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RESEARCH
Research Paper

Incorporating CT-Derived Body Composition Analysis Into the Global Leadership Initiative on Malnutrition Criteria Is Associated With Overall Survival: Findings From an International Cancer Cohort

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ABSTRACT

Background Cancer-associated malnutrition is highly prevalent and linked to adverse outcomes. However, studies evaluating malnutrition using the Global Leadership Initiative on Malnutrition (GLIM) criteria with inclusion of computed tomography (CT)-derived muscle mass are limited, particularly in Caucasian oncology populations. Moreover, the prevalence of GLIM-defined malnutrition and its association with overall survival across different treatment intents remains insufficiently characterized.

Objective This study investigates whether incorporating CT-derived body composition assessment into the GLIM criteria improves the detection of malnutrition in oncology patients and evaluates its association with overall survival across different treatment intent groups.

Design Secondary analysis of data from 2 observational, prospective studies in Ireland and the United Kingdom that both examined the effect of nutritional and inflammatory status on survival in patients. GLIM phenotypic and etiologic criteria were retrospectively applied using data available from these studies. Reduced muscle mass was derived from CT.

Participants/Setting Data were available for 1405 patients enrolled between 2011 and 2016; 1118 had evaluable CT scans. Treatment intent included curative (n = 428), palliative active treatment (n = 873), and supportive care (n = 104).

Main Outcome Prevalence of GLIM-diagnosed malnutrition incorporating CT muscle assessment and its association with overall survival (months) by treatment intent. Survival analysis was carried out using Kaplan-Meier curves and Cox regression.

Statistical Analysis Descriptive statistics characterized clinical characteristics and nutritional status. Analyses were conducted in SPSS, and statistical significance was considered at $P < .05$.

Results GLIM-malnutrition was identified in 40.4% (22.6% moderate; 17.8% severe). Among those with CT scans, 42.2% had low muscle mass, and only 24.8% had experienced >5% weight loss. CT analysis identified GLIM malnutrition in 22.8% of patients missed by weight/body mass index (BMI) criteria. Median follow-up was 102.4 months. Median survival was 30.4 months for well-nourished patients vs 13.5 months (moderate) and 6.4 months (severe) for malnourished patients ($P < .001$). Adjusted hazard ratios for death were 1.379 (moderate malnutrition) and 1.799 (severe malnutrition) ($P < .001$).

Conclusion GLIM-diagnosed malnutrition, particularly when incorporating CT-derived muscle mass, is common and strongly predicts poor survival across treatment intents. CT-based assessment identifies patients with muscle wasting who may be missed by conventional criteria, supporting its integration into GLIM phenotyping.
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PATIENTS WHO HAVE BEEN DIAGNOSED WITH CANcer are at an increased risk of developing malnutrition.[1] Involuntary weight loss is a hallmark of the disease, but cancer-associated malnutrition also includes an array of altered body composition types, including sarcopenia, low muscle attenuation, and cancer cachexia.[2,3] The severity of malnutrition is related to tumor type, cancer stage, and modality of systemic anti-cancer treatment.[2,3] However, the cause is multifactorial, complex, and not driven by simple starvation.[2,3] Malnutrition can stem from poor oral intake, nutrition impact symptoms, physiologic abnormalities, mechanical obstructions, or unique tumor-derived metabolic derangements, most notably systemic inflammation.[2,3]

Cancer-associated malnutrition is highly prevalent, with reported ranges of 50% to 80%, depending on tumor type, disease stage, and diagnostic tool used to identify malnutrition.[4,5] The difference in prevalence rates may be partly attributed to the inconsistent criteria used to diagnose malnutrition.[6] Complexity increases with the consideration that 40% to 60% of patients with cancer are overweight or obese, making it even more difficult to identify those who have lost considerable muscle mass.[7] Diagnosing malnutrition in those with cancer has become increasingly important because it is associated with reduced overall survival,[5,8,9] decreased quality of life,[10] and a higher prevalence of dose-limiting toxicities.[11-13]

The European Society for Clinical Nutrition and Metabolism emphasizes the need for early nutrition screening in patients with cancer to ensure the timely initiation of nutritional interventions.[1] Although diagnosing malnutrition has clear prognostic significance, until recently, there had been no consensus on which diagnostic tool to use.[6,14] The Global Leadership Initiative on Malnutrition (GLIM) criteria were published in 2019 as a means to standardize the diagnosis of malnutrition globally.[15] GLIM comprises a 2-step approach. First, screen for at-risk individuals using any validated malnutrition screening tool.[15] Then, malnutrition is diagnosed using the GLIM criteria if at least 1 phenotypic criterion (unintentional weight loss, low body mass index [BMI], or reduced muscle mass) and at least 1 etiologic criterion (reduced food intake/assimilation or disease burden/inflammation) is present.[15] Severity of malnutrition is then graded according to the phenotypic criteria.[15] Malnutrition can be graded as either stage 1 moderate or stage 2 severe malnutrition.[15]

The GLIM criteria have been developed to include a variety of measures for each criterion that can be used by any health care professional, in any setting, with or without nutrition expertise. This includes both objective and subjective measures of muscle mass,[15] which aims to improve generalizability across sites and medical conditions.[15] However, assessment of skeletal muscle is less commonly performed, particularly in settings that lack access to skilled clinical nutrition practitioners and specialized body composition methods.[16] Studies suggest that GLIM, although not oncology-specific, can be used as a valuable prognostic tool for predicting overall survival.[17-20] However, validation among all populations is still required.[15,18]

This study aims to evaluate whether incorporating computed tomography (CT)-derived body composition into the GLIM criteria improves the detection of malnutrition in oncology patients, and to examine its association with overall survival stratified by treatment intent.

RESEARCH SNAPSHOT

Research Question: Does the incorporation of computed tomography (CT)-derived body composition into the Global Leadership Initiative on Malnutrition (GLIM) criteria improve the detection of malnutrition in oncology patients, and how is this associated with overall survival when analyzed according to treatment intent?

Key Findings: Despite a substantial proportion of patients with cancer being classified as overweight or obese, malnutrition remains highly prevalent when diagnosed using the GLIM criteria (40.4%). This study found that median overall survival was significantly shorter in patients diagnosed with stage 1 moderate malnutrition (13.5 months) and stage 2 severe malnutrition (7.5 months) when compared with those without malnutrition (30.4 months) ($P < .001$). The inclusion of body composition analysis by CT scans identified patients with a high body mass index (BMI) but reduced muscle mass. Future research should focus on determining population-specific muscle cut-points for the severity staging component of the GLIM criteria.

METHODS

This is a secondary analysis of 2 observational studies that collected data from 18 centers (11 cancer centers and 7 specialist palliative care units) in Ireland ("An investigation of baseline nutritional status, lifestyle, quality of life and performance status in newly diagnosed cancer patients: effects on cancer stage, treatment tolerance and survival—SARCONC Study"[7,21]) and the United Kingdom ("A prospective cohort study comparing validated prognostic factors for use in patients with advanced cancer—IPAC Study"[22]). The SARCONC study enrolled n = 1015 subjects (of which n = 988 had an evaluable CT), and the IPAC study enrolled n = 478 (of which n = 247 had an evaluable CT). Of the n = 1493 participants enrolled in both studies, n = 1405 had clearly documented treatment intent and were included in the analysis. Both studies examined the nutritional and inflammatory status of patients diagnosed with cancer and receiving either anti-cancer treatment or supportive care measures between 2011 and 2016. For both studies, all data were collected at 1 baseline timepoint, with prospective follow-up for survival.

The SARCONC Study aimed to explore the nutritional, body composition, and inflammatory status of patients receiving ambulatory care and their relationship with survival. Adult oncology patients attending the ambulatory infusion centers of 1 of 2 regional cancer centers for systemic anti-cancer treatment provided written informed consent to participate. Ethical approval for the original study, including the exploratory analysis, was obtained (ECM 4 [g] 03/03/15).

The IPAC Study recruited adult patients with incurable cancer attending 9 regional cancer centers and 7 specialist palliative care units in the United Kingdom. The initial objective was to examine the prognostic impact of inflammation in advanced cancer. Ethical approval was granted for

secondary use of the dataset to explore nutrition and body composition (18/WS/0001).

The study design and data collected in both studies were similar. Both used convenience sampling, and enrollments were not restricted to a specific time point in the disease or treatment trajectory. The median time from initial diagnosis to baseline assessment for the original prospective studies was 122 days (interquartile range [IQR], 70–278 days). Of those prescribed systemic anti-cancer treatment (n = 1301), most (77.3%) were receiving first-line treatment. For the original prospective studies, data were collected primarily from routine clinical records (demographics, clinical history, weight history, laboratory, and radiology investigations). Trained researchers (dietitians, nutrition researchers, or nurses) collected the data. Combining these study datasets has allowed investigation of hypotheses in a large representative cohort of people receiving care for both early and advanced disease.[10,23-27] Because both studies captured variables that correspond to the GLIM consortium's etiologic (Malnutrition Screening Tool [MST],[28] inflammation markers) and phenotypic criteria (BMI, unintentional weight loss, CT assessment of muscle mass), the preexisting variables were used to establish the presence of GLIM-defined malnutrition. For the primary data collection, both oncology inpatients and outpatients were recruited. Exclusion criteria included those <18 years. Written informed consent was obtained from all participants who took part in the original prospective studies.

Data Collection

Demographic data were extracted from the original database along with clinical characteristics, including primary tumor site, tumor stage (according to Tumor Node Metastasis classification),[29] systemic anti-cancer treatment regimens, and laboratory blood parameters. Cancer types were grouped into Lung, Gastrointestinal (colorectal, gastric, hepato-biliary pancreas, esophageal, liver), Breast, Gynecologic (ovarian, endometrial, cervical), Genitourinary (prostate, bladder, testicular), Hematologic (leukemia, lymphoma, myeloma), and Other (head and neck, sarcoma, brain, melanoma). Performance status at the baseline timepoint was measured using the Eastern Oncology Cooperative Group (ECOG) performance status score.[30] Date of death was collected from the hospital online record system and recorded, where available, up until November 27, 2023.

Treatment Intent

Both prospective studies recorded treatment intent, recent therapy (≤3 months), and disease stage at the baseline timepoint. For the purposes of this secondary analysis, *Curative intent* was defined as those subjects receiving any form of systematic anti-cancer treatment with curative intent at enrollment. *Palliative intent (active treatment)* refers to those who were prescribed palliative systemic anti-cancer treatment at enrollment or within the previous 3 months. *Palliative intent (supportive care)* refers to subjects who were not considered to be curative and had not received any systemic anti-cancer treatment in the 3 months before enrollment, that is, receiving supportive care only. Patients in all groups were eligible to be included regardless of whether they had previously received systemic anti-cancer treatment, radiation therapy, or surgery. Because of heterogeneity, details of anti-cancer treatments were not included in this secondary analysis, and details of supportive care were not recorded.

Anthropometry

In the original studies, baseline weight (taken by a nurse on treatment day) was recorded from the prescription chart on the day of the survey by trained research staff. Weight history (unintentional weight loss within the 3–6 months before study enrollment and usual weight before cancer diagnosis) was self-reported at the baseline timepoint of the original prospective studies and confirmed using medical charts where possible. In the original prospective studies, height was self-reported and confirmed using medical charts where possible.

Body Composition Analysis

CT scans performed as part of routine patient care were obtained for the purpose of the previously described prospective studies. The median time between CT scan and date of enrollment was 84 days (IQR, 40–144 days). A cross-sectional area at the third lumbar vertebra was used as the standard landmark. Skeletal muscle area at this point has been reported to correlate with whole-body muscle mass.[31,32] Skeletal muscle was segmented manually and isolated by applying filters based on Hounsfield units (−29 to 150 HU). Analysis was conducted using OsiriX software version 4.1.1 (Pixmeo, Geneva, Switzerland).[33] To calculate skeletal muscle index (SMI), skeletal muscle area was normalized for stature (cm^2/m^2). Cut points proposed by Martin et al[34] were used to establish reduced muscle mass. Reduced muscle mass was defined as SMI <41 cm^2/m^2 for women, regardless of BMI, and <43 cm^2/m^2 for men with a BMI <25 or <53 cm^2/m^2 for men with a BMI >25.[34]

Study-Specific Application of the GLIM Criteria

The GLIM criteria define malnutrition as the presence of at least 1 phenotypic criterion (non-volitional weight loss, low BMI, or reduced muscle mass) and 1 etiologic criterion (reduced food intake/assimilation or presence of disease/inflammation).[15] The GLIM criteria were therefore retrospectively applied using data from the baseline timepoint of 2 previously conducted prospective studies.[15] In this study, C-reactive protein (CRP) and serum albumin were documented and subsequently used to calculate a modified Glasgow Prognostic Score (mGPS).[35] Participants with an mGPS score of 1 (CRP > 10 mg/dL) or 2 (CRP > 10 mg/dL and hypoalbuminemia < 35 g/L) fulfilled the disease burden/inflammation etiologic criteria. The presence of reduced food intake was evaluated using the validated MST and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30). The MST asks participants, *Have you been eating poorly because of decreased appetite?* with a *yes* answer fulfilling the etiologic criteria. The EORTC asks, *Have you lacked appetite*? with a score of 3 (Quite a bit) or 4 (Very much) fulfilling the etiologic criteria. Phenotypic criteria included low BMI (<20 for those <70 years, and < 22 for those >70 years), unintentional weight loss (>5% weight loss within 6 months or >10% weight loss in greater than 6 months), and reduced muscle mass (using

the Martin et al cut-points as described previously).[15,34] For subjects enrolled through the IPAC Study, only a 3-month weight history had been recorded; for these participants (n = 247), 3-month weight loss before study enrollment was used instead.

The severity of malnutrition was then graded according to the phenotypic criteria.[15] BMI <18.5 for those aged <70 years or <20 for patients aged ≥70 years was indicative of stage 2 severe malnutrition. For unintentional weight loss, values >10% within 6 months or >20% beyond 6 months were considered severe malnutrition.

STATISTICAL ANALYSIS

Descriptive statistics were used to characterize the nutritional, inflammatory, and body composition status of patients, including GLIM-diagnosed malnutrition. Descriptive statistics for all continuous variables were reported as means (standard deviation [SD]) or medians (interquartile range [IQR]) as appropriate. Differences between categorical variables were determined using chi-squared tests with Bonferroni adjustments. Kaplan-Meier curves and Mantel-Cox log-rank statistics were used to compare median survival across groups. Overall survival was calculated from the date of recruitment up until censoring. Mortality hazard ratios (HR) were estimated using Cox proportional-hazards models, with treatment intent (curative intent vs palliative (active treatment) vs palliative (supportive care) included in the model. Significant predictors from the univariate analysis (cancer site, ECOG, age, sex) were included in the multivariate analysis. Although significant in the univariate analysis, BMI, inflammation, and percentage weight loss are established prognostic factors and, as components of the GLIM criteria, would introduce collinearity into the model. The presence of metastatic disease, although significant in the univariate analysis, was also not included because it is colinear with treatment intent. Analysis was conducted in SPSS (version 28.0, SPSS Inc., Chicago, IL),[36] and statistical significance was considered at $P < .05$.

RESULTS

Over half of the 1405 participants recruited were male (52.5%), and the mean age was 62.7 years (SD, 12.1 years). Gastrointestinal cancer was the most common cancer (44.5%), followed by lung (20.3%) and breast (10.2%). Most (60.3%) had metastatic disease. In total, 30.5% (n = 428) were receiving systemic anti-cancer treatment with curative intent, 62.1% (n = 873) were treated with palliative intent (active treatment) at the time of enrollment to the original prospective studies, and 7.4% (n = 104) had not received active treatment in the past 3 months and were receiving supportive care only. Performance status was high, and most (70.2%) had an ECOG 0/1. Chemotherapy (45%) was the most common treatment modality. The most common regimen included fluorouracil (15.4%), carboplatin (12.2%), and paclitaxel (9.3%). A considerable number (16.5%) were receiving treatment regimens that included oxaliplatin. Baseline demographics, clinical characteristics, and anthropometric details can be found in Table 1, stratified by treatment intent.

Mean BMI at recruitment was 25.8 kg/m^2 (SD, 5.1 kg/m^2). A considerable number of participants were overweight (34.7%) or obese (19.4%) according to BMI. Conversely, only 11.1% were underweight (BMI < 20.0 kg/m^2). In the 3 to 6 months before study enrollment, 16.8% (n = 157) had experienced >10% weight loss, with an average weight loss of 3.9% (SD, 8.1%). However, almost half of the participants (48.5%) had remained weight stable or had gained weight.

Body Composition, Nutritional & Inflammatory Status

Of the 1118 patients with evaluable CT scans, 42.2% had low muscle mass, whereas only 24.8% experienced weight loss >5% within 3 to 6 months. A considerable number (72.7%) reported reduced oral intake because of poor appetite (using the MST/EORTC QLQ-C30). Median CRP was 10 g/L (IQR, 4–35 g/L). Systemic inflammation was common, with 14.8% of patients classified as mGPS 1 and 34.3% as mGPS 2.

GLIM-Diagnosed Malnutrition

Demographic characteristics stratified by GLIM malnutrition classification are detailed in Table 2. In total, 61% (n = 857) met at least 1 phenotypic criterion, and 62.8% met at least 1 etiologic criterion (Fig 1). As shown in Table 3, 40.4% of participants were diagnosed with malnutrition according to the GLIM criteria. Of those diagnosed, 22.6% (n = 317) had stage 1 moderate malnutrition, and 17.8% (n = 250) had stage 2 severe malnutrition. Figure 1 shows that 22.8% of subjects diagnosed using the GLIM criteria (ie, met both etiologic and phenotypic criteria) were identified solely by having low muscle mass, without accompanying weight loss or a low BMI. The prevalence of stage 2 severe malnutrition was significantly higher in the palliative cohort (receiving supportive measures) (37.5%, $P < .001$) and palliative (receiving active treatment) (18.9%, $P < .001$) when compared with patients being treated with curative intent (10.7%).

Survival Analysis. The results of the survival analysis are displayed in Table 4. Median follow-up time was 102.4 months (IQR, 99.6–105.2 months). At the time of censoring, 34.3% (n = 482) were alive. Median overall survival from univariate analysis was 30.4 months (95% confidence interval [CI], 23.5–37.2 months) for those not diagnosed with malnutrition, vs 13.5 months (95% CI, 10.2–16.8 months) for those with stage 1 moderate ($P < .001$) and 6.4 months (95% CI, 5.3–7.6 months) for those with stage 2 severe malnutrition ($P < .001$) (Fig 2A). The Kaplan-Meier curves for GLIM malnutrition stratified by treatment intent can be found in Fig 2B–D. Multivariate analysis demonstrated an HR of death of 1.379 (95% CI, 1.172–1.622; $P < .001$) for stage 1 moderate malnutrition and HR 1.799 (1.515–2.317; $P < .001$) for stage 2 severe malnutrition. The difference in survival time between those with stage 1 moderate and those with stage 2 severe malnutrition was found to be statistically significant ($P < .001$).

Treatment Intent. When stratified according to treatment intent, multivariate analysis (controlling for sex, age, cancer site, metastatic disease, GLIM malnutrition, and ECOG) showed that for curative intent (active treatment) patients (n = 428), no association was observed between the presence of stage 1 moderate malnutrition and survival (HR,

Table 1. Demographics and clinical characteristics of 1405 participants in an international cancer cohort stratified by treatment intent

	Total (n = 1405)	Curative[a] (n = 428)	Palliative (active)[b] (n = 873)	Palliative (supportive)[c] (n = 104)
Sex (n [%])	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
Male	738 (52.5%)	245 (57.2%)	443 (50.7%)	50 (48.1%)
Female	667 (47.5%)	183 (42.8%)	430 (49.3%)	54 (51.9%)
Age in years (mean [SD[d]])	(n = 1388)	(n = 428)	(n = 867)	(n = 93)
	62.7 (12.1)	60.2 (12.8)	62.9 (11.4)	72.2 (10.4)
Weight (kg) (mean [SD])	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
	73.6 (16.6)	76.4 (15.5)	73.1 (16.6)	66.0 (18.3)
Primary cancer (n [%])	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
Gastrointestinal	625 (44.5%)	234 (54.7%)	359 (41.1%)	32 (30.8%)
Lung	285 (20.3%)	36 (8.4%)	204 (23.4%)	45 (43.3%)
Breast	144 (10.2%)	59 (13.8%)	79 (9.0%)	6 (5.8%)
Hematologic	114 (8.1%)	64 (15%)	50 (5.7%)	-
Genitourinary	79 (5.6%)	19 (4.4%)	54 (6.2%)	6 (5.8%)
Gynecologic	76 (5.4%)	13 (3.0%)	63 (7.2%)	-
Other	82 (5.8%)	3 (0.7%)	64 (7.3%)	15 (14.4%)
Metastatic disease (n [%])	(n = 1364)	(n = 425)	(n = 851)	(n = 88)
	823 (60.3%)	51 (12.0%)[e]	708 (83.2%)	64 (72.7%)
ECOG Performance Score (n [%])[f]	(n = 1351)	(n = 420)	(n = 827)	(n = 104)
ECOG 0	497 (36.8%)	250 (59.5%)	245 (29.6%)	2 (1.9%)
ECOG 1	451 (33.4%)	122 (29.0%)	307 (37.1%)	22 (21.2%)
ECOG 2	31 (23.0%)	43 (10.2%)	216 (26.1%)	52 (50.0%)
ECOG 3	81 (6.0%)	5 (1.2%)	52 (6.3%)	24 (23.1%)
ECOG 4	11 (0.8%)	—	7 (0.8%)	4 (3.8%)
Serum albumin (g/L) (mean [SD])	(n = 1212)	(n = 368)	(= 741)	(n = 103)
	34.4 (5.1)	36.0 (4.6)	34.0 (5.1)	31.6 (5.4)
C-reactive protein (CRP) (median [IQR[g]])	(n = 1076)	(n = 288)	(n = 684)	(n = 104)
	10 [4–35.0]	5 [2–16.8]	10.8 [4–37.0]	34.5 [10.3–94.3]
Modified Glasgow Prognostic Score (n [%])	(n = 1053)	(n = 280)	(n = 669)	(n = 104)
0 (CRP <10 mg/L)	536 (50.9%)	187 (66.8%)	325 (48.6%)	24 (23.1%)
1 (CRP ≥10 mg/L & Albumin ≥35 g/L)	156 (14.8%)	40 (14.3%)	100 (11.5%)	16 (15.4%)
2 (CRP ≥10 mg/L & Albumin <35 g/L)	361 (34.3%)	53 (18.9%)	244 (36.5%)	64 (61.5%)
Body mass index (BMI) (kg/m^2)	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
Underweight: <20.0	156 (11.1%)	26 (6.1%)	103 (11.8%)	27 (26.0%)
Normal: 20.0–24.9	488 (34.7%)	138 (32.2%)	312 (35.7%)	38 (36.5%)
Overweight: 25–29.9	488 (34.7%)	174 (40.7%)	291 (33.3%)	23 (22.1%)
Obese: >30	273 (19.4%)	90 (21.0%)	167 (19.1%)	16 (15.4%)
BMI (mean [SD])	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
	25.8 (5.1)	26.5 (4.8)	25.7 (5.1)	24.1 (6.2)
% Weight change in the past 3–6 months (mean [SD])	(n = 1108)	(n = 385)	(n = 660)	(n = 63)
	−4.7 (8.7)	−2.8 (7.5)	−5.8 (9.1)	−12.4 (7.7)

(*continued on next page*)

Table 1. Demographics and clinical characteristics of 1405 participants in an international cancer cohort stratified by treatment intent (*continued*)

	Total (n = 1405)	Curative[a] (n = 428)	Palliative (active)[b] (n = 873)	Palliative (supportive)[c] (n = 104)
Presence of significant weight loss (n [%])	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
	543 (38.6%)	148 (34.6%)	343 (39.3%)	52 (50%)
Weight loss classifications (n [%])[h]	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
5% <3 months	348 (24.8%)	70 (16.3%)	226 (25.9%)	52 (50%)
5% <6 months	328 (23.3%)	132 (30.8%)	196 (22.5%)	—
10% >6 months	228 (16.2%)	74 (17.3%)	154 (17.6%)	—
Presence of reduced muscle mass determined by CT[i]	(n = 1405)	(n = 428)	(n = 873)	(n = 104)
	472 (33.6%)	143 (33.4%)	305 (34.9%)	24 (23.1%)

[a]Curative: Receiving active systemic anti-cancer treatment with curative intent.
[b]Palliative (active): Receiving active systemic anti-cancer treatment with palliative intent within the last 3 months.
[c]Palliative (supportive): Receiving supportive care measures and having not received systemic anti-cancer treatment in the last 3 months.
[d]SD = standard deviation.
[e]Likely includes colorectal patients with resectable metastases.
[f]ECOG = The Eastern Oncology Cooperative Group.
[g]IQR = interquartile range.
[h]Global Leadership Initiative (GLIM) Weight Loss Classification groups are not mutually exclusive.
[i]CT = computed tomography.

1.240; 95% CI, 0.876–1.756; $P = .226$). Conversely, stage 2 severe malnutrition was significantly associated with reduced survival in the curative intent cohort (HR, 1.775; 95% CI, 1.146–2.749; $P = .010$). For the palliative intent (active treatment) cohort (n = 873), the presence of stage 1 moderate (HR, 1.331; 95% CI, 1.096–1.617; $P < .001$) and stage 2 severe malnutrition (HR, 1.816; 95% CI, 1.484–2.223; $P < .001$) were both associated with reduced survival. For the palliative intent (supportive care) cohort (n = 104), both stage 1 moderate malnutrition (HR, 2.193; 95% CI, 1.018–5.335; $P = .049$) and stage 2 severe malnutrition (HR, 2.439; 95% CI, 1.203–4.943; $P = .0133$) were significantly associated with reduced survival (Tables 5–7).

DISCUSSION

Incorporating CT assessment of body composition adds value to the GLIM criteria. In this large cohort of patients diagnosed with cancer, 54% were overweight or obese. Despite this, 42.2% had low muscle mass when evaluated by CT. In addition, only 24.8% had experienced weight loss >5% in the 3 to 6 months before enrollment in the original prospective studies. This suggests the presence of hidden malnutrition (adverse muscle and fat changes not detected with weight or BMI alone). Therefore, incorporating CT assessment into the criteria led to a substantial increase in the detection of malnutrition. It has been estimated that even in the presence of metastatic disease, 40% to 60% of patients are overweight or obese.[7] Therefore, the use of basic anthropometric measurements is not appropriate because hidden malnutrition is masked by excess adiposity and may be underrecognized by health care professionals. This includes anthropometric techniques frequently incorporated into GLIM (eg, BMI, mid-upper arm circumference, calf circumference).[16] Health care professionals must recognize the severe consequences of hidden malnutrition and prioritize early identification and referral to dietetic services. CT assessment of body composition is considered the de facto gold standard, but it is labor-intensive, time-consuming, requires expertise in body anatomy, and is subject to interobserver variability.[37] Therefore, its use outside the research setting is limited.

A recent systematic review and meta-analysis conducted by Peng et al[38] has examined the prevalence of GLIM-diagnosed malnutrition in oncology populations. This review identified 22 studies (n = 14,573) and had a prevalence of GLIM malnutrition ranging from 12% to 88%.[38] Within this meta-analysis, only 4 studies incorporated CT assessment of body composition into their GLIM methodology, and 3 of these studies used SMI cut points specific to Asian populations.[20,39,40] These studies were also limited by focusing on single cancer types (eg, gastric, esophageal), had smaller sample sizes (117–895 participants), and examined heterogeneous outcomes such as postoperative complications, disease-free survival, and 6-month survival.[20,39–41] Therefore, this study, which includes a large sample size and cut-points relevant to a Western white oncology population, provides a unique contribution to this field.

Although the aim of the GLIM criteria is to standardize the diagnosis of malnutrition globally, variability reported across the existing evidence may reflect differences in how the criteria are applied.[38] In addition to the reduced muscle mass phenotypic criterion, studies in this area have also reported variation in the application of the disease burden/inflammation criteria.[15,42] Recent recommendations from the GLIM steering committee suggest that, in the absence of blood parameters, a malignancy diagnosis can fulfill the etiologic criteria.[42] In contrast, guidance from de Van der Schueren et al[43] states that laboratory measures of

Table 2. Demographics and clinical characteristics of 1405 participants in an international cancer cohort stratified by the presence of GLIM[a] diagnosed malnutrition (including severity stages), with significance between groups examined using chi-squared tests with Bonferroni adjustments

Variable	No malnutrition	Stage 1 moderate malnutrition	Stage 2 severe malnutrition	*P*
Sex (n [%])	(n = 838)	(n = 317)	(n = 250)	.141
Male	428 (51.1%)	182 (57.4%)	128 (51.2%)	
Female	410 (48.9%)	135 (42.6%)	122 (48.8%)	
Age in years (mean [SD[b]])	(n = 829)	(n = 309)	(n = 250)	.876
	61.4 (12.5)	64.4 (10.7)	64.2 (11.8)	
Weight (kg) (mean [SD])	(n = 838)	(n = 317)	(n = 250)	<.001
	76.5 (16.2)	74.0 (14.0)	63.5 (17.1)	
Primary cancer (n [%])	(n = 838)	(n = 317)	(n = 250)	<.001
Gastrointestinal	322 (38.4%)	162 (51.1%)	141 (56.4%)	
Lung	163 (19.5%)	68 (21.5%)	54 (21.6%)	
Breast	116 (13.8%)	18 (5.7%)	10 (4.0%)	
Hematologic	85 (10.1%)	19 (6.0%)	10 (4.0%)	
Genitourinary	52 (6.2%)	15 (4.7%)	12 (4.8%)	
Gynecologic	55 (6.6%)	8 (2.5%)	13 (5.2%)	
Other	45 (5.4%)	27 (8.5%)	10 (4.0%)	
Metastatic disease (n [%])	(n = 815)	(n = 309)	(n = 240)	<.001
	457 (56.1%)	201 (65%)	165 (68.8%)	
ECOG[c] Performance Score (n [%])	(n = 786)	(n = 315)	(n = 250)	<.001
ECOG 0	356 (45.3%)	91 (28.9%)	50 (20.0%)	
ECOG 1	264 (33.6%)	102 (32.4%)	85 (34.0%)	
ECOG 2	140 (17.8%)	87 (27.6%)	84 (33.6%)	
ECOG 3	26 (3.3%)	31 (9.8%)	24 (9.6%)	
ECOG 4	—	4 (1.3%)	7 (2.8%)	
Modified Glasgow Prognostic Score (n [%])	(n = 486)	(n = 317)	(n = 250)	<.001
0 (CRP <10 mg/L)	315 (64.8%)	124 (39.1%)	97 (38.8%)	
1 (CRP ≥10 mg/L and albumin ≥35 g/L)	59 (12.1%)	41 (12.9%)	26 (10.4%)	
2 (CRP ≥10 mg/L and albumin <35 g/L)	112 (23.0%)	152 (47.9%)	127 (50.8%)	
C-reactive protein (CRP)	(n = 504)	(n = 317)	(n = 250)	<.001
(median [IQR[d]])	6.0 (3–23)	14 [5–51]	16.5 [5–53]	
Body mass index (mean [SD])	(n = 838)	(n = 317)	(n = 250)	<.001
	26.9 (5.0)	25.7 (4.1)	22.7 (5.3)	
Body mass index (kg/m^2)	(n = 838)	(n = 317)	(n = 250)	<.001
Underweight: <20.0	48 (5.7%)	20 (6.3%)	88 (35.2%)	
Normal: 20.0–24.9	280 (33.4%)	116 (36.6%)	92 (36.8%)	
Overweight: 25–29.9	306 (36.5%)	138 (43.5%)	44 (17.6%)	
Obese: >30	204 (24.3%)	43 (13.6%)	26 (10.4%)	
% Weight change in the past 3–6 months (mean [SD])	(n = 614)	(n = 261)	(n = 233)	<.001
	−1.54 (7.2)	−3.8 (6.3)	−14.3 (8.1)	
Weight loss classifications (n [%])[e]	(n = 838)	(n = 317)	(n = 250)	<.001

(*continued on next page*)

Table 2. Demographics and clinical characteristics of 1405 participants in an international cancer cohort stratified by the presence of GLIM[a] diagnosed malnutrition (including severity stages), with significance between groups examined using chi-squared tests with Bonferroni adjustments (*continued*)

Variable	No malnutrition	Stage 1 moderate malnutrition	Stage 2 severe malnutrition	*P*
5% <3 months	86 (6.6%)	102 (32.2%)	160 (64%)	
5% <6 months	121 (14.4%)	87 (27.4%)	120 (48%)	
10% >6 months	79 (9.4%)	28 (8.8%)	121 (48.4%)	
Presence of significant weight loss (n [%])	(n = 838)	(n = 317)	(n = 250)	*<.001*
	157 (18.7%)	164 (51.7%)	222 (88.8%)	
Presence of reduced muscle mass determined by CT[f] (n [%])	(n = 838)	(n = 317)	(n = 250)	*<.001*
	181 (21.6%)	200 (63.1%)	91 (36.4%)	
Presence of reduced food intake determined by MST[g]/EORTC[h] (n [%])	(n = 838)	(n = 317)	(n = 250)	*<.001*
	513 (61.2%)	274 (86.4%)	235 (94%)	

[a]GLIM = Global Leadership Initiative on Malnutrition.[15]
[b]SD = standard deviation.
[c]ECOG = The Eastern Oncology Cooperative Group.
[d]IQR = interquartile range.
[e]GLIM Weight Loss Classification groups are not mutually exclusive.
[f]CT = computed tomography.
[g]MST = Malnutrition Screening Tool.
[h]EORTC = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire.

inflammation should be considered to improve reliability between studies. A small study conducted by Steer et al[17] found that in 188 patients with head and neck cancer, the prevalence of GLIM malnutrition was 22.6%. This prevalence is lower than that of this study, which estimated that 40.4% of participants had GLIM-diagnosed malnutrition. This is

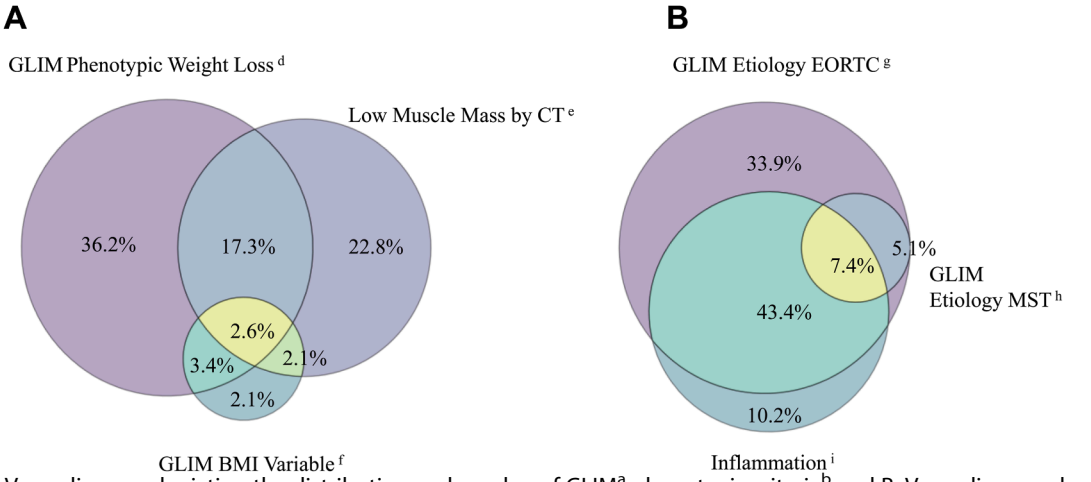


Figure 1. A, Venn diagram depicting the distribution and overlap of GLIM[a] phenotypic criteria[b] and B, Venn diagram depicting the distribution and overlap of GLIM[a] etiologic criteria.[c] [a]GLIM = Global Leadership Initiative on Malnutrition.[15] [b]GLIM phenotypic criteria = non-volitional weight loss; low body mass index (BMI); reduced muscle mass. [c]GLIM etiology criteria = Reduced food intake or assimilation; Presence of disease burden/inflammation. [d]GLIM Weight Loss = unintentional weight loss (>5% weight loss within 6 months or >10% weight loss greater than 6 months). [e]CT = computed tomography. Reduced muscle mass determined using the Martin et al cut points.[32] [f]BMI = body mass index. Defined as BMI (<20 for those <70 years of age, and <22 for those >70 years). [g]EORTC = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. Determine by a score of 3 (quite a bit) or 4 (very much) on the question *Have you lacked appetite*? [h]MST = Malnutrition Screening Tool.[28] Determined by a *yes* answer for the question *Have you been eating poorly because of decreased appetite?* [i]Modified Glasgow Prognostic Score (mGPS)[35] score of 1 (CRP > 10 mg/dL) or 2 (CRP >10 mg/dL and hypoalbuminemia <35 g/L).

Table 3. Prevalence of GLIM[a] diagnosed malnutrition[b] in 1405 patients with cancer, stratified by treatment intent

GLIM diagnosed malnutrition	Total (n = 1405)	Curative (n = 428)[c]	Palliative (Active)[d] (n = 873)	Palliative (Supportive)[e] (n = 104)
Not malnourished	838 (59.6%)	297 (69.4%)	504 (57.7%)	37 (35.6%)
GLIM malnutrition (stage 1 or 2)	567 (40.4%)	131 (30.6%)	369 (42.3%)	67 (64.4%)
Stage 1 moderate malnutrition	317 (22.6%)	85 (19.9%)	204 (23.4%)	28 (26.9%)
Stage 2 severe malnutrition	250 (17.8%)	46 (10.7%)	165 (18.9%)	39 (37.5%)

[a]GLIM = Global Leadership Initiative on Malnutrition.[15]

[b]The GLIM criteria are an internationally endorsed framework for the diagnosis of adult malnutrition, published in 2019 by a consortium of leading clinical nutrition societies.[15] The GLIM framework comprises both etiologic and phenotypic criteria, with the presence of at least 1 criterion from each category required to establish a diagnosis of malnutrition. Etiologic criteria include reduced food intake or assimilation (<50% of energy needs for >1 week) or the presence of disease burden/inflammation. Phenotypic criteria include weight loss (5% within past 6 months, or 10% beyond 6 months), low BMI (<20 if <70 years old or <22 if ≥70 years old or reduced muscle mass (by validated measures [eg, computed tomography, bioelectrical impedance, anthropometry]).

[c]Curative: Receiving active systemic anti-cancer treatment with curative intent.

[d]Palliative (active): Receiving active systemic anti-cancer treatment with palliative intent within the last 3 months.

[e]Palliative (supportive): Receiving supportive care measures and having not received systemic anti-cancer treatment in the last 3 months.

surprising given the array of nutrition impact symptoms commonly associated with head and neck malignancies.[17] In terms of methodology, Steer et al[17] used the presence of metastatic disease as a proxy for inflammation. As such, this may have potentially excluded those with locally advanced disease.[17] Because of the varying clinical presentation of participants in this study (ambulatory curative patients vs palliative hospice patients), a uniform cancer diagnosis was not considered appropriate, and mGPS was used.[44]

The findings from this study indicate that GLIM-diagnosed malnutrition is associated with overall survival independent of age, sex, ECOG, treatment intent, cancer site, and the presence of metastatic disease. For patients with incurable disease receiving systemic anti-cancer treatment, both stage 1 moderate malnutrition and stage 2 severe malnutrition were associated with worse overall survival when compared with those with no malnutrition. In curative cases, only stage 2 malnutrition was associated with overall survival. But in these patient groups, malnutrition is also linked to other important outcome measures, such as quality of life, which were not examined by this study.[10,12] For patients with incurable disease who are receiving supportive care, no statistically significant differences were observed in overall survival between stage 1 moderate and those not diagnosed with malnutrition. This may be explained by the fact that these patients were essentially receiving end-of-life care, and as such, the GLIM criteria may not be appropriate in this setting.

Nutrition and cancer guidelines from the European Society for Clinical Nutrition and Metabolism acknowledge the prognostic significance of even modest weight loss and recommend regular screening to detect nutritional issues.[1] Although these results suggest that the GLIM criteria can successfully establish the prevalence of malnutrition in oncology populations, this may be an underestimation. Martin et al[5] have previously reported that unintentional weight loss of as little as 2.4% independently predicts survival. Therefore, including >5% weight loss in 6 months as part of the GLIM phenotypic criteria may potentially exclude a considerable number of patients with cancer who are at risk of malnutrition. Therefore, it could be suggested that the sensitivity of GLIM could be improved by the introduction of oncology-specific criteria. Irish data from Daly et al[10] have shown that in a large cohort of adults with cancer (n = 1027), BMI-adjusted weight loss grading scales 3 and 4 (derived from Martin et al[5]) were independently associated with reduced overall survival (HR, 1.54; 95% CI, 1.22–1.93, $P < .001$; and HR, 1.87; 95% CI, 1.42–2.45; $P < .001$, respectively.[10] Incorporating the previously validated weight loss grading scales into the GLIM criteria may improve the prognostic capacity of the framework.

A key limitation of CT-based body composition research is the lack of reference data from diverse populations, hindering the application of consistent thresholds for diagnosing low skeletal muscle mass and identifying malnutrition using frameworks such as the GLIM criteria. Although GLIM aims to standardize malnutrition diagnosis globally, the absence of definitive cut-points leads to variability in their application across studies, resulting in inconsistent findings and limiting the integration of advanced body composition measures within GLIM. Notably, the Martin et al[34] cut points used in this study are based on mortality, rather than a more proximate measure of the presence of malnutrition. There is currently a gap in the literature for cut points that are derived from a healthy population and can be extrapolated to include various cancer cohorts. Work has been conducted by van der Werf et al,[45] who defined low muscle mass using the 5th percentile of a healthy sex-specific reference population (n = 420), but did not standardize for age. Future research to validate this methodology within oncology population groups is warranted because it may underestimate muscle wasting as a dynamic condition by focusing on population norms.[45] In this study, because specific cutoff points were unavailable, all participants with reduced muscle mass were subsequently classified as having moderate malnutrition. As a result, the prevalence of severe malnutrition is likely an underestimation. Recent guidance from the GLIM body composition working group acknowledges that future research to identify and validate sex- and ethnicity-specific cut-points for each technique (CT, bioelectrical impedance

Table 4. Estimated median survival, univariable and multivariable Cox regression analysis for variables associated with survival among 1405 patients with cancer

	No. of	Survival estimate		Univariate		Multivariate	
	events/Total N	Median survival (mo)	Log rank	Hazard ratio (95% CI[a])	*P*	Hazard ratio (95% CI)	*P*
Sex (ref. female)	414/660	16.767 (13.94–19.59)	0.103		.103		.600
Male	501/732	21.767 (16.79–26.74)		1.114 (0.978–1.269)		0.950 (0.830–1.087)	
Age (ref <65 years)	469/755	19.500 (15.265–23.735)	*<0.001*		<.001		.457
>65 years	437/620	17.900 (14.195–21.605)		1.326 (1.164–1.511)		1.040 (0.897–1.206)	
Cancer site (ref breast)	55/144	—	*<0.001*		<.001		*<.001*
Gastrointestinal	447/619	17.267 (13.982–20.551)		2.357 (1.781–3.119)	<.001	2.051 (1.518–2.772)	*<.001*
Genitourinary	57/79	20.500 (12.886–28.114)		2.355 (1.625–3.411)	<.001	1.730 (1.159–2.581)	*.007*
Gynecologic	56/76	14.133 (8.759–19.508)		2.632 (1.8113–3.819)	<.001	1.942 (1.335–2.825)	*<.001*
Hematologic	48/114	NR		0.857 (0.581–1.262)	.434	0.809 (0.523–1.159)	.218
Lung	203/281	9.400 (7.574–11.226)		4.521 (3.345–6.111)	<.001	2.944 (2.146–4.038)	*<.001*
Other	49/79	14.233 (8.496–19.971)		3.257 (2.213–4.794)	<.001	1.785 (1.197–2.663)	*.005*
ECOG[b] (ref ECOG 0–1)	575/944	30.400 (23.939–36.861)	*<0.001*				
ECOG 2–4	340/448	6.833 (5.740–8.197)		2.387 (2.083–2.735)	<.001	1.697 (1.473–1.955)	*<.001*
Metastatic disease (ref. No Mets)[c]	273/541	92.033 (65.096–118.971)	*<0.001*			N/A[d]	
Metastatic	631/823	11.067 (9.973–12.161)		3.176 (2.742–3.678)	<.001		
Treatment intent (ref. curative)[e]	196/428	—	*<0.001*				*<.001*
Palliative with active treatment[f]	653/868	12.300 (11.110–13.490)		3.870 (3.283–4.561)	<.001	3.366 (2.836–3.994)	*<.001*
Palliative with supportive measures[g]	66/96	3.300 (1.364–5.236)		12.725 (9.438–17.156)	<.001	7.608 (5.450–10.621)	*<.001*
GLIM[h] (ref. no malnutrition)	494/833	30.367 (23.546–37.188)	*<0.001*		<.001		*<.001*
Stage 1 moderate	225/314	13.533 (10.246–16.820)		1.572 (1.342–1.841)	<.001	1.379 (1.172–1.622)	*<.001*
Stage 2 severe	196/245	7.467 (5.836–9.098)		2.341 (1.981–2.766)	<.001	1.799 (1.515–2.317)	*<.001*
mGPS[i] 0 (ref. CRP <10 mg/L)[j]	301/532	32.067 (22.905–41.229)	*<0.001*		<.001	N/A[d]	
mGPS 1 = CRP ≥10 mg/L & Alb ≥ 35g/L	78/126	14.600 (8.621–20.579)		1.559 (1.247–1.949)	<.001		
mGPS 2 = CRP ≥10 mg/L & Alb <35	314/382	6.433 (5.310–7.556)		2.872 (2.437–3.384)	<.001		

(*continued on next page*)

Table 4. Estimated median survival, univariable and multivariable Cox regression analysis for variables associated with survival among 1405 patients with cancer (*continued*)

	No. of events/Total N	Survival estimate		Univariate		Multivariate	
		Median survival (mo)	Log rank	Hazard ratio (95% CI[a])	*P*	Hazard ratio (95% CI)	*P*
BMI categories (ref. 25−30) (kg/m^2)[j]	300/485	27.633 (19.989−35.278)	*<0.001*		<.001	N/A[d]	
Underweight	113/151	9.033 (4.702−13.364)		1.848 (1.488−2.295)	<.001		
Normal weight	328/484	14.167 (11.934−16.400)		1.301 (1.112−1.521)	<.001		
Obese	174/272	21.133 (13.129−29.137)		1.163 (0.965−1.402)	.112		
Weight change (ref. weight stable)[j]	162/272	16.600 (29.463−94.537)	*<0.001*		<.001	N/A[d]	
Weight gain	120/181	6.951 (19.243−46.490)		1.284 (1.014−1.626)	.038		
Weight loss (2%−4.9%)	111/153	5.299 (18.080−38.854)		1.488 (1.168−1.895)	<.001		
Weight loss (5%−9.9%)	125/171	3.468 (16.369−29.964)		1.409 (1.115−1.779)	.004		
Weight loss (>10%)	131/157	1.302 (9.748−14.852)		2.166 (1.1719−2.729)	<.001		

[a]CI = Confidence interval.
[b]ECOG = Eastern Cooperative Oncology Group Performance Status Scale.
[c]Not included in multivariate analysis as highly co-linear with treatment intent.
[d]N/A = Not applicable.
[e]Curative: Receiving active systemic anti-cancer treatment with curative intent.
[f]Palliative (active): Receiving active systemic anti-cancer treatment with palliative intent within the last 3 months.
[g]Palliative (supportive): Receiving supportive care measures and having not received systemic anti-cancer treatment in the last 3 months.
[h]GLIM = Global Leadership Initiative on Malnutrition.[15]
[i]mGPS = Modified Glasgow Prognostic Score.
[j]Not included in multivariate analysis as already a component of GLIM.

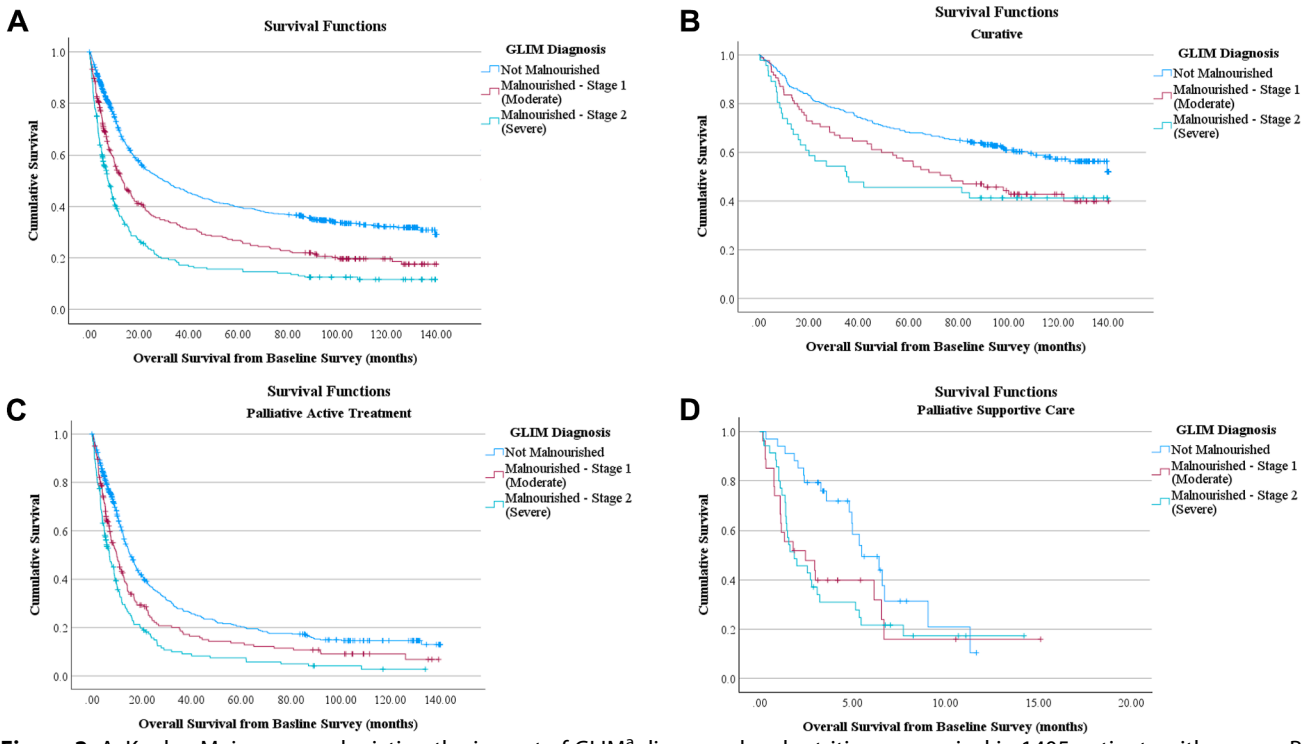


Figure 2. A, Kaplan Meier curves depicting the impact of GLIM[a] diagnosed malnutrition on survival in 1405 patients with cancer. B, Kaplan Meier curves depicting the impact of GLIM[a] diagnosed malnutrition on survival in 428 patients with cancer being treated with curative intent.[b] C, Kaplan Meier curves depicting the impact of GLIM[a] diagnosed malnutrition on survival in 873 patients with cancer receiving palliative (active) treatment.[c] D, Kaplan Meier curves depicting the impact of GLIM[a] diagnosed malnutrition on survival 104 of patients with cancer receiving palliative (supportive care) treatment.[d] [a]GLIM = Global Leadership Initiative on Malnutrition.[15] [b]Curative = Receiving active systemic anti-cancer treatment with curative intent. [c]Palliative (Active Treatment) = Patients who have received systemic anti-cancer treatment with palliative intent in the last 3 months. [d]Palliative (Supportive Care) = Patients who were receiving supportive care measures and had not received systemic anti-cancer treatment within the last 3 months.

analysis, and dual-energy X-ray absorptiometry) is required.[16]

A limitation of this study is that for a small number of participants, 6-month weight data were unavailable, and 3-month data were used, resulting in inconsistent application of the GLIM criteria. This approach may have missed people with more gradual weight loss, who would have met the >5% in 6 months criteria.[15] This may also be variable depending on time since diagnosis and exposure to prior treatment, which was not considered in this analysis. It is also important to acknowledge that previous research in cancer cachexia has refined diagnostic criteria related to weight loss, food intake, and severity of muscle depletion,[5,46,47] and the inclusion of both optional criteria and simplified yes/no responses may appear as a retrograde step. However, given the emerging prevalence of GLIM, it seems prudent to assess the criteria as proposed despite methodological limitations.[48]

Finally, another limitation of this study is the overall retrospective application of the GLIM criteria to a database of patients collected between 2011 and 2016. As such, crucial follow-up data (eg, dietitian referral rates, nutritional interventions) were not available and may have influenced survival outcomes.

The strengths of this study include its sizeable, international cohort of patients. To our knowledge, it is one of the largest to date to use de facto gold-standard CT scans to determine reduced muscle mass in the context of GLIM and using cut-points relevant to Western white oncology populations. Other large studies, Poulter et al,[49] for example, examined the ability of GLIM to predict 30-day outcomes in 2801 patients with cancer but used a subjective physical examination to determine muscle stores. Similarly, Liu et al[50] reported GLIM-diagnosed malnutrition prevalence in 2388 hospitalized patients with cancer by using calf circumference and hand grip strength as proxies for reduced muscle mass. Although body composition assessment methods such as mid-upper arm and calf circumference are included in GLIM, these measurements are considered less accurate,[15] and notably, our inclusion of CT assessments identified an additional 22.8% of patients as malnourished, despite being weight stable and in a normal to high BMI category. This highlights the importance of objective radiologic muscle assessment in routine cancer care. Additionally, this study offers an extensive follow-up period of 8.5 years, markedly longer than most previously published works.[20,41,51]

CONCLUSION

This study demonstrates the potential prognostic value of the GLIM criteria and its association with overall survival in adult patients with cancer. In this study, both stage 1 and stage 2 GLIM-diagnosed malnutrition are significantly associated with poorer overall survival compared with those without malnutrition. This study suggests that incorporating CT assessment of body composition into the GLIM criteria helps to identify patients with hidden malnutrition (muscle loss but not weight loss). Although this study offers valuable insights, the lack of standardized cut-points for muscle depletion makes determining severity a persistent challenge. Future research should focus on determining population-specific muscle cut-points for the severity staging component of the GLIM criteria.



PRACTICE IMPLICATIONS

What Is the Current Knowledge on This Topic?

Cancer-associated malnutrition is highly prevalent in oncology population groups, with an estimated prevalence rate of 50% to 80% depending on tumor type, stage of disease, and assessment tool used. This form of disease-related malnutrition is associated with reduced tolerance to treatment, poor quality of life, and decreased overall survival. Despite these debilitating consequences, there is still no global consensus on how best to identify malnutrition. Cancer-associated malnutrition is not just simple weight loss and includes an array of abnormal body composition phenotypes such as cancer cachexia, low muscle attenuation, and low muscle mass. It has been estimated that up to 60% of patients diagnosed with metastatic cancer are overweight or obese, and this can make malnutrition even harder to identify. The Global Leadership Initiative on Malnutrition (GLIM) criteria were published in 2019 with the aim of standardizing the diagnosis of malnutrition globally and across all medical conditions. The GLIM framework includes both objective and subjective measures to assess muscle mass, which may aid in identifying abnormal body composition phenotypes.

How Does This Research Add to Knowledge on This Topic?

This research study is 1 of the largest studies to date that uses computed tomography (CT) analysis of body composition within the GLIM framework to identify those patients with reduced muscle mass. CT assessment is considered the *de facto* gold standard of body composition analysis. This is the first study to stratify patients according to treatment modality within palliative intent (ie, patients receiving active cancer treatment with palliative intent vs patients receiving supportive palliative care only). This offers a unique perspective into the trajectory of patients diagnosed with cancer. This study also contains international data as patients were recruited from a variety of health care settings in both Ireland and the United Kingdom.

How Might This Knowledge Impact Current Dietetics Practice?

The results from this study show that incorporating CT assessment of reduced muscle mass into the GLIM criteria adds value to the framework. An estimated 22.8% of subjects were diagnosed with malnutrition based solely on the low muscle mass phenotype, without any significant weight loss or low body mass index (BMI). Therefore, for those with normal to high BMI and without significant weight loss, CT assessment inclusion in the criteria led to a significant increase in the detection of malnutrition.

Of the 1118 patients with evaluable CT scans, 42.2% had low muscle mass, whereas only 24.8% experienced weight loss >5% within 3 to 6 months, highlighting "hidden malnutrition" in the form of weight-stable muscle loss. In this study, more than half of the population had remained weight stable (or gained weight) in the preceding 3 to 6 months, and 54% had a BMI that was overweight or obese. Despite this, 40% were diagnosed with malnutrition according to the GLIM criteria. This suggests that clinical practice needs to move away from traditional malnutrition screening tools, which focus primarily on weight and BMI.

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Table 5. Estimated median survival, univariable, and multivariable Cox regression analysis for variables associated with survival for 428 patients with cancer receiving treatment with curative intent[a]

		Survival Estimate		Univariate		Multivariate	
	No. of events/ Total N	Median survival (months)	Log rank	Hazard ratio (95% CI[b])	*P*	Hazard ratio (95% CI)	*P*
Sex (ref. female)	69/183	139.700 (103.034-176.366)	*0.007*		.007		.520
Male	127/245	98.633 (NR)		1.497 (1.116−2.009)		1.112 (0.804−1.539)	
Age (ref <65 years)	167/258	NR[c]	*<0.001*		<.001		*<.001*
>65 years	65/170	68.233 (43.417−93.049)		2.032 (1.536−2.689)		1.637 (1.220−2.196)	
Cancer site (ref breast)	9/59	NR	*<0.001*		*<.001*		*<.001*
Gastrointestinal	127/234	90.233 (57.091−123.375)		4.320 (2.195−8.501)	*<.001*	2.921 (1.407−6.063)	*.004*
Genitourinary	7/19	NR		2.679 (0.996−7.208)	.051	2.121 (0.745−6.044)	.159
Gynecologic	6/13	NR		3.736 (1.330−10.500)	*.012*	3.646 (1.294−10.276)	*.014*
Hematologic	18/64	NR		1.834 (0.823−4.087)	.138	1.411 (0.614−3.242)	.417
Lung	28/36	25.967 (2.839−49.095)		9.055 (4.267−19.218)	*<.001*	6.127 (2.739−13.708)	*<.001*
Other	1/3	NR		2.028 (0.257−16.013)	0.502	2.223 (0.280−17.621)	.449
ECOG[d] (ref. ECOG 0−1)	162/372	139.700 (NR)	*0.004*				*.041*
ECOG 2−4	34/56	48.100 (13.958−82.24)		1.724 (1.191−2.496)	.004	1.483 (1.016−2.164)	
Metastatic disease (ref. no Mets)	160/374	NR	*<0.001*		<.001		<.001
Metastatic	35/51	26.633 (12.472−40.794)		2.256 (1.563−3.257)		3.070 (2.078−4.534)	
GLIM[e] (ref. no malnutrition)	120/297		*<0.001*		<.001		.032
Stage 1 moderate	49/85	NR		1.600 (1.147−2.231)	.006	1.240 (0.876−1.756)	.226
Stage 2 severe	27/46	76.9 (41.9−112.1)		1.898 (1.250−2.884)	.003	1.775 (1.146−2.749)	*.010*
mGPS[f] (ref. Score 0 CRP <10 mg/L)[g]	90/187	114.667 (NR)	*<0.001*		<.001	N/A[h]	
mGPS 1 = CRP ≥10 mg/L and Alb ≥ 35g/L	19/40	139.700 (74.459−204.941)		0.910 (0.554−1.494)	.708		
mGPS 2 = CRP ≥10 mg/L and Alb <35	36/53	27.33 (9.908−44.759)		2.047 (1.390−3.016)	<.001		
BMI categories (ref. 25−30)[g]	79/174	124.500 (NR)	0.267		.276	N/A[h]	
Underweight	16/26	43.6 (0.00−101.940)		1.653 (0.965−2.830)	.067		
Normal weight	59/138	139.7 (87.658−191.742)		0.968 (0.691−1.357)	.852		
Obese	42/90	139.700 (NR)		1.065 (0.733−15.49)	.741		

[a]Curative intent: Receiving active systemic anti-cancer treatment with curative intent.
[b]CI = Confidence interval.
[c]NR = Not reached.
[d]ECOG = Eastern Cooperative Oncology Group Performance Status Scale.
[e]GLIM = Global Leadership Initiative on Malnutrition.[15]
[f]mGPS = Modified Glasgow Prognostic Score.
[g]Not included in multi-variate analysis as already a component of GLIM.
[h]N/A = not applicable.

Table 6. Estimated median survival, univariable and multivariable Cox regression analysis for variables associated with survival for 873 patients with cancer in the palliative (active treatment)[a] cohort

	No. of	Survival Estimate		Univariate		Multivariate	
	events/ total N	Median survival (mo)	Log rank	Hazard ratio (95% CI[b])	*P*	Hazard ratio (95% CI)	*P*
Sex (ref. female)	313/428	12.300 (11.110−13.490)	0.073		.073		.825
Male	340/440	11.067 (9.683−12.451)		1.151 (0.987−1.342)		0.980 (0.757−1.049)	
Age (ref. <65 years)	370/479	12.633 (10.689−14.578)	*0.023*		.458		.166
>65 years	281/383	11.833 (10.464−13.203)		0.943 (0.807−1.101)		0.891 (0.757−1.049)	
Cancer site (ref. breast)	44/79	20.333 (7.637−33.030)	*<0.001*		*<.001*		*<.001*
Gastrointestinal	299/357	10.800 (9.109−12.491)		1.875 (1.366−2.574)	*<.001*	1.895 (1.341−2.677)	*<.001*
Genitourinary	46/54	17.467 (8.363−26.571)		1.505 (0.995−2.275)	.053	1.671 (1.057−2.643)	*.028*
Gynecologic	50/63	11.933 (9.230−14.637)		1.585 (1.057 -2.377)	*.026*	1.633 (1.084−2.461)	*.019*
Hematologic	30/50	67.067 (47.347−86.786)		0.642 (0.403−1.022)	.062	0.710 (0.433−1.164)	.175
Lung	146/203	9.700 (7.880−11.520)		2.622 (1.864−3.687)	*<.001*	2.648 (1.848−2.223)	*<.001*
Other	38/62	14.867 (8.837−20.896)		1.546 (1.001−2.388)	*.050*	1.514 (0.966−2.374)	.070
ECOG[c] (ref. ECOG 0−1)	401/548	14.500 (12.631−16.369)	*0.004*		*<.001*		<.001
ECOG 2−4	252/320	6.933 (5.304−8.563)		1.719 (1.467−2.014)		1.622 (1.378−1.909)	
Metastatic disease (ref. no Mets)	99/143	19.167 (013.389−24.945)	*<0.001*		*<.001*		
Metastatic	548/708	11.600 (10.459−12.741)		1.556 (1.255−1.931)		1.228 (0.981−1.538)	.073
GLIM[d] (ref. no malnutrition)	355/502	15.300 (13.235−17.365)	*<0.001*		*<.001*		*<.001*
Stage 1 moderate	157/202	9.900 (7.633−12.137)		1.435 (1.189−1.733)	*<.001*	1.331 (1.096−1.617)	*.004*
Stage 2 severe	141/164	6.967 (4.868−9.065)		2.018 (1.657−2.457)	*<.001*	1.816 (1.484−2.223)	*<.001*
mGPS[e] (ref. Score 0 CRP <10 mg/L)[f]	202/322	16.167 (13.137−19.196)	*<0.001*		*<.001*	N/A[g]	
mGPS 1 = CRP ≥10 mg/L & Alb ≥ 35 g/L	73/100	8.733 (6.533−10.933)		1.767 (1.351−2.312)	*<.001*		
mGPS 2 = CRP ≥10 mg/L & Alb <35	207/242	5.733 (4.470−6.997)		2.438 (2.003−2.966)	*<.001*		
BMI categories (ref. 25−30) (kg/m^2)[f]	207/289	15.167 (11.93−18.408)	*0.006*		*.006*	N/A[g]	
Underweight	80/102	8.667 (4.738−12.596)		1.402 (1.083−1.815)	*.010*		
Normal weight	243/289	11.067 (9.771−12.363)		1.352 (1.122−1.629)	*.002*		
Obese	123/167	12.33 (8.314−16.352)		1.252 (1.002−1.566)	*.048*		

[a]Palliative (active treatment): Receiving active systemic anti-cancer treatment with palliative intent within the last 3 months.
[b]CI = Confidence interval.
[c]ECOG = Eastern Cooperative Oncology Group Performance Status Scale.
[d]GLIM = Global Leadership Initiative on Malnutrition.[15]
[e]mGPS = Modified Glasgow Prognostic Score.
[f]Not included in multi-variate analysis as already a component of GLIM.
[g]N/A = not applicable.

Table 7. Estimated median survival, univariable and multivariable Cox regression analysis for variables associated with survival for 104 patients receiving palliative (supportive care) treatment[a]

	No. of	Survival Estimate		Univariate		Multivariate	
	events/ total N	Median survival (months)	Log rank	Hazard ratio (95% CI[b])	*P*	Hazard ratio (95% CI)	*P*
Sex (ref. female)	32/49	3.100 (2.339–3.861)	0.515		.516		.913
Male	34/47	4.833 (2.202–7.465)		1.174 (0.723–1.96)		1.037 (0.538–2.001)	
Age (ref. <65 years)	8/18	3.233 (1.169–3.924)	0.687		*.023*		*.024*
>65 years	51/67	2.967 (2.009–5.298)		2.414 (1.130–5.158)		2.599 (1.132–5.968)	
Cancer site (ref. breast)	2/6		0.348		.415		.067
Gastrointestinal	21/28	2.467 (1.257–3.677)		4.212 (0.981–18.091)	.053	8.240 (1.747–38.865)	*.008*
Genitourinary	4/6	5.167 (1.275–9.059)		3.036 (0.552–16.705)	.202	4.957 (0.757–32.478)	.095
Gynecologic	—	3.300 (0.777–5.823)		—	—	—	—
Hematologic	—	—		—	—	—	—
Lung	29/42	—		3.427 (0.814–14.434)	.093	4.883 (1.094–21.796)	*.038*
Other	10/14	1.100 (0.235–5.105)		3.647 (0.798–16.670)	.095	8.481 (1.629–44.152)	*.011*
ECOG[c] (ref. ECOG 0–1)	12/24	6.700 (2.543–10.857)	*0.007*		.009		*.003*
ECOG 2–4	54/72	2.800 (1.567–4.033)		2.319 (1.233–4.363)		3.211 (1.474–6.994)	
Metastatic disease (ref. no Mets)	14/24	5.367 (2.914–7.820)	0.109	1.620 (0.892–2.942)	.113		*.041*
Metastatic	48/64	2.567 (1.359–3.775)				3.211 (1.474–6.994)	
GLIM[d] (ref. no malnutrition)	19/34	5.500 (3.560–7.440)	*0.041*		.047		*.045*
Stage 1 moderate	19/27	2.467 (0.633–5.116)		1.952 (1.032–3.694)	.040	2.193 (1.018–5.335)	*.049*
Stage 2 severe	28/35	1.867 (0.247–3.103)		1.977 (1.100–3.552)	.023	2.439 (1.203–4.943)	*.013*
mGPS[e] (ref. Score 0 CRP <10 mg/L)[f]	9/23	9.067 (5.162–12.972)	<0.001		<.001	N/A[g]	
mGPS 1 = CRP ≥10 mg/L & Alb ≥ 35 g/L	12/16	2.367 (1.060–3.673)		4.626 (2.230–9.596)	<.001		
mGPS 2 = CRP ≥10 mg/L & Alb <35	45.57	1.867 (0.688–3.046)		4.768 (1.950–11.655)	<.001		
BMI categories (ref. 25–30) (kg/m^2)[f]	14/22	3.000 (0.00–6.079)	0.319		.322	N/A[g]	
Underweight	17/23	1.567 (0.836–2.297)		1.580 (0.766–3.216)	.207		
Normal weight	26/36	5.367 (3.008–7.726)		0.988 (0.515–1.894)	.970		
Obese	9/15	4.833 (0.657–9.009)		0.807 (0.348–1.872)	.618		

[a]Palliative (supportive care): Receiving supportive care measures and having not received systemic anti-cancer treatment in the last 3 months.
[b]CI = Confidence interval.
[c]ECOG = Eastern Cooperative Oncology Group Performance Status Scale.
[d]GLIM = Global Leadership Initiative on Malnutrition.[15]
[e]mGPS = Modified Glasgow Prognostic Score.
[f]Not included in multivariate analysis as already a component of GLIM.
[g]N/A = not applicable.