

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

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## 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

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## 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.<sup>1,2</sup> Up to 50% of cancer patients suffer from cachexia, and more than 20% of cancer patients die because of cachexia.<sup>3,4</sup> Patients with cachexia usually manifest with weight loss, muscle wasting, anorexia, and inflammation.<sup>5</sup> Moreover, cachexia can increase treatment-related toxicity, aggravate symptom burden, worsen quality of life, and shorten survival times for patients.<sup>6–8</sup>

In the international consensus,<sup>9</sup> 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  $\leq 5\%$  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

cancer cachexia are difficult to develop because of the complex mechanisms and multiple phenotypes of cachexia; however, developing these criteria is extremely important and useful for clinical treatment and prognosis. For this purpose, the cachexia score,<sup>10</sup> a new tool for staging cachexia cancer patients, was designed by Argiles *et al.* Although it was validated in clinical patients, its routine use was restricted due to a large number of measurements, questionnaires, and inflammatory parameters. For this reason, the minicachexia score,<sup>11</sup> a simplified form of the cachexia score, was developed. However, its discrimination regarding patient-related outcomes has not yet been validated. Vigano *et al.* successively applied the cancer cachexia stages<sup>12</sup> and routinely available criteria<sup>13</sup> to stage cancer cachexia, but these criteria could not effectively classify the pre-cachexia and cachexia stages. A similar problem exists for the study of Blum *et al.*<sup>14</sup>; 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.

## 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 for assessing symptom.<sup>15–18</sup> We used the MDASI to assess the symptom burden of our patients. In addition, two cachexia-specific symptoms, early satiety and taste/smell changes, were also assessed in our patients using a 0–10 numeric rating scale. Each symptom has a range of 0–10 with increasing severity. The FAACT scale is a specific and validated questionnaire for evaluating the quality of life of cachexia patients.<sup>19–22</sup> It consists of five subscales: physical well-being, social well-being (SWB), emotional well-being,

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.<sup>23–26</sup> 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 (cm<sup>2</sup>) at the third lumbar vertebra was measured by the ImageJ software using standard Hounsfield unit ranges (–29 to +150).<sup>27</sup> Then, the skeletal muscle index (SMI) (cm<sup>2</sup>/m<sup>2</sup>) was calculated by using the skeletal muscle cross-sectional area (cm<sup>2</sup>) and patient stature (m). Based on the international consensus, sarcopenia was defined as a SMI <39 cm<sup>2</sup>/m<sup>2</sup> in female patients or <55 cm<sup>2</sup>/m<sup>2</sup> in male patients.<sup>9</sup>

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).

### *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.<sup>10,12–14,28</sup> 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

**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 $\leq 5\%$	1
	Weight loss $> 5\%$ and $\leq 15\%$	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
	5–6	3
Appetite loss (0–10)	0–3	0
	4–6	1
	7–9	2
	10	3
Abnormal biochemistry: ①WBC $> 10 \times 10^9/L$ ; ②Alb $< 35$ g/L; ③Hb $< 120/110$ g/L (male/female)	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.

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  $\pm$  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 loss 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.

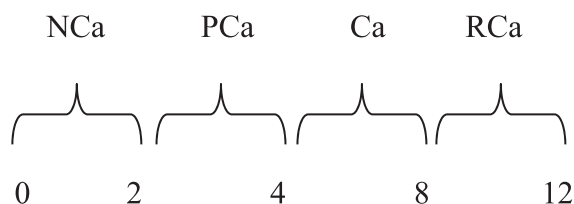
Patient demographics and clinical characteristics are summarized in Table 3. The mean age of our patients was  $50.6 \pm 12.6$  years, and 56.37% were males. The mean BMI ( $\text{kg}/\text{m}^2$ ), which was calculated by using weight (kg) and height (m), was  $21.83 (\pm 3.22)$  in our patients. The 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 2** Cachexia staging score

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



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.

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

Variables	No. of patients	Percentage
Age (mean $\pm$ SD) (y)	50.6 $\pm$ 12.6	—
Gender		
Female	113	43.63
Male	146	56.37
BMI (mean $\pm$ SD) (kg/m <sup>2</sup> )	21.83 $\pm$ 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.

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 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) <sup>a</sup>	8.44 (6.30) <sup>a, b</sup>	16.27 (7.36) <sup>a, b, c</sup>	<0.001
SARC-F (mean) (SD)	0.41 (0.79)	1.15 (1.08) <sup>a</sup>	2.70 (1.98) <sup>a, b</sup>	6.00 (1.97) <sup>a, b, c</sup>	<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%) <sup>a</sup>	9 (47.4%) <sup>a, b, c</sup>	
Appetite loss (mean) (SD)	1.20 (1.50)	3.03 (2.59) <sup>a</sup>	5.28 (2.78) <sup>a, b</sup>	8.47 (1.74) <sup>a, b, c</sup>	<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%) <sup>a, b</sup>	2 (20.0%) <sup>a, b, c</sup>	

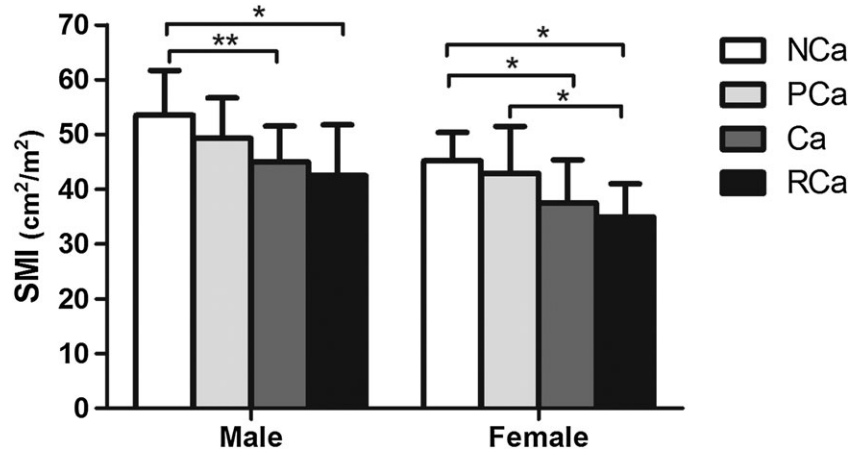
Ca, cachexia; ECOG PS, Eastern cooperative oncology group performance status; NcA, non-cachexia; PcA, pre-cachexia; RcA, refractory cachexia; SD, standard deviation.

<sup>a</sup>Statistically different from NcA.

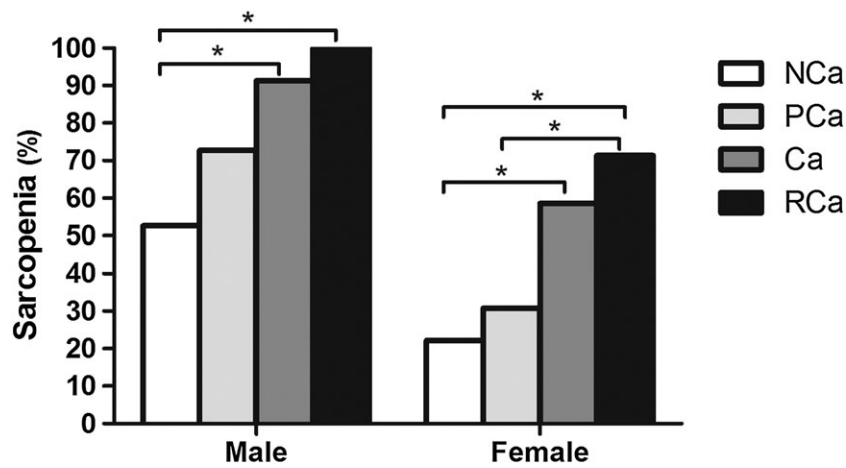
<sup>b</sup>Statistically different from PcA.

<sup>c</sup>Statistically different from Ca.

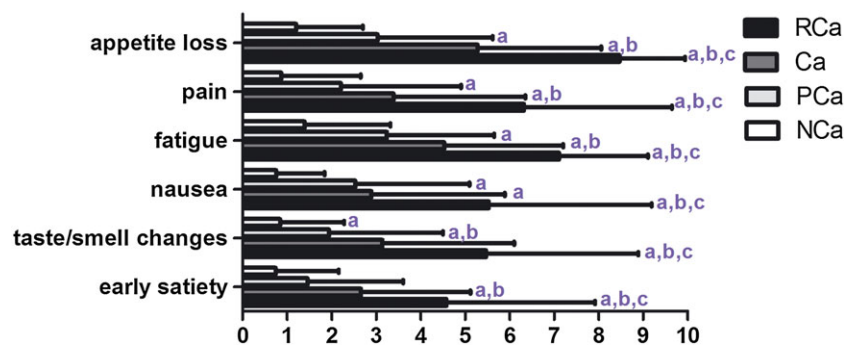
**Figure 1** Differences in skeletal muscle index (SMI) among male and female patients with different cachexia stages. Ca, cachexia; NCa, non-cachexia; PCa, pre-cachexia; RCa refractory cachexia; between groups comparisons: \* $P < 0.05$ , \*\* $P < 0.001$ .



**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; <sup>a</sup>Statistically different from NCa; <sup>b</sup>Statistically different from PCa; <sup>c</sup>Statistically 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 ( $P < 0.05$ ).

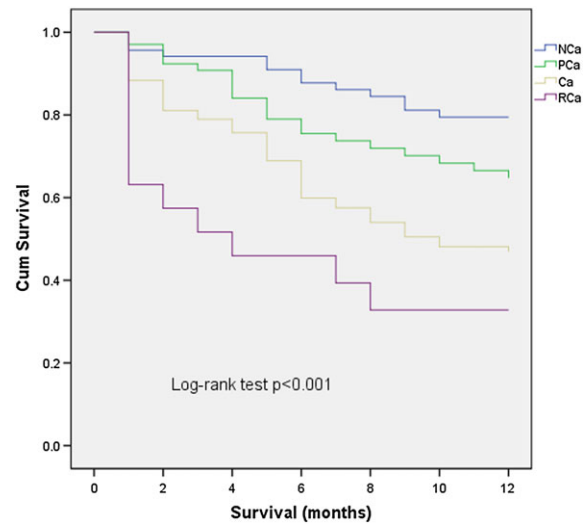
### Survival of patients in different cachexia stages

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

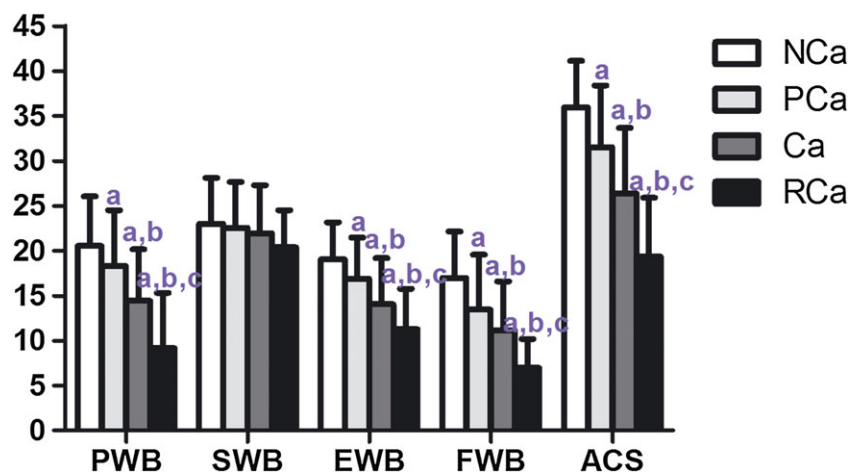
**Figure 5** Kaplan–Meier survival curves of patients with different cachexia stages. Ca, cachexia; NCa, non-cachexia; PCa, pre-cachexia; RCa refractory cachexia.



consists of five key cachexia components (weight loss, muscle function, appetite, performances 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.<sup>29</sup> 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

**Figure 4** Differences in quality of life among patients with different cachexia stages. ACS, anorexia–cachexia subscale; Ca, cachexia; EWB, emotional well-being; FWB, functional well-being; NCa, non-cachexia; PCa, pre-cachexia; PWB, physical well-being; RCa refractory cachexia; SWB, social well-being; <sup>a</sup>Statistically different from NCa; <sup>b</sup>Statistically different from PCa; <sup>c</sup>Statistically different from Ca.



to 3. These categories were referred to the validation study of consensus,<sup>14</sup> 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,<sup>30</sup> was recommended by the European working group on sarcopenia in older people using the presence of both low muscle mass and low muscle function.<sup>31</sup> 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.<sup>32–34</sup> Although different muscle mass measurements had little influence on the diagnosis of cachexia,<sup>35</sup> 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.<sup>25</sup> 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.<sup>36</sup> 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.<sup>37</sup>

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,<sup>38,39</sup> and in the international consensus on cachexia, low performance scores are a part of the definition for refractory cachexia.<sup>9</sup> 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 assessment<sup>40,41</sup> and nutrition risk screening 2002,<sup>42,43</sup> 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.<sup>44,45</sup> 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,<sup>12,13</sup> 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.*,<sup>12</sup> no difference was seen in body composition between pre-cachexia and cachexia stages, and in another study of Vigano *et al.*,<sup>13</sup> 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.<sup>13,14,18</sup>

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,<sup>14</sup> 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.<sup>12,13</sup> 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.

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## Conflict of interest

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

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