



Assessment of nutritional status using objective and subjective methods in Greek patients with cancer

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Summary

Purpose Malnutrition constitutes an important complication of cancer. Nutritional status is associated with the progression of malignant neoplasms. This study aimed to assess the nutritional status of patients with cancer using objective and subjective assessment methods.

Materials and methods The following validated questionnaires were used to assess the nutritional status of 152 patients with cancer recruited in Attica, Greece: Patient-Generated Subjective Global Assessment (PG-SGA), Nutritional Risk Screening-2002 (NRS-2002), Simplified Nutritional Appetite Questionnaire (SNAQ). Geriatric nutritional risk index (GNRI) was calculated, handgrip strength (HGS) test was carried out, and the arm circumference (MUAC) and triceps skinfold thickness (TSF) were measured.

Results Based on the PG-SGA assessment, 54.9% of the individuals were severely malnourished. Imminent risk was observed in 83.6% (NRS-2002) and 48.7% of participants were at increased risk of a 5% reduction in body weight within the next 6-months (SNAQ). Severely malnourished patients experienced significant weight reduction in the 6 months prior to recruitment and had lower HGS and TSF. MUAC was similar within the PG-SGA categories. High risk for malnutrition was estimated for geriatric patients (GNRI: 46.45 [IQR: 5.17]). Malnourishment, based on PG-SGA, was positively associated with percent weight loss within the past 6 months and negatively associated with body mass index (BMI), hemoglobin (Hgb), HGS, and MUAC (all $p \leq 0.05$).

Conclusion The present study highlighted a high risk of malnutrition in patients with cancer. Poor nutritional status was positively associated with weight loss, Hgb, and MUAC and negatively associated with BMI, HGS, and TSF.

K. Vamvakari and I. Evangelou contributed equally to this manuscript.

Data availability statement The data that support the findings of this study are available from the corresponding author, O. Androutsos, upon reasonable request.

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Keywords Neoplasms · Nutritional risk · Nutritional assessment · Patient-Generated Subjective Global Assessment · Malnutrition

Introduction

Malnutrition constitutes an important complication of cancer. Patients with cancer are at high risk for malnutrition, due to the disease itself and the treatments used [1, 2]. Inadequate nutritional intake is frequently observed, associated with weight loss and may arise for many reasons: dry mouth, intestinal obstruction, malabsorption, constipation, diarrhea, vomiting, reduced intestinal motility, chemosensory alteration, and side effects of drugs [1].

Malnutrition is a predictor of life expectancy, as it is estimated to be the cause of death in 20% of

cancer patients [3]. Early nutritional assessment and dietary intervention may reduce mortality and morbidity in patients with cancer [4]. Some challenges for oncology teams when facing cancer cachexia include identifying patients at risk, managing symptoms, and limited treatment options that can make management difficult [1]. Validated tools, such as Patient-Generated Subjective Global Assessment (PG-SGA), Nutritional Risk Screening-2002 (NRS-2002), Simplified nutritional Appetite Questionnaire (SNAQ), are commonly used to assess malnutrition in patients with cancer [5]. In combination with anthropometric measurements such as weight, mid-upper arm circumference (MUAC) and triceps skinfold thickness (TSF) are also used [6].

The present study aimed to assess the nutritional status of Greek patients with cancer and compare objective and subjective evaluation methods.

Materials and methods

Participants and experimental design

In total, 152 patients with cancer were recruited between April and October 2019. Participants were hospitalized or were undergoing cancer treatment at the Attikon University Hospital. Every year >15,000 patients with cancer are treated at Attikon University Hospital (inpatients and outpatients). The study was approved by the hospital bioethics committee (E.B.D. 315). Adult patients from the entire Greek territory were consecutively recruited and signed a consent form prior to their enrollment in the study. Bedridden patients at an advanced stage of the disease, were unable to participate due to inability of carry out the measurements.

Sociodemographic, lifestyle, and clinical factors

Participants self-completed a questionnaire on sociodemographic (age, gender, nationality, educational level, marital status, residence, occupation) and lifestyle data (smoking, alcohol consumption, quality and hours of sleep, screen time, physical activity). Clinical data (cancer type, cancer stage, type of treatment, comorbidity, medication, dietary supplements) were obtained from medical records.

Anthropometric measurements

Body weight was measured using a SECA-220 scale to the nearest 100 g and standing height using a stadiometer to the nearest 0.1 cm. Patients were measured with light clothing and no shoes, in the morning. MUAC was measured using anelastic tape, at the mid-point between the acromion and olecranon. TSF was measured using a Harpenden skinfold caliper (Ajanta Export Industries, India) at the same anatomic site [7].

Handgrip strength

For the evaluation of handgrip strength (HGS), the Saehan Hydraulic Hand Dynamometer (Saehan Corporation, Korea) was used. Three measurements were performed in the nondominant hand and the average was compared to a standard reference value based on the individual's gender and age [8].

Biochemical and hematological indices

Albumin, total protein, urine, creatinine, uric acid, potassium, sodium, calcium, magnesium, phosphorus, and hemoglobin (Hgb) levels were recorded from patients' medical files. The Geriatric Nutritional Risk Index (GNRI) was calculated, based on the equation: $GNRI = [14.89 \times \text{serum albumin (g/dL)}] + [41.7 \times (\text{actual body weight/ideal body weight})]$, where ideal body weight (kg) was calculated as: $[\text{height (m)}]^2 \times 22 \text{ (kg/m}^2\text{)}$. The ratio of body weight to ideal body weight was set to 1 when the patient's body weight exceeded the ideal body weight. Patients' GNRI scores were categorized as at: high risk (GNRI ≤ 89.3), moderate risk (GNRI 89.4 to < 94.9), low risk (GNRI 95 to ≤ 98), and no risk (GNRI > 98) [9].

Nutritional status assessment

The following validated nutritional screening tools were used: PG-SGA—a highly sensitive and specific tool, considered gold standard for oncology; NRS-2002—a valuable and reliable tool; and SNAQ—a validated tool to detect malnutrition in inpatients and outpatients [10].

- PG-SGA: Patients were categorized into 3 groups: category A (“good nutritional status”), category B (“moderately malnourished”), category C (“severely malnourished”) [11].
- NRS-2002: Total score < 3 was classified as without nutritional risk and ≥ 3 as with nutritional risk [12].
- SNAQ: scores range between 4–20. Scores < 14 indicated a significant risk of weight loss $> 5\%$ within 6 months; therefore, dietary intervention is considered necessary [13].

Statistical analysis

Continuous variables are presented as median values [interquartile range (IQR)] while the categorical variables as percentages (%). The non-parametric test Kruskal–Wallis H was used to compare differences between more than two independent groups and χ^2 to assess independence between categorical variables. Multivariable linear regression models were applied to investigate the relationship between subjectively assessed nutritional status and objective health indicators, while adjusting for the main confounding factors. The level of statistical significance was set in all analyses at $\alpha = 0.05$. All analyses were performed with the

Table 1 Demographic and lifestyle characteristics of the study participants (N= 152)

Demographic data	
Sex, men (%)	49.3
Age (years)	61.0 (14.0)
Education level	
None	0.7
Primary (%)	23.4
Secondary (%)	12.4
Higher (%)	63.4
Marital status: married/with partner (%)	74.5
Lifestyle characteristics	
Night sleep duration (h)	6.5 (2.3)
Sleep quality, self-reported	
Very good (%)	13.1
Good (%)	40.7
Bad (%)	29.7
Very bad (%)	16.6
Walking time (h/day)	0.25 (0.75)
Sedentary time (h/day)	16 (5.0)
Screen time (h/day)	3.6 (3.0)
Smoking habits	
Smokers (%)	20.0
Never smoked (%)	39.3
Stopped smoking (%)	40.7

statistical package SPSS Statistics (version 24.0; IBM, Armonk, NY, USA).

Results

The study consisted of 152 volunteers (50.7% women), with median age 61 years. The majority had a higher level of education (63.4%), were married or in a relationship (74.5%), had good or very good sleep quality (53.8%) and stated that they did not smoke during the study period (80.0%), that their main physical activity was walking (30.5 min/day) and the median of h/day spent on screen was 3.6 (Table 1). The most prevalent types of cancer were head, neck, and spinal (29.2%) and gastrointestinal (GI) tract and colorectal cancer (27%) and 47.3% of them were in cancer stage IV. A total of 25% of patients were newly diagnosed, with 5.8% being diagnosed at least 5 years prior to recruitment. The vast majority of volunteers (94.2%) followed chemotherapy as a treatment. The most common reported comorbidities were hypertension (17.2%) and diabetes mellitus (15.9%; Table 2).

Subjective assessment of patient's nutritional status indicated that 54.9% were severely malnourished, 83.6% were at nutritional risk, and 48.7% had high risk for weight loss within 6 months, according to PG-SGA, NRS-2002, and SNAQ, respectively. We calculated the percentage of patients with cachexia and we identified cancer cachexia in 50.7% of the sample. Objective assessment included anthropometric measurements

Table 2 Clinical and pathological characteristics of the study participants (N= 152)

Cancer morbidity years	
0, newly diagnosed (%)	25.2
1–5 (%)	37.0
≥ 6 (%)	37.8
Cancer stage	
I (%)	8.5
II (%)	24.0
III (%)	20.2
IV (%)	47.3
Cancer type	
Head, neck and spinal (%)	29.2
GI tract and colorectal (%)	27
Lung (%)	16.1
Breast (%)	13.1
Other types ^a (%)	14.6
Type of treatment	
Chemotherapy (%)	94.2
Radiotherapy (%)	49.3
Surgery (%)	40.6
Immunotherapy/biological therapy (%)	36.2
Hormone therapy (%)	5.8
Bone marrow or peripheral blood stem cell transplantation (%)	3.6
Comorbidities	
Hypertension (%)	17.2
DMt2 (%)	15.9
Dyslipidemia (%)	12.4
Hyperthyroidism (%)	8.3
None (%)	44.8
DMt2 Diabetes mellitus type 2, GI gastrointestinal	
^a Other types: tonsil, oropharynx, testes, liver, cholangiocarcinoma, bone, prostate, endometrium, esophagus, gallbladder, larynx, vulva, nasopharynx, ovaries, pharynx, stomach, thyroid gland, liposarcoma, lymphoma	

as well as biochemical and hematological parameters. Relative to the main biochemical and hematological markers associated with the nutritional status, median score for total protein, albumin, and Hgb were 7, 4.1, and 12.0 g/dl, respectively. The median body mass index (BMI) of the sample was 24.5 kg/m². The median value of MUAC, TSF, and HGS were 29.5 cm, 20.1 mm, and 26 kg, respectively. Based on GNRI, 53.6% of geriatric patients were at nutrition-related risk of morbidity and mortality (Table 3).

The prevalence of malnutrition risk across different cancer types and stages, assessed with different subjective assessment tools is shown in Fig. 1. The distribution of the prevalence was similar between the PG-SGA and NRS-2002 questionnaires, with higher scores in GI tract/colorectal and lung patients with cancer. Based on SNAQ, the prevalence of malnutrition was greater among breast and other cancer types. Malnutrition risk, based on PG-SGA and NRS-2002, was significantly higher within the later stages of cancer ($p=0.04$ and $p=0.05$, respectively). No significant dif-

Table 3 Questionnaires, anthropometric characteristics, biochemical–hematological parameters and GNRI

Questionnaires	
<i>PG-SGA</i>	
Well-nourished (%)	25.4
Moderate/suspected malnutrition (%)	19.7
Severely malnourished (%)	54.9
<i>NRS-2002</i>	
Nutritionally not at risk—weekly rescreening (%)	16.4
Nutritionally at risk—nutritional care plan initiated (%)	83.6
<i>SNAQ</i>	
Not at risk of weight loss within 6 months—no nutritional intervention needed (%)	51.3
High risk of >5% weight loss within 6 months—nutritional intervention needed (%)	48.7
Cancer cachexia (%) ^a	50.7
<i>Anthropometric characteristics</i>	
BMI (kg/m ²)	24.5 (6.0)
MUAC (cm)	29.5 (7.0)
TSF (mm)	20.1 (15.5)
HGS (kg)	26.0 (14.0)
% 6-month weight loss	5.3 (13.4)
<i>Biochemical and hematological parameters</i>	
Albumin (g/dl)	4.1 (0.6)
Total protein (g/dl)	7.0 (1.2)
Urine (mg/dl)	32.0 (15.1)
Creatinine (mg/dl)	0.8 (0.3)
Uric acid (mg/dl)	4.5 (2.2)
Potassium (mmol/L)	4.4 (0.7)
Sodium (mmol/L)	140.0 (4.7)
Calcium (mg/dl)	9.2 (0.7)
Magnesium (mg/dl)	2.0 (0.3)
Phosphorus (mg/dl)	3.5 (0.9)
Hgb (g/dL)	12.0 (2.6)
<i>GNRI (> 65 years: N = 28)</i>	
All risk (≤ 98) (%)	53.6
No risk (> 98) (%)	46.4
<i>PG-SGA Patient-Generated Subjective Global Assessment, NRS-2002 Nutrition Risk Screening, SNAQ Simplified Nutritional Appetite Questionnaire, BMI Body Mass Index, MUAC Mid-Upper Arm Circumference, TSF Triceps Skinfold Thickness, HGS Handgrip strength, Hgb Hemoglobin, GNRI Geriatric Nutritional Risk Index</i>	
^a Calculation was based on the following criteria: (1) Weight loss >5% or (2) BMI <20 and weight loss >2%. There are no available data as regards the 3rd criterion (i.e., sarcopenia and weight loss >2%)	

ference was observed between SNAQ and different cancer stages.

The results of the objective nutritional assessment methods were then compared to the PG-SGA-derived categories (Fig. 2). Severely malnourished patients experienced significant weight loss within 6 months prior to recruitment. Moreover, they had lower HGS (up to 25 kg) compared to well-nourished (HGS up to 30 kg). MUAC was similar within the three categories of PG-SGA, while TSF was higher in well-nourished individuals.

Table 4 Multivariable linear regression models for the association of PG-SGA categories with objective nutritional assessment tools

	B	Std. Error	P value
ln(HGS) (kg)	−0.11	0.44	0.02
ln(TSF) (mm)	−0.14	0.64	0.03
ln(MUAC) (cm)	−0.05	0.02	0.004
ln(BMI) (kg/m ²)	−0.06	0.02	0.003
ln(% 6-month weight loss)	1.26	0.18	1.56E-9
ln(Hgb) (g/dL)	−0.05	0.02	0.04

Each linear regression model has been adjusted for age, gender and type of cancer
BMI Body Mass Index, *Hgb* Hemoglobin, *HGS* Handgrip strength, *MUAC* Mid-Upper Arm Circumference, *TSF* Triceps Skinfold Thickness

HGS, TSF, MUAC, BMI, % 6-month weight loss, and Hgb were all significantly associated with PG-SGA categories (Table 4). A higher PG-SGA classification was negatively associated with ln(HGS) (beta = −0.11, *p* = 0.02), ln(TSF) (beta = −0.14, *p* = 0.03), ln(BMI) (beta = −0.06, *p* = 0.003), ln(MUAC) (beta = −0.05, *p* = 0.004), and ln(Hgb) (beta = −0.05, *p* = 0.04), after adjusting for age, gender, and cancer type. Moreover, PG-SGA classification was positively associated with ln(% 6-month weight loss) (beta = 1.26, *p* = 1.56E-9) after accounting for the same confounding factors.

Discussion

The present study showed that 74.6% of the patients were moderately/severely malnourished according to PG-SGA, which is concordant with previous studies [14, 15]. In line with other studies [16, 17], 83.6% of the current study sample were nutritionally at risk based on NRS-2002. In another study of Greek patients with cancer, the prevalence of malnutrition based on NRS-2002 (score of ≥ 3) was 45.5% at admission, which possibly is underestimated due to short hospital stay [18]. Using SNAQ, 48.7% was at high risk of >5% weight loss within 6 months. Nho et al. demonstrated that malnourished patients had lower scores of SNAQ, indicating risk for weight loss within 6 months and urgent need of nutritional support so as to prevent malnutrition [19]. Cancer cachexia is a leading cause of malnutrition in cancer patients [4], which may explain why half of our sample (50.7%) has cachexia.

The median BMI was 24.5 kg/m², which represents normal weight. In relevant studies, BMI has been shown to be within the upper limits of normal [20, 21], but in the study of Krishnasamy et al. was found lower, with an average value of 19.5 kg/m² [2]. Chaves et al. [22] stated that BMI and PG-SGA should be used complementarily, BMI to detect excess weight or obesity and PG-SGA to detect malnutrition. The median MUAC was 29.5 cm and the median TSF was 20.1 mm. These measurements are within the normal range for both genders, based on the median age of the sample.

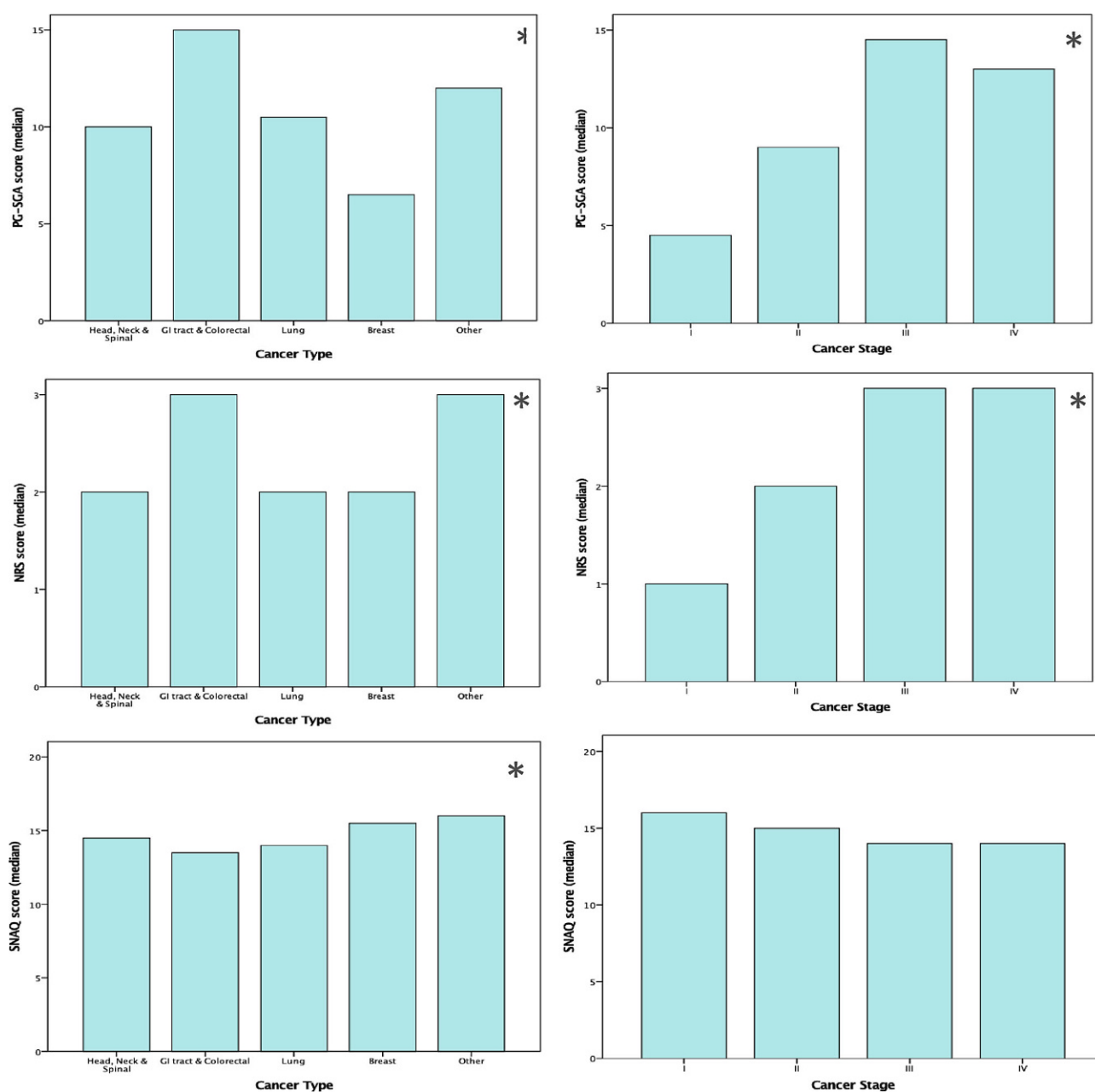


Fig. 1 Prevalence of malnutrition assessed with subjective nutritional assessment tools in various types and stages of cancer. PG-SGA Patient-Generated Subjective

Global Assessment, NRS NRS-2002: Nutrition Risk Screening, SNAQ Simplified Nutritional Appetite Questionnaire. *Kruskal-Wallis H p -values ≤ 0.05

In a recent study, MUAC and TSF were 26.99 cm and 16.02 mm, respectively, indicating similar results [23]. In their study, Fonseca et al. [16] reported contradictory results in terms of TSF, with the majority of patients having below normal values [16].

Herein, the evaluation of HGS for men and women was found within normal range (26 kg). However, HGS was significantly lower in malnourished patients compared to well-nourished ones. Similar results were previously reported [7, 8, 20, 21, 24]. The biochemical and hematological markers investigated were within normal range and in line with results from other studies [17, 20]. However, total protein was found to be

below normal reference ranges in 37.0% of the volunteers, particularly after a surgery [25]. GNRI revealed that 53.6% of patients were at nutritional risk. A recent study which aimed to detect malnutrition in patients with rectal cancer using GNRI demonstrated similar results [26].

The incidence of malnutrition in these patients varies, according to the type and stage of cancer. Higher prevalence of malnutrition was reported in GI/colorectal, lung and head, neck and spinal cancer. Moreover, the greater the cancer stage the greater the malnutrition (PG-SGA and NRS-2002). In their review, Bossi et al. mentioned that gastroesophageal, pan-

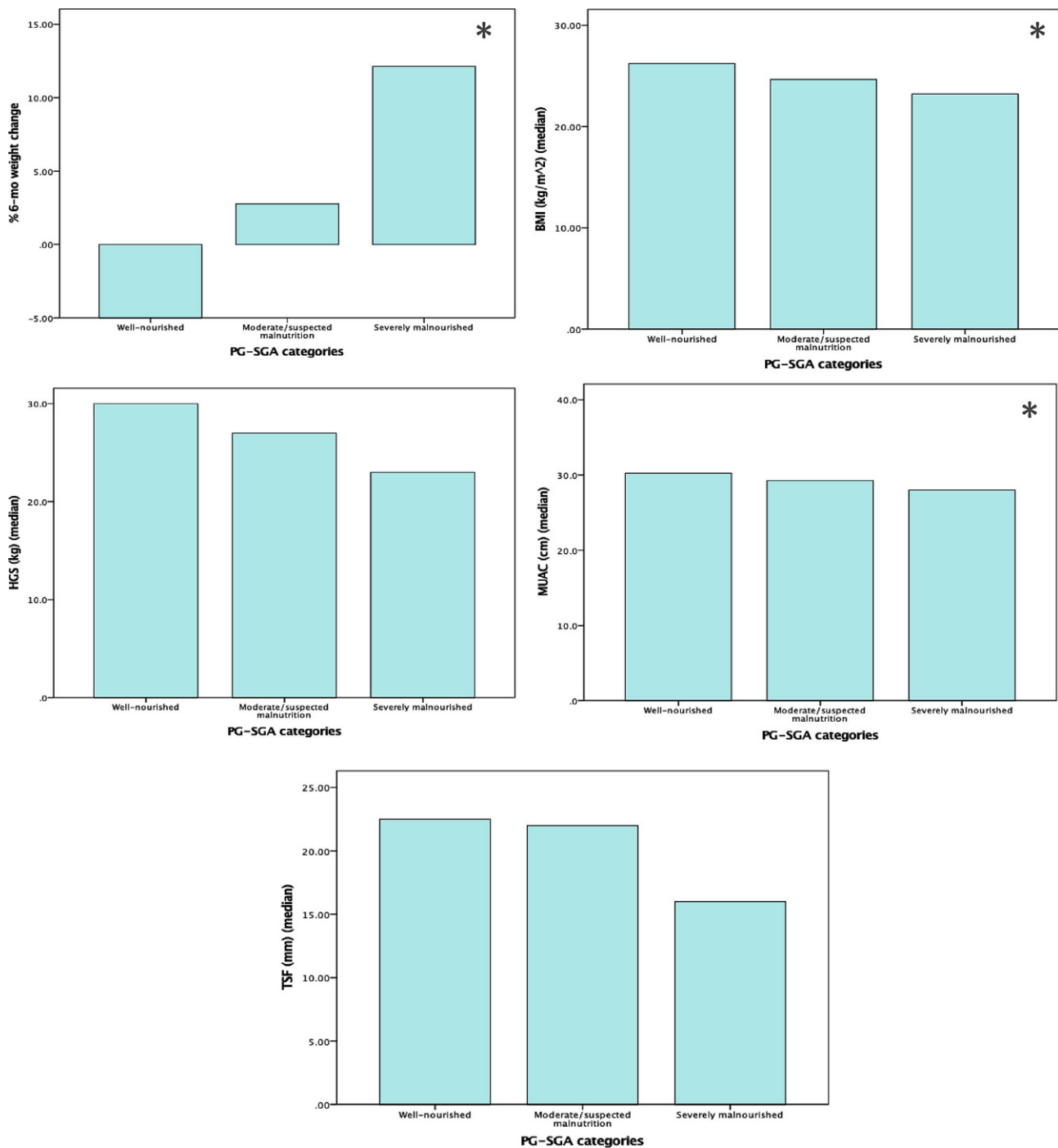


Fig. 2 Distribution of objective nutritional assessment parameters across PG-SGA categories. *PG-SGA* Patient-Generated Subjective Global Assessment, *HGS* Handgrip strength,

MUAC Mid-Upper Arm Circumference, *TSF* Triceps Skinfold Thickness. *Kruskal–Wallis H p -values ≤ 0.05

creas, and head and neck tumors pose the greatest risk of malnutrition [27]. In a similar Greek study, higher risk for malnutrition was linked to stomach and colorectal cancer [18]. These types of cancer are linked to protein-energy deficiency and cachexia [27]. SNAQ score was lower among patients with higher cancer stage, but it was not statistically significant. SNAQ assesses dietary habits and appetite which, depending on the location of the cancer, may not be

significantly affected. Furthermore, when disease is advanced, it is also possible that dietary habits may not differ significantly during the last period (e.g., from stage 3 to 4) and thus no significant difference can be observed. In a recent study, it was stated that SNAQ lacks accurate prediction of immediate weight loss in advanced cancer patients [28].

The multivariable linear regression analyses conducted in this study revealed an association between

PG-SGA and anthropometric measurements as well as Hgb. As the HGS increased, PG-SGA score decreased. Similar results were demonstrated by other studies [24, 29]. The relationship between HGS and PG-SGA could be explained by the relationship between muscle function and nutritional status. Skeletal muscle is the body's preferred energy source when malnutrition is present, resulting in loss of protein stores and deterioration in muscle strength and functionality. Muscle protein stores have been linked to quickly reintroduced food intake [8, 21]. The negative relationships between PG-SGA categories and TSF and MUAC are in agreement with relevant studies [7, 8, 20]. Patients with cancer tend to have high catabolism, which can lead to lower TSF and MUAC as a result of increased proteolysis and lipolysis, rapid weight loss, and disease severity [8]. BMI and % 6-month weight loss have been demonstrated to be major prognostic indicators of poor nutritional status in patients with cancer [21, 30]. Finally, as in earlier studies, the inverse relationship between PG-SGA categories and Hgb was demonstrated [20, 30].

To date, there are very limited studies which have compared objective and subjective measurements to assess malnutrition in Greek patients with cancer. The combination of these indicators reduces the potential risk of extracting invalid results. Still, the findings of this study should be interpreted under the light of its limitations. Due to its epidemiological design, it was not possible to establish cause-and-effect associations. The study sample was relatively small and obtained from a single hospital in Athens, so the results may not be applicable to the entire Greek population of cancer patients.

Conclusion

The present study reported high risk of malnutrition in Greek patients with cancer, as estimated by subjective nutritional tools, despite normal levels of several objective measurements. Furthermore, poor nutritional status, as assessed by PG-SGA, was positively associated with anthropometric measurements and Hgb levels. These findings highlight the need for multidisciplinary nutritional support teams in hospitals, which will i personalized interventions to prevent or treat malnutrition in patients with cancer.

Take home message

- All cancer patients should be assessed for nutritional risk at the time of diagnosis and throughout treatment.
- Healthcare providers should work closely with a registered dietitian to develop individualized nutrition plans for cancer patients.
- Cancer patients should be provided with education and resources on healthy eating during cancer treatment and recovery.

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Author Contribution O. Androutsos conceived, planned and supervised the study; I.P. Kalafati carried out the statistical analyses and contributed to the writing of the manuscript. All authors discussed the results and contributed to the final manuscript.

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Declarations

Conflict of interest K. Vamvakari, I. Evangelou, I.P. Kalafati, M. Kipouros, R.I. Kosti, A.N. Kasti and O. Androutsos declare that they have no competing interests.

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. The present study was approved by the Bioethics Committee of the Attikon University Hospital (E.B.D. 315).

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