



Applied nutritional investigation

Nutritional assessment by subjective methods versus computed tomography to predict survival in oncology patients

Paula Von Geldern R.D.^{a,b}, Claudio Salas M.D.^c, Pablo Alvaay M.D.^c, Claudio Silva M.D.^c,
 Maria Pía de la Maza M.D., M.Sc.^{b,c,*}

^a School of Nutrition and Dietetics, Mayor University, Santiago, Chile

^b Institute of Nutrition & Food Technology Dr. Fernando Monckeberg Barros (INTA), University of Chile, Santiago, Chile

^c Clínica Alemana de Santiago, Faculty of Medicine, Del Desarrollo University (UDD), Santiago, Chile

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ABSTRACT

Objectives: The aim of this study was to analyze the association between survival and two validated methods of nutritional assessment: body composition through computed tomography (CT) scans and Patient-Generated Subjective Global Assessment (PG-SGA).

Methods: Cancer-bearing patients (n = 103) hospitalized in the Oncology Ward of Clínica Alemana in Santiago, Chile, for palliative or curative treatment were assessed by both methods. Images from abdominal CT scans at the L3 level were analyzed by SliceOmatic (version 5.0), to measure muscle and fat areas and densities. Skeletal muscle mass index (MMI) was calculated using total abdominal mass area (psoas + rest of muscles)/ height². These were compared with those obtained for assessment of trauma of 130 healthy young adults (18–40 y of age), as reference control values. Sarcopenia was established as MMI < 1 SD compared with control participants.

Results: Patients with cancer had less muscle and higher abdominal fat areas compared with controls (P < 0.05). According to the PG-SGA, ~50% were classified as malnourished. Patients were followed for 38 mo, when 53% had died. Survival time was significantly and negatively correlated with PG-SGA score, cancer stage, and sarcopenia, independent of age and sex. Multivariate analysis included both cancer stage and nutritional assessment variables.

Conclusions: Together with cancer stage, both CT measurements and subjective assessment of nutritional status through PG-SGA can adequately identify cancer patients with a higher mortality risk, independent of age and sex. However, the latter is less costly and simple to use; it should be included as a valuable tool during management of patients with cancer.

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Introduction

The characteristic representation of malnutrition associated with neoplastic diseases is cancer cachexia, which can be defined according to the 2011 international consensus [1] as a “multifactorial syndrome defined by an 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.” It is a continuous process that consists of three stages of clinical relevance: precachexia, cachexia, and refractory cachexia [1]. The presence of cachexia is directly or indirectly responsible for the death of one-third of patients with cancer [2].

Sarcopenia was originally introduced as a term to define the age-related decline of muscle tissue [3]. It now includes loss of muscle mass and function associated with chronic diseases, including cancer [4]. Thus, all cachectic patients are sarcopenic although not all of these patients have cachexia [5]. Sarcopenia is associated with higher post-operative complications [6], with adverse events associated with anti-tumor treatments [7], leading to dose reduction or premature discontinuation of oncology treatments [1]. Therefore, the presence of sarcopenia in patients undergoing surgery for cancer, is a significant predictor of short- and long-term results [8].

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*Corresponding author. Tel.: +56 222 978 1502; fax.: +56-22214030.

E-mail address: mdelamazac@alemana.cl (M.P. de la Maza).

Several studies report associations between loss of muscle mass and drug toxicity [9,10] and increased mortality [11–13]. Regarding the response to antineoplastic treatments among patients with sarcopenia, data are few and discordant [14,15].

Detection of sarcopenia requires specific anthropometric measurements, or the use of equipment to assess muscle mass and function adequately [4]. The tomographic radiology images obtained from computed tomography (CT) allow the direct measurement of the adipose and skeletal muscular compartment of the whole body or body segments, and has been established as an excellent method to detect sarcopenia [16], especially among patients with cancer, which usually require repeated tomographic images during follow-up.

Subjective methods of nutritional evaluation such as the Patient-Generated Subjective Global Assessment (PG-SGA) have been also validated. Results of this assessment are delivered through a categorical classification (A, B, or C) or by numeric scores, recommending appropriate measures for its management. Thus, the PG-SGA is a very useful tool for the diagnosis of malnutrition and planning of nutritional care, being the most recommended for patients with cancer [6,17]. Subjective methods have both high sensitivity and specificity compared with objective nutritional variables [18]. Moreover, because the PG-SGA includes various clinical variables and evaluates the overall functionality of the patient, it can be considered as a method to approach the diagnosis of sarcopenia and cachexia. To date, several studies have found significant associations between PG-SGA and survival in patients with cancer. In short follow-up periods, studies have reported lower survival when PG-SGA scored ≥ 9 or was classified as B or C [19–21]. A retrospective Brazilian study also found a negative association between PG-SGA B and both 30- and 90-d mortality post-gastrectomy for cancer [22]. Thus, the PG-SGA could be considered a nutritional assessment tool as well as a predictor of mortality in oncology.

The aim of this study was to analyze the relationship between nutritional status, evaluated both through PG-SGA and by the objective measurement of muscle and fat mass using CT at the third lumbar vertebrae (L3), with global survival time, in a sample of hospitalized patients with cancer. Our hypothesis was that sarcopenia is a predictor of survival, independent of cancer stage.

Patients and methods

A cohort of adult cancer patients hospitalized in the oncology ward of Clínica Alemana (Santiago, Chile) from 2012 to 2014 was studied prospectively, during active cancer treatment with curative or palliative intent. We excluded patients with terminal illness in the agonic phase, patients with psychotic symptoms, and those with altered cognitive functions that prevented them from understanding the scope of the study and signing their consent. The study followed human ethics standards and was approved by the Scientific Ethics Committee from the Faculty of Medicine of Clínica Alemana–Del Desarrollo University. Each patient signed a written informed consent accepting the nutritional evaluation and use of their clinical data for further analysis.

Demographic information, diagnosis, treatments, and other clinical data were obtained from the electronic clinical record, and the PG-SGA through an interview and physical examination of the patient by one of the authors (PV).

The PG-SGA evaluates nutritional status through a brief clinical history and physical examination, including information of changes in weight and dietary intake, characteristic symptoms, functional capacity, cancer stage, and metabolic stress. The first section can be completed by the patient. The second part includes medical data such as physical examination, registering edema, ascites, loss of muscle mass and fat, and prescription of corticosteroids. Nutritional status is then classified as well nourished (A), moderately malnourished or at risk for malnutrition (B), or severely malnourished (C). This method also allows the calculation of a score if each section is quantified, making it less subjective. Scores < 4 are considered adequate nutritional status, scores 4 to 8 are considered malnutrition and implies recommendation of nutritional support provided by a dietitian, scores ≥ 9 indicate urgent need for improved symptom management, nutritional support, or both.

Muscle mass and fat were estimated on images obtained from abdominal CTs performed within 2 mo before or after the inclusion to the study, when available ($n = 64$). All CT scans were performed on 128- or 320-slice multidetector CT scanners (Siemens Definition AS+ or Toshiba Aquilion One, Siemens Healthineers, Forchheim, Germany Aquilion One; Toshiba Medical, Otawara, Japan), with 120 kVp,

210 mAs ref, and automatic dose modulation. Calibration was performed daily; test-retest variability of the obtained images are included in its software. Axial acquisition of the abdomen and pelvis was performed in a portal venous phase after injection of 80 to 120 cc of iodinated contrast media (Omnipaque 350 mgI/mL, GE Health Care, Waukesha, Wisconsin), with an injection rate of 3 to 5 mL/s followed by a saline chaser. A selected axial image at the L3 level was exported from our institution's PACS in DICOM format, and analyzed for muscle and fat mass using Slice-O-matic software (version 5.0, Tomovision, Montreal, Canada). Skeletal muscle mass index (MMI) was established by correcting muscle mass by height (m^2) [18]. To obtain the areas (cm^2) of muscle and adipose compartments, the following thresholds were used in Hounsfield units (HU):

- –29 to 150 HU for skeletal muscle'
- –190 to –30 HU for subcutaneous adipose tissue' and
- –150 to –50 HU for visceral fat tissue.

Negligible interobserver differences for estimation of muscle and fat areas and densities were observed (Lin's concordance correlation coefficient 0.96–0.99). As a reference standard for muscle mass, we included a sample of 130 adult men and women, 18 to 40 y of age, in which an abdominal CT was taken as part of standard trauma protocol [23]. The diagnosis of sarcopenia in cancer patients was established using a cutoff point of -1 SD compared with the control group of men and women. Attenuation or density of the psoas muscle was measured, by manually tracing the contours of the psoas muscles, on the L3 level, on the same software [24]. We considered as high abdominal fat or visceral fat, values over the median of the control group (> 206 and > 70 cm^2 in men and > 57 and > 18 cm^2 in women).

Patients were followed until death or up to 5 y, with a closing date of August 31, 2018. Survival of the patients was calculated from the date of entry into the study until the date of death verified by the clinical electronic records or through national death statistics. The survival time in months was analyzed against the nutritional status, stage of the disease, age, and sex.

Statistical analysis

Normality of the variables was analyzed through the Shapiro–Wilk test. Since most variables were distributed non-parametrically, demographic clinical and nutritional data were compared through Kruskal–Wallis. Then, simple correlation tests were carried out between the nutritional variables, cancer stage, and survival time, separated by sex. Using a cu-off point of -1 SD below values from previously health young men and women [25] comparison of the survival curves between sarcopenic and non-sarcopenic patients was carried out using the log-rank test and Kaplan–Meier survival curves. The same analysis was performed plotting PG-SGA (A, B, or C or numeric scores) and two TNM cancer stages (1 and 2 versus 3 and 4) with survival time. Significance was considered for $P < 0.05$. Finally, two Cox regression models to predict survival time were performed, including diagnosis of sarcopenia by CT scan or PG-SGA and stage of disease corrected by age and sex. Power for these associations was 0.46, 0.99, and 1, respectively.

All study data were entered into a database created with RedCap software (version 6.6, Vanderbilt University) and statistical analysis performed in Stata version 13 (StataCorp, College Station, TX, USA).

Results

We studied 103 patients (46 men, 57 women), 55 y of age on average, during hospitalization for cancer treatment (chemotherapy or radiotherapy) or management of complications, in the Oncology Ward of Clínica Alemana of Santiago. Analysis of survival was performed after a median follow-up of 38 mo.

Table 1 depicts localization of tumors according to sex. Table 2 shows general data from the patients. Owing to low frequency of cancer stages 1 and 2, the sample was grouped in two categories—TNM stages 1 and 2 versus 3 and 4. Staging was unknown in two

Table 1
Cancer sites according to sex

Cancer site	Men (n = 46), no./%	Women (n = 57), no./%
Digestive system	16/34.8	14/24.6
Hematologic	14/30.4	13/22.8
Gynecologic (breast, ovaries)	0	18/31.6
Lung	8/17.4	6/10.5
Testes	5/10.9	0
Other sites	3/6.5	6/10.5

Table 2
Demographic, anthropometric, and clinical stages of patients with cancer patients*

	Total (N = 103)	Men (n = 46)	Women (n = 57)
Age (y)	54.9 ± 13.5 56 (18–83)	55.7 ± 15.7 60 (18–83)	54.3 ± 11.6 55 (28–81)
Height (m)	1.67 ± 0.1 1.66 (1.49–1.88)	1.74 ± 0.08 1.75 (1.53–1.88)	1.61 ± 0.05 1.60 (1.49–1.75)
Weight (kg)	68.4 ± 14.2 67.9 (45–102)	78.4 ± 11.2 79.5 (49.5–102)	60.3 ± 10.7 58.8 (45–96.2)
BMI (kg/m ²)	24.4 ± 4 24 (16.7–36.7)	25.9 ± 3.4 25.7 (17.5–34.9)	23.3 ± 4.1 22.4 (16.7–36.7)
Stages 1–2, n/%	21/20.8	7/15.2	14/25.5
Stages 3–4, n/%	80/79.2	39/84.8	41/74.6

BMI, body mass index.

*Data expressed as mean ± SD and median (min–max) unless otherwise noted.

cases, and cases of leukemia were classified as stage 4. All patients were followed until death or until closure of the study.

Approximately 50% of patients with cancer were classified as undernourished according to the PG-SGA (B and C; 41% of men and 54% of women). PG-SGA scores (A, B, or C) correlated negatively and significantly with muscle and fat areas, and with MMI ($\rho = -0.52$; $P < 0.001$). PG-SGA numeric score averaged 14.3 ± 5.7 (5–30 points), without significant differences due to sex or cancer stage. Body mass index correlated negatively with PG-SGA ($\rho = -0.4$; $P < 0.01$) and positively with muscle areas, but not with survival time. Table 3 depicts variables according to PG-SGA categories.

As stated in the methodology, CT images at L3 from 130 individuals (83 men and 47 women) 18 to 40 y of age were analyzed for calculation of muscle and fat areas. These were considered the control values from young and previously healthy Chileans, for comparison with patients with cancer as no national standards are available. These images were stored in the databases of the Images Department, and have been obtained previously as part of the

workup in trauma patients. Total muscle area at the L3 level corrected by squared height (MMI) in control subjects averaged $58.6 \pm 7 \text{ cm}^2/\text{m}^2$ and $42.9 \pm 4.8 \text{ cm}^2/\text{m}^2$ in men and women, respectively, which was higher than values obtained in 64 cancer patients with available CT scans [26]. Fifteen male (58%) and 15 female patients (39.5%) were classified as sarcopenic (MMI <1 SD compared with healthy controls). Sarcopenic patients exhibited significantly higher PG-SGA scores (11.2 ± 3.8 versus 17.2 ± 6 ; $P < 0.001$). No statistical correlations were found between cancer stages with measured muscle and fat areas in either sex.

Fat areas were significantly higher among the patients than the controls, specifically at the visceral compartment, although we found no relation between fat compartments and survival. Muscle density as an indicator of tissue fat infiltration was also significantly lower among patients than controls (Table 4).

After a median follow-up time of 38 mo (0.2–66 mo), 55 patients had died (26 men and 29 women). Of the 55 who died, 1 died in stage 1, 5 in stage 3, and 48 in stage 4, TNM classification. According to univariate analysis, survival time was inversely correlated with age, cancer stage, PG-SGA but not with MMI nor abdominal fat area (data not shown). Kaplan–Meir survival estimates were significant for diagnosis of sarcopenia, cancer stage, and PG-SGA (Figs. 1 and 2).

A Cox regression model, including TNM staging and MMI expressed as a continuous variable or dichotomized (with or without sarcopenia), rendered both variables as significant predictors of survival, independent of age and sex. If muscle mass was exchanged for PG-SGA in the regression model, again both cancer stage and PG-SGA appeared as significant predictors of survival (Table 5). We did not include muscle mass and PG-SGA in the same model because both variables were significantly correlated.

The coexistence of sarcopenia with elevated total abdominal fat (over the median areas of healthy controls, that is, >206 in men and >157 cm² in women) was not correlated with survival time;

Table 3
Distribution of variables according to PG-SGA

	PG-SGA A (n = 54)	PG-SGA B (n = 42)	PG-SGA C (n = 7)	P-value
Age (y)	53 ± 14 54.5 (18–78)	58 ± 12 58.5 (31–83)	51 ± 12 55 (28–65)	0.14 0.17
Men/Women (n)	27/26	18/28	1/3	0.286
Cancer stage 1–2 vs 3–4 (n)	17/35	4/41	0/4	0.011
PG-SGA score	11.2 ± 3.9 10 (5–23)	16.4 ± 4.4 16.5 (7–26)	25.7 ± 2.6* 25 (22–30)	<0.001 0.0001
BMI (kg/m ²)	25.7 ± 4 25.2 (18.4–36.7)	23.7 ± 3.3 23.5 (16.7–31.6)	19.0 ± 1.3* 18.4 (17.5–20.7)	<0.001 0.0001
Psoas area (cm ²)	18.1 ± 5.3 ¹ 17.5 (10–30)	16.2 ± 5.8 15.1 (7.8–30.6)	10.5 ± 2.5 10.4 (7.8–14.7)	0.0086 0.0059
Total muscle area (cm ²)	136.0 ± 32.1 ¹ 134 (91.8–196.5)	120.5 ± 28.6 114.5 (72–162)	96.3 ± 23.4 89.2 (79.6–141.7)	0.0086 0.0065
Muscle mass index (cm ² /m ²)	48.0 ± 8.6 ¹ 47.9 (33–65.7)	43.3 ± 7.4 43.9 (28.9–59.6)	34.9 ± 4.7 35.7 (28.2–41.4)	0.0009 0.0017
Psoas density (HU)	49.0 ± 7.1 49.5 (30.1–62.3)	44.6 ± 7.5 43.8 (20.8–55.7)	44.3 ± 7.9 43.1 (36.3–57.9)	0.0591 0.0781
Total fat mass (cm ²)	347.2 ± 147.7 ² 375.2 (77.5–645.8)	248 ± 109 256.6 (66.9–493.3)	139.2 ± 77.6 118.1 (62.4–285.6)	0.0005 0.0009
Subcutaneous fat area (cm ²)	200.2 ± 32.1 ¹ 189.9 (52.8–455.3)	148.4 ± 54.7 150.9 (47.2–310.2)	76.2 ± 32.5 70.5 (45.7–121.3)	0.0003 0.0002
Visceral fat mass (cm ²)	147 ± 104.2 141.4 (20.5–406.3)	99.6 ± 66.3 85.4 (11.1–249.3)	63 ± 54.2 50.8 (12.6–164.3)	0.0347 0.0587

BMI, body mass index; PG-SGA, patient-generated subjective global assessment.

Data expressed as mean ± SD or ratios (first line) and median (min–max) below each variable. Statistical analysis by one-way analysis of variance (first line) and Kruskal–Wallis. Data on available computed tomography scans (n = 64).

Post hoc analysis:

*Significantly different to PG-SGA A and B.

¹Significantly different to PG-SGA A and C.²Significantly different to PG-SGA C.³Significantly different to PG-SGA B and C.

Table 4
Tomographic muscle and fat areas from patients and control group

	Male patients (n = 26)	Male controls (n = 83)	P-value	Female patients (n = 38)	Female controls (n = 47)	P-value
Psoas area (cm)	21.7 ± 4.2	27.8 ± 6	<0.001	13.1 ± 3.5	15.8 ± 3.2	0.004
	22.0 (14.7–30.6)	26.4 (17.4–45.5)	0.0001	12.5 (7.8–20.7)	15.8 (10.3–22.2)	0.0005
Total muscle area (cm ²)	157.2 ± 19.6	183.1 ± 22.2	<0.001	104.7 ± 18.2	116.4 ± 14.4	0.0014
	153.3 (116.2–196.5)	182.6 (126.3–268.7)	0.0001	103.8 (72–147)	115.4 (85.6–145.1)	0.0012
Muscle mass index (cm/cm ²)	51.2 ± 6.5	58.6 ± 7.0	<0.001	40.5 ± 7.2	42.9 ± 4.8	0.0743
	51 (38.4–65.7)	58.7 (39.5–82)	0.0001	39.8 (28.2–59.6)	42.8 (32.6–55.3)	0.0310
Psoas density (HU)	47.2 ± 8.3	55.5 ± 5.5	<0.001	46.5 ± 7.1	53.6 ± 6	<0.001
	48.3 (20.1–62.3)	56.2 (42.2–66.8)	0.0001	47.5 (20.8–57.9)	54.0 (40.1–66.7)	0.0001
Subcutaneous fat area (cm)	165.4 ± 50	147.8 ± 109.4	0.4281	168.9 ± 96.2	150 ± 82.2	0.3313
	179.8 (45.7–239.5)	119.2 (3.7–591.9)	0.0620	153.9 (47.2–455.3)	136.4 (20.5–369.2)	0.4686
Visceral fat area (cm)	178.3 ± 95.5	81.1 ± 70.7	<0.001	79.9 ± 60.9	25.3 ± 20.5	<0.001
	175.3 (24.7–406.2)	69.8 (2.1–369.4)	0.0001	54.5 (11.1–249.3)	18.2 (3.5–92.7)	0.0001
Total fat area (cm)	343.8 ± 126.7	230.3 ± 160.3	0.0013	248.8 ± 142.3	175.3 ± 99.3	0.0064
	355.5 (77.5–645.8)	205.8 (5.77–686.3)	0.0003	220.4 (62.4–627.2)	157.3 (24.1–427.4)	0.0178

Data expressed as mean ± SD (first line) and median (min–max) below each variable. Significant if $P < 0.01$ by analysis of variance or Kruskal–Wallis.

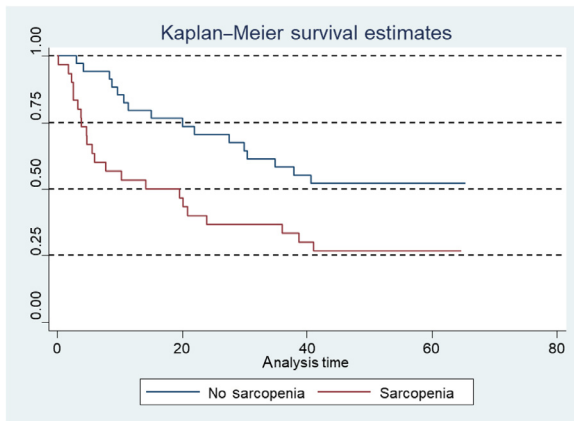


Fig. 1. Survival curves comparing patients with or without sarcopenia ($P = 0.0240$).

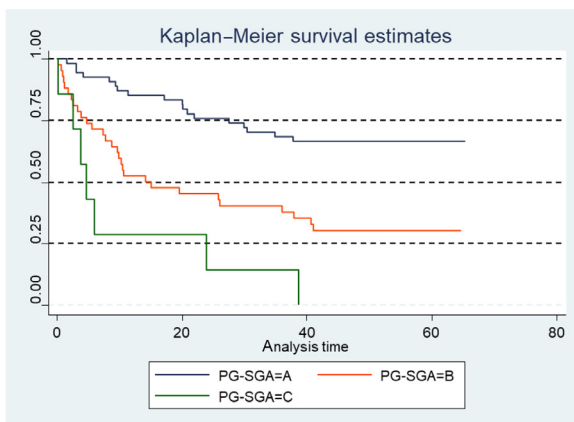


Fig. 2. Survival curves comparing patients according to PG-SGA classified as A, B, or C ($P = 0.0000$). PG-SGA, patient-generated subjective global assessment.

however, when considering sarcopenia with higher visceral abdominal fat (>70 in men and >18 cm² in women), a trend toward lower survival was observed ($P = 0.07$).

Discussion

The present study analyzed the relationship between nutritional status evaluated both through a subjective method (PG-SGA) and

Table 5
Cox regression models

Variables model 1	HR	SE	Z	$P > z $	95% CI	
Sex	1.02	0.34	0.07	0.94	0.53	1.96
TNM stage	12.5	12.90	2.46	0.01^a	1.67	94.10
Sarcopenia (Y/N)	2.38	0.80	2.59	0.01	1.23	4.60
Age	1.01	0.01	0.85	0.40	0.98	1.04
Variables model 2	HR	SE	Z	$P > z $	95% CI	
Sex	0.85	0.23	-0.59	0.56	0.50	1.46
TNM stage	15.4	15.6	2.69	0.01	2.10	112.74
PG-SGA	2.42	0.53	4.03	0.00	1.58	3.72
Age	1.01	0.12	0.98	0.33	0.99	1.04

PG-SGA, patient-generated subjective global assessment.

^a P -values in bold indicate significant survival predictor variables

the objective measurement of muscle and fat areas by CT at L3 with global survival in a heterogeneous group of patients with cancer. PG-SGA scores started from five points, suggesting that none of these patients should be considered nutritionally normal, although 52% were classified as A. This was not unexpected because, although nutritional assessment methods can be highly correlated, agreement between them can be moderate or low, as reported by Raeder et al. [25]. As expected, patients with advanced stages of disease had more nutritional deterioration and less survival time, but malnutrition contributed as well, independent of age and sex. Most importantly, the contribution of nutritional status was evident both when assessed through CT images or subjectively by PG-SGA. Coincidentally, a Brazilian study in patients with advanced cancer under palliative care found that a PG-SGA score ≥ 20 points was the best cutoff point for classifying patients predicted to be dead within 30 d, unlike the broader classification of malnutrition (B or C) [26], suggesting that the numeric score is more sensitive for detection of cachexia. Another retrospective Brazilian study suggests that the combination of PG-SGA with the Karnofsky Performance Status score should be the best approach for predicting survival and also focuses on the adequate management of specific symptoms during the terminal phases of this illness [27].

Using CT images, we detected sarcopenia (-1 SD below control values) in 58% of male and 40% of female patients. Cutoff points for sarcopenia were established as <1 SD compared with the control group, as 2 SD gave extremely low numbers and would have classified only nine patients as sarcopenic, whereas 1 SD behaved as an adequate predictor of survival both when expressed as a

continuous or dichotomic variable in the Cox regression models, although underpowered for univariate analysis because only 64 CTs were available. Average body mass indexes were within normal or overweight ranges in most patients, and although we detected only one sarcopenic obese patient in this sample, it is worth noting that abdominal fat, specifically the visceral compartment, and possibly muscle fat infiltration, was significantly higher in the patient group than in healthy controls. Low muscle area (either as absolute or corrected by squared height) was negatively correlated with survival time, and patients with sarcopenia and visceral fat areas over median values of the control group showed a non-significant trend toward less survival time, which was not evident among sarcopenic patients with higher subcutaneous fat area. These findings could suggest that the metabolic derangements responsible for muscle loss in cancer cachexia, could also induce alterations in adipose tissue, similar to those observed in ageing and in the metabolic syndrome, which could be attributed to circulating inflammatory cytokines [28].

The results of the present study are similar to those of Martin et al., who studied overweight and obese patients with advanced cancer and found that survival was associated with sarcopenia, myosteatosis, and PG-SGA score >9; however, Martin et al. employed a short form of this triage method [29]. Although we detected higher density in the psoas muscle, we do not have cutoff points of radiodensity to assess myosteatosis, and limitations for the analysis of radiologic attenuation in CT scans performed for clinical purposes must be considered [24]. This is due to the fact that variable contrast enhancement given by slight variation in acquisition timing, which have a significant effect on HU measurements, therefore rendering it flawed when used in clinical settings (beyond controlled clinical protocols).

Several studies using tomographic measurements of muscle mass have been performed in patients with cancer, and were shown to predict treatment toxicity and mortality [13,30,31], even better than subjective methods [32]. However, these cutoff values could not be employed for our patients because we found lower muscle mass and strength among Chileans [23,33]. The most widely employed cutoff points of MMI to define sarcopenia are those reported by Prado et al [9]: <52.4 cm²/m² for men and <38.6 cm²/m² for women. The present cutoff values were obtained using comparable methodology (values from a group of young and healthy individuals, similar to bone T scores, and not obtained from age-matched controls). Resulting cutoff values were <51.6 cm²/m² for men and 38.1 cm²/m² for women. Thus 30% of the cancer patients in the present study were classified as sarcopenic. Sarcopenia was significantly associated with malnutrition assessed by PG-SGA (among non-sarcopenic patients, 24% were classified as PG-SGA B or C compared with 80 % among patients with sarcopenia), but both sarcopenia and malnutrition were present in 38% of our patients, so again concordance between both measurements was low ($\kappa = -0.18$). An important aspect of these CT measurements and cutoff points is that they are usually corrected by squared height, which limits comparison between countries and ethnic groups, and also tend to “normalize” data from elderly individuals, who progressively lose stature [33]. Additionally, it deserves mentioning that quantification of psoas area, although easier (it can be performed even by economic available software), represents a low percentage of trunk muscles, so could fail to accurately reflect total body muscle mass, and therefore it is not recommended for assessment of sarcopenia [34,35].

The present study had several limitations, such as a reduced sample size, heterogeneous cancer sites and treatments, and images that were not available for all the patients. Cancer stage in leukemia was considered as TNM IV which can be questionable.

However, these data represent the reality of an oncologic ward, and has several strengths, such as the long-term follow-up (>5 y), and use of the best validated measurements for nutritional assessments among cancer patients. Young controls were chosen as local standard values following usual recommendations [23]; images were obtained as part of trauma assessment, otherwise costs and ethical limitations could preclude these measurements.

The best approach would be to analyze the evolution of tomographic measurements throughout cancer treatment to assess muscle and fat loss, and plot against treatment toxicity and patient survival, as studied retrospectively by Kays et al. [30].

Conclusion

In this sample, both PG-SGA and sarcopenia measured by CT, together with disease stage, were predictors of survival in patients with cancer, independent from other confounding variables such as age and sex. Although the former is simpler and has a lower cost, evidence suggests that it is better to express results through its numeric scoring system and thus identify which aspects are more compromised and plan adequate nutritional support. Body composition measurements should be obtained at diagnosis and followed for detection of muscle and fat wasting or accretion, to employ multimodal treatment strategies, able to counteract cachexia.

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References

- [1] 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.
- [2] Gómez Candela CI, Oliviar Roldán J, García M, Marín M, Madero R, Pérez-Portabella C, Planás M, Mokoroa A, Pereyra F, Martín Palmero A. Assessment of a malnutrition screening tool in cancer patients. *Nutr Hosp* 2010;25:400–5.
- [3] Rosenberg IH. Sarcopenia: origins and clinical relevance. *J Nutr* 1997;127:990S–1S.
- [4] Biolo G, Cederholm T, Muscaritoli M. Muscle contractile and metabolic dysfunction is a common feature of sarcopenia of aging and chronic diseases: from sarcopenic obesity to cachexia. *Clin Nutr* 2014;33:737–48.
- [5] 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.
- [6] Valenzuela-Landaeta K, Rojas P, Basfi-fer K. Nutritional assessment for cancer patient. *Nutr Hosp* 2012;27:516–23.
- [7] Awad S, Tan BH, Cui H, Bhalla A, Fearon KC, Parsons SL, et al. Marked changes in body composition following neoadjuvant chemotherapy for oesophagogastric cancer. *Clin Nutr* 2012;31:74–7.
- [8] Zhang S, Tan S, Jiang Y, Xi Q, Meng Q, Zhuang Q, et al. Sarcopenia as a predictor of poor surgical and oncologic outcomes after abdominal surgery for digestive tract cancer: a prospective cohort study. *Clin Nutr* 2019;38:2881–8.
- [9] Shachar SS, Deal AM, Weinberg M, Williams GR, Nyrop KA, Popuri K, et al. Body composition as a predictor of toxicity in patients receiving anthracycline and taxane based chemotherapy for early stage breast cancer. *Clin Cancer Res* 2017;23:3537–43.
- [10] Heidelberger V, Goldwasser F, Kramkimel N, Jouinot A, Huillard O, Boudou-Rouquette P, et al. Sarcopenic overweight is associated with early acute limiting toxicity of anti-PD1 checkpoint inhibitors in melanoma patients. *Invest New Drugs* 2017;35:436–41.
- [11] El Amrani M, Vermersch M, Fulbert M, Prodeau M, Lecolle K, Hebbat M, et al. Impact of sarcopenia on outcomes of patients undergoing pancreatotomy: a retrospective analysis of 107 patients. *Medicine (Baltimore)* 2018;97:e12076.
- [12] O'Brien S, Twomey M, Moloney F, Kavanagh RG, Carey BW, Power D, et al. Sarcopenia and post-operative morbidity and mortality in patients with gastric cancer. *J Gastric Cancer* 2018;18:242–52.
- [13] Mayr R, Fritsche HM, Zeman F, Reiffen M, Siebertz L, Niessen C, et al. Sarcopenia predicts 90-day mortality and postoperative complications after radical cystectomy for bladder cancer. *World J Urol* 2018;36:1201.

- [14] Rossi S, Di Noia V, Tonetti L, Strippoli A, Basso M, Schinzari G, et al. Does sarcopenia affect outcome in patients with non-small-cell lung cancer harboring EGFR mutations? *Future Oncol* 2018;14:919–26.
- [15] Zargar H, Almassi N, Kovac E, Ercole C, Remer E, Rini B, et al. Change in psoas muscle volume as a predictor of outcomes in patients treated with chemotherapy and radical cystectomy for muscle-invasive bladder cancer. *Bladder Cancer* 2017;3:57–63.
- [16] Murray TE, Williams D, Lee MJ. Osteoporosis, obesity, and sarcopenia on abdominal CT: a review of epidemiology, diagnostic criteria, and management strategies for the reporting radiologist. *Abdom Radiol* 2017;42:2376–86.
- [17] Mendes NP, Barros TA, Rosa COB, Franceschini SDCC. Nutritional screening tools used and validated for cancer patients: a systematic review. *Nutr Cancer* 2019;71:898–907.
- [18] Du H, Liu B, Xie Y, Liu J, Wei Y, Hu H, et al. Comparison of different methods for nutrition assessment in patients with tumors. *Oncol Lett* 2017;14:165–70.
- [19] Read JA1, Choy ST, Beale PJ, Clarke SJ. Evaluation of nutritional and inflammatory status of advanced colorectal cancer patients and its correlation with survival. *Nutr Cancer* 2006;55:78–85.
- [20] Ge T, Lin T, Yang J, Wang M. Nutritional status and related factors of patients with advanced lung cancer in northern China: a retrospective study. *Cancer Manag Res* 2019;11:2225–31.
- [21] Rodríguez CS, Lacerda MS, Chaves GV. Patient generated subjective global assessment as a prognosis tool in women with gynecologic cancer. *Nutrition* 2015;31:1372–8.
- [22] Poziomyck AK, Cavazzola LT, Coelho LJ, Lameu EB, Weston AC, Moreira LF. Nutritional assessment methods as predictors of postoperative mortality in gastric cancer patients submitted to gastrectomy. *Rev Col Bras Cir* 2017;44:482–90.
- [23] Alwayay P, Von Geldern P, De la Maza MP, Silva C. Área muscular abdominal determinada por tomografía computada como predictor de mortalidad en pacientes Oncológicos. *Abdominal muscle area measured by computed tomography as a predictor of mortality in oncologic patients. Rev Chil Radiología* 2015;21:133–7.
- [24] Boutin RD, Kaptuch JM, Bateni CP, Chalfant JS, Yao L. Influence of IV contrast administration on CT measures of muscle and bone attenuation: implications for sarcopenia and osteoporosis evaluation. *AJR* 2017;207:2046–54.
- [25] Ræder H, Henriksen C, Bøhn SK, O de Fey Vilbo AR, Henriksen HB, Kværner AS, et al. Agreement between PG-SGA category and fat-free mass in colorectal cancer patients. *Clin Nutr ESPEN* 2018;27:24–31.
- [26] Wiegert EVM, Padilha PC, Peres WAF. Performance of patient-generated subjective global assessment (PG-SGA) in patients with advanced cancer in palliative care. *Nutr Clin Pract* 2017;32:675–81.
- [27] Carvalho CS, Souza DS, Lopes JR, Castanho IA, Lopes AJ. Relationship between patient-generated subjective global assessment and survival in patients in palliative care. *Ann Palliat Med* 2017;6(suppl 1):S4–12.
- [28] Tisdale MJ. Mechanisms of cancer cachexia. *Physiol Rev* 2009;89:381–410.
- [29] Martin L, Gioulbasanis I, Senesse P, Baracos VE. Cancer-associated malnutrition and CT-defined sarcopenia and myosteatosis are endemic in overweight and obese patients. *JPEN J Parenter Enteral Nutr* 2012;44:227–38.
- [30] Degens JHRJ, Sanders KJC, de Jong EEC, Groen HJM, Smit EF, Aerts JG, et al. The prognostic value of early onset, CT derived loss of muscle and adipose tissue during chemotherapy in metastatic non-small cell lung cancer. *Lung Cancer* 2019;133:130–5.
- [31] Kazemi-Bajestani SM, Mazurak VC, Baracos V. Computed tomography-defined muscle and fat wasting are associated with cancer clinical outcomes. *Semin Cell Dev Biol* 2016;54:2–10.
- [32] Vashi PG, Gorsuch K, Wan L, Hill D, Block C, Gupta D. Sarcopenia supersedes subjective global assessment as a predictor of survival in colorectal cancer. *PLoS One* 2019;4:1–14.
- [33] Wigodski S, Carrasco F, Bunout D, Barrera G, Hirsch S, De la Maza MP. Sarcopenia: the need to establish different cutoff points of fat-free mass for the Chilean population. *Nutrition* 2019;57:217–24.
- [34] Baracos VE. Psoas as a sentinel muscle for sarcopenia: a flawed premise. *J Cachexia Sarcopenia Muscle* 2017;8:527–8.
- [35] Rutten IJG, Ubachs J, Kruitwagen RFP, Beets–Tan RGH, Olde Damink SWM, Van Gorp T. Psoas muscle area is not representative of total skeletal muscle area in the assessment of sarcopenia in ovarian cancer. *J Cachexia, Sarcopenia Muscle* 2017;8:630–8.