CT-defined Sarcopenia Prevalence in Patients With Metastatic Cancer: A Cross-sectional Multicenter French Study (the SCAN Study)

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Abstract

Background: Sarcopenia negatively impacts survival outcomes, treatment tolerability and functionality in cancer patients. However, there is a limited appreciation of its true prevalence, due inconsistent diagnostic methods and limited oncologist training.

Methods: 29 French healthcare establishments participated in this cross-sectional study, recruiting patients with those metastatic cancers most frequently encountered in routine practice (colon, breast, kidney, lung, prostate). The primary outcome was low muscle mass prevalence, as diagnosed by estimating the skeletal mass index (SMI) at the third-lumbar vertebrae (L3) level via computed tomography (CT). Other objectives included an evaluation of nutritional management, physical activity, and toxicities related to ongoing treatment.

Results: 766 patients (49.9% males) were enrolled with a mean age of 65.0 years. Low muscle mass prevalence was 69.1%. Cachexia prevalence among patients was 44.5%, but only one-third of sarcopenic patients benefited from nutritional support. Physicians highly underdiagnosed those patients identified with low muscle mass, as defined by the primary objective, by 74.3% and 44.9% in obese and non-obese patients, respectively. Multivariate analyses revealed a lower risk of low muscle mass for females (OR: 0.22, $P<0.01$) and those without brain metastasis (OR: 0.34, $P<0.01$). Low muscle mass patients were more likely to have delayed treatment administration due to toxicity (11.9% versus 6.8%, $P=0.04$).

Conclusions: There is a critical need to raise awareness of low muscle mass diagnosis among oncologists, and for improvements in nutritional management and physical therapies of cancer patients to curb potential sarcopenia. This calls for cross-disciplinary collaborations among oncologists, nutritionists and physiotherapists.

Introduction

Cancer cachexia is a complex metabolic syndrome characterized by involuntary muscle loss with or without loss of fat mass, systemic inflammation, and negative protein and energy balance. This condition cannot be completely reversed with conventional nutritional care and leads to progressive functional impairment in cancer patients [4, 13, 14]. Cancer cachexia is associated with an increased risk of postoperative complications, increased mortality in the metastatic phase, increased treatment intolerance, longer hospitalizations and alterations in patient quality of life [8, 18, 23, 31]. Deleterious effects increase with severity, delaying cancer management. Early care, prior to 5% bodyweight loss, is thus recommended [31]. Methods of cachexia diagnosis are variable, Fearon et al. [14] propose three different diagnostic criteria: 1) > 5% weight loss in the last 6 months, 2) < 20 kg/m² and ongoing weight loss > 2%, or 3) sarcopenia, evaluated using a muscular mass index, and ongoing weight loss > 2%.

The most clinically relevant phenotype of cachexia is sarcopenia, or loss of muscle mass and function. Different approaches to diagnosis exist, varying particularly between geriatrics and oncology [5]. In geriatrics sarcopenia is linked to a loss of muscle mass and function, associated with ageing. In

oncology, its diagnosis is generally based solely upon the loss of muscle mass. Dual-energy x-ray absorptiometry (DEXA) is the method of reference for measuring muscle mass [9, 11, 12]. Anthropometric evaluations via mid-arm muscle circumference and bio-impedance measurements are two techniques acknowledged by experts who have recently defined cachexia and cancer sarcopenia [14]. More recently, third-lumbar vertebra (L3) computed tomography (CT) cross-sections have been used to estimate body composition [21, 26]. Although this particular application of CT is not yet routinely implemented in France, it has been proposed as an objective measure for sarcopenia diagnosis among oncology patients [22]. Beyond muscular mass assessments, current interest also lies in diagnosing muscular strength and performance, as suggested by the European Working Group on Sarcopenia in Older People (EWGSOP) guidelines [11, 12]. The diagnosis is based on documentation of low muscle mass with either low muscle strength or physical performance (e.g.: the hand-grip test's prognostic value has already been validated in patients with locally advanced or metastatic cancers [19]).

Precise estimates of sarcopenia prevalence among cancer patients remain scarce and vary widely. As such, the primary objective of this cross-sectional, multi-centric study conducted in France was to evaluate the prevalence of low muscle mass as measured by a L3 cross-sectional CT scans in patients diagnosed with metastatic cancers. Moreover, misdiagnoses by oncologists and nutritional strategies available to cancer patients were explored.

Methods

Study population and design

This study was conducted in accordance with the Declaration of Helsinki. All persons provided their informed consent prior to enrollment. The protocol was in line with French data protection regulations (CNIL, approval no. 2066086) and approved by the French ethical research committee, "Le Comité de Protection des Personnes" (CPP), on the 6 July 2017 (approval no. 2017-A01648-45).

This cross-sectional study was conducted within the investigators' oncology practices in 29 public and private hospitals in France, between September and October 2017. Patients were men or women aged ≥ 18 years, diagnosed with metastatic lung, kidney, colon, breast or prostate cancer, and with ongoing chemotherapy, targeted therapy or immunotherapy. Patients had to have a CT scan including an L3 cross-section suitable for SMI evaluation of low muscle mass, performed between 6 weeks before and 4 weeks after inclusion. Patients were excluded if diagnosed with two or more malignant pathologies, if being treated exclusively by radiotherapy, if they had surgery in the previous 30 days, or if they had a concomitant neurological comorbidity, other than cerebral metastasis.

The investigating pair in each center consisted of an oncologist-radiologist duo. Radiologists were trained in cross-sectional skeletal muscle area (TMS) measurement with CT, using a standardized approach, adapted based on the instrument manufacturer's software available on site. The use of different software was considered acceptable, as this does not impact the accuracy and precision of the measures obtained

[35]. Oncologists recorded the following information during the inclusion visit: current weight, weight 1 and 6 months ago, height, dietary and nutritional support for each patient, physical activity, food intake assessment at the previous meal using a visual analogue scale (VAS, wherein 10 signifies normal, healthy food intake for the patient)[33], and performance status (PS) scores using the Eastern Cooperative Oncology Group (ECOG) scale of 0 (fully active) to 5 (death)[24]. Additionally, the oncologist was required to assess for sarcopenia as per their habitual practice (no specific predefined method), while being blinded to the CT results. C-reactive protein (CRP) and serum albumin (SA) data were collected from test results between a month before and a week after the CT-scan to assess malnutrition in line with local guidelines [2] and the patients' Glasgow Prognostic Scores (GPS), categorizing patient prognosis on a scale of 0 (best) to 2 (worst)[15].

Malnutrition severity was defined according to criteria provided by the French national health authorities [17] using the thresholds listed below by age group: moderate malnutrition < 70 years old: BMI ≤ 18.5 to 16 kg/m² or SA < 30 to 20 g/L, and ≥ 70 years old: BMI < 21 to 18 kg/m² or SA < 35 to 30 g/L, and severe malnutrition < 70 years old: BMI ≤ 16 kg/m² or SA < 20 g/L, and ≥ 70 years old: BMI < 18 kg/m² or SA < 30 g/L

Study objectives

The primary objective was to determine the prevalence of low muscle mass in patients with metastatic cancer of the lung, kidney, colon, breast or prostate, by estimating the Skeletal Muscle Index (SMI) at the L3 level. First, the cross-sectional muscle area at L3 level was manually contoured by radiologists; then, pre-established Hounsfield unit (HU) thresholds (-29 to + 150 HU) were applied to quantify the skeletal muscle. Low muscle mass was subsequently determined by calculating the SMI (TMS/ height²), with cut-off values < 55cm²/m² and < 39 cm²/m² indicating low muscle mass in men and women, respectively [14].

Other outcomes included an evaluation of the level of agreement between CT measurements and oncologists' evaluations of sarcopenia (for the total study population, and for obese (Body mass index [BMI] ≥ 30 kg/m²) and non-obese sub-groups (BMI < 30 kg/m²), an assessment of the nutritional management and physical activity trends of cancer patients (using simple survey questions addressed to treating oncologists), and an evaluation of toxicities related to ongoing anti-cancer treatment and their impact on dosage modifications, treatment delays due to toxicity, treatment interruptions and the occurrence of adverse events (AE) $\geq$ grade 3. Cachexia prevalence was estimated, according to each of the three criteria defined by Fearon et al. [14], that were elaborated in the introduction. Multivariate analyses of the relationship between presence of low muscle mass and patient age, sex, primary tumor site, weight loss, current BMI, serum albumin, PS score, VAS for food intake and brain metastasis were also performed.

Statistical analyses

Data management and statistical analyses were performed by Kantar Health (Paris, France), using DAISIE (version 2.4.25 & 2.4.45) and R i386 3.0.1. Descriptive analyses (means, SD, median and range) are provided for continuous variables, percentages for categorical variables. Due to the sample size, it was assumed that the data was distributed normally: the Z-test or t-test were used for comparisons between two groups; a sensitivity analysis was performed using the Wilcoxon test, where similar results were obtained. Cohen's kappa coefficient (κ) denoted the reliability of oncologists' assessments of sarcopenic low muscle mass. Logistic regression evaluating the relationship between the presence of low muscle mass and selected exploratory variables are expressed in OR with 95% confidence intervals (CI). *P*-values for comparisons between the groups with and without low muscle mass were calculated; *P* < 0.05 was considered statistically significant.

Results

A participant flow diagram for this study is presented in Fig. 1.

Low muscle mass prevalence in cancer patients and their clinical characteristics

The patients' demographic and disease characteristics are presented in Table 1. Males and females were equally represented in the study, with an average age of 65.0 ± 11.8 years; cancer types were colon (37.1%), lung (25.5%), breast (22.6%), kidney (7.8%) and prostate (7.0%). Average times since diagnosis of the primary tumor was 46.9 ± 60.7 months. The majority of patients (40.5%) were undergoing their first line of treatment.

CT-defined sarcopenia, or low muscle mass, was considered to be present for patients whose SMI was < $55\text{cm}^2/\text{m}^2$ in men and < $39\text{cm}^2/\text{m}^2$ in women. In the total population of 766 patients, 529 were assessed as to have low muscle mass, denoting a CT-defined sarcopenia prevalence of 69.1%.

Low muscle mass was more prevalent in men than women: 83.0% (317/382) versus 55.2% (212/384) (*P* < 0.01), and patients with low muscle mass were older than those without. Low muscle mass was most prevalent in prostate cancer patients (94.4%, 51/54), compared to only 54.3% (94/173) in breast cancer patients; prevalence in the kidney, colon and lung cancer sub-groups were comparable to that of the total population (76.7%, 70.4% and 70.8%, respectively). Patients with low muscle mass were twice as likely to have brain metastasis than their counterparts (12.7% versus 5.9%, *P* < 0.01). PS scores were poorer for patients without low muscle mass: 40.1% had a "good" PS score versus 29.7% among those with low muscle mass (PS 0, *P* < 0.01) and 10.5% of patients without low muscle mass had a "poor" PS score of 2, compared to 17.2% of low muscle mass patients (*P* = 0.02).

Malnutrition and cachexia prevalence among cancer patients with low muscle mass

Nutrition related data are summarized in Table 2. About four-times the proportion of patients without low muscle mass were obese compared to the low muscle mass group. Food intake during the previous meal, evaluated with a VAS, revealed that 9.5% of low muscle mass versus 5.1% of without low muscle mass patients had very abnormal food intake (score 0–4, $P = 0.04$) and 9.8% of low muscle mass patients versus 2.5% of their counterparts were moderately malnourished ($P < 0.01$). Serum albumin and GPS was found to be similar between both groups, nevertheless, CRP levels were significantly elevated in low muscle mass patients (mean 29.7 ± 48.8 versus 17.9 ± 31.3 in non-sarcopenic patients). Overall cachexia prevalence was estimated at 44.5% (28% of patients with more than 5% of weight loss in last 6 months, 8% with a BMI $< 20 \text{ kg/m}^2$ and $> 2\%$ weight loss in last 6 months, and 31% with CT-defined sarcopenia and weight loss $> 2\%$ in last 6 months).

Multivariate analysis of the determinants of low muscle mass in cancer patients

Only patients for whom serum albumin data were available ($n = 561$) were included in the multivariate analysis, as this was an exploratory variable (see Methods). Associations ($P < 0.05$) were found between low muscle mass and moderately malnourished status (OR 5.28, 95%CI 1.74–16.00), severely malnourished status (OR 5.00, 95%CI 1.05–23.82) and age ≥ 70 years (OR 2.09, 1.14–3.83). Females (OR 0.23, 95%CI 0.14–0.38) and those not having a brain metastatic site (OR 0.26, 0.11–0.58) were found to have a lower risk of low muscle mass ($P < 0.05$) – Table S1.

Low muscle mass diagnosis and management in real-life practice

Figure 2 presents the level of disagreement between low muscle mass diagnosis via SMI measurement and the oncologist's assessment of sarcopenia. Whereas underestimation by physicians in non-obese patients with low muscle mass (44.9%) was comparable to that found in the total population, non-diagnosis in obese cancer patients was much higher, reaching 74.3% ($P < 0.01$). Only 34.0% and 28.4% of patients with low muscle mass received personalized dietetic counselling and nutritional management, respectively, and 16.3% received physiotherapy. Mean daily spent-in-bed time was also higher for low muscle mass patients (10.3 ± 3.3 hours/day) than those with without low muscle mass (9.3 ± 2.9 hours/day, $P < 0.01$) – Table 3.

Impact of low muscle mass on ongoing cancer therapy tolerability

Dose reductions, treatment interruptions and occurrence of AE of grade 3 and greater related to ongoing treatment were comparable between low muscle mass patients and their counterparts. However, a higher number of low muscle mass patients (11.9%) experienced treatment delays due to toxicities, compared to patients without low muscle mass (6.8%, $P = 0.04$). Low muscle mass patients were also significantly

more likely to have experienced at least two treatment-related AEs (13.8% versus 8.4% among their counterparts; $P = 0.03$) – Table S2).

Discussion

Our prospective study represents the largest multicenter sample of metastatic cancer patients collected in France, assessing low muscle mass prevalence was among 766 patients. Although EWGSOP guidelines [11, 12] recommend a holistic approach involving both muscle mass and strength assessments to diagnose sarcopenia, cut-offs for strength assessments have yet to be validated in large cohorts. So despite collecting hand-grip test measures in 666 patients – of which 205 (30.8%) presented with both myopenia and dynapenia – our study has concentrated on evaluating muscle mass. As previously reported with different cut-offs for SMI [25, 32], low muscle mass was found to be highly prevalent among these cancer patients (69.1%). These data demonstrate how commonly available CT imagery may be used to objectively measure the myopenic component of sarcopenia, thus facilitating diagnosis and subsequent treatment of this common condition in cancer patients.

We found that low muscle mass was significantly more prevalent in men than women. Multivariate analyses also confirmed a strong association between low muscle mass prevalence and gender, with females being at lower risk. A similar gender-based association has been previously reported in other cancer sarcopenia populations [3, 7, 27]. Low muscle mass prevalence was found to be highest in prostate cancer (94.4%) and lower in breast cancer patients (54.3%). Indeed, prostate cancer patients have multiple risk factors for muscle mass loss, such as advanced age, advanced cancer and testosterone deprivation. In our study, prostate cancer patients had a mean age of 70.6 ± 8.5 versus 60.4 ± 13.4 years in breast cancer patients. Among sex-neutral cancers in this study, sarcopenia was similarly prevalent in each sex. Multivariate analysis did not reveal any associations between cancer type and the presence of low muscle mass.

The choice of the cut-off may be another factor explaining the differences in low muscle mass prevalence by gender. In studies where notably different SMI cut-off values were used, no significant differences in sarcopenia prevalence by gender was identified, such as in a recent study by Cortellini *et al.* [10], where L3 SMI thresholds for low muscular mass were $< 43 \text{ cm}^2/\text{m}^2$ for men with $\text{BMI} \leq 25$, $< 53 \text{ cm}^2/\text{m}^2$ for men with $\text{BMI} \geq 25$, and $\leq 41 \text{ cm}^2/\text{m}^2$ for women. A 2016 literature review reported a sarcopenia prevalence ranging from 5 to 89%, depending on the malignancy and methods used for sarcopenia diagnosis [29]. Elsewhere, a prevalence of 25–30% has been reported, equivalent to about 1 million cancer patients in Europe [36]. There could also be other confounding factors influencing the apparent differences in sarcopenia prevalence by gender, such as behavioral characteristics (smoking, alcoholism, food habits). Nevertheless, an analysis that accounts for confounding factors was beyond the scope of our study, which is not longitudinal and was intended to be descriptive.

Our study is the first to demonstrate a potential association between brain metastases and low muscle mass. Patients with cerebral metastases are often prescribed corticosteroids, resulting in greater fatigue,

and they also are at risk of developing hemiplegia. Both factors may lead to an overall reduction in the patients' physical activity, increasing the risk of low muscle mass.

We documented a cachexia prevalence of 45.4% in low muscle mass patients (Fig. 2), which is higher compared to Fearon's [14] definitions of cachexia measurement that assessed only percentage weight loss and BMI. Thus, these differences vouch for the use of CT imagery to detect low muscle mass defined sarcopenia, promising a more reliable diagnosis of cachexia.

The most worrying result of our study is that despite its high prevalence, practitioners were unable to recognize sarcopenia in nearly half of those patients with low muscle mass during the survey, even while completing nutritional status data. Low muscle mass was more poorly recognized in obese patients (Fig. 2). Our findings also demonstrate the general lack of nutritional and physical therapy support available to cancer patients in France. Sarcopenic patients have a higher risk of being bedridden for longer durations and having abnormal food intake. It is well known that suitable nutritional programs and physical exercise regimes are helpful countermeasures to prevent muscle wasting, and hence cachexia development [1, 4].

These observations are sadly not novel, as highlighted in the cross-sectional NutriCancer2012 study [16, 20] that evaluated malnutrition prevalence in over 2000 cancer patients in France. Malnutrition prevalence was around 40%, and it was often diagnosed belatedly. Approximately 10% of these patients lacked any type of nutritional management, and there was only 70% concordance between the patients' true conditions and the physicians' evaluations. The study explained that such a low recourse to nutritional management was due to a lack of knowledge on malnutrition diagnosis and nutritional treatments (64% of interviewed physicians) and the lack of a nutrition team in the hospital (56% of physicians)[28].

While we could describe the existing nutrition and physical activity trends in patients with and without low muscle mass as part of this study, a longitudinal study would be better suited to investigate the link between these factors, their development and progression.

Sarcopenic patients have been reported to be more likely to accumulate treatment-related events [6, 30, 34]. In our study, we found an effect of low muscle mass on increased delay in treatment administration due to treatment-related toxicities. However, no links could be established with dose reductions, treatment interruptions, and occurrence of grade 3 AEs. We suggest that our study design was such that it favored the selection of patients with low toxicity prevalence. This might also be explained by the relative heterogeneity in our sample with regards to ongoing treatment and cancer type (compared to other studies assessing sarcopenia and treatment toxicity [6, 30, 34]). However, the principal objective of this study was not to assess such toxicity, but to evaluate low muscle mass prevalence in a population of patients with metastatic cancers most frequently encountered in clinical settings.

We aimed to demonstrate the prevalence and impact of low muscle mass in a population of metastatic cancer patients in various healthcare settings in France. Measures taken to ensure data quality included

the study's multicentric design, large sample size, oncologist and radiologist training in data collection and collaboration with a coordinating center. However, some limitations were duly noted. This was a cross-sectional study that evaluated a patient's low muscle mass status at a certain timepoint, using their medical records to obtain much of the historical data reported. Such a study design offers limited control over center-based variability in the level of completeness, methods of measuring and recording of past data. Additionally, a cross-sectional design is inadequate for obtaining data on the development and evolution of cancer related low muscle mass over the course of a person's illness, the evaluation of contributing factors, and its eventual impact on patient outcomes. Future longitudinal prospective studies, with a reasonable follow-up durations, will be required to better understand this complex disorder.

Conclusions

Low muscle mass was found to be highly prevalent, at 69.1%, in patients with metastatic cancers in French clinical practice as evaluated by L3 level CT imagery muscle mass measurements. Nutritional and physical therapy support were only provided to a minority of patients. Low muscle mass was often underdiagnosed by the oncologist, even more so in obese patients, highlighting a worrying gap in the oncologists' understanding of sarcopenia diagnosis and management. Our findings underline the necessity for improvements in oncologist education of diagnostic tools and the nutritional aspects of cancer management, and the need for an increased involvement of dieticians, nutritionists, physiotherapists and fitness counselors in the regular, long-term management of cancer related low muscle mass and sarcopenia as part of a more wholistic standard of care.

Declarations

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Conflicts of interest/competing interests

All authors were remunerated for their participation as investigators in the SCAN study.

Availability of data and material

N/A

Code availability

N/A

Authors' contributions

B. Raynard, F. Pigneur, M. Di Palma, E. Deluche and F. Goldwasser equally contributed to the conception and design of the research; B. Raynard, F. Pigneur, M. Di Palma, E. Deluche and F. Goldwasser equally contributed to the acquisition and analysis of the data; B. Raynard contributed to the interpretation of the data; and B. Raynard drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Ethics approval

This study, conducted in accordance with the Declaration of Helsinki, was approved by the French ethical research committee, "Le Comité de Protection des Personnes" (CPP), on the 6 July 2017 (approval no. 2017-A01648-45). National data protection regulations were also met (CNIL, approval no. 2066086).

Consent to participate

All persons provided their informed consent prior to enrollment.

Consent for publication

All persons were informed that this study would be submitted for publication

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Tables

Table 1 Demographic and cancer characteristics of patients with and without sarcopenia, as assessed by the L3 computed tomography imaging method.

Sarcopenia is present if the skeletal mass index (SMI) is $< 55\text{cm}^2/\text{m}^2$ in men and $< 39\text{cm}^2/\text{m}^2$ in women. In the total population of 766 patients, 529 were assessed as sarcopenic, denoting a sarcopenia prevalence of 69.1%. Results are presented by N (%) or mean $\pm$ SD. NS not significant, NA not applicable. Non-responses are not shown.

	Total Patients	Sarcopenic	Non- sarcopenic	<i>P</i>
SMI, cm²/m²	n = 766	n = 529	n = 237	
Mean ± SD, median (range)	43.2 ± 8.7, 42.6 (18.8 – 76.6)	40.6 ± 7.6, 38.7 (18.8 – 54.8)	49.1 ± 8.2, 46.0 (39.0 – 76.6)	<i>P</i> < 0.01
Male, n (%)	n = 766	n = 529	n = 237	
	386 (49.9)	317 (59.9)	65 (27.4)	<i>P</i> < 0.01
Age (years)	n = 762	n = 527	n = 235	
Mean ± SD, median (range)	65.0 ± 11.8, 65.6 (18.7 – 97.8)	66.1 ± 11.8, 66.7 (25.5 – 97.8)	62.5 ± 11.3, 63.1 (18.7 – 86.9)	<i>P</i> < 0.01
Site of primary tumour, n (%)	n = 766	n = 529	n = 237	
Colon	284 (37.1)	200 (37.8)	84 (35.4)	NS
Lung	195 (25.5)	138 (26.1)	57 (24.1)	NS
Breast	173 (22.6)	94 (17.8)	79 (33.3)	<i>P</i> < 0.01
Kidney	60 (7.8)	46 (8.7)	14 (5.9)	NS
Prostate	54 (7.0)	51 (9.6)	3 (1.3)	<i>P</i> < 0.01
Time since diagnosis of primary cancer (months)	n = 762	n = 529	n = 237	
Mean ± SD, median (range)	46.9 ± 60.7, 23.2 (0 – 400.0)	45.7 ± 61.4, 20.8 (0 – 396.0)	49.7 ± 58.9, 28.1 (1.0 – 400.0)	NS
Time since diagnosis of metastatic disease (months)	n = 756	n = 524	n = 232	
Mean ± SD, median (range)	25.1 ± 31.2, 14.5 (0 – 285.0)	25.4 ± 33.5, 13.6 (0 – 285.0)	24.5 ± 25.0, 17.5 (0 – 160.0)	NS
Main metastatic sites, n (%)	n = 766	n = 529	n = 237	
Hepatic	323 (42.2)	224 (42.3)	99 (41.8)	NS

Pulmonary	310 (40.5)	208 (39.3)	102 (43.0)	NS
Lymph nodes	275 (35.9)	198 (37.4)	77 (32.5)	NS
Bones	259 (33.8)	178 (33.6)	81 (34.2)	NS
Peritoneal	90 (11.7)	64 (12.1)	26 (11.0)	NS
Cerebral	81 (10.6)	67 (12.7)	14 (5.9)	$P < 0.01$
Treatment line, n (%)	n = 766	n = 529	n = 237	
First line of treatment	310 (40.5)	207 (39.1)	103 (43.5)	NS
Second line of treatment	217 (28.3)	154 (29.1)	63 (26.6)	NS
Third or higher	208 (27.2)	144 (27.2)	64 (27.0)	NS
Non-responses	31 (4.0)	24 (4.5)	7 (3.0)	NS
Current therapies, n (%)	n = 766	n = 529	n = 237	
Chemotherapy	530 (69.2)	375 (70.9)	155 (65.4)	NS
Hormonotherapy	72 (9.4)	48 (9.1)	24 (10.1)	NS
Targeted therapy	305 (39.8)	192 (36.3)	113 (47.7)	$P < 0.01$
Immunotherapy	118 (15.4)	89 (16.8)	29 (12.2)	NS
PS-score, n (%)	n = 766	n = 529	n = 237	
0	252 (32.9)	157 (29.7)	95 (40.1)	$P < 0.01$
1	353 (46.1)	250 (47.3)	103 (43.5)	NS
2	116 (15.1)	91 (17.2)	25 (10.5)	$P = 0.02$
3	27 (3.5)	19 (3.6)	8 (3.4)	NS
Non-responses	18 (2.3)	12 (2.3)	6 (2.5)	NS

Table 2 Nutritional status, body weight measures and Glasgow Prognostic Score (GPS in metastatic cancer patients with and without sarcopenia.

Results are presented as N (%) or mean $\pm$ SD. NS not significant

	Total patients	Sarcopenic patients	Non-sarcopenic Patients	<i>P</i>
	n = 722	n = 500	n = 222	
Weight before cancer diagnosis (kg)	73.7 ± 16.3 71.7 (39.0 – 134.0)	73.4 ± 15.4 72.4 (39.0 – 130.0)	74.2 ± 18.2 69.7 (45.0 – 134.0)	NS
	n = 760	n = 525	n = 235	
Current weight (kg)	69.2 ± 15.4 67.5 (35.0 – 136.0)	68.1 ± 14.5 67.2 (35.0 – 120.0)	71.6 ± 17.1 69.1 (40.0 – 136.0)	<i>P</i> < 0.01
	n = 766	n = 529	n = 237	
> 2% weight loss in 1 month	157 (20.5)	120 (22.7)	37 (15.6)	<i>P</i> = 0.02
> 5% weight loss in 1 month	59 (7.7)	46 (8.7)	13 (5.5)	NS
> 5% weight loss in 6 months	217 (28.3)	164 (31.0)	53 (22.4)	<i>P</i> = 0.01
> 10% weight loss in 6 months	93 (12.1)	74 (14.0)	19 (8.0)	<i>P</i> = 0.03
Current BMI (kg/m²) ^a	n = 766	n = 529	n = 237	
Severely malnourished	20 (2.6)	17 (3.2)	3 (1.3)	NS
Moderately malnourished	58 (7.6)	52 (9.8)	6 (2.5)	<i>P</i> < 0.01
Non-responses	10 (1.3)	6 (1.1)	4 (1.6)	NS
Obese (BMI ≥ 30 kg/m ²)	96 (12.5)	35 (6.6)	61 (25.7)	<i>P</i> < 0.01
	n = 760	n = 525	235	
Mean ± SD, median (range)	24.6 ± 4.6, 23.9 (14.0 – 44.9)	23.7 ± 4.1, 23.2 (14.0 – 42.5)	26.6 ± 5.0 25.8 (15.4 – 44.9)	<i>P</i> < 0.01
VAS for food intake at latest meal (by the patient) ^b	n = 766	n = 529	n = 237	
0-4 very abnormal	62 (8.1)	50 (9.5)	12 (5.1)	<i>P</i> = 0.04
5-7 abnormal	199 (26.0)	146 (27.6)	53 (22.64)	NS
8-10 normal	481 (62.8)	316 (59.7)	165 (69.6)	<i>P</i> <

Serum albumin (SA, g/l) ^a	n = 766	n = 529	n = 237	
Normal	476 (62.1)	329 (62.2)	147 (62.0)	NS
Moderate Malnutrition	59 (7.7)	45 (8.5)	14 (5.9)	NS
Severe malnutrition	26 (3.4)	19 (3.6)	7 (3.0)	NS
Non-responses	205 (26.8)	136 (25.7)	69 (29.1)	NS
	n = 564	n = 395	n = 169	
Mean ± SD, median (range)	37.2 ± 6.0, 37.3 (4.0 – 50.0)	37.2 ± 5.9, 37.4 (4.0 – 49.0)	37.0 ± 6.2, 37.1 (4.0 – 50.0)	NS
C-reactive protein (mg/l)	n = 381	n = 273	n = 111	
Mean ± SD, median (range)	26.3 ± 44.8, 7.3 (0 – 374.0)	29.7 ± 48.8, 7.9 (0 – 374.0)	17.9 ± 31.3, 6.3 (0 – 177.0)	<i>P</i> < 0.01
Glasgow Prognostic Score (GPS)	n = 348	n = 249	n = 99	
0	166 (47.7)	113 (45.4)	53 (53.5)	NS
1	103 (29.6)	75 (30.1)	28 (28.3)	NS
2	79 (22.7)	61 (24.5)	18 (18.2)	NS

^a Nutritional status based on patient **BMI** and **serum albumin** was calculated according to the following thresholds:

Moderate malnutrition:

- < 70 years old: BMI ≤ 18.5 to 16 kg/m² or SA < 30 to 20 g/L
- ≥ 70 years old: BMI < 21 to 18 kg/m² or SA < 35 to 30 g/L

Severe malnutrition:

- < 70 years old: BMI ≤ 16 kg/m² or SA < 20 g/L
- ≥ 70 years old: BMI < 18 kg/m² or SA < 30 g/L

^b VAS: 0 (No food intake) – 10 (Normal food intake)

Table 3 Nutritional management and physical activity interventions in metastatic cancer patients, with and without sarcopenia.

Unknown responses and non-responses are not reported in the Table.

	Total patients	Sarcopenic patients	Non-sarcopenic Patients	p
Patients currently benefiting from personalized nutrition counselling	n = 766	n = 529	n = 237	
Yes	237 (30.9)	180 (34.0)	57 (24.1)	<i>P</i> < 0.01
No	527 (68.8)	347 (65.6)	180 (75.9)	
If no, is any personalized nutritional counselling planned? ^a	n = 527	n = 347	n = 180	
Yes	66 (12.5)	55 (15.9)	11 (6.1)	<i>P</i> < 0.01
Patients currently under specific nutritional management	n = 766	n = 529	n = 237	
Yes	183 (23.9)	150 (28.4)	33 (13.9)	<i>P</i> < 0.01
Oral nutritional supplements	172 (22.5)	140 (26.5)	32 (13.5)	<i>p</i> < 0.01
Enteral nutrition	6 (0.8)	6 (1.1)	0 (0.0)	NS
Parenteral nutrition	7 (0.9)	6 (1.1)	1 (0.4)	NS
No	580 (75.7)	377 (71.3)	203 (85.7)	<i>P</i> < 0.01
If NO, is any personalized nutritional management planned?	n = 580	n = 377	n = 203	
Yes	56 (9.7)	44 (11.7)	12 (5.9)	<i>P</i> = 0.05
Current patient physical activity ^a				
Number of hours spent in bed per day (hours/day) ^a	n = 591	n = 412	n = 179	
Mean ± SD, median (range)	10.0 ± 3.2, 8.8 (0 – 23.0)	10.3 ± 3.3, 9.0 (0 – 23.0)	9.3 ± 2.9, 8.4 (0 – 20.0)	<i>P</i> < 0.01
≥ 11 hours bedridden per day	185 (31.2)	141 (34.2)	44 (24.6)	<i>P</i> < 0.05

Patients practicing physical exercises	n = 628	n = 429	n = 199	
Frequency of 30-minute physical exercises per week [Mean $\pm$ SD, median (range)]	2.9 $\pm$ 3.8, 1.2 (0 – 35)	2.9 $\pm$ 3.7, 1.1 (0 – 28)	3.0 $\pm$ 3.9, 1.4 (0 – 35)	NS
	n = 766	n = 529	n = 237	
Patients undertaking physiotherapy	122 (15.9)	86 (16.3)	36 (15.2)	NS
Patients consulting a sports coach	22 (2.9)	12 (2.3)	10 (4.2)	NS

^a Including sleeping time

Figures

Figure 1

Flow diagram representing the sample population enrolled in the SCAN study. Of 818 CRFs received in October 2017, 52 were excluded as they did not meet selection criteria or lacked essential information; 766 CRFs were included in the study analysis.

Figure 2

Differences sarcopenia evaluations of sarcopenia by oncologist versus the L3 CT-Scan method within the low muscle mass sub-population. Oncologists' diagnosis of sarcopenia are compared to the L3 scan method using a stacked bar graph for the total low muscle mass population, and for low muscle mass non-obese and obese sub-populations. Concordant and non-concordant oncologist assessments were calculated as a percentage of the low muscle mass population (y-axis); 249 of 529 patients in the low

muscle mass population (47.1%), were incorrectly evaluated as non-sarcopenic by their oncologist; 220 of 490 (44.9%) of non-obese low muscle mass patients were incorrectly evaluated. Among obese patients the discordance was much higher, with 26 out of 35 (74.3%) of low muscle mass patients being erroneously assessed as not having sarcopenia. The Cohen's kappa coefficient for inter-rater agreement between the two assessment methods was low at 0.186, implying that any concordances are likely to be random rather than correlated.

Supplementary Files

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