SARC-F proposed for the Brazilian population was used, where the measurement of calf circumference is added [8].

To assess functional independence and mobility, the Barthel Index was used and the evolution of the complete blood count was also monitored, which is already performed before each chemotherapy cycle [9].

Finally, the caloric and protein consumption of the patients was evaluated through the 24-hour recall (24HR) and calculated using the NutriSoft® software.

Patients showed good adherence to the consumption of nutritional supplements, consuming >75% for the entire recommended period.

Results

Regarding nutritional status, only patient 1 showed weight loss, although not significant, which occurred between C1 (cycle 1) and C2 (cycle 2) and from C2 to cycle 3 (C3), maintaining his weight in the other chemotherapy cycles. Patient 2 presented weight gain between C1 and C2 and after that, maintained his weight. Both maintained PG-SGA grade A – well nourished, throughout the follow-up period, with score 2. This score refers to the fact that they are cancer patients and elderly. None of the patients reported symptoms of nutritional impact in the PG-SGA, thus showing good tolerance to the treatment and absence of symptoms related to food (Table 1). Likewise, calf circumference remained adequate (≥34cm), with slight changes.

Table 1: Evolution of nutritional status

Patient	Cycle	Weight (kg)	BMI (kg/m²)	%WL	CC	PG-SGA (score/ classification)
1	C1	78	26,3	0	34,5	2/A
	C2	77,3	26,1	0,89	34	2/A
	C3	77	26	0,38	34,5	2/A
	C4	77	26	0	34,5	2/A
2	C1	75,5	24,3	0	35	2/A
	C2	76,5	24,7	0	35,5	2/A
	C3	76,5	24,7	0	35	2/A
	C4	76,5	24,7	0	35,5	2/A

Legend: BMI: Body Mass Index; %WL: weight loss; CC: calf circumference; PG-SGA: Patient Generated Subjective Global Assessment

HGS showed evolution and variations between periods in both patients. The HGS remained within the adequate range throughout the follow-up, according to reference values (≥27kg) (Figure 2), and an improvement in the values was observed between cycles C1 and C2 and C2 and C3 in both patients. Although there was a reduction in HGS between C3 and C4, this decrease was not significant and the values remained above the appropriate level.

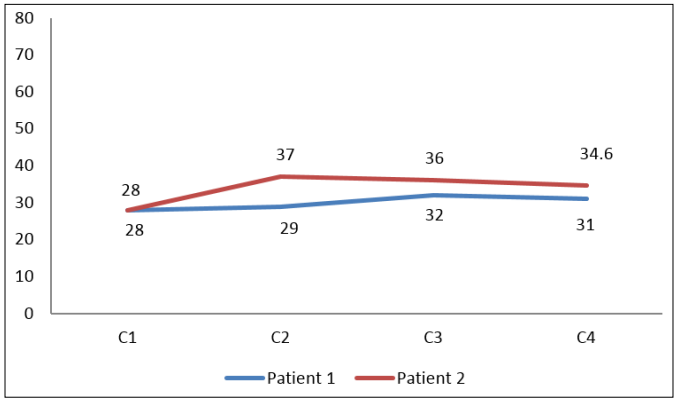

Figure 2: Evolution of Handgrip Strength (kg)

In the assessment of sarcopenia, which began with screening with SARC-F, according to the algorithm, the 2 patients did not score at any time during the assessment, that is, they were not at risk for sarcopenia during the entire follow-up. From the functionality point of view, throughout the intervention period, the patients scored 100 on the Barthel Index, showing that they were totally independent in their daily activities.

The assessment of food consumption by 24HR showed that patient 1 had a mean food intake of 1,828 calories and 105 grams of protein. Patient 2 had an mean food intake of 1,800 calories and 90 grams of protein. Both patients showed improvement in protein intake through the use of nutritional supplements, reflecting the achievement of the goal, as shown in the graph (Figure 3). Caloric intake exceeded 75% among patients, however, the goal was not reached, considering the estimates based on the predictive equations of 2,340 kcal and 2,265 kcal for patient 1 and 2, respectively.

Regarding the biochemical tests, the values of the complete blood count were considered, patient 1 had hemoglobin reductions between cycles, but only in cycle 4 (C4) he had markers below the minimum reference value (12.5g/dL). Patient 2 showed slight changes in hemoglobin, but remained within normal levels (13.5 to 17.5g/dL). On the other hand, under leukocyte analysis, both patient 1 and patient 2 remained within normal levels (3,500 to 10,500 mm3. Likewise, the platelets of both patients remained within normal levels (150,000 to 450,000 mm³). No patient discontinued treatment or needed to postpone any chemotherapy/ immunotherapy cycle.

Discussion

Malnutrition is common in cancer patients, occurring in about 40% of cases, and its prevalence is observed to vary according to the location of the tumor, stage of the disease and the type of treatment. According to the Society of Clinical Oncology of Australia, the diagnosis of lung cancer and chemotherapy are high nutritional risk factors, increasing the incidence of malnutrition [10].

The decline in muscle mass during cancer therapy can be partially attributed to the uncontrolled catabolism of muscle proteins that intensifies as the tumor progresses. In addition, adverse events during treatment, such as fatigue, inappetence, nausea, vomiting and diarrhea, can negatively affect food intake and physical activity, contributing to significant loss and changes in muscle mass [11].

Nutritional intervention through the use of oral nutritional supplements brings several benefits, among them, improved food intake, reduced weight loss during cancer treatment, greater tolerance to toxicities, and consequently, improved clinical results. In addition, nutritional strategies are updated and used to decrease the inflammatory and catabolic effects of cancer, therefore, specialized nutrients, anti-catabolic and inflammation suppressors are suggested and should be considered as part of the intervention [2].

According to Prieto et al. immunonutrition improves the immune and inflammatory system by modulating its functional capabilities, increasing receptor densities on immune cell membranes and improving the ability to react against pathogens, maintaining CD4/CD8 lymphocytes and TNF-α levels, improving T cell functions and NK cytotoxicity [12].

The use of immunomodulatory nutrients has shown benefits during systemic treatment. Vasson et al. showed an improvement in the increase in body weight and its composition, with an increase in lean mass, when compared to standard supplementation in patients undergoing chemotherapy [13]. In a systematic review carried out by Zheng et al it is possible to conclude that immunonutrition reduces weight loss during chemotherapy, as well as reduces the severity of toxicities, thus helping to improve the patient's food intake and, consequently, maintenance/recovery of nutritional status [14]. Still, it is seen an opportunity to use these specialized nutrients in the survival of cancer patients. In a double-blind phase III study, Boisselier et al, observed that overall survival and disease-free survival were significantly higher in the group treated with immunonutrition vs standard formula [15].

Conclusion

The present case report showed that there may be a benefit of nutritional intervention with immunonutrition in chemotherapy and immunotherapy. Supplementation combined with immunonutrition associated with a protein supplementation resulted in better treatment tolerance, important progression of hand grip strength, weight maintenance during chemotherapy and immunotherapy cycles and better protein intake. However, randomized clinical trials are needed to prove this relationship.

Nutritional therapy should be considered an important pillar in the cancer patient's journey. We need to increase our understanding of nutritional therapy in cancer, prioritizing nutrients to: regulate excess catabolism, optimize the effectiveness of cancer treatments, and protect non-tumor tissues from treatment toxicity.

Author's contribution:
Conception and design: TMM, PCF, VASR
Data analysis and interpretation: TMM, MAVM, PCF
Manuscript writing: TMM, PCF
Final approval of manuscript: All authors.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflict of Interest Disclosures: PCF and VASR are Nestle HealthScience employees. The other authors have no conflict to declare.

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