



Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrn.com

Applied nutritional investigation

Nutritional risk and malnutrition rates at diagnosis of cancer in patients treated in outpatient settings: Early intervention protocol



Elena Álvaro Sanz, Ph.D.^a, Marga Garrido Siles, Pharm.D., Ph.D.^{a*}, Laura Rey Fernández, Dietitian^a, Rosa Villatoro Roldán, Ph.D., M.D.^b, Antonio Rueda Domínguez, Ph.D., M.D.^b, Jimena Abilés, Ph.D.^a

^a Pharmacy and Nutrition Service, Costa del Sol Hospital, Marbella (Málaga), Spain

^b Oncology service, Costa del Sol Hospital, Marbella (Málaga), Spain

ARTICLE INFO

Article History:

Received 19 January 2018

Received in revised form 13 April 2018

Accepted 29 May 2018

Keywords:

Nutritional screening

Cancer

Oncology outpatients

Malnutrition

Nutriscore

Protocol

ABSTRACT

Objectives: Malnutrition is frequent in patients with cancer and is associated with a higher rate of morbidity and mortality. However, a significant number of patients at nutritional risk remain undetected due to the lack of a routine screening procedure during diagnosis. Costa del Sol Hospital in Marbella (Málaga), Spain has implemented a protocol for outpatients with cancer aimed at identifying and treating malnutrition at an early stage. The aim of this study was to determine the prevalence of nutritional risk and the rate of malnutrition when cancer is diagnosed.

Methods: We conducted a complete assessment of the nutritional status of patients with cancer of the upper digestive tract (esophagus, stomach, pancreas, or biliary tract) or head and neck cancer. Using the Nutriscore tool at the first oncology consultation, a screening for nutritional risk was performed for patients with other solid tumors. When nutritional risk was detected, a complete nutritional assessment was conducted.

Results: Of 295 consecutive patients, 21.4% were found to be at nutritional risk (Nutriscore ≥ 5). After complete assessment, a moderate degree of malnutrition was observed in 76% and severe malnutrition in 12%. Among patients with colorectal cancer or tumors of gynecologic origin, only 7.5% presented nutritional risk, but 52.8% presented cachexia.

Conclusion: The high rate of malnutrition observed and the identification of cachexia at an early stage highlight the importance of obtaining early identification of patients at risk to improve the efficacy of nutritional interventions.

Published by Elsevier Inc.

Introduction

Patients with cancer form a heterogeneous group in which the prevalence of malnutrition is very significant, ranging from 20% to 80% depending on the location of the tumor, the patient's age, and the stage of the disease. In this respect, patients with gastrointestinal tract or head or neck cancers are at an especially high risk [1–4].

A.R.D. and J.A. contributed equally to the manuscript as senior authors. E.A.S., M.G.S., J.A., and A.R.D. equally contributed to the conception and design of the research. All authors contributed to the generation, collection, and assembly of the data. E.A.S., M.G.S., and J.A. equally contributed to the analysis and interpretation of the data and wrote the paper. All authors read and critically revised the manuscript, and agree to be fully accountable for ensuring the integrity and accuracy of the work. E.A.S., M.G.S., J.A., and A.R.D. approved the final version of the manuscript. M.G.S. and J.A. have participated in a Fresenius-Kabi Advisory Board. The authors have no conflicts of interest to declare.

* Corresponding author: Tel.: +34 649 911480; Fax: +34 951 976882.

E-mail address: Marga.garrido@hotmail.com (M. Garrido Siles).

Many factors may contribute to the deterioration of nutritional status in patients with cancer, including mechanical, functional, or metabolic disorders related to the neoplastic process; side effects of surgery, chemotherapy, radiotherapy or immunotherapy; patient-related questions (physical deterioration, personal habits, psychological aspects, etc.); issues regarding health care personnel (absence of nutritional assessment, lack of knowledge or training to detect malnutrition, delay in initiating adequate nutritional treatment, etc.); or aspects related to health care authorities (such as the lack of multidisciplinary care units) [5].

The patient's nutritional status can influence the oncologic process, and studies have reported an association between malnutrition and increased postoperative complications [6,7], greater toxicity of treatments [8,9], a poorer response to antineoplastic therapy and greater risk for mortality [6], worse quality of life [10], increased duration of hospital stay, and higher associated costs [11].

Among the different prognostic factors in these patients (e.g., type of tumor, disease stage), weight loss is potentially sensitive to therapeutic intervention. In this respect, the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend nutritional assessment for all patients with cancer at the time of diagnosis, and in situations of risk, the performance of a complete nutritional assessment to facilitate diagnosis and the provision of appropriate nutritional support according to the patient's requirements and clinical condition [12].

However, despite the effects of malnutrition and the importance of early intervention in the clinical evolution of these patients, the lack of a routine screening procedure during diagnosis means that a significant number of patients at nutritional risk remain undetected and therefore that the possibility of an early intervention, which a priori would be more effective, is lost. This unsatisfactory situation persists despite the regular monitoring and follow up of patients with cancer by health care personnel [13]. In this respect, Hebeturne et al. [14] reported that only 30% to 60% of patients with cancer who were at risk for malnutrition received nutritional treatment. Indeed, on many occasions even patients diagnosed with severe malnutrition fail to receive an appropriate nutritional intervention [3,15].

Costa del Sol Hospital in Marbella (Málaga), Spain has defined and implemented a nutritional protocol for patients with cancer, to be applied after diagnosis but before the planned treatment is implemented. The protocol aims to identify and treat malnutrition at an early stage. The long-term objectives of this policy are to determine the prevalence of nutritional risk; to evaluate the capability of Nutriscore, a new validated screening method in oncologic patients; and thus to identify nutritional risk at diagnosis. The aim of the present study was to assess the rate of malnutrition when

cancer is diagnosed in order to determine its association with certain variables related to the tumor and to the patient.

Materials and methods

Study population

Adult patients (≥18 y of age) diagnosed with solid tumors for whom chemotherapy was started between April 2016 and June 2017 were eligible for inclusion in the study. The patients presented different stages of cancer, from early diagnosis to advanced stages. Patients were excluded if they had previously received chemotherapy or were unable to understand the purpose of the study. The study protocol was carried out according to the guidelines established by the Declaration of Helsinki and was approved by the Local Ethics Committee for Clinical Research. All study patients granted informed consent in writing to participate in the study.

Study design

A working group that included oncologists, specialists in oncology pharmacy, and nutritionists was tasked with devising an early approach protocol for patients with cancer who have malnutrition, after diagnosis of the neoplastic process. The protocol defines two levels of action depending on the location of the tumor.

Patients with localized cancer in the gastrointestinal tract (esophagus, stomach, pancreas, or biliary tract) or cancerous tumors of the head or neck comprised group 1. These patients were referred directly for nutritional consultation, either by the corresponding oncology committee or during the hospital procedure in which the tumor pathology was diagnosed. The nutritional consultation consisted of a screening (performed by the nutritionist), a complete assessment of nutritional status, and a nutritional diagnosis, before reaching a decision regarding the most appropriate treatment for the patient's requirements and characteristics.

Patients with solid tumors not included in the above category made up group 2. In this group, the screening for nutritional risk was performed at the first consultation with the oncologist by the doctor or at the outpatient pharmacy consultation by the specialist pharmacist, and in any case before chemotherapy is initiated. When a risk for malnutrition is identified, nutritional status was assessed and the procedure shown in Figure 1 was followed.

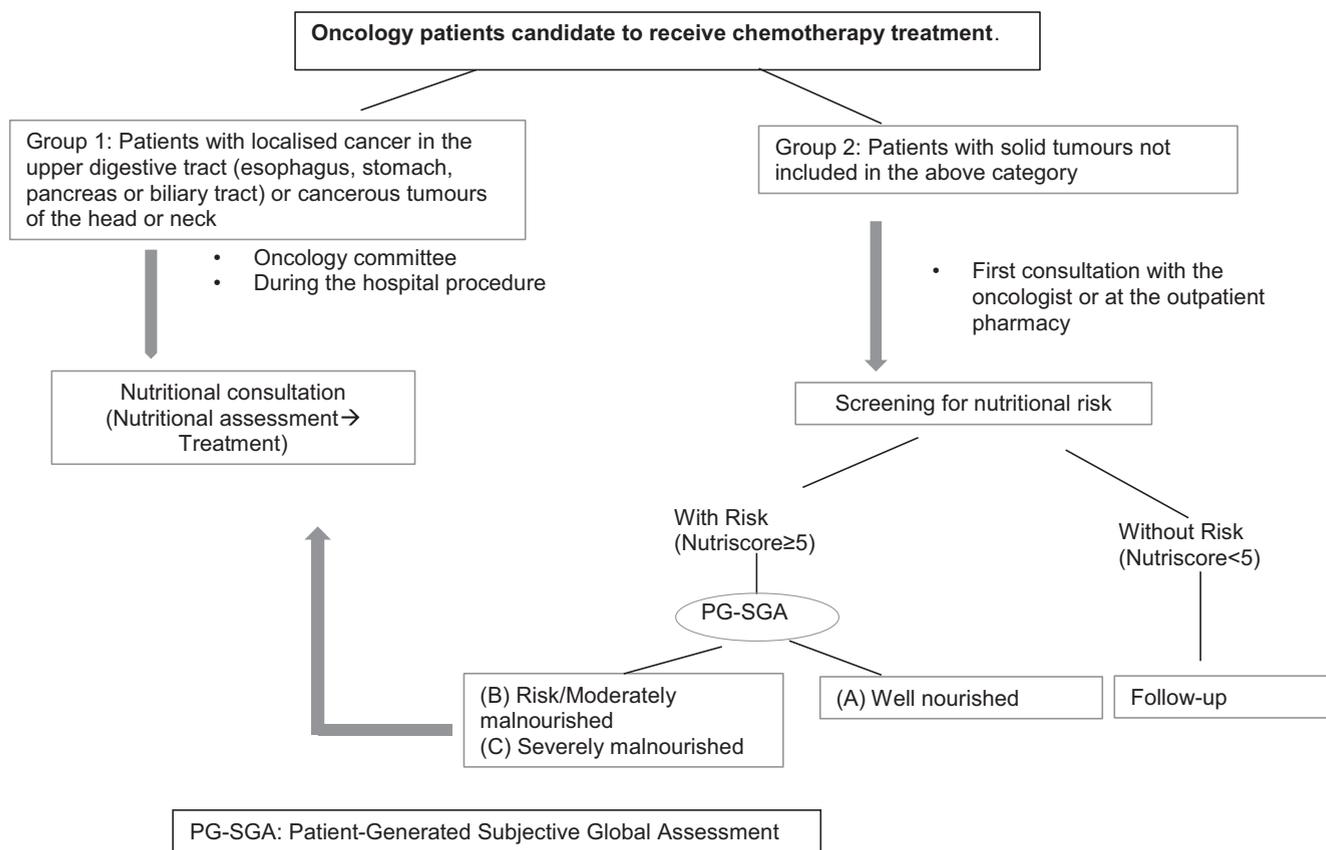


Fig. 1. Performance algorithm.

During monitoring and follow up, the patient's weight was determined on day 1 of each cycle of chemotherapy, together with an assessment of adherence and tolerance to the oral supplementation prescribed. The patient was referred to the nutritionist if weight loss or poor tolerance to the nutritional treatment was observed. In addition, all patients in group 1 were invited to a nutritional consultation on completion of every two cycles of chemotherapy.

Patients at nutritional risk were identified using Nutriscore [16], a nutritional screening test for outpatients with cancer, which takes into account involuntary weight loss in the previous 3 mo, decreased appetite, tumor location, and oncology treatment. Patients were considered at risk when the Nutriscore was ≥ 5 points (9 points is the maximum score). Nutriscore is a screening method that has been validated in the Spanish population by reference to the Patient-Generated Subjective Global Assessment (PG-SGA) and the Malnutrition Score Tool (MST), with a sensitivity of 97.3% and a specificity of 95.9%. The Nutritional Risk Screening (NRS02) was used for hospitalized patients, in accordance with the hospital's standard protocol.

The PG-SGA was used to evaluate patients' nutritional status [17]. This instrument measures weight loss, incorporates the patient's clinical history (diagnosis, current treatment, medication, and analytical results), includes a physical examination and, moreover, involves the patients themselves, who are asked to provide information regarding their symptoms, the type of diet followed, and their daily activity. The PG-SGA classifies patients as well nourished, at nutritional risk or moderately malnourished, or severely malnourished. The PG-SGA is carried out at the nutrition consultation (for the patients in group 1) or in the oncology pharmacy consultation, in both cases by personnel trained to carry out the evaluation.

In all cases, the presence or absence of cachexia was evaluated at the outset, following the definition proposed by Fearon et al.: weight loss $> 5\%$ during the previous 6 mo (in the absence of simple undernourishment); or body mass index (BMI) $< 20 \text{ kg/m}^2$ and any degree of weight loss $> 2\%$ or appendicular skeletal muscle index consistent with sarcopenia (men $< 7.26 \text{ kg/m}^2$, women $< 5.45 \text{ kg/m}^2$) and any degree of weight loss $> 2\%$ [18]. In addition, markers of inflammation and their possible relationship with nutritional risk were determined using the Glasgow Prognostic Score (GPS) and the Inflammatory-Nutritional Index (INI), as systemic inflammation-based prognostic scores [19–21]. For this study, INI values < 0.35 were considered to reflect risk for malnutrition. The cutoff points of normal values for serum albumin and C-reactive protein (CRP) were 3.5 g/dL and 10 mg/dL, respectively.

In determining the implementation of nutritional measures, the time elapsed between nutritional risk screening and the start of chemotherapy was taken into account.

Statistical analysis

A descriptive analysis was performed using mean and SD values (median and interquartile range [IQR] for samples with < 30 patients per subgroup) for the quantitative variables and the frequency distribution for qualitative variables. The differences in the presence of nutritional risk were evaluated by the Student's *t* test for quantitative variables (Mann–Whitney U test when distribution was non-normal), and the χ^2 test for qualitative variables. Finally, a multivariate logistic regression model was obtained, taking the presence of nutritional risk as the outcome variable. The level of statistical significance was set at $P < 0.05$.

Results

The present study included 295 patients, with a mean age of 61 ± 11 y. Of these patients, 24.7% were ≥ 70 y of age. The most prevalent

Table 1
Patient characteristics

	N	%
Overall	295	
Sex		
Female	158	53.6
Male	137	46.4
Median age,y (IQR)	62 (17)	
Site of primary tumor		
Head-neck	12	4.1
Colon-rectum	53	18
Esophagus-gastric	16	5.4
Gynecologic	35	11.9
Breast	73	24.7
Pancreas-bile ducts	17	5.8
Lung	64	21.7
Urothelial	12	4.1
Other	13	4.4
Treatment intention		
Curative/Radical	172	58.3
Palliative	123	41.7
GPS		
0	131	44.4
1	120	40.7
2	15	5.1
INI risk	119	44.7
Cachexia	118	40
BMI (mean \pm SD)	26.6 \pm 4.9	
Nutritional Risk (Nutriscore)		
≥ 5	63	21.4
< 5	232	78.6

BMI, body mass index; GPS, Glasgow Prognostic Score; INI, Inflammatory-Nutritional Index; IQR, interquartile range.

tumors corresponded to breast, lung, and colorectal cancer. Table 1 shows the clinical features and characteristics of the patients.

All patients underwent nutritional screening, and 21.4% were found to be at nutritional risk (Nutriscore ≥ 5). By type of tumor, the patients with esophagus-gastric and pancreas-bile duct neoplasms were at highest nutritional risk, at diagnosis (Table 2).

At diagnosis, 58.3% of the patients had suffered weight loss in the previous 3 mo, although the median weight loss value when nutritional screening was performed was only 3% (IQR, 8.8%). In 63.2% of the patients, the weight loss was $\leq 10\%$ and in 36.8% it was $> 10\%$. In patients with pancreas-bile duct or esophagus-gastric tumors, nearly 100% had experienced weight loss, meaning that virtually all patients with this kind of tumor are at risk for malnutrition at diagnosis. The average weight loss among these patients was about 10%.

Among patients with colorectal cancer or tumors of gynecologic origin, only 7.5% presented nutritional risk, but screening revealed

Table 2
Nutritional and prognostics parameters of the study population

Tumor type	Patients at nutritional risk, %	Patients with weight loss, %	Weight loss, % (median)	BMI, kg/m^2 (median, IQR)	Cachexia, %	GPS% (0/1/2)	INI-risk, % per patient
Esophagus-gastric	75	93.8	9.8 (14.9)	24.4 (7, 4)	65.5	50/43.8/63	31.3
Pancreas-bile ducts	70.6	94.1	10.6 (7.6)	24.9 (5, 0)	88.2	37.5/50/12.5	62.5
Head-neck	33.3	50	2.2 (16.9)	25.1 (6, 5)	41.7	41.7/50/8.3	50
Gynecology	28.6	71.4	6 (11.5)	26.1 (5, 3)	54.3	54.8/35.5/9.7	41.9
Lung	26.6	59.4	3.9 (8.8)	24.7 (5, 9)	42.2	19/72.4/8.6	75.9
Colon-rectum	7.5	75.5	5.8 (9.3)	26.2 (4, 8)	52.8	45.1/54.9/0	47.1
Breast	0	21.9	0 (–2.1)	26.6 (8, 4)	5.5	88.5/9.8/1.6	8.2
Urothelial	0	66.7	2.2 (9.9)	29.8 (4, 3)	33.3	36.4/63.6/0	41.7
Other	30.8	61.5	5 (14.4)	22.8 (2, 2)	46.2	30/50/20	70
Total	21.4	58.3	3				

BMI, body mass index; GPS, Glasgow Prognostic Score; INI, Inflammatory-Nutritional Index.

Table 3
Comparison for nutritional risk

	NO nutritional risk, % (n)	Nutritional risk, % (n)	P-value
Age (y)			
<70	78.4 (174)	21.6 (48)	0.976
≥70	79.5 (58)	20.5 (15)	
Sex			
Male	73 (100)	27 (37)	0.039
Female	83.5 (132)	16.5 (26)	
Grouped tumor location			
Upper gastrointestinal/Head and Neck	37.8 (17)	62.2 (28)	<0.001
All others	86 (215)	14 (35)	
Treatment intention			
Curative/Radical	86.6 (149)	13.4 (23)	<0.001
Palliative	67.5 (83)	32.5 (40)	
Weight loss at diagnosis, % (median)	0 ± 5.4	13.5 ± 7.1	<0.001
GPS			
0	87.8 (115)	12.2 (16)	
1	74.2 (89)	25.8 (31)	<0.001
2	26.7 (4)	73.3 (11)	
INI risk	38.9 (208)	65.5 (58)	<0.001
Cachexia			
Presence of cachexia	50.8 (60)	49.2 (58)	<0.001
Absence of cachexia	97.2 (172)	2.8 (5)	

GPS, Glasgow Prognostic Score; INI, Inflammatory–Nutritional Index

that 75.5% had experienced weight loss and >50% presented cachexia. In all the subgroups of patients, the median BMI was within the normal range, with a mean value of 26.6 ± 4.9 kg/m². Regarding the inflammatory marker-based index, the highest proportion of patients with INI risk were those with tumors of the lung, pancreas, head or neck, or those with colorectal cancer. Only patients with pancreatic cancer presented an association between INI risk and the presence of nutritional risk according to Nutriscore (Table 2).

Patients at risk for malnutrition were mostly male with a primary tumor located in the upper digestive tract or head and neck and being treated with palliative chemotherapy. These patients were more likely to present cachexia and recorded higher values for ECOG performance status, GPS and INI risk. Regarding age, no significant differences were found. The corresponding data are shown in Table 3.

An assessment of nutritional status (PG-SGA) was performed for 95% of the patients considered to be at nutritional risk. A moderate degree of malnutrition was observed in 76% and severe malnutrition in 12%. The remaining 12% of patients presented good nutritional status at the time of assessment.

With respect to the time elapsed between nutritional risk screening and the start of treatment, 27% of patients were screened ≥1 wk before the first cycle of chemotherapy. On average, this period was 31.7 ± 22.1 d for patients at greatest risk (those with pancreatic cancer, and esophagus-gastric, head and neck tumors).

Discussion

Oncology is one of the areas of medicine where recent advances can significantly improve outcomes for patients. Nevertheless, there are various factors that can limit the response to even the best therapies. Malnutrition is common, especially among patients with cancer [6,14] and is acknowledged to be an important prognostic factor [4].

The high risk for malnutrition, resulting both from the physical and metabolic effects of the cancer and from the influence of anti-cancer treatment, together with its major effects on survival rates,

makes this patient population very sensitive to strategies that may prevent, delay, or overcome malnutrition [6]. Therefore, nutritional risk screening is performed to increase awareness and to facilitate early recognition and treatment.

Previous recommendations and guidelines [12] have been issued for the inclusion of nutritional management in the global approach to this disease. The main contribution of this study was to present the evaluation of malnutrition in a global population of patients with cancer and to perform a screening at the time of diagnosis. The results that have been published in this regard show there is a high prevalence of malnutrition risk, reaching 31.8% among outpatients [4] and 33.9% among hospitalized patients [11]. Our own study group recorded a prevalence of nutritional risk of 21.4%, a value considerably lower than that published elsewhere [4,22,23], especially compared with the results obtained in Mexico [24], the Czech Republic [25], and Norway [26]. A possible explanation for this discrepancy lies in the fact that most other studies have been performed with hospitalized patients, who may be in a more delicate condition than those treated in an ambulatory setting. Moreover, hospitalization per se, regardless of the treatment provided, is associated with a deterioration of nutritional status [27–29].

It should be noted that the present study was based on mixed populations, and the inclusion of a large proportion of patients with breast cancer, who do not present the same nutritional risk or degree of weight loss as patients with other types of tumors [1], might reduce the proportion of patients at risk, compared to the findings of other studies. Moreover, all of these studies used the NRS02 screening method. Although NRS02 is reported to perform well for hospitalized patients, the Nutriscore method was specially designed to detect the risk for malnutrition in cancer outpatients and has been validated in the Spanish population [16].

Although a cancer patient's nutritional status generally worsens as the disease progresses, and with the administration of cytotoxic treatment [30–33], malnutrition can appear at any time during the disease, even at diagnosis [30].

In the present study, 36.8% of patients experienced weight loss >10%, a value that is considered clinically relevant because it is associated with functional impairment and a worse outcome [12]. This prevalence is within the range reported by Dewys et al., who found that 31% to 87% of cancer patients experienced weight loss before receiving chemotherapy [34].

In the present study population, the distribution of body weight loss and the nutritional risk was not homogeneous, and was associated with the type of primary tumor and the treatment provided. More than 90% of patients with pancreas-bile duct or esophagus-gastric cancer experienced weight loss of ~10%. A Nutriscore >5, a value suggesting the need for more extensive nutritional assessment and potential intervention, was recorded in ~75% of the patients with pancreas-bile duct or esophagus-gastric cancer. In a previous study conducted with patients with gastrointestinal tract cancer, 70% of those with tumours in the lower intestinal tract, 78% of those with esophageal or stomach cancer, and 87% of those with pancreatic tumors presented weight loss at diagnosis [35]. According to a related study, ~50% of patients with pancreatic or stomach cancer were at risk for malnutrition [4].

Although in our population BMI values were lower in patients at risk than in those not at risk, both groups had BMI values close to normality. We conclude, therefore, that BMI alone is not a sufficient indicator of nutritional status.

Clearly, the satisfactory outcome of mandatory screening depends on appropriate action being taken in response to an abnormal screening result and on the treatment strategies initiated being effective.

The presence of risk does not always include the condition of malnutrition, but refers to the risk for it developing. In fact, our results demonstrated that 12% of the patients at nutritional risk were in fact classified as well nourished. The recorded prevalence of malnutrition (18.5%) was below the range reported in previous research (34%–61%) for different types of tumors [1,2,6,11,14,36].

The maximum expression of malnutrition in cancer is tumor cachexia, which is directly or indirectly responsible for death in one-third of patients with cancer [37]. In a consensus document, Fearon et al. defined this condition as a multifactorial syndrome characterized by 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 [18]. Cachexia is defined as a weight loss >5% during 6 mo (in the absence of simple starvation). Hence, with chronic illness, even a low rate of weight loss can give rise to cachexia. Based on this criterion, we found that 40% of patients had cachexia at diagnosis. Although the previous lack of a definition and of commonly accepted diagnostic and classification criteria during the past decade make comparison with published data difficult, it should be noted that cachexia-anorexia syndrome has been described in 20% to 40% of patients at diagnosis [38].

Interestingly, in the present study although there were a low proportion of patients with colorectal cancer and nutritional risk, more than half were classified as cachectic. Clearly, patients with cancer might present with malnutrition (secondary to anorexia or starvation), cachexia or both (these are two different processes). In an earlier study, Rosenberg [39] focused on the changes in body composition that are characteristic of cachexia, coining the term *sarcopenia* or muscle wasting. This condition is not restricted to individuals who appear thin or wasted. Indeed, in the present study, patients with colorectal cancer were characterized by their heavy stature, with a median BMI of 26.6 kg/m² (IQR, 4.8). Although we did not specifically measure sarcopenia, earlier studies have reported a significant prevalence of sarcopenia in colorectal cancer associated with treatment toxicity, poor functional status, and decreased survival [40–43], which leads us to believe that this group of patients, although not detected in screening as being at risk, are in need of special attention.

There is good evidence that a chronic systemic inflammatory response provokes the cardinal features of cancer cachexia and plays an important role in its genesis and progression [19,44,45]. The most common measure of the systemic inflammatory response in patients with cancer is an elevated CRP concentration [18]. Other measures that have recently been employed include systemic inflammation-based scores such as the GPS and the INI [20,46]. In the present study, high GPS were observed, and most patients had an INI score <0.35. Several studies have found GPS to be a mortality predictor in patients with colorectal, lung, or gastric cancer and that a high GPS is associated with a linear reduction in survival [47,48]. Other studies have shown that INI is an independent predictor of survival and is associated with GPS [21].

The use of these scores facilitates the identification of patients who have or are likely to develop cachexia, present a poor response to treatment, and are likely to have poor survival.

The clinical management of cachexia is currently both limited and complex. Various procachectic mechanisms are involved, and these should be assessed and ranked according to importance and reversibility before a management plan is adopted [49–54].

Although it is generally accepted that nutritional support is ineffective at advanced stages of the disease, recent research has shown that at earlier stages, when the nutritional status is only marginally compromised, personalized nutritional counseling may prove beneficial, even concerning the final oncologic outcome.

Conclusion

Although it has been known since the early 1980s that weight loss frequently affects patients with cancer and that it depends on the type of tumor, the stage of the disease, and the oncologic treatment received, the present study nevertheless adds new information [36,55]. To our knowledge, this is the first investigation to make systematic use of Nutriscore to define the nutritional risk of cancer outpatients. Moreover, the high rate of malnutrition observed and the identification of cachexia at an early stage highlight the importance of obtaining early identification of patients at risk in order to change the timing of interventions and improve their efficacy.

Acknowledgments

The authors acknowledge the hospital day staff and patients for their collaboration. They also acknowledge the research team at the Costa del Sol Hospital for their support. This study was partially presented at the V National Oncology and Oncology-Pharmacy Congress “Tendiendo puentes” held in Toledo, Spain, in November 2017, where it received the second prize for best study presented. The present study is part of a PhD research program being conducted at the University of Málaga.

References

- Wie GA, Cho YA, Kim SY, Kim SM, Bae JM, Joung H. Prevalence and risk factors of malnutrition among cancer patients according to tumor location and stage in the National Cancer Center in Korea. *Nutrition* 2010;26:263–8.
- Silva FR, de Oliveira MG, Souza AS, Figueroa JN, Santos CS. Factors associated with malnutrition in hospitalized cancer patients: a cross-sectional study. *Nutr J* 2015;14:123.
- Attar A, Malka D, Sabate JM, Bonnetain F, Lecomte T, Aparicio T, et al. Malnutrition is high and underestimated during chemotherapy in gastrointestinal cancer: an AGEO prospective cross-sectional multicenter study. *Nutr Cancer* 2012;64:535–42.
- Bozzetti F, Mariani L, Lo vullo S, Mario ML, Biffi R, Caccialanza R, et al. The nutritional risk in oncology: a study of 1453 cancer outpatients. *Support Care Cancer* 2012;20:1919–28.
- Virizuela JA, Cambor-Alvarez M, Luengo-Perez LM, Grande E, Alvarez-Hernandez J, Sendrós-Madroño MJ, et al. Nutritional support and parenteral nutrition in cancer patients: an expert consensus report. *Clin Transl Oncol* 2018;20:619–29.
- Pressoir M, Desne S, Berchery D, Rossignol G, Poiree B, Meslier M, et al. Prevalence, risk factors and clinical implications of malnutrition in French comprehensive cancer centres. *Br J Cancer* 2010;102:966–71.
- Fukuda Y, Yamamoto K, Hirao M, Nishikawa K, Maeda S, Haraguchi N, et al. Prevalence of malnutrition among gastric cancer patients undergoing gastrectomy and optimal preoperative nutritional support for preventing surgical site infections. *Ann Surg Oncol* 2015;22(suppl 3):778–85.
- Aaldriks AA, van der Geest LG, Giltay EJ, le Cessie S, Portielje JE, Tanis BC, et al. Frailty and malnutrition predictive of mortality risk in older patients with advanced colorectal cancer receiving chemotherapy. *J Geriatr Oncol* 2013;4:218–26.
- Seo SH, Kim SE, Kang YK, et al. Association of nutritional status-related indices and chemotherapy-induced adverse events in gastric cancer patients. *BMC Cancer* 2016;16:900.
- Gellich NC, Handschel J, Holtmann H, Kruskemper G. Oral cancer malnutrition impacts weight and quality of life. *Nutrients* 2015;7:2145–60.
- Planas M, Alvarez-Hernandez J, Leon-Sanz M, Celaya-Perez S, Araujo K, Garcia de Lorenzo A, et al. Prevalence of hospital malnutrition in cancer patients: a sub-analysis of the PREDyCES study. *Support Care Cancer* 2016;24:429–35.
- Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr* 2017;36:11–48.
- Orrevall Y, Tishelman C, Permet J, Cederholm T. Nutritional support and risk status among cancer patients in palliative home care services. *Support Care Cancer* 2009;17:153–61.
- Hebuterne X, Lemaire E, Michallet M, de Montreuil CB, Schneider SM, Goldwasser F. Prevalence of malnutrition and current use of nutrition support in patients with cancer. *JPEN J Parenter Enteral Nutr* 2014;38:196–204.
- Segura A, Pardo J, Jara C, Zugazabeitia L, Carulla J, de las Penas R, et al. An epidemiological evaluation of the prevalence of malnutrition in Spanish patients with locally advanced or metastatic cancer. *Clin Nutr* 2005;24:801–14.
- Aribas L, Hurtos L, Sendrós MJ, Peiró I, Salleras N, Fort E, et al. Nutriscore: a new nutritional screening tool for oncological outpatients. *Nutrition* 2017;33:297–303.
- Read JA, Crockett N, Volker DH, MacLennan P, Choy ST, Beale P, et al. Nutritional assessment in cancer: comparing the Mini-Nutritional Assessment

- (MNA) with the scored Patient-Generated Subjective Global Assessment (PGSGA). *Nutr Cancer* 2005;53:51–6.
- [18] Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011;12:489–95.
- [19] McMillan DC. The systemic inflammation-based Glasgow Prognostic Score: a decade of experience in patients with cancer. *Cancer Treat Rev* 2013;39:534–40.
- [20] Pastore CA, Orlandi SP, Gonzalez MC. The Inflammatory-Nutritional Index; assessing nutritional status and prognosis in gastrointestinal and lung cancer patients. *Nutr Hosp* 2014;29:629–34.
- [21] Pastore CA, Orlandi SP, Gonzalez MC. Association between an inflammatory-nutritional index and nutritional status in cancer patients. *Nutr Hosp* 2013;28:188–93.
- [22] Gur AS, Atahan K, Aladag I, Durak E, Cokmez A, Tarcan E, et al. The efficacy of Nutrition Risk Screening–2002 (NRS-2002) to decide on the nutritional support in general surgery patients. *Bratisl Lek Listy* 2009;110:290–2.
- [23] Gheorghie C, Pascu O, Iacob R, Vadan R, Iacob S, Goldis A, et al. Nutritional risk screening and prevalence of malnutrition on admission to gastroenterology departments: a multicentric study. *Chirurgia (Bucur)* 2013;108:535–41.
- [24] Alvarez-Altamirano K, Delgadillo T, García-García A, Alatriste-Ortiz G, Fuchs Tarlovsky V. Prevalence of nutritional risk evaluated with nrs-2002 in Mexican oncology population. *Nutr Hosp* 2014;30:173–8.
- [25] Illa P, Tomíšková M, Skříčková J. Screening of malnutrition risk versus indicators of nutritional status and systemic inflammatory response in newly diagnosed lung cancer patients. *Klin Onkol* 2014;27:261–8.
- [26] Tangvik RJ, Tell GS, Guttormsen AB, Eisman JA, Henriksen A, Nilsen RM, et al. Nutritional risk profile in a university hospital population. *Clin Nutr* 2015;34:705–11.
- [27] Hosseini S, Amirkalali B, Nayeby N, Heshmat R, Larijani B. Nutrition status during hospitalization, Teheran, Iran. *Nutr Clin Pract* 2006;21:518–21.
- [28] Ravera E, Bozzetti F, Ammatuna M, Radaelli G. Impact of hospitalization on the nutritional status of cancer patients. *Tumori* 1987;73:375–80.
- [29] Weinsier RL, Hunker EM, Krumdieck CL, Butterworth CE. Hospital malnutrition. A prospective evaluation of general medical patients during the course of hospitalization. *Am J Clin Nutr* 1979;32:418–26.
- [30] Tong H, Isenring E, Yates P. The prevalence of nutrition impact symptoms and their relationship to quality of life and clinical outcomes in medical oncology patients. *Support Care Cancer* 2009;17:83–90.
- [31] Olsson U, Bosaeus I, Svedlund J, Bergbom I. Patients' subjective symptoms, quality of life and intake of food during the recovery period 3 and 12 months after upper gastrointestinal surgery. *Eur J Cancer Care (Engl)* 2007;16:74–85.
- [32] Russi EG, Raber-Durlacher JE, Sonis ST. Local and systemic pathogenesis and consequences of regimen-induced inflammatory responses in patients with head and neck cancer receiving chemoradiation. *Mediat Inflamm* 2014;2014:518261.
- [33] Silver HJ, Dietrich MS, Murphy BA. Changes in body mass, energy balance, physical function, and inflammatory state in patients with locally advanced head and neck cancer treated with concurrent chemoradiation after low-dose induction chemotherapy. *Head Neck* 2007;29:893–900.
- [34] Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. *Am J Med* 1980;69:491–7.
- [35] Baldwin C, McGough C, Spiro A, Thomas K, Cunningham DC, Andreyev HJN. Nutritional and clinical characteristics of patients with gastrointestinal tract (GI) cancers at presentation. *Proc Nutr Soc* 2009;68(OCE1):E18.
- [36] Freijer K, Lenoir-Wijnkoop I, Russell CA, Koopmanschap MA, Kruijzena HM, Lhachimi SK, et al. The view of European experts regarding health economics for medical nutrition in disease-related malnutrition. *Eur J Clin Nutr* 2015;69:539–45.
- [37] Tisdale MJ. The 'cancer cachectic factor'. *Support Care Cancer* 2003;11:73–8.
- [38] Pérez Camargo DA, Allende Pérez SR, Meneses García A, De Nicola Delfin L, Copca Mendoza ET, Sánchez López MS, et al. Frecuencia de anorexia-caquexia y su asociación con síntomas gastrointestinales, en pacientes paliativos del Instituto Nacional de Cancerología, México. *Nutr Hosp* 2014;30:891–5.
- [39] Rosenberg IH. Epidemiologic and methodologic problems in determining nutritional status of older persons. *Am J Clin Nutr* 1989;50:1121–235.
- [40] Muscaritoli M, Anker SD, Argilés J, Aversa Z, Bauer JM, Biolo G, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: Joint document elaborated by Special Interest Groups (SIG) “cachexia-anorexia in chronic wasting diseases” and “nutrition in geriatrics”. *Clin Nutr* 2010;29:154–9.
- [41] Antoun S, Baracos VE, Birdsell L, Escudier B, Sawyer MB. Low body mass index and sarcopenia associated with dose-limiting toxicity of sorafenib in patients with renal cell carcinoma. *Ann Oncol* 2010;21:1594–8.
- [42] Prado CM, Antoun S, Sawyer MB, Baracos VE. Two faces of drug therapy in cancer: drug-related lean tissue loss and its adverse consequences to survival and toxicity. *Curr Opin Clin Nutr Metab Care* 2011;14:250–4.
- [43] van Vledder MG, Levolger S, Ayez N, Verhoef C, Tran TC, Ijzermans JN. Body composition and outcome in patients undergoing resection of colorectal liver metastases. *Br J Surg* 2012;99:550–7.
- [44] Roxburgh CS, McMillan DC. Cancer and systemic inflammation: treat the tumour and treat the host. *Br J Cancer* 2014;110:1409–12.
- [45] Laird BJ, Kaasa S, McMillan DC, Fallon MT, Hjermstad MJ, Fayers P, et al. Prognostic factors in patients with advanced cancer: a comparison of clinicopathological factors and the development of an inflammation-based prognostic system. *Clin Cancer Res* 2013;19:5456–64.
- [46] McMillan DC. Systemic inflammation, nutritional status and survival in patients with cancer. *Curr Opin Clin Nutr Metab Care* 2009;12:223–6.
- [47] Elahi MM, Mc Millan DC, McArdle CS, Angerson WJ, Sattar N. Score based on hypoalbuminemia and elevated C-reactive protein predicts survival in patients with advanced gastrointestinal cancer. *Nutr Cancer* 2004;48:171–3.
- [48] Meek CL, Wallace AM, Forrest LM, McMillan DC. The relationship between the insulin-like growth factor-1 axis, weight loss, an inflammation-based score and survival in patients with inoperable non-small cell lung cancer. *Clin Nutr* 2010;29:206–9.
- [49] Yavuzsen T, Davis MP, Walsh D, LeGrand S, Lagman R. Systematic review of the treatment of cancer-associated anorexia and weight loss. *J Clin Oncol* 2005;23:8500–11.
- [50] Bosaeus I. Nutritional support in multimodal therapy for cancer cachexia. *Support Care Cancer* 2008;16:447–51.
- [51] Kubrak C, Olson K, Jha N, Jensen L, McCargar L, Seikaly H, et al. Nutrition impact symptoms: key determinants of reduced dietary intake, weight loss, and reduced functional capacity of patients with head and neck cancer before treatment. *Head Neck* 2010;32:290–300.
- [52] Chopard A, Hillock S, Jasmin BJ. Molecular events and signalling pathways involved in skeletal muscle disuse-induced atrophy and the impact of countermeasures. *J Cell Mol Med* 2009;13:3032–50.
- [53] Paddon-Jones D, Sheffield-Moore M, Cree MG, Hewlings SJ, Aarsland A, Wolfe RR, et al. Atrophy and impaired muscle protein synthesis during prolonged inactivity and stress. *J Clin Endocrinol Metab* 2006;91:4836–41.
- [54] Reid J, McKenna HP, Fitzsimons D, McCance TV. An exploration of the experience of cancer cachexia: what patients and their families want from healthcare professionals. *Eur J Cancer Care* 2010;19:682–9.
- [55] Bozzetti F, Migliavacca S, Scotti A, Bonalumi MG, Scarpa D, Baticci F, et al. Impact of cancer, type, site, stage and treatment on the nutritional status of patients. *Ann Surg* 1982;196:170–9.