

Sipping as a nutritional supplement in ambulatory palliative oncology care – A pilot study with non-invasive methods.

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Abstract

Objective. The implementation of nutritional support is a basic need of patients in palliative oncological care. This pilot study optimized the use of sipping to improve the nutritional status of cancer patients in palliative care.

Method. The pilot study included 63 patients, aged 61.3 years on average (range: 32 – 82 years of age). The patients were assigned to either group A (no nutritional support n=39 patients) or group B (sipping as nutritional support n=24 patients). The latter consisted of one nutridrink (12g protein, 36.8g saccharide, 11.6g fat, and 300kcal) per day, for at least three weeks. The patients were evaluated through by non-invasive methods, *i.e.* body weight, waist and arm circumference, and triceps skinfold, all of which were measured during the patients' visit to the clinic. The body fat and fat-free mass ratio were evaluated with a bioimpedance analysis. Voluntary muscle strength was determined using dynamometry. Quality of life was assessed through modified questionnaires.

Results. In contrast with group A, group B did not have a significant weight loss, *i.e.* A: 81.9±15.8 kg - 80.5±15.8 kg (p=0.028); B: 73.9±14.9 kg - 73±16 kg. BMI A: 29±5 kg/m² - 28.5±5 kg/m² (p=0.007); B: 25.3±4.7 kg/m² - 25±4.9 kg/m² (p=0.614). Waist circumference A: 93.5±15.1 cm – 92.5±14.8 cm (p=0.008); B: 80.1 ± 13.2 cm – 80.6 ± 12.3 cm (p=0.234). Triceps skinfold A: 12.3±7.2 mm - 11±6.7 mm (p=0.001); B: 8.2±6.1 mm - 7.9±5.7 mm (p=0.207). Fat free mass A: 54.8 ±11.5 kg -52.8 ±11.6 kg (p=0.018); B: 54.7±10.9 - 52.8±11.5 kg (p=0.207). Significantly lower dynamometer values were recorded in both groups A: 25.6±10.4 kg – 23.1±10.3 kg (p=0.010); B: 27.4±9.9 kg – 24.3±9.1 kg (p=0.009). In contrast to group B, the patients in group A showed slight variations in their health status, thus decreasing their scores into the significance limit (p= 0.072).

Conclusion. Our results suggest that providing nutritional support in the form of sipping (~12g proteins, 300 kcal) on a daily basis prevents the loss of active tissue mass in palliative oncology patients. Based on these results, we recommend the inclusion of this simple nutritional support to prevent malnutrition in cancer patients in palliative care.

Introduction

The treatment of oncological patients requires a multidisciplinary approach, among which palliative treatment and care are an essential part since their goal is to maintain the best possible quality of life for the patients [1]. However, palliative oncology care is not only focused on patients in the pre-terminal and terminal stages of cancer, and it is currently moving into the ambulatory setting, *i.e.* early palliative care [2]; however, its provision requires proper timing before it is initiated [3]. Further, adequate palliative care needs the correct diagnosis and treatment of the symptoms related to the underlying disease, treatment side effects, and the general condition of the patient. Oncology patients often undergo harsh anti-tumor therapy and, during the course of treatment, up to 70–80% of the patients inevitably suffer from malnutrition [4, 5].

Malnutrition is a very serious problem and the patients that become severely affected display symptoms such as fatigue, weakness, anorexia, apathy, depression, and a significant impact in both mental and physical condition. Because the disease can be perceived differently by each patient, either at the hospital or at home, we respect the wishes of the patient as a general rule. In palliative cancer care, the patient often prefers outpatient care. It is important to note that malnutrition and cachexia are common in cancer patients and are indicators of poor prognosis, *i.e.* reduced survival, and increased number and frequency of complications [6].

The concept of nutrition in patients with cancer has changed significantly in recent years, both in theoretical and practical terms. The same is true for the patients in palliative cancer care, where cachexia and/or anorexia play a significant role. The former is a complex, systematic disease that negatively affects the metabolic pathways in various tissues [7]; whereas that anorexia is an almost universal component of cachexia. The patients in palliative care often have a reduced caloric intake, which may be more severe in cases of dysphagia, mental depression, appetite disorders, or chronic nausea. The latter is a common symptom of progressive malignancies and can be caused by a dysfunctional autonomic nervous system, treatment drugs, constipation, or impaired digestive system. Cancer-related cachexia includes metabolic abnormalities such as increased lipolysis, insulin resistance, and protein loss, which cause a profound catabolic imbalance [8].

The nutritional support of palliative oncology patients seeks to prevent or ameliorate further risk to their health condition. This kind of supportive treatment includes oral feeding, oral supplements, enteral and parenteral nutrition, and hydration. However, some of the issues encountered during the patient's nutrition may include nausea or vomiting, anorexia, early satiety, taste and smell disorders, and difficulty masticating or swallowing. Some medications have beneficial effects on these symptoms, *e.g.* corticosteroids, which also have antiemetic and analgesic effects, or progestational drugs (*e.g.* medroxyprogesterone and megestrol acetate) which may substantially improve appetite and caloric intake, although it is unclear how [9]. The modern approach consists in the application of pharmaconutrients, *i.e.* arginine and leucine, or polyunsaturated fatty acids, *i.e.* eicosapentaenoic and docosahexaenoic acids.

Malnutrition and quality of life can be screened through several instruments that have been recently introduced [7,10–12]. One of such instruments is the Karnofsky performance status scale (KPS), which quantifies the functional status of cancer patients [13]. However, only a limited set of instruments are available for clinical practice when concerning palliative care cancer patients, *e.g.* Edmonton Symptom Assessment system [14, 15] and Palliative Performance Scale [16]. Other tools, such as the patient-generated-subjective global assessment (PG-SGA) include questions regarding the presence of nutritional symptoms and short-term weight loss [17], whereas that the Kaplan-Meier survival estimation can be used to compare early and late groups of patients in palliative care [18]. Regardless of the method, minimally invasive procedures should be considered at all times [19]. Nutritional support in palliative care patients qualifies as such, since it is focused on the alleviation of malnutrition and improvement in the quality of life [20].

A patient diagnosed with tumor cachexia should be examined in detail and, based on international consensus, it is recommended to assess the condition in four main domains, such as food intake, catabolic factors, muscle value, and the effect of cachexia on the patient's functional status [6, 10]. The assessment of the patient's condition in the mentioned domains is mostly subjective, which has limited significance when evaluating malnutrition. With this in consideration, we developed a malnutrition monitoring method in an outpatient setting, which may correct this subjective assessment. Thus, a monitoring program for patients with a high risk of malnutrition was created based on previous clinical experience in ambulatory palliative oncology care. Great emphasis was set on the domain related to muscle mass in this program, *i.e.* body weight, sarcopenia, muscle mass quality, and dynapenia. The effect of cachexia on the patient's functional status was another of the domains included, *i.e.* physical performance, normal daily activity, quality of life, and psychological status [20]. Outpatient practice has shown that sipping is an adequate substitute when typical nutritional efforts are insufficient. The administration of sipping is recommended in small volume preparations of liquid enteral nutrition (125–300 ml), often referred to as oral nutritional supplement (ONS). In most cases, these ONS have a complex composition of three main nutrients, and also includes minerals, trace elements, and vitamins. ONS are characterized by a high content of calories, proteins, and other nutrients in a balanced ratio [21, 22]. The latter is one of the main reasons why it is frequently used in the nutritional support of palliative oncology patients, which are often at risk of malnutrition or are already malnourished. The patients in palliative oncology care are classified into a specific group where the early administration of nutritional support plays an important role, as it seeks to maintain their quality of life [22]. The energetic density of ONS is usually within the range of 1.5-2 kcal/ml, *e.g.* 300–400 kcal per 200 ml. It must be noted that the protein content varies considerably, *i.e.* 8-20g, as it also does the total carbohydrate content, *i.e.* 35-45g. There's little available evidence on the effect of ONS intervention alone, in part because most authors evaluate their effect in conjunction with dietary advice as part of a joint oral nutrition intervention. The minimum assessment period of a nutritional intervention is at least 60 days, which is similar to previous studies when ONS nutritional intervention, with an energy content of 350 kcal/day, was evaluated after 56 days, when it showed a positive result [24, 25].

This pilot study evaluated the nutritional status and quality of life of patients in palliative care and the efficacy of sipping as a source of nutrition. Sipping, as nutritional support for palliative cancer patients, is often used as therapeutic intervention; however, there are no clear indications for such procedure. The experience obtained to date shows how important it is to start this nutritional intervention early, especially in an outpatient setting, where it is important to determine the correct timing and minimum nutritional intake needed to maintain the best possible quality of life.

Methods

Design

This non-randomized, prospective, open label pilot study recruited patients from the Palliative Oncology Program in the Complex Oncology Centre of the University Hospital Hradec Kralove. The study was done in accordance with the ethical standards of the institutional ethics committee (reference number

201311S20P). Informed consent was provided by 111 patients, in whom a minimum of 5% decrement in body weight was detected. Of these patients, 48 (43.2%) were excluded during the clinical examination in visit 1 (baseline) due to a deteriorated health and performance status (PS), *i.e.* worse than 3 or hospitalization. A total of 63 patients (57.8%) were maintained in the study. Further inclusion in the clinical study was accepted by 39 patients, who agreed to the planned clinical examinations and measurements for a period of up to two months without sipping (group A). On the other hand, 24 patients agreed to use sipping as explained in the proposed methodology (group B). The follow up period was of two months (Fig. 1).

Inclusion criteria

Patients (≥ 18 years of age) with discontinued active anticancer treatment in palliative cancer care, with a performance status (PS) better than 3 (PS 0–3), or a life expectancy of more than 6 months.

Exclusion criteria

Patients undergoing palliative chemotherapy, radiotherapy, immunotherapy, or biologic therapy. Neither were included those patients with duplicate cancer, megastrol acetate, or in another nutritional program.

Participants

Of the initial 111 patients, with an average of 68.2 years of age (min. 32 years, max. 91 years), were evaluated in the course of one year. Of these patients, 48 were later excluded in virtue of unexpected changes in their health condition (*e.g.* disease progression and hospitalization). As a result, the study only included the analysis of 63 patients with an average of 61.3 years of age (min. 32 years, max. 82 years). The minimum criterion for inclusion in the statistical analysis was at least 3 examinations in the clinic (*i.e.* one per month) and survival for at least one month after the last examination.

Nutritional support

Nutritional support consisted of an unflavored sipping preparation, consisting of at least one nutridrink (12g protein, 36.8g saccharide, 11.6g fat, and 300kcal) on a daily basis for at least three weeks, provided in the form of sipping according to the standard protocol of the University Hospital Hradec Kralove.

Anthropometric parameters, body composition, and dynamometry

Bioimpedance is widely available, cheap, non-invasive, and fast. However, it is incompatible with a pacemaker, and movement on behalf of the patient prior to measurement can induce data fluctuations. The baseline values for males are: $15 \pm 5\%$ fat mass (*i.e.* $85 \pm 5\%$ fat free mass, including total body

water), and for females: $23 \pm 5\%$ fat mass (*i.e.* $77 \pm 5\%$ fat free mass, including total body water). Whereas that the normal triceps skinfold values are 12.5 and 16.5 mm for males and females, respectively. Dynamometry measures the force exertion capacity of a person, determining their strength based on isometric muscle contraction. Simple piezometric tensometers or dynamometers for larger muscle groups can also be used. The maximum strength of individual limbs can be compared and used as interpreted values. In this regard, hand grip is commonly used in clinical settings since it is the simplest method to assess muscle function; further, its results are reliable across all ages. On the other hand, dynamometry is primarily used for its simplicity and its reference values are evaluated according to weight and age (nomograms).

The body weight (Omron BF, Japan), waist and arm circumference, and triceps skinfold (Caliper Fat Meter, Czech Republic) of the patients was measured during their monthly visit to the clinic. Body fat and fat-free mass ratio were evaluated through a bioimpedance analysis (Bodystat Ltd., UK), voluntary muscle strength was determined with an electronic dynamometer (Digital Tenzometry DT1, CR).

Statistical methods

The obtained data was evaluated with a One-way Anova Repeated method using the Sigmastat software (Systat, USA) and compared between the groups. The data is shown as mean \pm SD ($p < 0.05$).

Results

Sixty-three patients were evaluated, during at least three examinations in the clinic, and included in the study. Group A comprised 39 patients (without nutrition) whereas that 24 were assigned to group B (with nutritional support). The average was of 68.1 ± 11.6 years of age in group A and of 66.3 ± 10.7 years in group B. Table 1 lists the gender frequency (%), type of cancer, and performance status (ECOG) of patients included to study (median).

Table 1
Patient characteristics. (Group A – without nutrition; Group B – with nutrition).

% Occurrence	Group A	Group B	P value
Man	48.7	62.5	<i>0,311</i>
Woman	51.3	37.5	
Liver and pancreas cancer	28.2	25	<i>1,0</i>
Stomach and colon cancer	35.9	54.1	<i>0,197</i>
Gynecology cancer	20.5	12.5	<i>0,509</i>
Other localizations	15.4	8.4	<i>0,669</i>
Performance status (ECOG) (median)	2	2	<i>n.s.</i>

Data were compared with a Fisher exact test with contingency tables. The incidence of males and females was compared in both groups. Individual types of tumors and their occurrence were always compared to the total number of other types of tumors

Both somatic and anthropometric parameters were evaluated, which were measured during the initial clinical examination (Visit 1), then after one (Visit 2) and 2 months (Visit 3) of follow-up. At the initial clinical examination (Visit 1), group A had an average weight of 81.9 kg (\pm 15.8) and group B had an average weight of 73.9 kg (\pm 14.8). During the follow-up at Visits 2 and 3, a significant weight loss was recorded in group A ($p = 0.028$). No significant weight loss was recorded in group B during the same period ($p = 0.383$). The initial BMI value in group A was 29 (\pm 5) and 25.3 (\pm 4.7) in group B. During the follow-up, group A recorded a significant decrement in BMI ($p = 0.007$) in contrast with group B, where no significant change was recorded ($p = 0.614$) (Table 2). The anthropometric measurements were limited to waist circumference and triceps skinfold in this pilot study. We confirmed that the somatic values (body weight and BMI) correlated with the data obtained from the anthropometric parameters. The average waist circumference at Visit 1 was of 93.6 cm (\pm 15.1) in group A and 80.1 cm (\pm 13.2) in group B. This was significantly lower ($p = 0.008$) for group A as time progressed, but not in group B ($p = 0.234$) (Table 2). During this same Visit, an average value of 12.3 mm (\pm 13.2) and 8.2 mm (\pm 6.1) was found for triceps skinfold in groups A and B, respectively. This was also significantly lower in group A ($p = 0.001$) in posterior Visits, whereas that any change in group B was non-significant ($p = 0.207$) (Table 2).

Table 2

Weight, BMI and anthropometrics (group A – without nutrition, group B – with nutrition); Visit 1, 2, 3 (1 – baseline, 2–30 days, 3–60 days).

	Group	Visit 1 (mean)	\pm SD 1	Visit 2 (mean)	\pm SD 2	Visit 3 (mean)	\pm SD 3	<i>p</i> value
Weight (kg)	A	81.9	15.8	81.4	17.3	80.5	15.3	0.028
	B	73.9	14.9	76.1	15.5	73	16	0.383
BMI (kg/m ²)	A	29	5	28.1	5.2	28.5	5	0.007
	B	25.3	4.7	25.7	5	25	4.9	0.614
Waist circumference (cm)	A	93.5	15.1	91.1	16.1	92.5	14.8	0.008
	B	80.1	13.2	77.5	12.4	80.6	12.3	0.234
Triceps skinfold (mm)	A	12.3	7.2	12.1	6.63	11	6.7	0.001
	B	8.2	6.1	7.8	5.9	7.9	5.7	0.207

The parameters of fat and fat-free mass bioimpedance and dynamometry were evaluated. At Visit 1, the average Fat mass for group A was of 27.1 (\pm SD 12.4) and for group B it was 19.1 (\pm SD 10.3). No significant differences in Fat mass ($p = 0.555$) were found in group A nor B ($p = 0.735$) (Table 3). At Visit 1, Fat free mass in group A was of 54.8 (\pm SD 11.5) and 54.7 (\pm SD 10.9) in group B. A significant difference ($p = 0.018$) was found in group A during follow up, compared to group B ($p = 0.207$), where this difference was not significant. During Visit 1, the average dynamometry value was of 25.6 (\pm SD 10.4) for group A and 27.4 (\pm SD 9.9) for group B. These values were significantly lower at later measurements ($p = 0.010$ and $p = 0.009$, for groups A and B, respectively) (Table 3).

Table 3

Bioimpedance (fat and fat-free mass) and dynamometry (group A – without nutrition, group B – with nutrition); Visit 1, 2, 3 (1 – baseline, 2–30 days, 3–60 days).

	Group	Visit 1 (mean)	\pm SD 1	Visit 2 (mean)	\pm SD 2	Visit 3 (mean)	\pm SD 3	<i>p</i> value
Fat mass (kg)	A	27.1	12.4	26.1	11.4	28.4	11.2	0.555
	B	19.1	10.3	19.2	10.6	20.2	11.3	0.735
Fat free mass (kg)	A	54.8	11.5	55.4	10.3	52	9.8	0.018
	B	54.7	10.9	56.9	12.1	52.8	11.6	0.207
Dynamometry (kg)	A	25.6	10.4	27	10.8	23.1	10.3	0.010
	B	27.4	9.9	26.4	8.3	24.3	9.1	0.009

A standardized questionnaire containing nutritional care related questions was applied to assess the quality of life of the patients. The score was rated from 0-100. In the area of physical function, a score of 45 (\pm 22.1) for group A and 45.4 (\pm 22.8) for group B was found during initial examination (Visit 1). A significantly lower score was found in group B ($p = 0.125$) during follow-up. In the social function area, no significant differences were found in the scores, which was also true for body pain, vitality, and general mental health. However, a drop in the score of the patients was recorded for health change perception in group A ($p = 0.072$). No significant differences were recorded in other parameters, such as nutritional status or gastrointestinal symptoms (Table 4).

Table 4: Questionnaire scores. (group A – without nutrition, group B with nutrition); Visit 1, 2, 3 (1 – baseline, 2–30 days, 3 – 60 days)

	Group	Visit 1 (mean)	\pm SD 1	Visit 2 (mean)	\pm SD 2	Visit 3 (mean)	\pm SD 3	<i>p</i> value
Physical functioning	A	45	22.1	47.5	22.1	42.7	23.5	0.707
	B	45.4	22.8	41.8	19.36	34.5	21.5	0.125
Social functioning	A	66.2	18.4	72.6	18.0	68.2	17	0.335
	B	67.3	19.9	63.3	17.9	31.2	20.3	0.545
Body pain	A	77.7	23.5	76.5	22.3	80.7	22	0.427
	B	67.3	25.3	69.6	20.4	71.8	20.8	0.74
Vitality (energy and fatigue)	A	40.1	14.3	38.1	13.1	38.9	13.6	0.305
	B	34.8	12.9	33.4	14.6	43.7	33.4	0.635
General mental health	A	62.3	16.5	60.9	14.3	61.9	14.8	0.922
	B	56.7	10.3	54.5	14.4	52.2	14.5	0.418
Health change	A	51.9	17.5	44.2	17.8	46.1	22.9	0.072
	B	51.1	22.5	44.1	20.8	47.3	20.3	0.436
Nutritional status	A	72.2	12.2	74.8	10.8	74.2	11.8	0.805
	B	67.8	12.3	70.6	16.4	66	14.9	0.85
Gastrointestinal symptoms	A	89.3	8.8	90.2	6.4	90.8	7.3	0.676
	B	85.9	10.4	86.2	10.8	83.5	10.5	0.943

Discussion

Palliative oncology includes critical therapeutic interventions for patients in advanced and pre-terminal stage, such as pain management and nutritional support. Nutritional supplements often need to be administered after chemotherapy, as anorexia and cachexia are known side effects of the treatment. Thus, dietotherapy and nutritional support (sipping) are included in palliative care to prevent these potentially serious issues; however, their effects are yet to be determined [6]. Regardless, its importance should not be neglected, especially in outpatients, whose malnutrition often goes undiagnosed and intervention comes too late to have any clinical effect.

A diagnosis of malnutrition is made through the evidence of substantial weight loss, according to the patient's clinical history. Relatively uncomplicated measurements are required, *e.g.* weight measurement and body mass index calculation. Other straightforward parameters involve triceps or subscapular skin folds (*i.e.* body fat), and arm muscle circumference (*i.e.* body lean mass). These parameters can be used to monitor any changes in nutritional status or the effect of palliative treatment in oncology patients. At present, the validation of these assessment tools is rather ambiguous in palliative oncology care; therefore, they are widely foregone in patients with advanced stages of cancer [8].

Malnutrition in oncology patients is often caused by the primary disease and by chemotherapeutic treatments, both of which provoke a negative energy balance that leads to muscle atrophy and subcutaneous fat loss; further, an inflammatory response triggered by the tumor also plays a role in the pathogenesis of malnutrition in oncology patients [4]. Palliative oncology treatment and care seeks to achieve the highest possible quality of life for the patient, although the socio-economic impact of the treatment still remains a matter of discussion. The nutritional intervention and pain management of cancer patients are crucial to maintain their quality of life as long as possible. In this regard, the effects of some intervention strategies must be evaluated in a multidimensional frame in which the analysis of several parameters must be readily available and sensitive enough to the changes in the field and over time [6, 8].

The preparation of a nutritional plan is essential for the patients in ambulatory palliative care, where great emphasis must be placed in the simplicity and effectiveness of the proposed procedure. This clinical study had an expanded focus on the nutritional status of the included patients during palliative oncology care and simple procedures were used to evaluate muscle mass (body weight, sarcopenia, muscle mass quality, and dynapenia) and to determine the effect of cachexia on the functional status of the patients. Nutritional support, provided in the form of sipping, is often indicated to counteract the effect of insufficient food intake, increased energy expenditure, and protein loss (shown as fever, progressive weight loss, *etc.*). Therefore, nutritional support therapy seeks to increase energy and protein intake to promote an anabolic state, preferably during pre and postoperative periods, to modulate or ameliorate tumor induced cachexia and thus reduce the risk of comorbid infections, among other complications [10, 28].

The current recommendations for sipping, as nutritional support, suggest the use of enteral nutrition preparations in small volumes (*i.e.* 125–300 ml), mostly because it is not intended to replace basal food

intake. The patients in ambulatory palliative oncology care are classified within a specific group where the early initiation of nutritional support plays a significant role in the early stages of palliative care. Previously published recommendations [11, 28], supported by the personal experience of our team, describe the basic concept behind the choice of nutritional intervention (*i.e.* 12g protein, 36.8g carbohydrates, and 11.8g fat), which has an energy density of 300 kcal and it is thus within the optimal range of 1.5-2 kcal/ml in a volume of 200 ml. This support must have a minimum duration of 3 weeks, providing 1–2 preparations per day. Previous clinical studies in this regard [24, 25] have monitored the patients in two sessions (30 and 60 days) and a 6-month follow-up.

To perform an objective assessment, the data obtained from the patient's anamnesis and anthropometric parameter values must be correlated. A proper comparison must be made between their weight prior to cancer diagnosis and the current one to establish the impact of sarcopenia and fluid redistribution (*i.e.* edema, ascites, and fluidothorax). Further, the BMI values of the patients can be reevaluated and objectively assessed through the evaluation of muscle strength and overall physical activity. However, accurately assessing the nutritional status of cancer patients is not a straightforward task [28, 30], therefore, it is often difficult to correctly determine when the nutritional intervention should start and how long it should be [28, 29]. Considerable attention was paid to the patients included in this clinical study and, based on the observations made during its course, we highly suggest that nutritional intervention should be initiated at the first appearance of malnutrition symptoms, *e.g.* lack of appetite, difficulties with food intake, *etc.* An inappropriate nutritional preparation before surgery can accelerate problems and accentuate the malnutrition symptoms, which can lead to a significant nutritional disorder.

Clinical implication

The results of our pilot study suggest that nutritional intervention in the form of sipping can be easily integrated in the care plan, although correct timing for implementation is important. We found that the first signs of malnutrition risk can be observed during outpatient care, especially in patients whose weight loss was greater than 5% in a relatively short period of time, *i.e.* 1–2 months. Some clinical studies recommend an early nutritional intervention, starting with oncological treatment [31]. The obtained results by our group confirm that the nutritional deficit cannot be fully corrected if the nutritional intervention is not started in the time. The symptoms of malnutrition in these patients progressively worsen and the management options become far more demanding. Therefore, the early diagnosis of a nutritional problem is crucial to ensure its proper treatment in both cancer patients and those at high risk of malnutrition [5, 32]. A plausible solution for good clinical results would be the use of standardized protocols, screening tests, and the inclusion of nutritional parameters supporting the preparation and update of the palliative oncology care plan. Our pilot study attempts to get closer to these problems, primarily by designing the timely inclusion of patients into a nutritional intervention. However, the preparation of suitable methodology for malnutrition diagnosis and monitoring, along with the evaluation of the nutritional intervention, still remains an issue. A collective of Italian authors described the problems related to malnutrition in oncology patients, considering the timing of nutritional assessment and intervention, in the expansion of Enhanced Recovery after Surgery (ERAS®) protocols, including also the

cost-effectiveness of these nutritional interventions [32]. Further research is needed to specify the correct timing of nutritional intervention in an outpatient setting, as well as to establish the form and composition of the nutritional intervention and its availability. Sipping has some advantages in this regard, such as its availability, but it is not without shortcomings, as its use can imply a risk for diabetes or poor tolerance to some of the formulation components [33]. A long term protocol is used for nutritional intervention in ambulatory patient care, in which the optimal volume and composition of sipping is sought after. If done correctly, this can be used in most patients without the need for further monitoring or nutritional adjustment. The patients under nutritional intervention included in this study tolerated sipping in a satisfactory manner and full compliance was recorded. An early nutritional intervention, initiated at the first appearance of malnutrition symptoms, significantly reduces the risk and frequency of said symptoms. However, the diagnosis of malnutrition in cancer patients requires non-invasive methods, such as anthropometric parameters and physiological functions. Recently published reports have verified prognostically significant parameters that may be useful to identify cancer patients at nutritional risk and who may require early nutritional support [34, 35]. It is certain that healthcare workers should be trained in this regard and that standard protocols should be implemented to detect malnutrition in patients in palliative oncology care, thus facilitating early nutritional intervention during anti-cancer treatment.

Study limitation

Our study was the first to investigate how to optimize nutritional intervention (sipping) based on the non-invasive examination of patients in ambulatory palliative oncology care. It must be mentioned that the study was hampered by the low number of patients included, mostly because 43.2% of the original population could not be considered due to hospitalization, or poor health and performance status. Moreover, only 38% of the patients agreed to use sipping as nutritional support and to comply with the evaluations of the study. Despite these shortcomings, not a single event of non-compliance was recorded. Further, the enrolled patients were examined correctly and the submitted questionnaires did not contain erroneous data, which allowed its accurate analysis and statistical evaluation. However, the distribution of patients between the groups was non-homogeneous; therefore, randomization was not possible due to the small number of patients. Regardless, the obtained results have an informative character and indicate the need of a prospective randomized study including a larger number of patients under nutritional support.

Conclusions

An optimal nutritional support prevents malnutrition in oncological outpatients. This is an important aspect of palliative oncology care because malnourishment often goes undiagnosed and, in several cases, intervention comes too late to have any clinical effect. The diagnosis of malnutrition is simplified by the appearance of distinctive symptoms, such as substantial weight loss. Further, its diagnosis requires relatively uncomplicated parameters, *e.g.* weight and BMI, and can include additional straightforward measurements, such as triceps or subscapular skin folds (for body fat), and arm muscle

circumference (for lean body mass). These parameters can be used to monitor the nutritional status of the patient and the effect of palliative treatment. However, their validation remains ambiguous and their use in patients in advanced stages of an oncological disease is still limited. Our method enables a personalized approach to palliative oncology care, which is also associated with a better quality of life and benefit cost.

Declarations

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Author contributions

AT conducted laboratory analysis and wrote the manuscript, AH and AT conducted laboratory and statistical analysis, VM, PP collection of clinical data, SF performed of search strategy, data extraction and quality assessment. All authors have read and approved the manuscript.

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Data availability

The datasets obtained from this study are available upon reasonable request.

Ethics approval

All the procedures performed in this study involving human participants adhered to the ethical standards of the institutional ethics committee (reference number 201311S2OP) and the Helsinki declaration of 1964 and its later amendments or comparable ethical standards.

Consent to participate

Patients provided informed consent for participation.

References

1. Pastrana T, Jünger S, Ostgathe C, Elsner F, Radbruch L (2008) A matter of definition – key elements identified in a discourse analysis of definitions of palliative care. *Palliat Med* 22(3): 222–32

2. Just J, Schmitz MT, Grabenhorst U, Joist T, Horn K, Engel B et al (2021) Factor influencing length of survival in ambulatory palliative care – a cross sectional study based on secondary data. *BMC Palliat Care* 20(1): 69
3. Hui D, Hannon BL, Zimmermann C, Bruera E (2018) Improving patient and caregiver outcomes in oncology: Team-based, timely, and targeted palliative care. *CA Cancer J Clin* 68(5): 356–76
4. Aktas A, Couto MM, Walsh D. (2020) We report performance status in oncology-but not nutritional status? *Support Care Cancer* 28(12): 5605–607
5. Cotogni P, Stragliotto S, Ossola M, Collo A, Riso S (2021) The role of nutritional support for cancer patients in palliative care. *Nutrients* 13(2): 306
6. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC et al (2017) ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr* 36(1): 49–64
7. Peixoto Da Silva S, Santos JMO, Costa E Silva MP, Da Costa RMG, Medeiros R et al (2020) Cancer cachexia and its pathophysiology: links with sarcopenia, anorexia and asthenia. *J Cachexia Sarcopenia Muscle* 11(3): 619–35
8. Marceca GP, Londhe P, Calore F (2020) Management of Cancer Cachexia: Attempting to Develop New Pharmacological Agents for New Effective Therapeutic Options. *Front Oncol* 10: 298
9. Currow DC, Glare P, Louw S, Martin P, Clark K, Fazekas B et al (2021) A randomized double blind, placebo-controlled trial of megestrol acetate or dexamethasone in treating symptomatic anorexia in people with advanced cancer. *Sci Rep* 11(1): 2421
10. Arends J, Bodoky G, Bozzetti F, Fearon K, Muscaritoli M, Selga G et al (2006) ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology. *Clin Nutr* 25(2): 245–59
11. Yalcin S, Gumus M, Oksuzoglu B, Ozbemir F, Evrensel T, Sarioglu AA et al (2019) Nutritional aspect of cancer in medical oncology patients. *Clin Ther* 41(11): 2382–96
12. Reber E, Schönenberger KA, Vasiloglou MF, Stanga Z (2021) Nutritional risk screening in cancer patients: The first step toward better clinical outcome. *Front Nutr* 8: 603936
13. Celtek NY, Süren M, Demir O, Okan I (2019) Karnofsky performance scale validity and reliability of Turkish palliative cancer patients. *Turk J Med Sci* 49(3): 894–98
14. Wong A, Tayjasant S, Rodriguez-Nunet A, Park M, Liu D, Zapata KP et al (2021) Edmonton symptom assessment scale time duration of self-completion versus assisted completion in patients with advanced cancer: A randomized comparison. *Oncologist* 26(2):165–71
15. Hallet J, Davis LE, Isenberg-Grzeda E, Mahar AL, Zhao H, Zuk V, et al (2020) Gaps in the management of depression symptoms following cancer diagnostics: A population-based analysis of prospective patient-reported outcomes. *Oncologist* 25(7): e1098-108
16. Baik D, Russell D, Jordan L, Dooley F, Bowles KH, Masterson Creberet RM (2018) Using the palliative performance scale to estimate survival for patients at the end of life: A systematic review of the literature. *J Palliat Med* 21(11): 1651–61

17. Yin L, Cheng N, Chen P, Zhang M, Li N, Lin X, et al (2021) Association of malnutrition as defined by the PG-CGA, ESPEN 2015, and GLIM criteria, with complications in esophageal cancer patients after esophagectomy. *Front Nutr* 8: 632546
18. Bakitas MA, Tosteson TD, Li Z, D'Lyons K, Hull GJ, Li Z et al (2015) Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial. *J Clin Oncol* 33(13): 1438–45
19. Chu L, Hawley P, Munk P, Mallinson P, Clarkson P (2015) Minimally invasive palliative procedures in oncology: A review of a multidisciplinary collaboration. *Support Care Cancer* 23(6): 1589–96
20. Costa de Oliveira L, Travassos Abreu G, Calixto Lima L, Azevedo Aredes M, Weigert EVM (2020) Quality of life and its relation with nutritional status in patients with incurable cancer in palliative care. *Support Care Cancer* 28(10): 4971–78
21. Blackwood HA, Hall ChC, Balstad TR, Solheim TS, Fallon M, Haraldsdottir E et al (2020) A systematic review examining nutrition support intervention in patients with incurable cancers. *Support Care Cancer* 28(4): 1877–89
22. Mulazzani GEG, Corti F, Della Valle S, Di Bartolomeo M (2021) Nutritional support indications in gastroesophageal cancer patients: From perioperative to palliative systemic therapy. A comprehensive review of the last decade. *Nutrients* 13(8): 2766
23. Göksel F, Senel G, Oguz G, Özdemir T, Aksakal H, Türkkan MH et al (2020) Development of palliative care services in Turkey. *Eur J Cancer Care* 29(6): e13285.
24. Breikreutz R, Tesdal K, Jentschura D, Haas O, Leweling H, Holm E (2005) Effects of a high-fat diet on body composition in cancer patients receiving chemotherapy: a randomized controlled study. *Wien Klin Wochenschr* 117(19–20): 685 – 92
25. Clemente-Suárez VJ, Redondo-Flórez L, Rubio-Zarapuz A, Martínez-Guardado I, Navarro-Jiménez E, Tornero-Aguilera JF (2022) Nutritional and exercise interventions in cancer-related cachexia: an extensive narrative review. *J Environ Res Public Health* 19(8): 4604
26. Ware J, Sherbourne C. (1992) The MOS 36-item short-form health survey (SF-36): I. conceptual framework and item selection. *Med Care* 30(6): 473–83
27. Bauer J, Capra S, Ferguson M (2002) Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr* 56(8): 779–85
28. Zhao XH, Yang T, Ma DX, Qi XY, Lin YY, Chen ZY et al (2020) Heterogeneity of nutrition care procedure in nutrition guidelines for cancer patients. *Clin Nutr* (39(6): 1692–704
29. de Las Peñas R, Majem M, Perez-Altozano J, Virizuela JA, Cancer E, Diz P, Donnay O et al (2019) SOEM clinical guidelines on nutrition in cancer patients (2018). *Clin Transl Oncol* 21(1):87–93
30. Ruggeri E, Giannantonio M, Agostini F, Ostan R, Puroni L, Pannuti R (2021) Home artificial nutrition in palliative care cancer patients: Impact on survival and performance status. *Clin Nutr* 39(11): 3346–53

31. Aprile G, Basile D, Giaretta R, Schiavo G, La Verde N, Corradi E et al (2021) The clinical value of nutritional care before and during active cancer treatment. *Nutrients* 13(4): 1196
32. Bossi P, De Luca R, Ciani O, D'Angelo E, Caccialanza R (2022) Malnutrition management in onkology: An expert view on controversial issues and future perspectives. *Front Oncol* 12:910770
33. Durán-Poveda M, Jimenez-Fonseca P, Sirvent-Ochando M, Gardía-Luna PP, Pereira-Cunill JL, Lema-Marqués B et al (2018) Integral nutritional approach ti the care of cancer patients: results from a Delphi panel. *Clin Transl Oncol* 20(9): 1202–211
34. Bertoli S, Battezzati A, Petruzzi A, Leone A, De Amicis R, Tramacere E et al (2018) Anthropometrics and body composition in adults with high-grade gliomas: Effects od disease-related variables. *Nutr Cancer* 70(3): 431–40
35. Cereda E, Caraccia M, Klersy C, Cappello S, Turri A, Borioli V et al (2021) Validation of a new prognostic body composition parameter in cancer patients. *Clin Nutr* 40(2): 615–23

Figures

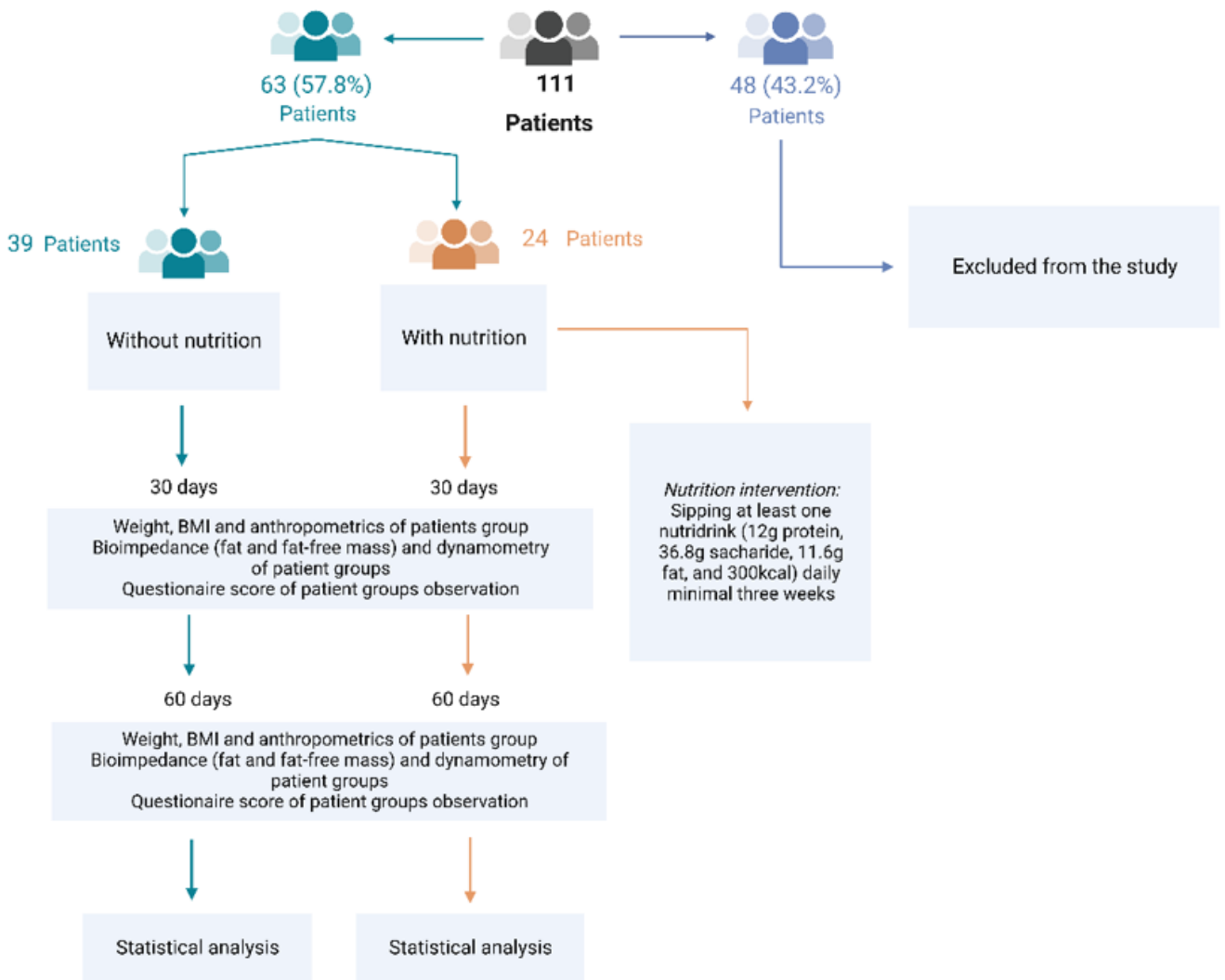


Figure 1

Study design.