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# Fat mass assessment using the triceps skinfold thickness enhances the prognostic value of the Global Leadership Initiative on Malnutrition criteria in patients with lung cancer

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## Abstract

The present study evaluated whether fat mass assessment using the triceps skinfold (TSF) thickness provides additional prognostic value to the Global Leadership Initiative on Malnutrition (GLIM) framework in patients with lung cancer (LC). We performed an observational cohort study including 2672 LC patients in China. Comprehensive demographic, disease and nutritional characteristics were collected. Malnutrition was retrospectively defined using the GLIM criteria, and optimal stratification was used to determine the best thresholds for the TSF. The associations of malnutrition and TSF categories with survival were estimated independently and jointly by calculating multivariable-adjusted hazard ratios (HR). Malnutrition was identified in 808 (30·2 %) patients, and the best TSF thresholds were 9·5 mm in men and 12 mm in women. Accordingly, 496 (18·6 %) patients were identified as having a low TSF. Patients with concurrent malnutrition and a low TSF had a 54 % (HR = 1·54, 95 % CI = 1·25, 1·88) greater death hazard compared with well-nourished individuals, which was also greater compared with malnourished patients with a normal TSF (HR = 1·23, 95 % CI = 1·06, 1·43) or malnourished patients without TSF assessment (HR = 1·31, 95 % CI = 1·14, 1·50). These associations were concentrated among those patients with adequate muscle mass (as indicated by the calf circumference). Additional fat mass assessment using the TSF enhances the prognostic value of the GLIM criteria. Using the population-derived thresholds for the TSF may provide significant prognostic value when used in combination with the GLIM criteria to guide strategies to optimise the long-term outcomes in patients with LC.

**Key words:** **Malnutrition: GLIM: Triceps skinfold thickness: Lung cancer: Survival**

Lung cancer (LC) is a major disease burden both in China[(1)] and worldwide[(2)]. Despite recent advances in the diagnostic and therapeutic domains, the prognosis of LC remains poor[(3,4)]. Thus, the management strategies for patients with LC are still evolving, and interdisciplinary treatment solutions are being increasingly sought[(5)].

Nutritional care is an integral component of multi-disciplinary anti-cancer treatments and has been shown to optimise the

**Abbreviations:** GLIM, Global Leadership Initiative on Malnutrition; HR, hazard ratio; LC, lung cancer; MAC, mid-arm circumference; QOL, quality of life; TSF, triceps skinfold.

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clinical outcomes for patients with various cancers[6–9]. Malnutrition frequently develops in oncology patients due to either the tumour itself or various anti-cancer treatments and can lead to poorer clinical outcomes[6]. In the context of LC, the incidence of malnutrition ranges from 20 %[10] to 72 %[11] as defined by different assessment tools, which is associated with multiple adverse outcomes, including reduced treatment tolerance[12], poorer pulmonary rehabilitation[13], a reduced quality of life (QOL)[W14] and shorter survival[15]. Thus, the early detection[16] and treatment[17] of malnutrition among patients with LC have been emphasised in practice[7].

However, since there is not yet a universally accepted guideline[18], the methods used to detect malnutrition vary greatly across different institutions[10–12,14–16], which has made it difficult to implement a standardised management pathway in patients who can benefit from nutritional intervention. To address this challenge, the Global Leadership Initiative on Malnutrition (GLIM) criteria were recently proposed by several of the major global clinical nutrition societies after extensive discussion[19]. The criteria recommend a two-step approach (risk screening, then diagnosis) for diagnosing malnutrition. For the second step, three phenotypic criteria (weight loss, low BMI and reduced muscle mass) and two etiologic criteria (reduced food intake or assimilation and inflammation or disease burden) were proposed. At least one phenotypic criterion and one etiologic criterion should be met to confirm a diagnosis of malnutrition. Many studies have reported the effectiveness of this novel framework for diagnosing malnutrition[20] or predicting short-term outcomes[21]. Its value in predicting survival has also been described in several oncology populations[22–25].

Despite its potential to gain global acceptance, the GLIM framework was essentially based solely on expert opinions[19], some of the components of the GLIM might require refinement or adjustment, such as the best thresholds and combinations of parameters to reflect the full spectrum of malnutrition[26]. However, evidence for the refinement of the GLIM components has so far been limited. Of note, a major concern that has been raised is that the GLIM criteria only include the muscle mass and do not include fat mass assessment as a component, which is different from the Patient-Generated Subjective Global Assessment[27], a conventional assessment tool validated for use in oncology populations. Previous studies have shown the importance of fat mass assessment, independently or jointly with muscle mass assessment, in providing additional prognostic information in cancer patients[28,29]. Fat mass loss has also been related to worse survival in patients with LC[30,31]. As we have described in our previous work, GLIM-defined malnutrition is an independent risk factor for LC survival[32]. However, due to the current architecture of the GLIM, it remains unknown if the inclusion of a fat assessment would enhance the prognostic value of the GLIM in LC patients.

To address this question, we investigated whether using the triceps skinfold (TSF) thickness, a cost-effective anthropometric measurement, that reflects the fat mass, can provide additional prognostic value to the GLIM-based diagnosis of malnutrition by identifying specific risk groups. The secondary objective was to determine the optimal, survival-oriented and sex-specific thresholds of the TSF to facilitate the identification of a low fat mass in patients with LC.

## Methods

### Study design and population

This was a multicentre, observational cohort study. Patients were derived from the Investigation on Nutrition Status and Clinical Outcome of Common Cancers (INSCOC) project of China (chictr.org.cn, ChiCTR1800020329)[33]. For the present study, we included 2672 patients aged 18 to 87 years who were pathologically diagnosed with LC and/or were hospitalised for LC treatment from November 2012 to December 2018 at the Daping Hospital of Army Medical University ($n$ 773) and the First Hospital of Jilin University ($n$ 1899) in China. All patients were followed via face-to-face inquiry or telephone interview until death, last contact on March 31, 2020. This study was approved by the Institutional Ethics Committee of Daping Hospital.

### Data acquisition

The baseline information was acquired by a trained researcher upon patient admission and included the age, sex, smoking status (active tobacco smoker), whether they consumed alcohol (once a week or more frequent alcohol consumption, regardless of amount, in the past one year), place of residence (urban $v.$ rural), family cancer history, co-morbidities (chronic obstructive pulmonary disease, diabetes, hypertension and CHD), the Nutritional Risk Screening 2002 score (NRS2002, $\geq 3$ indicating nutritional risk)[34], the Karnofsky Performance Status score[35] and the European Organization for Research and Treatment of Cancer QLQ-C30 score (QLQ-C30)[36]. For the QLQ-C30, the global QOL scale was used in the present study, with a higher score indicating a better QOL.

### Disease and treatment

The following clinical characteristics of patients were obtained from electronic medical records collected during hospitalisation: clinical cancer stage, pathological differentiation grade, anti-cancer therapies received (radical surgery, radiotherapy, curative chemotherapy, postoperative adjuvant chemotherapy, targeted therapy or any other therapies) and laboratory measurements (total protein, albumin, prealbumin, transferrin, haemoglobin, C-reactive protein, neutrophil:lymphocyte ratio and white blood cell counts, measured using fasting blood samples drawn upon admission).

### Anthropometric measurements

Anthropometric parameters were measured upon admission. The height and body weight were measured to the nearest 0·1 cm and 0·1 kg, respectively, with the patient dressed in light indoor clothing without shoes. The percentages of unintentional weight loss (within and beyond six months) were then calculated as (self-reported historic weight minus weight measured)/historic weight ×100 %. The BMI was calculated as the weight in kilograms divided by the height in metres squared

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(kg/m$^2$). The hand grip strength (non-dominant arm, kg) was measured by a hand grip dynamometer (CAMRY, model EH101). The calf circumference (CC, left calf) and mid-arm circumference (MAC, non-dominant arm) were measured to the nearest 0·1 cm using a flexible and non-elastic tape. The TSF (non-dominant arm, mm) was measured using an adipometer (PZJ-01). The mid-arm muscle circumference (non-dominant arm) was calculated as MAC − 3·14 × TSF (cm).

### *Global Leadership Initiative on Malnutrition diagnosis*

The GLIM diagnosis was retrospectively defined according to a previously described approach[19]. Briefly, for patients at risk of malnutrition (NRS2002 ≥ 3), at least one phenotypic criterion and one etiologic criterion should be positive to establish the GLIM diagnosis in the present study. For the phenotypic criteria, the unintentional weight loss was assessed as described in the GLIM[19]. The BMI was assessed based on a set of thresholds (moderate: <18·5 kg/m$^2$ if <70 years, <20 kg/m$^2$ if ≥ 70 years; severe: <17·0 kg/m$^2$ if <70 years, <17·8 kg/m$^2$ if ≥ 70 years) validated in Asians[37]. The reduced muscle mass criterion was assessed based on validated CC thresholds (moderate: <30·5 cm in men and <29 cm in women; severe: <28·1 cm in men and <27 cm in women) in Asians[37,38] (online Supplementary Table S1). For the etiologic criteria, since all patients in the study cohort were pathologically diagnosed with and/or treated for LC, the entire study population was considered to be positive for the disease burden-related etiologic criterion[23].

### *Threshold determination and subgroup definitions*

Based on a previously described method[39,40], the optimal thresholds for the TSF were determined by maximising the between-group log-rank statistic with regard to the overall survival. The selected thresholds were then used to define the normal TSF (≥ threshold) and low TSF (<threshold) groups. Based on the GLIM diagnosis, the study population were further categorised into three groups: well-nourished, malnourished + normal TSF (patients with malnutrition and a normal TSF) and malnourished + low TSF (patients with malnutrition and a low TSF).

### *Statistical analysis*

The normality of continuous data was tested using a Kolmogorov–Smirnov test, and the variance equality was tested using a Levene's test. Continuous variables are shown as the means ± standard deviation (SD) and were compared using an ANOVA. Data with unequal variance were compared using an ANOVA with Welch correction. Dunnett's test was used for post hoc analysis by setting the malnourished + low TSF group as the reference. Categorical data are expressed as a number (percentage) and were compared using a $\chi^2$test. False discovery rate adjustment was used for the multiple comparison of the $\chi^2$ test. The least absolute shrinkage and selection operator method was used to screen the prognostic factors for multivariable adjustment. A ten-fold cross-validation and one standard error criterion (lambda.1se) were used to select the optimal model.

The univariate associations between the study subgroups and survival were evaluated using Kaplan–Meier curves and log-rank tests. Multivariable-adjusted Cox proportional hazard models were used, and hazard ratios (HR) with 95 % CI were calculated to estimate the associations between the subgroups and survival. The Kaplan–Meier curves and the Schoenfeld individual test were used to visually and statistically estimate the proportional hazards assumption. Incremental models with increasing numbers of variables were generated. Model 1 was an unadjusted model. Model 2 was adjusted for age (continuous) at baseline. Model 3 was adjusted for the least absolute shrinkage and selection operator-screened predictors plus age and sex. Sensitivity analyses were performed to test the robustness of the multivariable Cox regression models by excluding those patients who died within the first 3 months (model 4), first 6 months (model 5) and first 12 months (model 6) after admission. Multiplicative interactions between the study subgroup and other covariates were tested by adjusting the cross-product terms. Patients were stratified by the variables showing interactive effects to evaluate the modification of the associations. All tests were two-sided, and $P < 0·05$ was regarded as statistically significant. All analyses were performed using the open source software, R (version 3.6.3, http://www.rproject.org).

## Results

### *Baseline characteristics*

The study included 899 females and 1773 males with a mean age of 59 years. Based on the two-step approach, it was found that 966 (36·2 %) patients were considered to be at nutritional risk based on the NRS2002, and malnutrition was subsequently identified in 808 (30·2 %) patients by the GLIM criteria. The optimal stratification method showed that the best thresholds for the TSF were 9·5 mm (statistic = 6·71) in men and 12 mm (statistic = 2·51) in women. Accordingly, 496 (18·6 %) patients were identified as having a low TSF.

The baseline characteristics of the study population, as stratified by the GLIM and TSF categories, are shown in Table 1. The GLIM and TSF categories were both associated with age, sex, smoking, chronic obstructive pulmonary disease, hypertension, albumin, prealbumin, haemoglobin, BMI, MAC, mid-arm muscle circumference, CC, weight loss (both within and beyond six months) and quality of life. In contrast, drinking, diabetes, the clinical stage, radical surgery, adjuvant chemotherapy, other anticancer therapy, total protein, C-reactive protein, neutrophil:lymphocyte ratio, white blood cell count, hand grip strength and Karnofsky Performance Status score were only associated with the GLIM. The differentiation grade was only associated with the TSF (all $P < 0·05$). Furthermore, a low TSF was associated with elevated nutritional risk (54·8 % *v.* 31·9 %, $P < 0·001$) and the incidence of malnutrition (49·8 % *v.* 25·8 %, $P < 0·001$).

Based on the GLIM diagnosis and the TSF categories, the study population was further sub-categorised into well-nourished (*n* 1864), malnourished + normal TSF (*n* 561) and malnourished + low TSF (*n* 247) groups for further analysis. The overall and group-specific baseline characteristics of the study population are presented in Table 2. The patient age, sex, smoking, drinking, chronic obstructive pulmonary disease, diabetes,

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**Table 1.** Baseline characteristics stratified by the Global Leadership Initiative on Malnutrition (GLIM) and triceps skinfold (TSF) categories (Number and percentages; median and standard values, *n* 2672)

| | GLIM | | | | | TSF | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Well-nourished (*n* 1864) | | Malnourished (*n* 808) | | | Normal (*n* 2176) | | Low (*n* 496) | | |
| Characteristics | *n* | % | *n* | % | *P* | *n* | % | *n* | % | *P* |
| General information | | | | | | | | | | |
| Age, years | | | | | | | | | | |
| Median | 58·78 | | 60·54 | | < 0·001 | 58·97 | | 60·82 | | < 0·001 |
| SD | 9·28* | | 10·38 | | | 9·60 | | 9·80 | | |
| Sex, male | 1337 | 71·7 | 436 | 54·0 | < 0·001 | 1417 | 65·1 | 356 | 71·8 | 0·005 |
| Smoking, yes | 1213 | 65·1 | 472 | 58·4 | 0·001 | 1350 | 62·0 | 335 | 67·5 | 0·025 |
| Drinking, yes, | 546 | 29·3 | 174 | 21·5 | < 0·001 | 577 | 26·5 | 143 | 28·8 | 0·321 |
| Residency, urban | 1371 | 73·6 | 590 | 73·0 | 0·812 | 1589 | 73·0 | 372 | 75·0 | 0·400 |
| Family cancer history, yes | 321 | 17·2 | 118 | 14·6 | 0·105 | 369 | 17·0 | 70 | 14·1 | 0·140 |
| COPD, yes | 26 | 1·4 | 25 | 3·1 | 0·005 | 33 | 1·5 | 18 | 3·6 | 0·003 |
| Diabetes, yes | 202 | 10·8 | 65 | 8·0 | 0·032 | 227 | 10·4 | 40 | 8·1 | 0·133 |
| Hypertension, yes | 371 | 19·9 | 122 | 15·1 | 0·004 | 422 | 19·4 | 71 | 14·3 | 0·010 |
| Coronary disease, yes | 116 | 6·2 | 54 | 6·7 | 0·718 | 144 | 6·6 | 26 | 5·2 | 0·303 |
| Disease and treatment | | | | | | | | | | |
| Clinical stage | | | | | < 0·001 | | | | | 0·131 |
| I | 266 | 14·3 | 80 | 9·9 | | 292 | 13·4 | 54 | 10·9 | |
| II | 305 | 16·4 | 112 | 13·9 | | 341 | 15·7 | 76 | 15·3 | |
| III | 603 | 32·3 | 210 | 26·0 | | 672 | 30·9 | 141 | 28·4 | |
| IV | 690 | 37·0 | 406 | 50·2 | | 871 | 40·0 | 225 | 45·4 | |
| Differentiation grade | | | | | 0·856 | | | | | 0·013 |
| Well | 144 | 7·7 | 58 | 7·2 | | 149 | 6·8 | 53 | 10·7 | |
| Medium | 831 | 44·6 | 358 | 44·3 | | 979 | 45·0 | 210 | 42·3 | |
| Poor | 889 | 47·7 | 392 | 48·5 | | 1048 | 48·2 | 233 | 47·0 | |
| Radical surgery, yes | 442 | 23·7 | 162 | 20·0 | 0·042 | 505 | 23·2 | 99 | 20·0 | 0·133 |
| Radiotherapy, yes | 179 | 9·6 | 94 | 11·6 | 0·128 | 219 | 10·1 | 54 | 10·9 | 0·643 |
| Adjuvant chemotherapy, yes | 256 | 13·7 | 86 | 10·6 | 0·033 | 280 | 12·9 | 62 | 12·5 | 0·883 |
| Curative chemotherapy, yes | 716 | 38·4 | 275 | 34·0 | 0·035 | 818 | 37·6 | 173 | 34·9 | 0·281 |
| Targeted therapy, yes | 138 | 7·4 | 71 | 8·8 | 0·252 | 175 | 8·0 | 34 | 6·9 | 0·426 |
| Other anticancer therapy, yes | 545 | 29·2 | 277 | 34·3 | 0·011 | 674 | 31·0 | 148 | 29·8 | 0·659 |
| Laboratory findings | | | | | | | | | | |
| | Median | SD | Median | SD | | Median | SD | Median | SD | |
| Total protein, g/l | 68·00 | 6·62 | 66·44 | 7·49 | < 0·001 | 67·65 | 6·88 | 67·00 | 7·12 | 0·060 |
| Albumin, g/l | 39·33 | 6·22 | 36·98 | 5·75 | < 0·001 | 38·88 | 6·30 | 37·46 | 5·45 | < 0·001 |
| Prealbumin, mg/l | 225·51 | 144·26 | 201·14 | 139·16 | < 0·001 | 222·05 | 150·03 | 201·01 | 106·33 | 0·003 |
| Transferrin, g/l | 4·36 | 20·58 | 5·32 | 41·50 | 0·425 | 4·70 | 29·92 | 4·48 | 21·66 | 0·878 |
| Haemoglobin, g/l | 129·64 | 20·07 | 120·43 | 20·39 | < 0·001 | 127·98 | 19·92 | 121·93 | 22·72 | < 0·001 |
| C-reactive protein, mg/l | 17·29 | 50·03 | 25·45 | 39·70 | < 0·001 | 19·52 | 50·21 | 20·80 | 31·43 | 0·587 |
| NLR | 3·89 | 10·74 | 5·45 | 13·91 | 0·002 | 4·29 | 12·82 | 4·67 | 5·51 | 0·518 |
| White blood cells, $10^9$ | 6·89 | 3·19 | 7·73 | 5·33 | < 0·001 | 7·11 | 4·07 | 7·29 | 3·51 | 0·358 |
| Anthropometric measurements | | | | | | | | | | |
| BMI, kg/m$^2$ | 23·65 | 3·31 | 19·17 | 3·45 | < 0·001 | 22·81 | 3·86 | 20·04 | 3·45 | < 0·001 |
| Mid-arm circumference, cm | 27·89 | 3·27 | 24·90 | 3·20 | < 0·001 | 27·45 | 3·45 | 24·96 | 3·11 | < 0·001 |
| Triceps skinfold thickness, mm | 16·93 | 6·78 | 13·91 | 6·15 | < 0·001 | 17·97 | 5·85 | 7·42 | 1·92 | < 0·001 |
| Hand grip strength, kg | 27·55 | 9·44 | 22·25 | 9·07 | < 0·001 | 26·09 | 9·70 | 25·32 | 9·39 | 0·107 |
| MAMC, cm | 22·58 | 3·33 | 20·54 | 3·10 | < 0·001 | 21·81 | 3·44 | 22·65 | 3·10 | < 0·001 |
| Calf circumference, cm | 34·84 | 3·74 | 31·36 | 3·62 | < 0·001 | 34·26 | 4·04 | 31·72 | 3·30 | < 0·001 |
| Weight loss within 6 months, % | 0·69 | 1·30 | 5·09 | 5·15 | < 0·001 | 1·86 | 3·42 | 2·73 | 4·43 | < 0·001 |
| Weight loss beyond 6 months, % | 2·33 | 3·95 | 8·83 | 7·76 | < 0·001 | 3·85 | 5·67 | 6·24 | 7·70 | < 0·001 |
| Nutritional status | | | | | | | | | | |
| | *n* | % | *n* | % | | *n* | % | *n* | % | |
| NRS2002, ≥ 3 | 158 | 8·5 | 808 | 100·0 | < 0·001 | 694 | 31·9 | 272 | 54·8 | < 0·001 |
| TSF, low | 249 | 13·4 | 247 | 30·6 | < 0·001 | 0 | 0·0 | 496 | 100·0 | < 0·001 |
| GLIM, malnourished | 0 | 0·0 | 808 | 100·0 | < 0·001 | 561 | 25·8 | 247 | 49·8 | < 0·001 |
| GLIM severity grade | | | | | < 0·001 | | | | | < 0·001 |
| Well-nourished | 1864 | 100·0 | 0 | 0·0 | | 1615 | 74·2 | 249 | 50·2 | |
| Moderate malnutrition | 0 | 0·0 | 445 | 55·1 | | 335 | 15·4 | 110 | 22·2 | |
| Severe malnutrition | 0 | 0·0 | 363 | 44·9 | | 226 | 10·4 | 137 | 27·6 | |
| Quality of life (QOL) | | | | | | | | | | |
| | Median | SD | Median | SD | | Median | SD | Median | SD | |
| Global QOL by the QLQ-C30 | 66·38 | 18·81 | 60·67 | 21·10 | < 0·001 | 65·03 | 19·87 | 62·99 | 18·91 | 0·037 |
| KPS score, continuous | 89·00 | 10·10 | 84·52 | 14·05 | < 0·001 | 87·84 | 11·13 | 86·75 | 13·55 | 0·059 |

Low TSF, < 12 mm in women and < 9·5 mm in men; COPD, chronic obstructive pulmonary disease; NLR, neutrophil:lymphocyte ratio; MAMC, mid-arm muscle circumference; NRS2002, the nutritional risk screening 2002; QLQ-C30, the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 score; KPS, the Karnofsky Performance Scale.

* Median ± standard deviation, all such values.

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**Table 2.** Baseline characteristics of the study population stratified by the Global Leadership Initiative on Malnutrition (GLIM) and triceps skinfold (TSF) subgroups
(Number and percentages; median and standard values)

| | Overall (*n* 2672) | | Well-nourished (*n* 1864) | | Mal + normal TSF (*n* 561) | | Mal + low TSF (*n* 247) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Characteristics | *n* | % | *n* | % | *n* | % | *n* | % | *P* overall* | PN *v.* L† |
| General information | | | | | | | | | | |
| Age, years | | | | | | | | | | |
| Median | 59·31 | | 58·78 | | 60·24 | | 61·22 | | < 0·001 | 0·264 |
| SD | 9·66‡ | | 9·28 | | 10·33 | | 10·48 | | | |
| Sex, male | 1773 | 66·4 | 1337 | 71·7 | 294 | 52·4 | 142 | 57·5 | < 0·001 | 0·208 |
| Smoking, yes | 1685 | 63·1 | 1213 | 65·1 | 329 | 58·6 | 143 | 57·9 | 0·005 | 0·903 |
| Drinking, yes | 720 | 26·9 | 546 | 29·3 | 125 | 22·3 | 49 | 19·8 | < 0·001 | 0·493 |
| Residency, urban | 1961 | 73·4 | 1371 | 73·6 | 409 | 72·9 | 181 | 73·3 | 0·954 | 0·989 |
| Family cancer history, yes | 439 | 16·4 | 321 | 17·2 | 84 | 15·0 | 34 | 13·8 | 0·224 | 0·734 |
| COPD, yes | 51 | 1·9 | 26 | 1·4 | 12 | 2·1 | 13 | 5·3 | < 0·001 | 0·048 |
| Diabetes, yes | 267 | 10·0 | 202 | 10·8 | 54 | 9·6 | 11 | 4·5 | 0·007 | 0·028 |
| Hypertension, yes | 493 | 18·5 | 371 | 19·9 | 93 | 16·6 | 29 | 11·7 | 0·003 | 0·096 |
| CHD, yes | 170 | 6·4 | 116 | 6·2 | 38 | 6·8 | 16 | 6·5 | 0·893 | 0·998 |
| Disease and treatment | | | | | | | | | | |
| Clinical stage | | | | | | | | | < 0·001 | 0·759 |
| I | 346 | 12·9 | 266 | 14·3 | 58 | 10·3 | 22 | 8·9 | | |
| II | 417 | 15·6 | 305 | 16·4 | 77 | 13·7 | 35 | 14·2 | | |
| III | 813 | 30·4 | 603 | 32·3 | 150 | 26·7 | 60 | 24·3 | | |
| IV | 1096 | 41·0 | 690 | 37·0 | 276 | 49·2 | 130 | 52·6 | | |
| Differentiation grade | | | | | | | | | 0·713 | 0·682 |
| Well | 202 | 7·6 | 144 | 7·7 | 36 | 6·4 | 22 | 8·9 | | |
| Medium | 1189 | 44·5 | 831 | 44·6 | 254 | 45·3 | 104 | 42·1 | | |
| Poor | 1281 | 47·9 | 889 | 47·7 | 271 | 48·3 | 121 | 49·0 | | |
| Radical surgery, yes | 604 | 22·6 | 442 | 23·7 | 112 | 20·0 | 50 | 20·2 | 0·115 | 1·000 |
| Radiotherapy, yes | 273 | 10·2 | 179 | 9·6 | 65 | 11·6 | 29 | 11·7 | 0·281 | 1·000 |
| Adjuvant chemotherapy, yes | 342 | 12·8 | 256 | 13·7 | 54 | 9·6 | 32 | 13·0 | 0·038 | 0·296 |
| Curative chemotherapy, yes | 991 | 37·1 | 716 | 38·4 | 193 | 34·4 | 82 | 33·2 | 0·094 | 0·801 |
| Targeted therapy, yes | 209 | 7·8 | 138 | 7·4 | 53 | 9·4 | 18 | 7·3 | 0·272 | 0·580 |
| Other anticancer therapy, yes | 822 | 30·8 | 545 | 29·2 | 200 | 35·7 | 77 | 31·2 | 0·015 | 0·372 |
| Laboratory findings | | | | | | | | | | |
| | Median | SD | Median | SD | Median | SD | Median | SD | | |
| Total protein, g/l | 67·53 | 6·93 | 68·00 | 6·62 | 66·64 | 7·53 | 65·98 | 7·39 | < 0·001 | 0·301 |
| Albumin, g/l | 38·62 | 6·17 | 39·33 | 6·22 | 37·31 | 5·61 | 36·23 | 6·00 | < 0·001 | 0·033 |
| Prealbumin, mg/l | 218·14 | 143·15 | 225·51 | 144·26 | 206·22 | 141·07 | 189·60 | 134·29 | < 0·001 | 0·191 |
| Transferrin, g/l | 4·66 | 28·57 | 4·36 | 20·58 | 6·08 | 48·70 | 3·60 | 15·75 | 0·381 | – |
| Haemoglobin, g/l | 126·85 | 20·60 | 129·64 | 20·07 | 121·93 | 20·02 | 117·02 | 20·85 | < 0·001 | 0·003 |
| C-reactive protein, mg/L | 19·76 | 47·29 | 17·29 | 50·03 | 24·97 | 40·42 | 26·55 | 38·05 | < 0·001 | 0·831 |
| NLR | 4·36 | 11·81 | 3·89 | 10·74 | 5·43 | 16·06 | 5·48 | 6·87 | 0·007 | 0·997 |
| White blood cells, $10^9$ | 7·14 | 3·98 | 6·89 | 3·19 | 7·79 | 5·85 | 7·57 | 3·89 | < 0·001 | 0·636 |
| Anthropometric measurements | | | | | | | | | | |
| BMI, kg/m$^2$ | 22·29 | 3·94 | 23·65 | 3·31 | 19·78 | 3·54 | 17·78 | 2·79 | < 0·001 | < 0·001 |
| Mid-arm circumference, cm | 26·99 | 3·53 | 27·89 | 3·27 | 25·55 | 3·17 | 23·42 | 2·75 | < 0·001 | < 0·001 |
| Triceps skinfold thickness, mm | 16·02 | 6·74 | 16·93 | 6·78 | 16·72 | 5·15 | 7·54 | 2·22 | < 0·001 | < 0·001 |
| Hand grip strength, kg | 25·95 | 9·64 | 27·55 | 9·44 | 22·33 | 9·06 | 22·09 | 9·11 | < 0·001 | 0·901 |
| MAMC, cm | 21·97 | 3·39 | 22·58 | 3·33 | 20·30 | 3·23 | 21·09 | 2·71 | < 0·001 | 0·003 |
| Calf circumference, cm | 33·78 | 4·03 | 34·84 | 3·74 | 31·93 | 3·65 | 30·06 | 3·22 | < 0·001 | < 0·001 |
| Weight loss within 6 months, % | 2·02 | 3·65 | 0·69 | 1·30 | 5·17 | 5·08 | 4·92 | 5·33 | < 0·001 | 0·392 |
| Weight loss beyond six months, % | 4·29 | 6·17 | 2·33 | 3·95 | 8·34 | 7·37 | 9·92 | 8·49 | < 0·001 | < 0·001 |
| QOL and physical performance | | | | | | | | | | |
| Global QOL by the QLQ-C30 | 64·65 | 19·70 | 66·38 | 18·81 | 61·71 | 21·47 | 58·33 | 20·08 | < 0·001 | 0·039 |
| KPS score, continuous | 87·64 | 11·62 | 89·00 | 10·10 | 85·13 | 13·07 | 83·12 | 16·02 | < 0·001 | 0·035 |
| Malnutrition | | | | | | | | | | |
| GLIM diagnosis | | | | | | | | | < 0·001 | < 0·001 |
| | *n* | % | *n* | % | *n* | % | *n* | % | | |
| Well-nourished | 1864 | 69·8 | 1864 | 100·0 | 0 | 0·0 | 0 | 0·0 | | |
| Moderate malnutrition | 445 | 16·7 | 0 | 0·0 | 335 | 59·7 | 110 | 44·5 | | |
| Severe malnutrition | 363 | 13·6 | 0 | 0·0 | 226 | 40·3 | 137 | 55·5 | | |

Mal, malnutrition; Low TSF, < 12 mm in women and < 9·5 mm in men; Mal + normal TSF, malnourished patients with a normal TSF; Mal + low TSF, malnourished patients with a low TSF; N *v.* L, Malnourished + normal TSF group *v.* malnourished + low TSF group; COPD, chronic obstructive pulmonary disease; NLR, neutrophil:lymphocyte ratio; MAMC, mid-arm muscle circumference; QOL, quality of life; QLQ-C30, the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 score; KPS, the Karnofsky Performance Scale.

* Calculated by one-way ANOVA for continuous variables and $\chi^2$ test for categorical variables.

† Dunnett's test was used for post hoc analysis by setting the Mal + low TSF group as the reference, and false discovery rate (FDR) adjustment was used for the multiple comparison of the $\chi^2$ test.

‡ Median ± standard deviation, all such values.

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hypertension, adjuvant chemotherapy, other anticancer therapy, total protein, albumin, prealbumin, haemoglobin, C-reactive protein, neutrophil:lymphocyte ratio, white blood cell count, BMI, MAC, TSF, hand grip strength, mid-arm muscle circumference, CC, weight loss within and beyond six months, global QOL scores, Karnofsky Performance Status scores and the severity of malnutrition differed across the three groups (all $P < 0{\cdot}05$). Such differences were not observed for the place of residence, family cancer history, CHD, differentiation grade, radical surgery, radiotherapy, curative chemotherapy, targeted therapy or the transferrin level (all $P > 0{\cdot}05$).

Subsequent multiple comparisons showed that compared with the malnourished + normal TSF group, patients in the malnourished + low TSF group had less/lower diabetes, albumin, haemoglobin, BMI, MAC, TSF, CC, global QOL scores and Karnofsky Performance Status scores, but had more/higher chronic obstructive pulmonary disease, mid-arm muscle circumference, weight loss beyond six months and severe malnutrition (all $P < 0{\cdot}05$).

### *Univariate survival analysis*

There were 1090 deaths among the 2672 patients during a median follow-up time of 751 d. Kaplan–Meier curves demonstrated that patients with malnutrition had a worse survival (HR = 1·52, 95 % CI = 1·35, 1·72, median overall survival (MOS) = 39 months) than those in the well-nourished group (MOS = 83 months, $P < 0{\cdot}0001$, Fig. 1(a)). In addition, patients in the low TSF group had worse survival (HR = 1·64, 95 % CI = 1·42, 1·88, MOS = 33 months) than those in the normal TSF group (MOS = 83 months, $P < 0{\cdot}0001$, Fig. 1(b)). After further stratifying the study population into three subgroups, patients in the malnourished + low TSF showed a higher death risk (HR = 1·91, 95 % CI = 1·59, 2·29, MOS = 20 months) compared with those in the malnourished + normal TSF group (HR = 1·38, 95 % CI = 1·19, 1·58, MOS = 53 months) and the well-nourished group (MOS = 83 months, $P < 0{\cdot}0001$, Fig. 1(c)).

### *Multivariable models*

The results of the multivariable Cox proportional hazards models are shown in Table 3. Covariates for adjustment were chosen based on the predictor screening results using the least absolute shrinkage and selection operator method (including the clinical tumour stage, radical surgery, curative chemotherapy, CC and haemoglobin, Fig. 2) plus age and sex. Concurrent malnutrition and a low TSF were associated with a 54 % (HR = 1·54, 95 % CI = 1·25, 1·88) greater death hazard compared with the well-nourished group (reference) and a 31 % greater death hazard compared with the malnourished + normal TSF group (HR = 1·23, 95 % CI = 1·06, 1·43). The combination of GLIM-diagnosed malnutrition and a low TSF also showed greater prognostic value than GLIM-defined malnutrition alone (regardless of the severity of malnutrition, HR = 1·31, 95 % CI = 1·14, 1·50) or a low TSF alone (HR = 1·39, 95 % CI = 1·20, 1·61) in other independent models.

To minimise the possibility of reverse causality to support the robustness of the results, we also performed sensitivity analyses by excluding those patients who died within the first 3 months

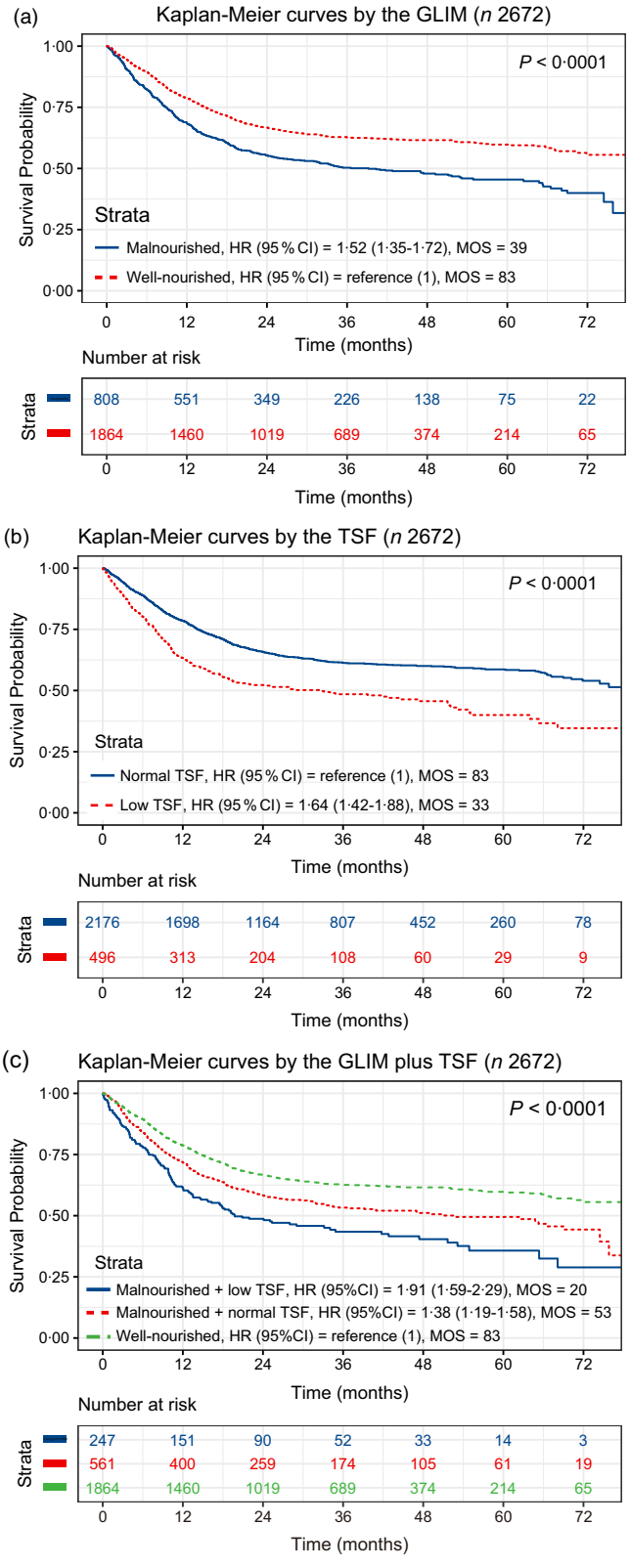


**Fig. 1.** The association of the combination of the Global Leadership Initiative on Malnutrition (GLIM)-defined malnutrition and triceps skinfold (TSF) thickness with survival. Low TSF, < 12 mm in women and < 9·5 mm in men; MOS, median overall survival. (a) Kaplan–Meier curves stratified by the GLIM diagnosis. (b) Kaplan–Meier curves stratified by the TSF. (c) Kaplan–Meier curves stratified by GLIM diagnosis plus the TSF.

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**Table 3.** Multivariable models for the Global Leadership Initiative on Malnutrition (GLIM) and triceps skinfold (TSF)

| | Overall population | | | | | | | | Sensitivity analysis | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Model | No./events | Model 1* | | Model 2† | | Model 3‡ | | No./events | Model 4§ | | No./events | Model 5‖ | | No./events | Model 6¶ | |
| GLIM, independent | | | | | | | | | | | | | | | | |
| Well-nourished | 1864/686 | 1 (Reference) | | 1 (Reference) | | 1 (Reference) | | 1765/587 | 1 (Reference) | | 1667/490 | 1 (Reference) | | 1460/290 | 1 (Reference) | |
| Malnourished | 808/404 | 1·52 | 1·35–1·72 | 1·50 | 1·33–1·7 | 1·31 | 1·14–1·50 | 732/328 | 1·29 | 1·11–1·50 | 666/262 | 1·29 | 1·09–1·53 | 551/151 | 1·31 | 1·05–1·62 |
| TSF, independent | | | | | | | | | | | | | | | | |
| Normal | 2176/831 | 1 (Reference) | | 1 (Reference) | | 1 (Reference) | | 2054/709 | 1 (Reference) | | 1935/591 | 1 (Reference) | | 1698/364 | 1 (Reference) | |
| Low | 496/259 | 1·64 | 1·42–1·88 | 1·61 | 1·40–1·85 | 1·39 | 1·20–1·61 | 443/206 | 1·37 | 1·17–1·61 | 398/161 | 1·37 | 1·14–1·64 | 313/77 | 1·14 | 0·88–1·48 |
| GLIM plus TSF, joint | | | | | | | | | | | | | | | | |
| Well-nourished | 1864/686 | 1 (Reference) | | 1 (Reference) | | 1 (Reference) | | 1765/587 | 1 (Reference) | | 1667/490 | 1 (Reference) | | 1460/290 | 1 (Reference) | |
| Malnourished + Normal TSF | 561/264 | 1·38 | 1·19–1·58 | 1·36 | 1·18–1·57 | 1·23 | 1·06–1·43 | 518/221 | 1·24 | 1·05–1·46 | 473/176 | 1·22 | 1·02–1·47 | 400/106 | 1·26 | 0·99–1·59 |
| Malnourished + Low TSF | 247/140 | 1·91 | 1·59–2·29 | 1·88 | 1·56–2·25 | 1·54 | 1·25–1·88 | 214/107 | 1·46 | 1·16–1·84 | 193/86 | 1·53 | 1·18–1·97 | 151/45 | 1·47 | 1·04–2·09 |

Low TSF, < 12 mm in women and < 9·5 mm in men.
* Model 1 is the unadjusted crude model.
† Model 2 is adjusted for age at baseline (continuous).
‡ Model 3 is adjusted for age at baseline (continuous), sex (reference = female), tumour stage (reference = I), radical surgery (reference = no), curative chemotherapy (reference = no), calf circumference (continuous) and haemoglobin (continuous).
§ Model 4 is adjusted for all covariates in model 3 but excluded those patients who died within the first 3 months after admission.
‖ Model 5 is adjusted for all covariates in model 3 but excluded those patients who died within the first 6 months after admission.
¶ Model 6 is adjusted for all covariates in model 3 but excluded those patients who died within the first 12 months after admission.

(model 4), 6 months (model 5) or 12 months (model 6) after admission. The results were similar to those in the overall population, indicating that concurrent malnutrition and a low TSF was associated with a 46 % (HR = 1·46, 95 % CI = 1·16, 1·84), 53 % (HR = 1·53, 95 % CI = 1·18, 1·97) and 47 % (HR = 1·47, 95 % CI = 1·04, 2·09) greater death hazard, respectively, compared with the well-nourished group (reference). The death hazard was also higher than the malnutrition group in the independent GLIM models, as shown in model 4 (HR = 1·29, 95 % CI = 1·11, 1·50), model 5 (HR = 1·29, 95 % CI = 1·09, 1·53) and model 6 (HR = 1·31, 95 % CI = 1·05, 1·62), or the low TSF group in the independent TSF models as shown in model 4 (HR = 1·37, 95 % CI = 1·17, 1·61), model 5 (HR = 1·37, 95 % CI = 1·14, 1·64) and model 6 (HR = 1·14, 95 % CI = 0·88, 1·48). In model 6, concurrent malnutrition and a normal TSF were not associated with the survival outcome, while the malnourished + low TSF group still held prognostic value, which remained higher than the malnutrition group in the independent GLIM model (HR = 1·31, 95 % CI = 1·05, 1·62). A low TSF alone was not associated with survival in the sensitivity analysis in model 6.

### *Interaction analysis*

We screened all of the covariates for potential multiplicative interactions and found that the CC had a significant interaction ($P = 0·011$), while no such interaction was observed for any other covariates (all $P > 0·05$). To comprehensively assess the modification of the associations in different CC groups, we categorised the study population into normal CC and low CC strata using two independent methods, namely, the optimal stratification method (a low CC was defined as <35·9 cm in men and <34 cm in women, based on the present data) and the Asian Working Group for Sarcopenia (AWGS) 2019 standards (a low CC was defined as <34 cm in men and <33 cm in women)[41]. For the malnourished + low TSF group, the death hazard was concentrated in the normal CC stratum based on both the optimal stratification method (HR = 2·69, 95 % CI = 1·50, 4·82) and the AWGS 2019 standards (HR = 2·17, 95 % CI = 1·36, 3·44). For the optimal stratification method, concurrent malnutrition and a normal TSF was an independent risk factor only in the low CC stratum (HR = 1·22, 95 % CI = 1·03, 1·45) but not in the normal CC stratum. In contrast, this association was only observed in the normal CC stratum (HR = 1·41, 95 % CI = 1·12, 1·77), but not in the low CC stratum, for the AWGS method (Table 4).

## Discussion

The present multicentre, observational cohort study demonstrated that additional fat mass assessment using the TSF enhances the prognostic value of GLIM criteria-defined malnutrition in patients with LC. Furthermore, compared with those with malnutrition but a normal TSF, patients with concurrent malnutrition and a low TSF had a significantly reduced QOL and physical performance. We also defined survival-related thresholds to facilitate the identification of a low TSF in the clinical setting. For clinicians, the study implies that routine assessment of the TSF based on these thresholds can provide significant prognostic

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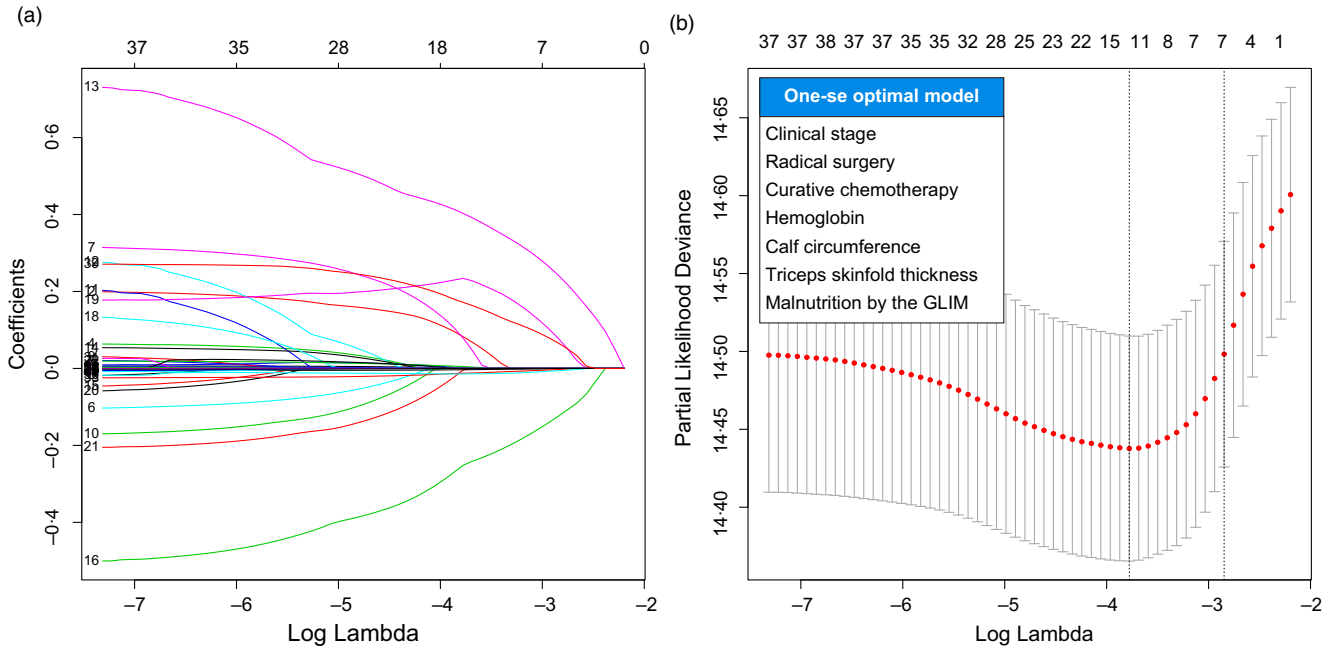


**Fig. 2.** Prognostic factors were screened using the least absolute shrinkage and selection operator (LASSO). Global Leadership Initiative on Malnutrition (GLIM), the Global Leadership Initiative on Malnutrition. (a) The LASSO coefficient profiles of the baseline characteristics in the model. (b) Selection of the optimal model (using the 1se criterion) in the LASSO via 10-fold cross-validation.

information that outperforms the GLIM diagnosis alone and will help to guide interventions to optimise the survival outcomes in patients with LC. Although preliminary, these results may also imply that fat mass assessment is an important component of patient risk stratification, but may be underestimated during the diagnosis of malnutrition under the existing GLIM framework.

The impact of body size on patient outcomes has recently been garnering great clinical interest[28,42,43]. The BMI is the best known index among the various parameters developed to assess body size. However, it is limited by being unable to identify different body components[44]. Thus, excess fat can be masked by a low BMI, while reduced muscle can be masked by a high BMI. In addition, since previous studies have reported strong evidence to support the importance of muscle mass on patient outcomes[41,45], the GLIM framework has include a reduced muscle mass as one of the three phenotypic criteria[19] because it provides more accurate information about the body composition. Interestingly, in the present study, although the CC was already used to assess the muscle mass to diagnose malnutrition, it remained in the optimal model as an independent prognostic factor for survival after the least absolute shrinkage and selection operator screening (Fig. 2). This result was consistent with several previous studies emphasising the clinical usefulness of the CC for identifying patients at an elevated risk of death[32,46].

A previous study showed that obese LC patients, as indicated by the BMI, had a significantly better survival relative to normal weight patients[47]. Consistent with this finding, a high TSF was also identified as a protective factor, independent of the diagnosis of malnutrition and the CC (Fig. 2). However, since the prognostic effect of the TSF in the present study was evaluated in addition to the GLIM, not as a component of the GLIM, future studies are needed to clarify whether integration of the fat mass assessment would increase the performance of the GLIM framework for diagnosing malnutrition. Nevertheless, to our knowledge, this is the first large-scale study to provide sex-specific, population-derived TSF thresholds that can be applied to other patients newly diagnosed with LC. Moreover, adding the TSF to the GLIM did increase the ability to identify those patients who would experience a worse QOL and poorer physical performance (Table 2). Similarly, although it is not listed as a criterion in the GLIM framework, the TSF assessment did significantly increase the performance of the GLIM to identify severely malnourished patients, as indicated by the results of multiple comparisons (55·5 % *v.* 40·3 %, false discovery rate adjusted $P < 0{\cdot}001$, Table 2). Therefore, these findings might support including a fat mass assessment as a component in the GLIM criteria, at least for LC patients. However, since the prognostic value of obesity or overweight (as defined by the BMI) in other cancers is controversial[42], it is unclear whether these findings are generalisable to other cancer populations.

Interestingly, during the interaction analysis, patients in the malnourished + normal TSF group had different modifications associated with the CC, depending on the stratification method used (optimal stratification or AWGS 2019 standards, Table 4). A possible explanation is the different thresholds used, where the AWGS 2019 uses lower CC cut-offs (< 34 cm in men and < 33 cm in women) to screen for potential sarcopenia[41]. In contrast, the CC thresholds calculated by the optimal stratification (< 35·9 cm in men and < 34 cm in women) were sample-based and survival-related and are thus likely to better reflect the prognostic dimension. Indeed, in an exploratory univariate Cox analysis, a low CC among patients as defined by the optimal stratification showed a higher death hazard (HR = 1·54,

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**Table 4.** Interaction analysis for the multivariable model

| Model | Total no./events | No./events | Well nourished | No./events | Malnourished + Normal TSF | | No./events | Malnourished + Low TSF | | *P trend* |
|---|---|---|---|---|---|---|---|---|---|---|
| Model 1* | 2672/1090 | 1864/686 | 1 (Reference) | 561/264 | 1·38 | 1·19–1·58 | 247/140 | 1·91 | 1·59–2·29 | < 0·001 |
| Model 2†,‡ | 2672/1090 | 1864/686 | 1 (Reference) | 561/264 | 1·23 | 1·06–1·43 | 247/140 | 1·54 | 1·25–1·88 | < 0·001 |
| CC, optimal stratification | | | | | | | | | | |
| Normal | 998/336 | 869/281 | 1 (Reference) | 112/43 | 1·19 | 0·86–1·64 | 17/12 | 2·69 | 1·50–4·82 | 0·006 |
| Low | 1674/754 | 995/405 | 1 (Reference) | 449/221 | 1·22 | 1·03–1·45 | 230/128 | 1·47 | 1·19–1·81 | < 0·001 |
| CC, AWGS 2019 | | | | | | | | | | |
| Normal | 1429/528 | 1207/419 | 1 (Reference) | 191/90 | 1·41 | 1·12–1·77 | 31/19 | 2·17 | 1·36–3·44 | < 0·001 |
| Low | 1243/562 | 657/267 | 1 (Reference) | 370/174 | 1·16 | 0·95–1·42 | 216/121 | 1·50 | 1·20–1·89 | 0·001 |

TSF, triceps skinfold thickness; low TSF, female < 12 mm or male < 9·5 mm; CC, calf circumference; CC (optimal stratification), low CC, < 35·9 cm in men and < 34 cm in women; AWGS 2019, Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment; CC (AWGS 2019), low CC, < 34 cm in men and < 33 cm in women.

* Model 1 is the unadjusted crude model.

† Model 2 is adjusted for age at baseline (continuous), sex (reference = female), tumour stage (reference = I), radical surgery (reference = no), curative chemotherapy (reference = no), calf circumference (continuous) and haemoglobin (continuous).

‡ *P* values for the interaction, age = 0·701, sex = 0·549, clinical stage = 0·174, curative surgery = 0·521, curative chemotherapy = 0·117, calf circumference = 0·011, haemoglobin = 0·090.

95 % CI = 1·36, 1·76, $P < 0·001$) than a low CC defined by the AWGS 2019 standards (HR = 1·36, 95 % CI = 1·20, 1·53, $P < 0·001$), which might support this explanation. It is also possible that the optimal stratification-derived thresholds are better than the AWGS standards for LC patients, since the positive association of the muscle mass with survival has been well described in previous studies[28,44,46]. Of note, this effect modification might also be ascribed to the limited numbers of patients in each group in the present study, so future studies with a larger sample size are needed to address this issue.

There are several limitations associated with the present study. First, as is the nature of all observational studies, unmeasured potential confounding factors might have altered the relationships observed. However, we used a comprehensive screening approach to select the covariates in the multivariable analysis to balance the generalisability of the regression results, as well as to control for confounding factors. Second, reverse causality may have influenced our findings. However, the observed associations still persisted after the exclusion of the patients who died within 3, 6 and 12 months after admission. Although this does not completely eliminate the risk, it should at least reduce this possibility. Third, compared to the more sophisticated technologies used to assess body composition, such as dual energy x-ray absorptiometry[48], imaging technologies[49] or bioelectrical impedance analysis[50], the TSF might be less accurate when used to measure the fat mass. However, due to its non-invasive nature, simplicity and cost-effectiveness, the TSF can be conveniently used at smaller institutions and in community settings, where more advanced technologies may not be available. Nevertheless, future studies using more advanced technologies for fat mass assessment are needed to confirm our findings. Fourth, it is unclear whether the results will be generalisable to other ethnic groups. Fifth, due to the limited sample size used for the multivariable analysis, the malnutrition group could not be further stratified into moderate and severe malnutrition groups, so larger studies with more patients who can be further sub-grouped might provide additional insights. Sixth, limited to the scope of the present study, information on the incidence of complications after anti-cancer treatment was not collected for analysis. In summary, our present results suggest that adding the TSF to a GLIM-based assessment can help stratify LC patients into different prognostic groups. However, future studies are needed to address the above issues.

In conclusion, the addition of fat mass assessment using the TSF enhances the prognostic value of GLIM criteria-defined malnutrition in patients with LC. We also identified thresholds that can be used to facilitate the identification of a low TSF in the clinical setting. Due to its simplicity, measurement of the TSF can be rapidly and cost effectively performed by the nurses, dietitians or clinicians upon patient admission and can be repeated during hospitalisation to reflect changes in the fat mass. The fat mass represents a potentially modifiable risk factor in oncology patients. Therefore, in addition to weight and muscle loss, our results suggest that the clinicians should also consider interventions to improve the fat mass in LC patients, such as more individualised nutritional supplementation. These findings emphasise the importance of fat mass assessment to guide strategies to optimise the long-term outcomes in patients with LC.

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## Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1017/S0007114521002531.

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