Development and validation of a clinically applicable score to classify cachexia stages in advanced cancer patients

Ting Zhou¹, Bangyan Wang¹, Huiquan Liu¹, Kaixiang Yang², Sudip Thapa¹, Haowen Zhang¹, Lu Li¹ & Shiying Yu¹*

¹Cancer Center of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, Hubei Province, China, ²Cell and Molecular Biology Laboratory, Department of Orthopedics, Alpert Medical School of Brown University/Rhode Island Hospital, Providence, RI 02903, USA

Abstract

Background  Cachexia is a multifactorial syndrome that is highly prevalent in advanced cancer patients and leads to progressive functional impairments. The classification of cachexia stages is essential for diagnosing and treating cachexia. However, there is a lack of simple tools with good discrimination for classifying cachexia stages. Therefore, our study aimed to develop a clinically applicable cachexia staging score (CSS) and validate its discrimination of clinical outcomes for different cachexia stages.

Methods  Advanced cancer patients were enrolled in our study. A CSS comprising the following five components was developed: weight loss, a simple questionnaire of sarcopenia (SARC-F), Eastern Cooperative Oncology Group, appetite loss, and abnormal biochemistry. According to the CSS, patients were classified into non-cachexia, pre-cachexia, cachexia, and refractory cachexia stages, and clinical outcomes were compared among the four groups.

Results  Of the 297 participating patients, data from 259 patients were ultimately included. Based on the CSS, patients were classified into non-cachexia (n = 69), pre-cachexia (n = 68), cachexia (n = 103), and refractory cachexia (n = 19) stages. Patients with more severe cachexia stages had lower skeletal muscle indexes (P = 0.002 and P = 0.004 in male and female patients, respectively), higher prevalence of sarcopenia (P = 0.017 and P = 0.027 in male and female patients, respectively), more severe symptom burden (P < 0.001), poorer quality of life (P < 0.001 for all subscales except social well-being), and shorter survival times (P < 0.001).

Conclusions  The CSS is a simple and clinically applicable tool with excellent discrimination for classifying cachexia stages. This score is extremely useful for the clinical treatment and prognosis of cachexia and for designing clinical trials.

Keywords  Cancer; Cachexia; Classification; Quality of life; Survival

Introduction

Cancer cachexia is a multifactorial syndrome that is characterized by unstoppable muscle wasting with or without fat wasting, and it cannot be reversed by nutritional supplementation.¹² Up to 50% of cancer patients suffer from cachexia, and more than 20% of cancer patients die because of cachexia.³⁴ Patients with cachexia usually manifest with weight loss, muscle wasting, anorexia, and inflammation.⁵ Moreover, cachexia can increase treatment-related toxicity, aggravate symptom burden, worsen quality of life, and shorten survival times for patients.⁶⁻⁸

In the international consensus,⁹ the definition of cancer cachexia was used, and cancer cachexia was classified as pre-cachexia, cachexia, and refractory cachexia stages. In pre-cachexia, patients had weight loss ≤5% with anorexia and metabolic changes. Patients with weight loss >5% or weight loss >2% when body mass index (BMI) <20 or sarcopenia were classified into the cachexia stage, and they often had reduced food intake or systemic inflammation. For refractory cachexia, patients had a low performance status, were not responsive to anticancer treatments, and had an expected survival time of <3 months. These are basic definitions that lack specific criteria. Criteria for staging...
Methods

Patients and data collection

This study was prospectively conducted at the Cancer Center of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. Patients no less than 18 years old and with a diagnosis of advanced cancer (cancer stage III/IV) were included in this study. Each patient was asked to sign an informed consent before participation, and approval for this study was provided by the Tongji Medical College Research Ethics Board.

All patients completed two questionnaires: the M.D. Anderson symptom inventory (MDASI) and the Functional Assessment of Anorexia Cachexia Therapy (FAACT) scale, to assess their symptom burden and quality of life. The MDASI has been validated and is a frequently used questionnaire to assess their symptom burden and quality of life. The MDASI Assessment of Anorexia Cachexia Therapy (FAACT) scale, to simplify the criteria of cachexia stages, we developed a simplified form of the cachexia score, but these criteria could not effectively classify the pre-cachexia and cachexia stages. A similar problem exists for the study of Blum et al.; their criteria based on weight loss did not well distinguish patients in the non-cachexia and pre-cachexia stages.

To date, there is a lack of precise and simple tools for the classification of cancer cachexia stages. Therefore, our study aimed to develop a clinically applicable cachexia score for staging cancer cachexia and validate its discrimination of clinical outcomes, such as patient muscle mass and function, symptom burden, quality of life, and survival time.

Classification of cancer cachexia stages and scoring methods

According to studies of cancer cachexia stages and the international consensus, some of the criteria used in the past included weight loss, sarcopenia (muscle mass/function), anorexia, decreased performance status, quality of life, inflammation, and metabolic disturbances. To simplify the criteria of cachexia stages, we developed a cachexia staging score (CSS) for clinical use in advanced cancer patients. The CSS consists of five components (details shown in Table 1): weight loss in 6 months (score range: 0–3), a simple SARC-F questionnaire for assessing muscle function and sarcopenia (score range: 0–3), ECOG performance status (score range: 0–2), appetite loss (score range: 0–2), and abnormal biochemistry (score range: 0–2).

After scores for the five components were given, the total cachexia score was then calculated. Patients were classified into four stages of cachexia (Table 2): non-cachexia (score: 0–2), pre-cachexia (score: 3–4), cachexia (score: 5–8), and functional well-being, and the anorexia–cachexia subscale. Higher scores on this questionnaire indicate a better quality of life.

Participating patients were also asked to complete a simple clinical symptom index called the SARC-F to assess muscle function. The SARC-F is a simple questionnaire for rapidly assessing patient muscle function and screening for sarcopenia. It comprises five items: strength, assistance in walking, rising from a chair, climbing stairs, and falls. Each item is scored according to a range of 0–2, and the higher the total score is, the worse the patients’ muscle function is. Patients who had abdominal computed tomography (CT) images within 1 month were analysed for body composition. Skeletal muscle cross-sectional area (cm²) at the third lumbar vertebra was measured by the ImageJ software using standard Hounsfield unit ranges (−29 to +150). Then, the skeletal muscle index (SMI) (cm²/m²) was calculated by using the skeletal muscle cross-sectional area (cm²) and patient stature (m). Based on the international consensus, sarcopenia was defined as a SMI <39 cm²/m² in female patients or <55 cm²/m² in male patients.

Patient demographics (age, gender, height, and weight) and clinical characteristics (tumour diagnoses and stages and types of therapy) were collected from the medical records, and weight loss in 6 months was reported by the patients. Eastern Cooperative Oncology Group (ECOG) performance status of the patients was assessed by clinicians. Routine blood tests, including white blood cell (WBC) count and haemoglobin and albumin levels, were performed at their clinical visit. Survival data of patients were assessed from the date of inclusion in our study until the patient died or were lost to follow-up or until the end of follow-up (March 2017).
refractory cachexia (score: 9–12). Obviously, higher scores indicated worse the cachexia syndrome. After classifying the patients into the different cachexia stages, we compared the outcomes of the five components of the CSS among the patient groups. In addition, we validated the CSS by comparing differences in muscle mass, sarcopenia, symptom burden, quality of life, and survival time among the four groups.

Statistical analysis

Patient demographics and clinical characteristics were summarized with descriptive statistics. Differences in continuous variables with variance homogeneity were tested by analysis of variance with mean ± standard deviation; otherwise, Kruskal-Wallis tests were used. Chi-square tests were used for comparing differences in categorical variables, but when more than one-fifth of the expected frequency was <5 or one expected frequency was <1, Fisher’s exact tests were used. Non-parametric tests followed by pairwise comparisons were used to compare differences between groups. Differences in survival were determined by Kaplan–Meier analyses with log-rank tests. All statistical analyses were performed by SPSS software version 20.0 (SPSS, Inc., Chicago).

Results

Patient demographics and clinical characteristics

A total of 297 patients were enrolled in our study. Of these, 18 patients did not complete the MDASI scale and lost the assessment of appetite loss, 11 patients did not complete the SARC-F scale, and 9 patients did not have the blood test data; thus, these patients were excluded from this study. Ultimately, data from 259 patients were collected for analysis. Patient demographics and clinical characteristics are summarized in Table 3. The mean age of our patients was 50.6 ± 12.6 years, and 56.37% were males. The mean BMI (kg/m²), which was calculated by using weight (kg) and height (m), was 21.83 (±3.22) in our patients. The top three most common tumour types in these patients included lung cancer (31.66%), digestive system cancer (27.03%), and gynaecological cancer (12.74%). Almost three-quarters of the patients were diagnosed with stage IV tumours, and more than 80% of the patients received chemotherapy at this time of hospitalization.

Cachexia stages of advanced cancer patients

According to the CSS, 69 patients were classified in the non-cachexia stage, 68 patients were classified in the pre-cachexia stage, 103 patients were classified in the cachexia stage, and 19 patients were classified in the refractory cachexia stage. We compared the differences in the five components of the CSS among the patients in the four cachexia stages. As

Table 1 A new cachexia staging score to classify cachexia stages

| Measurements                  | Values                          | Point |
|-------------------------------|---------------------------------|-------|
| Weight loss in 6 months       | Weight stable or weight gain    | 0     |
|                               | Weight loss ≤5%                 | 1     |
|                               | Weight loss >5% and ≤15%        | 2     |
|                               | Weight loss >15%                | 3     |
| SARC-F                        | 0                               | 0     |
|                               | 1–3                             | 1     |
|                               | 4–6                             | 2     |
|                               | 7–10                            | 3     |
| ECOG PS                       | 0                               | 0     |
|                               | 1–2                             | 1     |
|                               | 3–4                             | 2     |
| Appetite loss (0–10)          | 0–3                             | 0     |
|                               | 4–6                             | 1     |
|                               | 7–10                            | 2     |
| Abnormal biochemistry:        | All normal                      | 0     |
|                               | One of the three abnormal       | 1     |
|                               | More than one abnormal          | 2     |

Alb, albumin; ECOG PS, Eastern cooperative oncology group performance status; Hb, haemoglobin; WBC, white blood cell.

Table 2 Cachexia staging score

\[
\text{WL} (0-3) + \text{SARC-F} (0-3) + \text{ECOG PS} (0-2) + \text{AL} (0-2) + \text{AB} (0-2)
\]

\[
\begin{array}{cccccc}
\text{NCa} & \text{PCa} & \text{Ca} & \text{RCa} \\
0 & 2 & 4 & 8 & 12 \\
\end{array}
\]

AB, abnormal biochemistry; AL, appetite loss; Ca, cachexia; ECOG PS, Eastern cooperative oncology group performance status; NCa, non-cachexia; PCa pre-cachexia; RCa refractory cachexia; WL, weight loss.
summarized in Table 4, patients in the refractory cachexia stage had a significantly greater weight loss, higher SARC-F score, poorer ECOG performance status, worse appetite, and higher prevalence of abnormal biochemical indexes than patients in the non-cachexia, pre-cachexia, and cachexia stages, and differences in all five components among the four groups were statistically significant (all \( P < 0.001 \)).

### Body composition of patients in different cachexia stages

A total of 127 patients (male patients: 69 and female patients: 58) had abdomen CT scans within 1 month, and we measured the muscle mass at the third lumbar vertebra of these patients. A total of 19, 22, 23, and 5 male patients, respectively, and 9, 13, 29, and 7 female patients, respectively, were classified into the non-cachexia, pre-cachexia, cachexia, and refractory cachexia stages. As shown in Figure 1, SMI values were lower in the cachexia and refractory cachexia groups than in the non-cachexia and pre-cachexia groups; \( P = 0.002 \) and \( P = 0.004 \) in the male and female patients, respectively. For comparisons between groups, both male and female patients in the non-cachexia group had higher SMI values than patients in the cachexia and refractory cachexia groups, and female patients in the pre-cachexia group had higher SMI values than female patients in the refractory cachexia group (\( P < 0.05 \)).

Based on the sarcopenia criteria in the international consensus on cachexia, we compared the prevalence of sarcopenia in these four groups. As shown in Figure 2, the prevalence rates of sarcopenia in the cachexia and refractory cachexia groups were higher than in the non-cachexia and pre-cachexia groups; \( P = 0.017 \) and \( P = 0.027 \) in male and female patients, respectively. For comparisons between groups, higher prevalence rates of sarcopenia were seen in the cachexia and refractory cachexia groups than in the non-cachexia group, and female patients in the refractory cachexia group had higher prevalence rates of sarcopenia than those in the pre-cachexia group (\( P < 0.05 \)).

### Symptom burden and quality of life in patients with different cachexia stages

Symptoms were reported by patients using the MDASI scale, and two cachexia specific symptoms (early satiety and taste/smell changes) were reported using numeric rating scales. Patients in the refractory cachexia stage suffered more severe symptoms than patients in the other cachexia stages, and the differences among the four groups were statistically significant (all \( P < 0.001 \)). Details of six cachexia-related symptoms in the four groups are shown in Figure 3, and the scores of the symptoms were increased with cachexia stage severity.

### Table 3 Patient demographics and clinical characteristics (n = 259)

| Variables               | No. of patients | Percentage |
|-------------------------|-----------------|------------|
| Age (mean ± SD) (y)     | 50.6 ± 12.6     | —          |
| Gender                  |                 |            |
| Female                  | 113             | 43.63      |
| Male                    | 146             | 56.37      |
| BMI (mean ± SD) (kg/m²) | 21.83 ± 3.22    | —          |
| Tumour types            |                 |            |
| Lung cancer             | 82              | 31.66      |
| Digestive system cancer | 70              | 27.03      |
| Gynaecological cancer   | 33              | 12.74      |
| Head/neck cancer        | 28              | 10.81      |
| Lymphoma                | 25              | 9.65       |
| Others                  | 21              | 8.11       |
| Tumour stages           |                 |            |
| III                     | 69              | 26.64      |
| IV                      | 190             | 73.36      |
| Treatments              |                 |            |
| Chemotherapy            | 220             | 84.94      |
| Radiotherapy            | 11              | 4.25       |
| Palliative care         | 28              | 10.81      |

BMI, body mass index; SD, standard deviation.

A clinical applicable cachexia score to classify cachexia stages

### Table 4 Differences in five criteria according to different cachexia stages (n = 259)

| Variables               | NCa (n = 69) | PCa (n = 68) | Ca (n = 103) | RCa (n = 19) | \( P \) value |
|-------------------------|--------------|--------------|--------------|--------------|--------------|
| Weight loss (%) (mean) (SD) | 0.18 (0.82)  | 2.41 (3.31)a | 8.44 (6.30)a b | 16.27 (7.36)a b c | <0.001 |
| SARC-F (mean) (SD)      | 0.41 (0.79)  | 1.15 (1.08)a | 2.70 (1.98)a b | 6.00 (1.97)a b c | <0.001 |
| ECOG PS                 |              |              |              |              | <0.001 |
| 0                       | 3 (4.4%)     | 0            | 0            | 0            | —            |
| 1                       | 51 (73.9%)   | 49 (72.0%)   | 64 (62.1%)   | 5 (26.3%)    | —            |
| 2                       | 15 (21.7%)   | 18 (26.5%)   | 30 (29.1%)   | 5 (26.3%)    | —            |
| 3                       | 0            | 1 (1.5%)     | 9 (8.8%)b c  | 9 (47.4%)a b c | —            |
| Appetite loss (mean) (SD) | 1.20 (1.50) | 3.03 (2.59)a | 5.28 (2.78)a b | 8.47 (1.74)a b c | <0.001 |
| Abnormal biochemistry   |              |              |              |              | <0.001 |
| All normal              | 50 (72.5%)   | 32 (47.1%)   | 29 (28.2%)   | 0            | —            |
| One abnormal            | 19 (27.5%)   | 35 (51.5%)   | 47 (45.6%)   | 10 (52.6%)   | —            |
| Two abnormal            | 0            | 1 (1.5%)     | 19 (18.4%)   | 7 (36.8%)    | —            |
| Three abnormal          | 0            | 0            | 8 (7.8%)a b  | 2 (20.0%)a b c | —            |

Ca, cachexia; ECOG PS, Eastern cooperative oncology group performance status; NCa, non-cachexia; PCa, pre-cachexia; RCa, refractory cachexia; SD, standard deviation.

aStatistically different from NCa.
bStatistically different from PCa.
cStatistically different from Ca.

DOI: 10.1002/jcsm.12275
Figure 1  Differences in skeletal muscle index (SMI) among male and female patients with different cachexia stages. Ca, cachexia; NCa, non-cachexia; PCa, pre-cachexia; RCa refractory cachexia; between groups comparisons: *$P < 0.05$, **$P < 0.001$.

Figure 2  Differences in prevalence of sarcopenia among male and female patients with different cachexia stages. Ca, cachexia; NCa, non-cachexia; PCa, pre-cachexia; RCa refractory cachexia; between groups comparisons: *$P < 0.05$.

Figure 3  Differences in symptom burden among patients with different cachexia stages. Ca, cachexia; NCa, non-cachexia; PCa, pre-cachexia; RCa refractory cachexia; *Statistically different from NCa; bStatistically different from PCa; cStatistically different from Ca.
For comparisons between groups, patients in the refractory group had a significantly higher symptom burden than patients in the other groups ($P < 0.05$).

Of the 259 patients, 23 patients did not complete the FAACT scale, and data from 236 patients (non-cachexia: 61 patients; pre-cachexia: 64 patients; cachexia: 93 patients; and refractory cachexia: 18 patients) were used for assessing the quality of life. According to the scoring methods for the FAACT scale, we calculated the subscale scores of patients in the four cachexia groups and then calculated the total score, which represents patient quality of life. As shown in Figure 4, patients in the non-cachexia and pre-cachexia stages had higher scores for each subscale than patients in the cachexia and refractory cachexia stages, and the differences were statistically significant for all subscales except SWB ($P = 0.241$ for SWB and $P < 0.001$ for all others). These data suggested that patients with worse cachexia stages had lower scores on the FAACT scale, which represents poor quality of life. Moreover, significant differences were seen in the comparisons between any two groups for all subscales except SWB ($P < 0.05$).

**Survival of patients in different cachexia stages**

Kaplan–Meier survival curves for patients in the four cachexia stages are shown in Figure 5. Survival was worse in patients with more severe cachexia stages. Differences in survival were statistically significant among the four groups ($P < 0.001$).

**Discussion**

Our study provides a clinically applicable CSS for clinicians to classify the cachexia stages of cancer patients; the CSS consists of five key cachexia components (weight loss, muscle function, appetite, performance status, and abnormal biochemistry). This cachexia score turned the definition of cachexia stages into diagnosis criteria and has excellent discrimination for separating patients in different cachexia stages according to patient-related outcomes, including body composition, symptom burden, quality of life, and survival.

Weight loss was the main symptom of cachexia, and BMI-adjusted weight loss was associated with cancer patients’ survival.29 We divided weight loss into four categories for the CSS: weight stable or gain, weight loss $\leq 5\%$, weight loss $\leq 15\%$, and weight loss $>15\%$ with increasing score from 0 to 4.
to 3. These categories were referred to the validation study of consensus,14 but weight loss was not the only determinant of cachexia. Therefore, the diagnostic criteria for the cachexia stages based on weight loss and BMI alone were not sufficient to classify the different stages of cancer cachexia.

Sarcopenia, another key symptom associated with cachexia and shorter survival in cancer patients,30 was recommended by the European working group on sarcopenia in older people using the presence of both low muscle mass and low muscle function.31 The definition of sarcopenia recommended by the European working group on sarcopenia in older people was applied to patients who were not able to rise from a chair or who had a gait speed of less than 1 min/s and who had low muscle mass measured by dual energy X-ray, CT, magnetic resonance imaging (MRI), or ultrasound.32–34 Although different muscle mass measurements had little influence on the diagnosis of cachexia,35 the muscle mass measurements are not applicable for the rapid screening of cachexia. Therefore, we chose the simple SARC-F questionnaire and classified its score into four categories for rapidly assessing the muscle function of patients. A study from Cao et al. showed that the SARC-F was a simple and useful tool for screening elderly Chinese people with impaired physical function and grip strength.25 Another study by Woo et al. suggested that the SARC-F screening tool yielded similar results for predicting physical limitations and mortality as the criteria used for sarcopenia diagnoses derived from the European, Asian, and international consensus.36 In addition, a study from Malmstrom et al. proved that SARC-F is a consistent and valid tool for screening people with adverse outcomes from sarcopenia in different populations.37

In the CSS, we added the ECOG performance score to reflect the patients’ physical function, which was simple and already used in clinical practice. Previous studies have suggested that cachexia can impair patients’ performance status,38,39 and in the international consensus on cachexia, low performance scores are a part of the definition for refractory cachexia.9 Therefore, the physical performance of patients should be an important component of staging cachexia.

Cancer cachexia has now been recognized as a cancer anorexia and cachexia syndrome. Obviously, anorexia and appetite loss are also key components of cancer cachexia, which lead to nutrition problems for cancer patients. Many instruments, such as scored patient-generated subjective global assessment40,41 and nutrition risk screening 2002,42,43 have been used to assess nutrition and anorexia in cancer patients. Because of the complexity of these methods, we chose a patient-reported numerical rating scale with a range of 0–10 with increasing severity to assess their appetite loss; this measurement is more suitable for clinical use in rapid screening.

Inflammation and malnutrition are frequently observed in cachexia patients and have been associated with poor outcomes. C-reactive protein, which is a biomarker of inflammation, has been shown to be associated with cancer cachexia and patient outcomes.44,45 Another common biomarker of inflammation is the WBC count. Because the WBC count is more commonly reported in routine blood tests than C-reactive protein levels, and it has been used in several cachexia staging studies,12,13 we chose it as a biomarker for inflammation in patients. In addition, haemoglobin and albumin levels were considered as biomarkers of patient nutrition and were also used as criteria for these cachexia staging studies. Therefore, we included all the three routine blood biomarkers (WBC and haemoglobin and albumin) in our CSS.

After we developed the CSS, we validated the discrimination of the four cachexia stages for clinical outcomes. Regarding the body composition results, patients in the more severe cachexia stages had lower SMI values and higher prevalence rates of sarcopenia, regardless of their gender. Differences in any two cachexia groups were statistically significant. In a study of cancer cachexia stages of Vigano et al.,12 no difference was seen in body composition between pre-cachexia and cachexia stages, and in another study of Vigano et al.,13 no difference in body composition was found in female patients. These findings suggest that our results had better discrimination for the body composition than other cachexia staging studies.

Symptom burden and quality of life were assessed in our patients. As a result, patients in the refractory cachexia stage had the highest symptom burden, and patients in the non-cachexia stage had the lowest symptom burden. Similar results were found for the quality of life assessment. Patients in the refractory cachexia stage had the poorest quality of life according to physical well-being, emotional well-being, functional well-being, and anorexia–cachexia subscale, and patients in the non-cachexia stage had the best quality of life. Differences in any two groups were all statistically significant. These findings suggest that the more severe the cachexia syndrome is, the higher the symptom burden and the poorer the quality of life will be. Similar results were found in previous studies.13,14,18

For survival analysis, significant differences among the four groups were seen according to Kaplan–Meier survival curves. Patients in the refractory cachexia stage had the shortest survival time, and patients in the non-cachexia had the longest survival time. In the consensus validation study,14 there was no difference in survival between the non-cachexia and pre-cachexia stages. Two cachexia staging studies from Vigano et al. showed that there was no difference in survival between the pre-cachexia and cachexia stages.12,13 These results suggest that our CSS can better classify cachexia stages for survival than previous studies.

Some limitations exist in our study. First, our study was conducted at only one cancer centre in mainland China and had a small sample size, which could affect the generalization of the results. Second, although our study was a prospective study, we did not repeatedly assess the cachexia status in our patients; therefore, changes in cachexia stages over time were not obtained. Third, for developing a simple and clinically
available score to classify cachexia stages, we used the SARC-F instead of muscle function assessment (e.g. grip strength and walk speed) and muscle mass assessment (e.g. dual-energy X-ray absorptiometry and CT) to determine muscle function and sarcopenia in our patients; we also used a numerical rating scale of 0–10 instead of other frequently used nutrition assessment tools, such as patient-generated subjective global assessment and nutrition risk screening 2002, to assess appetite in our patients.

In conclusion, our study has developed a simple and clinically available CSS for the classification of cachexia stages; the CSS showed good discrimination among the four cachexia stages for patient-related outcomes, including body composition, symptom burden, quality of life, and survival. The CSS in our study had better discrimination than previous studies and can be used easily in clinical practice. Moreover, it is beneficial for early recognition, diagnosis, and treatment of cachexia. Because this was a single centre study with a small sample size, multicentre studies with larger sample sizes are needed to further validate the CSS.

Acknowledgements

The authors certify that they comply with the Ethical guidelines for authorship and publishing in the Journal of Cachexia, Sarcopenia and Muscle. This work was supported by the National Natural Science foundation of China number 81372852 and 11602155.

Conflict of interest

No potential conflicts of interest were existed in the research, authorship, and publication of this article.

References

1. Fearon KC, Voss AC, Hustead DS. Cancer Cachexia Study G. Definition of cancer cachexia: effect of weight loss, reduced food intake, and systemic inflammation on functional status and prognosis. Am J Clin Nutr 2006;83:1345–1350.
2. Penet MF, Bhujwalla ZM. Cancer cachexia, recent advances, and future directions. Cancer J 2015;21:117–122.
3. Tisdale MJ. Mechanisms of cancer cachexia. Physiol Rev 2009;89:381–410.
4. Argiles JM, Lopez-Soriano FJ, Busquets S. Mechanisms and treatment of cancer cachexia. Nutr Metab Cardiovasc Dis 2013;23:S19–S24.
5. Mondello P, Mian M, Aloisi C, Fama F, Mondello S, Pitini V. Cancer cachexia syndrome: pathogenesis, diagnosis, and new therapeutic options. Nutr Cancer 2015;67:12–26.
6. Vaughan VC, Martin P, Lewandowski PA. Cancer cachexia: impact, mechanisms and emerging treatments. J Cachexia Sarcopenia Muscle 2013;4:95–109.
7. Srdic D, Plestina S, Sverko-Peternav A, Nikolac N, Simundic AM, Samarzija M. Cancer cachexia, sarcopenia and biochemical markers in patients with advanced non-small cell lung cancer-chemotherapy toxicity and prognostic value. Support Care Cancer 2016;24:4495–4502.
8. Takayama K, Atagi S, Immamura F, Tanaka H, Minato K, Harada T, et al. Quality of life and survival survey of cancer cachexia in advanced non-small cell lung cancer patients-Japan nutrition and QOL survey in patients with advanced non-small cell lung cancer study. Support Care Cancer 2016;24:3473–3480.
9. 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;12:489–495.
10. Argiles JM, Lopez-Soriano FJ, Toledo M, Betancourt A, Serpe R, Busquets S. The cachexia score (CASCOS): a new tool for staging cachectic cancer patients. J Cachexia Sarcopenia Muscle 2011;2:87–93.
11. Argiles JM, Betancourt A, Guardia-Olmos J, Pero-Cebollero M, Lopez-Soriano FJ, Madeddu C, et al. Validation of the Cachexia SCOré (CASCOS). Staging cancer patients: the use of miniCASCOS as a simplified tool. Front Physiol 2017;8:92.
12. Vigano AA, Del Fabbro E, Bruera E, Borod M. The cachexia clinic: from staging to managing nutritional and functional problems in advanced cancer patients. Crit Rev Oncog 2012;17:293–303.
13. Vigano AA, Morais JA, Ciutto L, Rosenthall L, di Tomasso J, Khan S, et al. Use of routinely available clinical, nutritional, and functional criteria to classify cachexia in advanced cancer patients. Clin Nutr 2016;36:1378–1390.
14. Blum D, Stene GB, Solheim TS, Fayers P, Hjermstad MJ, Baracos VE, et al. Validation of the consensus-definition for cancer cachexia and evaluation of a classification model—a study based on data from an international multicentre project (EPCR CSA). Ann Oncol 2014;25:1635–1642.
15. Wang XS, Wang Y, Guo H, Mendoza TR, Hao XS, Cleeeland CS. Chinese version of the M. D. Anderson symptom inventory: validation and application of symptom measurement in cancer patients. Cancer 2004;101:1890–1901.
16. Jain P, Keating M, Renner S, Cleeeland C, Xuelin H, Gonzalez GN, et al. Roxulitinib for symptom control in patients with chronic lymphocytic leukemia: a single-group, phase 2 trial. Lancet Haematol 2017;4:e67–e74.
17. George GC, Iwuanyanwu EC, Anderson KO, Yusuf A, Zinner RG, Pihal-Paul SA, et al. Sleep quality and its association with fatigue, symptom burden, and mood in patients with advanced cancer in a clinic for early-phase oncology clinical trials. Cancer 2016;122:3401–3409.
18. Zhou T, Yang K, Thapa S, Liu H, Wang B, Yu S. Differences in symptom burden among cancer patients with different stages of cachexia. J Pain Symptom Manag 2017;53:919–926.
19. Cella DF, Tulsky DS, Gray G, Saraffan B, Linn E, Bonomi A, et al. The functional assessment of cancer therapy scale: development and validation of the general measure. J Clin Oncol 1993;11:570–579.
20. LeBlanc TW, Samsa GP, Wolf SP, Locke SC, Cella DF, Abernethy AP. Validation and real-world assessment of the functional assessment of anorexia–cachexia therapy (FAACT) scale in patients with advanced non-small cell lung cancer and the cancer anorexia-cachexia syndrome (CACS). Support Care Cancer 2015;23:2341–2347.
21. Salsman JM, Beaumont JL, Wortman K, Yan Y, Friend J, Cella D. Brief versions of the FACIT-fatigue and FAACT subscales for patients with non-small cell lung cancer cachexia. Support Care Cancer 2015;23:1355–1364.
22. Zhou T, Yang K, Thapa S, Fu Q, Jiang Y, Yu S. Validation of the Chinese version of functional assessment of anorexia–cachexia therapy (FAACT) scale for measuring quality of life in cancer patients with cachexia. Support Care Cancer 2017;25:1183–1189.
23. Malmstrom TK, Morley JE. SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. J Am Med Dir Assoc 2013;14:531–532.
24. Morley JE, Cao L. Rapid screening for sarcopenia. J Cachexia Sarcopenia Muscle 2015;6:312–314.

25. Cao L, Chen S, Zou C, Ding X, Gao L, Liao Z, et al. A pilot study of the SARC-F scale on screening sarcopenia and physical disability in the Chinese older people. J Nutr Health Aging 2014;18:277–283.

26. Woo J, Leung J, Morley JE. Validating the SARC-F: a suitable community screening tool for sarcopenia? J Am Med Dir Assoc 2014;15:630–634.

27. Richards CH, Roxburgh CS, MacMillan MT, Isswiasi S, Robertson EG, Guthrie GK, et al. The relationships between body composition and the systemic inflammatory response in patients with primary operable colorectal cancer. PLoS One 2012;7:e41883.

28. Bozzetti F, Mariani L. Defining and classifying cancer cachexia: a proposal by the SCRINIO Working Group. J Parenter Enteral Nutr 2009;33:361–367.

29. Vagnildhaug OM, Blum D, Wilcock A, Fayers P, Strasser F, Baracos VE, et al. The applicability of a weight loss grading system in cancer cachexia: a longitudinal analysis. J Cachexia Sarcopenia Muscle 2017;8:789–797.

30. Choi MH, Oh SN, Lee IK, Oh ST, Won DD. Sarcopenia is negatively associated with long-term outcomes in locally advanced rectal cancer. J Cachexia Sarcopenia Muscle 2017. https://doi.org/10.1002/jcsm.12234

31. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on sarcopenia in older people. Age Ageing 2010;39:412–423.

32. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. J Am Med Dir Assoc 2011;12:249–256.

33. Paris MT, Lafleur B, Dubin JA, Mourtzakis M. Development of a bedside viable ultrasound protocol to quantify appendicular lean tissue mass. J Cachexia Sarcopenia Muscle 2017;8:713–726.

34. Nijholt W, Scagfoglieri A, Jager-Wittenaar H, Hobbelen JSM, van der Schans CP. The reliability and validity of ultrasound to quantify muscles in older adults: a systematic review. J Cachexia Sarcopenia Muscle 2017;8:702–712.

35. Blauwhoff-Buskermolen S, Langius JAE, Parenter Enteral Nutr 2017;41:367.

36. Woo J, Leung J, Morley JE. Defining sarcopenia in terms of incident adverse outcomes. J Am Med Dir Assoc 2015;16:247–252.

37. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle 2016;7:28–36.

38. Bye A, Sjoblom B, Wentzel-Larsen T, Gronberg BH, Baracos VE, Hjermstad MJ, et al. Muscle mass and association to quality of life in non-small cell lung cancer patients. J Cachexia Sarcopenia Muscle 2017;8:759–767.

39. LeBlanc TW, Nipp RD, Rushing CN, Samsa GP, Locke SC, Kamal AH, et al. Correlation between the international consensus definition of the cancer anorexia–cachexia syndrome (CACS) and patient-centered outcomes in advanced non-small cell lung cancer. J Pain Symptom Manag 2015;49:680–689.

40. Bauer J, Capra S, Ferguson M. Use of the scored patient-generated subjective global assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr 2002;56:779–785.

41. Tan CS, Read JA, Phan VH, Beale PJ, Peat JK, Clarke SJ. The relationship between nutritional status, inflammatory markers and survival in patients with advanced cancer: a prospective cohort study. Support Care Cancer 2015;23:385–391.

42. Orell-Kotikangas H, Osterlund P, Saariluhti K, Ravasco P, Schwab U, Makitie AA. NRS-2002 for pre-treatment nutritional risk screening and nutritional status assessment in head and neck cancer patients. Support Care Cancer 2015;23:1495–1502.

43. Bozzetti F, Mariani L, Lu Vullo S, Amerio ML, Biffi R, Caccialanza R, et al. The nutritional risk in oncology: a study of 1,453 cancer outpatients. Support Care Cancer 2012;20:1919–1928.

44. Bye A, Wesseltoft-Rao N, Iversen PO, Skjegstad G, Holven KB, Ulven S, et al. Alterations in inflammatory biomarkers and energy intake in cancer cachexia: a prospective study in patients with inoperable pancreatic cancer. Med Oncol 2016;33:54.

45. Wallengren O, Lundholm K, Bosaeus I. Diagnostic criteria of cancer cachexia: relation to quality of life, exercise capacity and survival in unselected palliative care patients. Support Care Cancer 2013;21:1569–1577.

46. von Haehling S, Morley JE, Coats AJ, Anker SD. Ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2015. J Cachexia Sarcopenia Muscle 2015;6:315–316.