

Advanced cancer: nutritional impact and the importance of integrating palliative care in a public health service

Câncer avançado: impacto nutricional e a necessidade de integração dos cuidados paliativos em um serviço público de saúde

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ABSTRACT

Background: Cancer patients usually require palliative care. One of the reasons for this is malnutrition, which is common in these patients, affecting their prognosis and quality of life. Data on nutritional care in palliative care are still scarce. **Objective:** To characterize the diagnosis and nutritional care in palliative care cancer patients hospitalized in a public health setting. **Methods:** Descriptive retrospective cohort study on clinical, laboratory, and nutritional data obtained from medical records of cancer patients in palliative care. **Results:** A total of 128 admissions of cancer patients in palliative care were analyzed. Main primary cancer sites were in digestive, urologic and pulmonary systems. Mean age was 64.3 ± 16.6 years. Patients were clinically and nutritionally compromised – mean performance status of 17.77 ± 7.15 , hemoglobin 9.6 ± 2.37 U/dL, albumin 2.64 ± 0.64 g/dL, C-reactive protein 125.37 ± 68.37 ml/L, and 60.8% of malnutrition (mean BMI of 20.19 ± 5.57 kg/m²). Oral route was the main route of administration (62.5%) and analysis of agreement revealed nutritional provision in excess of estimated daily requirements. No association was found between fasting condition, hospitalization outcome (death) and nutritional diagnosis ($p=0.51$). **Conclusions:** These cancer patients received palliative care just at the end stage of life, when most of them were malnourished, symptomatic, without specific oncologic treatment, and with a poor performance status. There was a preference for oral nutritional therapy, however, energy and protein supply were higher than the estimated nutritional requirements. The realization of fasting during hospitalization in the moments before death was not associated with the patient's outcome.

Keywords: Palliative Care. Cancer. Nutritional Status. Nutritional Therapy. Nutrition. Public Health.

RESUMO

Introdução: Pacientes com câncer necessitam de cuidados paliativos. Uma das razões para isso é a desnutrição, frequentemente observada nesses pacientes, afetando seu prognóstico e qualidade de vida. No entanto, dados sobre a atenção nutricional em cuidados paliativos ainda são escassos.

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Objetivo: Caracterizar o diagnóstico e o cuidado nutricional em pacientes em cuidados paliativos hospitalizados em um serviço de saúde pública. **Métodos:** Estudo de coorte retrospectivo descritivo sobre dados clínicos, laboratoriais e nutricionais obtidos de prontuários de pacientes oncológicos em cuidados paliativos. **Resultados:** Foram analisadas 128 internações de pacientes oncológicos em cuidados paliativos. Os principais sítios tumorais primários estavam nos sistemas digestivo, urológico e pulmonar. A média de idade foi de $64,3 \pm 16,6$ anos. Os pacientes estavam clínica e nutricionalmente comprometidos - desempenho médio de $17,77 \pm 7,15$, hemoglobina $9,6 \pm 2,37$ U/dL, albumina $2,64 \pm 0,64$ g/dL, proteína C-reativa $125,37 \pm 68,37$ ml/L e 60,8% de desnutrição (IMC médio de $20,19 \pm 5,57$ kg/m²). A via oral foi a principal via de administração (62,5%) e a análise de concordância revelou o suprimento nutricional em excesso às necessidades diárias estimadas. Não foi encontrada associação entre condição de jejum, desfecho da hospitalização (morte) e diagnóstico nutricional ($p = 0,51$). **Conclusões:** Esta população de pacientes oncológicos recebeu cuidados paliativos no estágio final de vida, quando a maioria estava desnutrida, sintomática, sem tratamento oncológico e com baixo desempenho funcional. Houve a preferência pelo uso da via oral para a realização da terapia nutricional, contudo, observou-se fornecimento energético e proteico superior às necessidades nutricionais estimadas. A realização de jejum durante o período de internação hospitalar que antecede o óbito não foi associada com o desfecho dos pacientes.

Palavras-chave: Cuidados Paliativos. Câncer. Estado Nutricional. Terapia Nutricional. Nutrição. Saúde Pública.

INTRODUCTION

It is estimated that 14 million people are diagnosed with cancer in the world every year, and approximately 8.2 million died of cancer in 2012¹. The incidence of cancer is 11 times greater in the elderly², and approximately 60% of the cases diagnosed and 70% of deaths from cancer occur in individuals older than 65 years³.

According to the World Health Organization (WHO) report, more than 19 million adults require palliative care, and cancer accounts for 34% of the underlying diseases in this population⁴.

Palliative care is defined by the WHO as an approach aimed at improving the quality of life of patients and their families facing health problems that can threaten an individual's life continuity through the prevention and relief of suffering⁵.

Cancer is associated with deterioration of nutritional status that can progress to severe malnutrition depending on tumor extension, histological subtype, adverse events to treatment, and intrinsic characteristics of patients^{6,7}. This reflects an imbalance between nutritional and tumor requirements, and direct and indirect effects of oncologic therapy on one side of the scale, and nutrient availability in the body on the other

side⁸. This culminates in malnutrition, that directly affects patients' prognosis^{6,8}.

Despite the direct association between nutrition and quality of life, there is a gap in the literature regarding the existence and application of guidelines on nutritional care in palliative care patients. This is also evident in the context of public health services, in which nutritional assistance is usually provided late, in attempt to reverse an already established malnutrition and debilitating symptoms. There are few available data on the use of nutritional therapy as a routine practice in palliative care patients⁹.

Understanding of how nutritional care has been provided to palliative care cancer patients may contribute to the development of a more adequate approach to this type of patient. Therefore, this study aimed at characterizing nutritional therapy, nutritional diagnosis, and metabolic changes in hospitalized cancer patients in palliative care in a public health setting.

METHODS

This was a descriptive, retrospective cohort study of palliative care cancer patients who received nutritional care during hospitalization at

the department of palliative care of Americo Brasiliense Hospital in the period from June 2011 to June 2013. Patient's data were collected from medical records. A total of 805 cancer patients in palliative care were admitted in this period, and the first 128 admissions were included in this study.

Data collection

Clinical laboratory data and nutritional data were collected from patients' medical records, as described below:

- Clinical laboratory data: time of hospitalization, sociodemographic characteristics, comorbidities, symptoms, performance status (Karnofsky Performance Status, KPS) at admission, laboratory data, medications and oncologic diagnosis;
- Nutritional data: nutritional care in the first 72 hours of admission; measured or estimated¹⁰ current body weight (kg); measured or estimated¹¹ current height, body mass index (BMI) (weight [kg]/height² [m]) and respective cutoff points for underweight, normal weight, overweight and obesity¹²; arm circumference (AC) (cm) and calculation of percentage adequacy¹³. Patients were classified into malnourished, at nutritional risk, normal weight, at risk of overweight, overweight and obese. In addition, the percentage of weight loss was calculated and classified as: significant loss or severe weight loss over time¹⁴.

In addition, patients' nutritional requirements were calculated as follows:

- Basal metabolic rate (BMR) using the Harris-Benedict equation (1919)¹⁵, total energy expenditure (TEE) calculated by three different methods – by multiplying BMR by activity factor, stress factor, temperature factor¹⁶ ("TEE – 1" in this study), by multiplying patient's current body weight by 25 ("TEE – 2") or 35 ("TEE – 3"), according to the Brazilian National Cancer Institute¹⁷ recommendations;
- Minimum and maximum recommended daily protein intake – 1.0 to 1.5g of protein / kg of current body weight / day¹⁷;

Information of patients' diet:

- Feeding routes – oral, enteral and/or parenteral;

- Characteristics and composition of diet – diet composition was analyzed using the Brazilian Food Composition Table¹⁸. Composition of pre-packed formulas administered orally or enterally was obtained by the manufacturer.
- Period (hours) of the hospital patient's fast, based on the medical prescription information and the evolution of the multidisciplinary team.

Data analysis

Collected data were transferred to a spreadsheet and analyzed using the SAS software (SAS Institute, 1999). The Kruskal-Wallis test followed by Dunn's test was used for comparisons involving three or more independent groups. Associations between two qualitative variables were examined using the Fisher's exact test. The coefficient of agreement proposed by Lin¹⁹ was also used. A $p < 0.05$ was set as statistically significant.

Ethical issues

The study was approved by the Research Ethics Committee of the General Hospital of Ribeirao Preto Medical School, University of Sao Paulo (approval number 497.327).

RESULTS

Data of 128 hospitalized oncology patients in palliative care were analyzed. The majority of patients were older (median age 64 years); clinical demographic data are described in Table 1.

The most prevalent symptoms during hospitalization were: pain (60.9%), constipation (53.1%), anorexia, (43.7%) and dyspnea (42.2%).

Patients' general well-being at admission was evaluated by the Karnofsky scale. Mean KPS was 19.77 ± 7.15 , with a median of 20 (10 - 40), indicating that patients were very sick, requiring hospitalization and active supportive treatment.

With respect to laboratory data, mean values of serum hemoglobin and albumin (9.6 ± 2.37 U/dL and 2.64 ± 0.64 g/dl, respectively) were lower than reference values. Increased serum levels were found for creatinine (1.37 ± 1.33 mg/dL), urea (76.96 ± 60.2 ml/dL), direct bilirubin (1.87 ± 3.28 ml/dL), total bilirubin (3.45 ± 5.81 mg/dL), reactive C protein (125.37 ± 68.37 ml/L), aspartate aminotransferase (110.64 ± 143.82 U/L), and alanine transaminase (56.82 ± 60.22 U/L).

Table 1
Clinical and demographic characteristics of patients (n=128)

Characteristics	Results	
	n°	(%)
Age (years)		
Mean ± standard deviation	64.27 ± 16.64	
Median	64.5	
Sex		
Male	73	(57.03%)
Female	55	(42.97%)
Hospital stay duration (days)		
Mean ± Standard deviation	12.77 ± 12.88	
Median	8.0	
Reason for hospitalization		
Control of signs and symptoms	63	(49.22%)
Decrease in general well-being	20	(15.63%)
Infection	24	(18.75%)
End-of-life care	21	(16.41%)
Outcome of hospitalization		
Death	83	(64.85%)
Hospital discharge	43	(33.59%)
Primary tumor site		
Digestive system	41	(32.03%)
Head and neck	20	(15.63%)
Urologic system	20	(15.63%)
Pulmonary system	19	(14.84%)
Gynecologic / breast	17	(13.28%)
Others	11	(8.59%)
Metastasis	77	(60.16%)
Metastatic sites		
Visceral	57	(44.53%)
Bones	30	(23.44%)
Brain	18	(14.06%)
Lymph node	9	(7.03%)
Previous oncologic therapy		
Chemotherapy / Hormonal therapy	73	(57.03%)
Surgery	57	(44.53%)
Radiotherapy	40	(31.25%)
Radiotherapy	36	(28.13%)
Comorbidities		
Systemic arterial hypertension	84	(65.63%)
Renal failure	49	(38.28%)
Depressive disorder	29	(22.66%)
Diabetes Mellitus	22	(17.19%)
Diabetes Mellitus	18	(14.06%)
Others	36	(28.13%)

Legend: n = number of patients; % = percentage

Another outcome measured was the routine use of medications. The most frequently used were opioids (34.4%) and non-opioid analgesics (20.3%) for oncologic pain (Table 2).

Table 2
Classes of medications used by the study population

Classes of medications	n	(%)
Non-opioid analgesics	26	(20.31%)
Antihistamines	2	(1.56%)
Antibiotics	18	(14.06%)
Antidepressants	22	(17.19%)
Antiemetic agents	14	(10.94%)
Anti-inflammatories	9	(7.03%)
Corticosteroids	16	(12.5%)
Diuretics	20	(15.63%)
Appetite stimulants	3	(2.34%)
Laxatives	10	(7.81%)
Opioids	44	(34.38%)
Nutritional / vitamin supplements	8	(6.25%)

Body weight was measured in 96 patients, with a mean of 53.09 ± 13.96 Kg, and a severe weight loss (22) was identified in 25% of these patients. Mean BMI was 20.19 ± 5.57 Kg/m², with 60.8% of patients classified as malnourished. This was significantly associated ($p < 0.01$) with the percentage of weight loss and values of AC.

There was a statistically significant association between nutritional status (categorized by BMI) and the percentage of previous weight loss (p value < 0.01), arm circumference (p value < 0.01); but not between nutritional diagnosis and the length hospitalization (p value = 0.62), according to the table 3.

Regarding nutritional approach, 62.5% of patients received soft (38.7%) or pureed (34.7%) diet. Also, 46.1% of these patients received an individualized diet according to their desire and preference. Oral nutritional supplementation was performed in 25% of patients, mostly with a 1.5 cal/mL formula. Fifty-three patients received enteral diet during hospitalization, mainly (49.1%)

Table 3
Analysis of association between nutritional diagnosis and the percentage of previous weight loss, arm circumference, hospitalization period and hospitality fast.

Nutritional Status	N	Mean	Standard Sdeviation	Median	P value
Percentage of previous weight loss					
Malnutrition	58	28,65	11,33	26,13 *	<0.01
Normal weight	28	13,7	7,12	11,6 §	
Overweight	5	0	0	0	
Obesity	5	6,99	0,68	6,99 §	
Arm circumference (centimeters)					
Malnutrition	58	21,45	3,37	21 *	<0.01
Normal weight	28	27	2,24	27 §	
Overweight	5	30,8	2,89	31,5 §	
Obesity	5	34,13	3,57	34 §	
Period of hospitalization (days)					
Malnutrition	58	15,1	13,34	10	0.62
Normal weight	28	15,5	14,53	10,5	
Overweight	5	13	9,64	10	
Obesity	5	21,2	13,33	21	
Fasting during hospitalization					
	Death (N)	Hospital discharge (N)		P value	
Nutritional Status	9	11		0.51	
Malnutrition	1	2			
Normal weight	1	1			
Overweight	1	1			

a 1.0 cal/mL formula. No patient received parenteral nutrition during the study period.

Another aspect analyzed in our study was fasting period. Of the 128 patients included, 61 (47.7%) patients fasted during hospital stay (mean of 22.44 ± 26.50 hours [0.43 to 110.42 hours]), mainly during the days prior to death. Eight patients remained fasted throughout their hospitalization period with a mean of 1.63 ± 0.74 days [1 to 3 days]. Patients total fasting time were 22.53 ± 19.80 hours, representing $58.59 \pm 41.8\%$ of the total hospitalization period.

Considering 61 patients who were fasted during hospitalization, 45 had a nutritional status diagnosis according to BMI. When analyzing the data, we identify that there was no statisti-

cally significant association ($p=0.51$) between the fasting and the patient's outcome, even considering their nutritional status diagnosis (Table 3).

Means of energy, macronutrients (carbohydrates, proteins and fats) and dietary fiber provided during patients' hospital stay was also analyzed. Mean energy delivered was 1819 ± 699 Kcal/day ($53.97 \pm 8.82\%$ carbohydrates, $16.36 \pm 2.31\%$ of proteins, $29.37 \pm 6.30\%$ of fats) and 17.29 ± 7.56 gram of fiber daily. Dietary protein and energy provided was greater than estimated requirements (Table 4).

A weak agreement (Lin's concordance correlation coefficient) was found between estimated nutritional requirements and the amounts of energy and protein supplied, as detailed in Table 5.

Table 4
Comparative analysis of dietary energy and protein provided with estimated nutritional requirements

Variables	Mean	Standard deviation	Median
% Energy provided /day vs. TEE-1	114.55	43.62	113.16
% Energy provided /day vs. TEE-2	192.39	87.74	168.96
% Energy provided /day vs. TEE-3	109.94	50.14	96.55
% Protein provided /day vs. minimum recommended amount /day	163.4	81.79	142.76
% Protein provided /day vs. maximum recommended amount /day	96.99	52.28	84.95

TEE: total energy expenditure

Table 5
Agreement analysis of estimated energy and protein requirements with the amount delivered to the study population

	ccc	95%	CI
BMR vs. total energy provided (Kcal)	0.03	-0.02	0.08
TEE – 1 vs. total energy provided (Kcal)	0.08	-0.05	0.21
TEE – 2 vs. total energy provided (Kcal)	0.02	-0.04	0.08
TEE – 3 vs. total energy provided (Kcal)	0.08	-0.11	0.26
Minimum recommended protein level (g/day) vs. total provided (g)	0.02	-0.07	0.11
Maximum recommended protein level (g/day) vs. total provided (g)	0.06	-0.12	0.24

BMR: basal metabolic rate (Kcal/day); TEE: total energy expenditure (Kcal/day); ccc: Lin's concordance correlation coefficient; CI: confidence interval

DISCUSSION

Analysis of clinical, oncological, and nutritional aspects of a population of cancer patients in palliative treatment revealed interesting particularities that may contribute to the remodeling of palliative care processes and clinical routines in the context of public health. Most patients were elderly, with diagnosis of advanced-stage cancer, without specific treatment, symptomatic and debilitated, with significant metabolic changes, high prevalence of malnutrition and delayed access to palliative care.

In agreement with previous studies, socio-demographic characteristics of the sample reflected the current epidemiological transition, with increasing demand for palliative care in elderly patients^{9,20,21}. In addition, the presence of weak, symptomatic patients in advanced stage of cancer disease at hospital admission is corroborated by the high percentage of in-hospital death and low KPS in our sample.

These findings suggest a delayed referral to palliative care services, whose beneficial effects on quality of life and well-being, provided by patient- and family-centered care, are limited by patients' severity and risk of imminent death. Similar conclusions were reported by other studies that investigated difficulties encountered by patients in getting access to palliative care^{22,23}.

Considering cancer specific treatments as chemotherapy; target-therapy; radiotherapy and surgery, only 57% of patients received at least one treatment. According to a North American paper, they verified that only 12.3% of the 113,885 patients with invasive cancer did not receive any cancer treatment and, the fact of not receiving oncologic treatment increased significantly with age and cancer stage. In fact, patients with stage II or III disease were twice as likely to not receive treatment as those with early-stage disease (stage I), and stage IV cancers were six times more likely to not be treated²⁴. Thus, the high percentage of cancer patients with inadequate treatment access verified in our study suggests that patients are mostly admitted for end-of-life care, with a delayed diagnosis and limited access to tertiary services with cancer treatment and assistance.

This situation is even worse taking into account characteristics of the elderly population, including higher incidence of cancer and chronic diseases. Also, these patients may have low educational attainment and low income, and thereby rely on public health services²⁵.

A high prevalence of metastatic patients (60.2%) with comorbidities (65.6%), as observed in our sample, makes the action of multidisciplinary teams and use of specific therapies difficult, in addition to increase the frequency of recurrent hospitalization, particularly in the elderly^{26,27}.

The requirement of hospitalization for control of symptoms, particularly cancer-related pain, resulting from the progression of oncologic disease^{26,27}, has been associated with decreased quality of life²⁶ and impaired nutritional status^{6,28,29} in palliative care patients. Opioids and non-opioids analgesics were the most commonly used drugs to treat cancer-related pain. This symptom involves not only physical manifestations, but also psychological, spiritual and social spheres that are carefully addressed by the palliative care team, in combination with standard drug treatment, since early stages of cancer diagnosis. However, in terminal stages of the disease, even total pain is treated with medications that do not control all symptom dimensions^{28,30}.

In our patients, altered biochemical parameters characterize a chronic consumptive disease of inflammatory stress (anemia, increased inflammatory tests, decreased albumin) associated with organ failure (e.g. kidney, liver), that are directly correlated with lower survival rates, as previously described^{28,30}.

In our study, 60.8% of patients had a diagnosis of malnutrition according to BMI. Malnutrition is commonly observed in patients with cancer and negatively affects functional state, immune response, quality of life and survival^{28,29}. It is directly associated with death in more than 20% of cancer patients, particularly when diagnosed in the terminal phase and in patients with low functionality^{29,30}.

Among anthropometric parameters, weight loss prior to admission and AC measurements corroborate nutritional deficits in palliative care patients, and are associated with in-hospital mortality^{31,32}.

With respect to the route of diet administration, we found that oral route was predominant in our study population. Oral nutrition is the route of choice for nutritional therapy; it is directly correlated with benefits to patients' quality of life, and stimulates the pleasure of eating³³. Enteral nutrition was also reported in palliative care patients^{6,28,34}. Indication of this route of nutrition support should consider the potential risks and benefits of nutritional therapy to the patient, as well as its impact on survival and quality of life^{6,34,35}.

Estimates of energy, macronutrients and fibers delivered to patients corroborate the results reported by other authors³⁶. Changes and decline in energy and nutrient intake are commonly observed in cancer patients, especially during the end of life stage³⁷. Under these circumstances, nutritional intake did not reach the current recommended levels for energy and protein in most advanced cancer patients; worsening prognosis and quality of life³⁸.

Therefore, it is essential to associate the evaluation and adequacy of the quantity and quality of nutritional intake (calories, macronutrients and fibers) with clinical signs and symptoms of nutritional status to obtain an adequate nutritional assistance, according to the real needs of the patient during the different phases of cancer disease⁶. However, it is important to remember that the retrospective nature of our study is a limitation, as we could not quantify the actual consumption in relation to the amount provided.

It is important to be aware of the effects of overfeeding in palliative care patients. Water and nutrient excess can cause an overload that may result in patients' discomfort³⁴. Several studies have reported that provision of macronutrients in amounts greater than patients' requirements offers no benefits in treatment response, survival rate or patients' well-being, and can even be deleterious to their quality of life^{39,40}.

However, analyses of agreement between the amount of nutrients provided and nutritional requirements calculated for each patient showed a disagreement between them, with provision in excess of estimated needs. This finding calls for the importance of the individualization of nutritional therapy according to patients' actual needs.

Individualization of dietary prescription may improve acceptance of the diet and reduce food waste, restore the feelings of pleasure and satisfaction of eating, and promote benefits to quality of life²⁹.

Fasting in palliative care of patients in end-of-life stage is controversial. The decision to withdraw nutritional support has been questioned due to the fact that both nutrition and hydration are considered basic necessities of human life^{34,41}. In our study, 61 patients spent some days in fasting conditions during hospitalization. In addition, progressive decrease in oral intake may be associated with cachexia-anorexia syndrome, which is quite common in advanced cancer and other chronic conditions³⁰.

The decision to withdraw nutrition support from these patients, therefore, should be discussed by healthcare providers, taking into account patients' and families' desire and expectations, patients' health status and prognosis, their nutritional requirements and quality of life⁴¹.

In addition, we found no significant association between fasting and hospitalization outcome, even when considering the diagnosis of nutritional status. In a qualitative study⁴², a voluntary, gradual decrease in food intake was observed in palliative care patients at the end of life. The authors reported that no sign of physical suffering attributable to the decline in oral intake was identified.

The major strength of this study was that we presented data from patients with cancer in palliative care in the public health scenario, bringing up for discussion not only organizational issues (including the flow of healthcare delivery) but also the need for nutritional protocols specific for palliative care patients, that may contribute to the construction of knowledge by healthcare professionals and provide benefits to routine health care practice for this population.

CONCLUSION

Advanced cancer has a significant negative impact on quality of life, resulting from worsening of symptoms associated with tumor progression / invasion, toxicity of cancer treatment, aggravation of previous comorbidities and progressive

functional decline. In this context, a comprehensive palliative care is crucial to fulfill patients' needs that are beyond the physical realm.

Most of our study population was malnourished, with important nutritional deficits. The offer of energy and macronutrients was a priority in nutritional therapy, and exceeded estimated nutritional requirements. Fasting was not correlated with death or nutritional deficit at the end stage of life.

Malnutrition, impairment of body energy store, metabolic changes and the presence of symptoms that affect food intake were detected in palliative care cancer patients. This highlights the importance of individualization of dietary plan and its relevance and impact on palliative care.

Thus, nutritional care should provide adequate amounts of nutrients, respecting patients' nutritional needs, desire and preferences, as well as the decrease in food intake at the end stage of life.

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