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RESEARCH ARTICLE

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Malnutrition defined by GLIM criteria identifies a higher incidence of malnutrition and is associated with pulmonary complications after oesophagogastric cancer surgery, compared to ICD-10-defined malnutrition

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Abstract

Background & Objectives: Low muscle mass, measured using computed tomography (CT), is associated with poor surgical outcomes. We aimed to include CT-muscle mass in malnutrition diagnosis using the Global Leadership Initiative on Malnutrition (GLIM) criteria, compare it to the International Classification of Diseases 10th Revision (ICD-10) criteria, and assess the impact on postoperative outcomes after oesophagogastric (OG) cancer surgery.

Methods: One hundred and eight patients who underwent radical OG cancer surgery and had preoperative abdominal CT imaging were included. GLIM and ICD-10 malnutrition data were assessed against complication and survival outcomes. Low CT-muscle mass was determined using predefined cut-points.

Results: GLIM-defined malnutrition prevalence was significantly higher than ICD-10-malnutrition (72.2% vs. 40.7%, $p < 0.001$). Of the 78 patients with GLIM-defined malnutrition, low muscle mass (84.6%) was the predominant phenotypic criterion. GLIM-defined malnutrition was associated with pneumonia (26.9% vs. 6.7%, $p = 0.010$) and pleural effusions (12.8% vs. 0%, $p = 0.029$). Postoperative complications did not correlate with ICD-10 malnutrition. Severe GLIM (HR: 2.51, $p = 0.014$) and ICD-10 (HR: 2.15, $p = 0.039$) malnutrition were independently associated with poorer 5-year survival.

Conclusions: GLIM criteria appear to identify more malnourished patients and more closely relate to surgical risk than ICD-10 malnutrition, likely due to incorporating objective muscle mass assessment.

KEYWORDS

cancer surgery, esophageal, gastric, GLIM criteria, malnutrition, muscle mass

1 | INTRODUCTION

Surgical resection of oesophageal and gastric cancer is the mainstay of the multimodal curative treatment pathway and is associated with high postoperative morbidity, especially pulmonary complications.[1,2] Postoperative complications lead to delayed recovery, impaired quality of life, and reduced overall and disease-free survival.[3,4] Therefore, it is essential to identify potentially modifiable patient factors associated with complications, such as malnutrition, that, when improved, may mitigate the risk of adverse surgical outcomes. Identifying and treating malnutrition is particularly pertinent for patients with oesophagogastric (OG) cancer whose tumor location and treatment interventions contribute to more significant weight loss than other types of gastrointestinal cancer.[5]

Loss of skeletal muscle (SM) is prevalent in patients with cancer[6] and is a predictor of surgical complications and reduced long-term survival after resection of OG cancer.[7,8] Muscle mass assessment is included in the diagnostic criteria for malnutrition developed by the Global Leadership Initiative on Malnutrition (GLIM).[9] The GLIM consensus incorporates phenotypic (low body mass index, weight loss, and reduced muscle mass) and etiologic (reduced food intake or assimilation and inflammation or disease burden) criteria.

The GLIM criteria have been validated against a range of preexisting definitions of malnutrition.[10–12] In patients undergoing resection of gastrointestinal cancer, GLIM showed good interrater reliability and moderate agreement with the Subjective Global Assessment (SGA).[13] However, few studies incorporate an objective assessment of muscle mass in the phenotypic component of GLIM.

The International Classification of Diseases, 10th Edition (ICD-10) definition of malnutrition is widely used in the acute clinical setting, and within our institution. However, this definition incorporates a subjective visual assessment of muscle wasting, not an objective measure. Body composition assessment using computed tomography (CT) is a valid and reliable method to estimate SM mass.[14] CT images are part of routine cancer staging in OG cancer surgery and present an opportunity to identify patients with low muscle mass who are known to have a higher risk of adverse surgical outcomes.[7,8] Therefore, this study aimed firstly to compare the prevalence of malnutrition using the GLIM and ICD-10 criteria and secondly to determine their impact on postoperative complications and long-term survival after OG cancer surgery.

2 | MATERIALS AND METHODS

2.1 | Patient selection and study design

This single-center retrospective cohort study involved patients who underwent radical resection of oesophageal, OG junction, or gastric carcinoma from July 2007 to May 2018 at Alfred Health, a metropolitan tertiary center in Melbourne, Victoria, Australia. The selected cohort represents an overlapping spectrum of diseases that are faced by upper gastrointestinal cancer surgeons and oncologists in clinical practice at our institution. Patients who had an assessable abdominal CT image taken preoperatively were included. Patients with palliative or secondary resection and those with poor-quality CT images unsuitable for body composition analysis were excluded. Ethical approval was obtained from The Alfred Human Research and Ethics Committee (project no. 366/15).

2.2 | Clinical management

All patients diagnosed with OG cancer were assessed and managed in a dedicated outpatient clinic at diagnosis, preoperatively (after neoadjuvant therapy) and post discharge after surgery. For primary tumors staged T2 or greater, preoperative chemotherapy (MAGIC protocol for gastric cancer and esophageal adenocarcinoma before 2012[15]) and CROSS chemoradiotherapy[16] (after 2012) were standard of care. All other patients did not receive neoadjuvant treatment. Preoperative CT scans were performed within 4 weeks before surgical resection, following the completion of preoperative therapy. Surgical resection was a modified radical en bloc oesophagectomy or gastrectomy (D1), aiming to clear all first and second-tier lymph node stations. There were no pancreatic or splenic resections unless directly involved. Surgical outcomes from our center have been previously described.[17]

2.3 | Data collection sources

Baseline characteristics, oncological, surgical, and outcome data were sourced from the Oesophago-Gastric and Bariatric Surgery Unit's database. The prospectively maintained and clinician-verified database contains detailed information on all patients with OG cancer.

Oncological data included primary tumor site, disease pathology, tumor stage according to the TNM classification,[18] and completion of neoadjuvant chemoradiation regimens. Surgical data recorded preoperative health status according to the American Society of Anaesthesiologists (ASA) score,[19] resection type, and lymph node resection count. Postoperative complications were graded according to the Clavien–Dindo Classification of Surgical Complications Criteria.[20] Severe complications were ≥ Grade 3. Postoperative length of stay (LOS) was recorded from the day of surgery to the day of discharge from the tertiary center. Survival was measured in months from the date of tissue diagnosis to survival status and presence of disease to assess 5-year overall survival (OS) and disease-free survival (DFS), respectively. The final follow-up date to determine the OS and DFS status was December 2019. Patients who were alive or disease-free at this time were censored and included in the survival analysis. Information that was not already included in the database (e.g., anthropometric measures and malnutrition diagnostic criteria) was obtained from the medical records. CT images were sourced from the hospital's Picture Archiving and Communication System (PACS).

2.4 | Malnutrition diagnosis

Preoperative body weight, height, and body mass index (BMI) from the nutrition assessment were collected from the medical records. Preoperative percentage loss of weight (LOW) was taken from either a past documented weight or if no previous documentation, was patient-reported.

2.4.1 | ICD-10 criteria

Mild-moderate malnutrition, according to the ICD-10 criteria, was confirmed if patients had a low BMI (<18.5 kg/m^2) and/or unintentional weight loss (>5%) over any time period, along with reduced food intake (any reported reduction in food intake) and mild/moderate muscle wasting (as documented in dietitian's initial assessment).[12] Patients were categorized as having severe malnutrition if unintentional weight loss was >10% over any time period and/or severe muscle wasting was reported.

2.4.2 | GLIM criteria

According to the GLIM criteria for the diagnosis of malnutrition consensus report,[9] patients were identified as malnourished if they met ≥1 phenotypic criterion and ≥1 etiologic criterion. The phenotypic criteria used to diagnose malnutrition were unintentional weight loss (>5% in ≤3 months or >10% in ≥6 months), low BMI (<20 kg/m^2 if <70 years; <22 kg/m^2 if ≥70 years), and low muscle mass (low skeletal muscle index [SMI] using CT). The phenotypic criteria thresholds for moderate malnutrition were weight loss of 5%−10% in <6 months or 10%−20% in ≥6 months; BMI of <20 kg/m^2 if <70 years, or <22 kg/m^2 if ≥70 years; reduced muscle mass (mild to a moderate deficit of SM using CT). The thresholds for severe malnutrition were weight loss >10% in 6 months, or >20% in ≥6 months; BMI of <18.5 kg/m^2 if <70 years, or <20 kg/m^2 if ≥70 years; reduced muscle mass (severe deficit of SM using CT). The etiologic criterion used was inflammation associated with malignant disease. Supportive laboratory measures for inflammation and quantifiable documentation of reduced food intake or assimilation were not consistently available.

2.5 | CT assessment of body composition

A single slice of an axial abdominal CT image at the level of L3 was analyzed to estimate body composition. Every SM at L3 was included (psoas, erector spinae, quadratus lumborum, transverse abdominus, external and internal obliques, and rectus abdominus). All CT images were contrast-enhanced with contrast in the portal venous phase. SliceOmatic software Version 5 (TomoVision) allowed a semiautomated segmentation of body tissues. Specific tissue attenuation thresholds, measured in Hounsfield Units (HU), were applied to SM −29 to +150 HU, subcutaneous adipose tissue −190 to −30 HU, visceral adipose tissue −50 to −150 HU, and intramuscular adipose tissue (IMAT) −190 to −30 HU, and cross-sectional area (CSA, cm^2) of each were measured. Contrast-enhanced SM radio-density was quantified as mean SM attenuation (HU). Two trained assessors who were blinded to patient outcomes analyzed the CT images. The inter- and intra-rater coefficient of variations was a mean of 0.73% for SM and 2.83% for adipose tissue. There was a minimum of 1 month between each CT analysis to assess intra-rater variability.

SM CSA was normalized for height (m^2) to obtain skeletal muscle index (SMI). Low SMI was defined according to gender-specific SMI cut-points of <52.4 cm^2/m^2 for men and <38.5 cm^2/m^2 for women.[21] SMI cut-points were established from this data set in the absence of predefined and validated thresholds for the severity grading of GLIM-defined malnutrition. Values below the above-mentioned gender-specific SMI cut-points were further separated into tertiles. The lowest tertile indicated a severe deficit of SM mass and was categorized as severe GLIM-defined malnutrition. The highest and middle tertiles indicated a mild-moderate deficit of SM mass, respectively, and were grouped to form the mild-moderate GLIM-defined malnutrition category.

Myosteatosis, a consequence of excess IMAT infiltration, was determined using BMI-specific SM attenuation thresholds of <41 HU for patients who were underweight (BMI < 18.5 kg/m^2) or had a healthy BMI (18.5–24.9 kg/m^2) and <33 HU for patients within the overweight (25–29.9 kg/m^2) or obese (≥30 kg/m^2) BMI category.[22]

2.6 | Statistical analysis

Statistical analysis was undertaken using SPSS Statistics Version 23 (IBM Corp.). The distribution of data was assessed using the Kolmogorov−Smirnov test. Continuous variables are reported as mean ± standard deviation (parametric) or median ± interquartile range (nonparametric). Malnutrition, as a dichotomous variable, was divided into well-nourished and malnourished groups for the ICD-10 and GLIM diagnostic criteria. Differences between well-nourished and malnourished groups within these malnutrition definitions were assessed using independent *T*-tests and χ^2 tests for continuous and categorical variables, respectively. Mann−Whitney and Fisher's exact tests were applied for nonparametric data. A comparison of malnutrition prevalence between ICD-10 and GLIM-defined malnutrition was determined using McNemar's test.

The impact of malnutrition on postoperative complications was analyzed using logistic regression. The univariate analysis included known or probable predictors of outcomes, and multicollinearity was considered. Variables with $p \le 0.1$ were included in the multivariate regression model. Overall and DFS between malnutrition groups was compared with Kaplan−Meier analysis using Log-rank values. A significance threshold of $p < 0.05$ was applied.

Cox regression analysis was used to determine predictors of 5-year OS. Malnutrition was assessed as a dichotomous variable (well-nourished vs. malnourished) and using severity categories (well-nourished, mild to moderate, and severe). Variables with $p \le 0.2$ at univariate analysis were included in the multivariate model. Several regression models were required to account for multicollinearity between variables that make up malnutrition diagnostic criteria (weight loss and BMI). A significance threshold of $p < 0.05$ was applied.

The published overall complication rate after esophageal and gastric cancer resection at Alfred Health is 55.2% (3). This study was powered to detect a 50% increase in the incidence of overall complications in patients with malnutrition compared to well-nourished patients. With an error level of 5% and power of 80%, the minimum sample size to detect a significant difference in the overall complication rate between the two groups was 80 patients.

3 | RESULTS

3.1 | Baseline characteristics

The baseline characteristics of the 108 patients included are described in Table 1. The mean age was 66.4 years (±9.9), and 75% ($n = 81$) were male. The primary tumor sites were predominantly gastric (43.5%) and oesophageal (38%), with 84% adenocarcinoma. Types of surgical resection were evenly distributed. There were no differences in baseline characteristics, including tumor location, between patients diagnosed with malnutrition and those who were well-nourished, using the ICD-10 and GLIM criteria (data not shown).

For the entire cohort, the mean body weight was 76.9 kg (±19.2), and the median BMI was 25.9 kg/m^2 (IQR: 6.9). The anthropometric and body composition measures of well-nourished compared to malnourished patients for both malnutrition diagnostic criteria are shown in Table 2. Most malnourished patients had a BMI in the healthy weight range (ICD-10: 63.6%, and GLIM: 57.7%).

3.2 | Malnutrition diagnosis

The proportion of patients diagnosed with malnutrition was significantly higher using the GLIM criteria compared to ICD-10 ($n = 78$, 72.2% vs. $n = 44$, 40.7%, $p < 0.001$). Figure 1 shows the difference in the distribution of malnutrition categories between the GLIM and ICD-10 diagnostic criteria. There was a significantly greater proportion of severely malnourished patients when using GLIM criteria compared to ICD-10 ($n = 33$, 31% vs. $n = 12$, 11%, $p < 0.001$). Overall, when combining the outcome of using both malnutrition definitions, 25% ($n = 28$) of patients were well nourished, 2% ($n = 2$) were malnourished according to ICD-10, 33% ($n = 36$) were malnourished using the GLIM definition, and 39% ($n = 42$) had malnutrition detected by both the ICD-10 and GLIM criteria.

3.2.1 | GLIM criteria

Of the 78 patients with GLIM-defined malnutrition, reduced muscle mass ($n = 66$, 84.6%) made the most significant contribution to the phenotypic criteria, followed by weight loss ($n = 46$, 59.0%) and low

TABLE 1 Baseline characteristics of all oesophagogastric cancer surgery patients ($n = 108$).

Age years mean (SD)	66.4 (9.9)
Gender *n* (%)	
Male	81 (75)
Female	27 (25)
Comorbidities *n* (%)	
History of smoking	64 (59.3)
Cardiac	31 (28.7)
Respiratory	27 (25)
Diabetes	15 (13.9)
Renal	11 (10.2)
Primary tumor site *n* (%)	
Gastric	47 (43.5)
Oesophageal	41 (38)
Oesophago-gastric junction	20 (18.5)
Disease pathology *n* (%)	
Adenocarcinoma	91 (84.3)
Squamous cell carcinoma	12 (11.1)
Other	5 (4.6)
Neoadjuvant treatment *n* (%)	
Chemotherapy	56 (51.9)
Chemoradiation	23 (21.3)
No neoadjuvant therapy	29 (28.2)
ASA score *n* (%)	
Grade I	6 (5.6)
Grade II	32 (29.6)
Grade III	64 (59.3)
Grade IV	6 (5.6)
Resection type *n* (%)	
Gastrectomy	55 (50.9)
Oesophagectomy	53 (49.1)
Pathologic T stage *n* (%)	
T0	8 (7.4)
T1	23 (21.3)
T2	20 (18.5)
T3	50 (46.3)
T4	7 (6.5)
Pathologic N stage *n* (%)	
N0	56 (51.9)
N1	25 (23.1)
N2	15 (13.9)
N3	12 (11.1)

TABLE 1 (Continued)

Pathologic M stage *n* (%)	
M0	103 (95.4)
M1	5 (4.6)
Pathological TNM stage groups *n* (%)	
Stage 0	7 (6.5)
Stage 1	29 (26.9)
Stage 2	38 (35.2)
Stage 3	29 (26.9)
Stage 4	5 (4.6)
Lymph node yield *n* (%)	
Oesophagectomy (*n* = 53)	
Node count mean (SD) (nodes)	18.5 (10.8)
1–5	4 (7.5)
6–14	15 (28.3)
≥15	33 (62.3)
Missing	1 (1.9)
Gastrectomy (*n* = 55)	
Node count median (IQR) (nodes)	23 (19.5)
1–14	11 (20)
15–24	17 (30.9)
≥25	26 (47.3)
Missing	1 (1.8)

Abbreviation: ASA, American Society of Anaesthesiology; IQR, interquartile range; SD, standard deviation; TNM, Tumour Node Metastasis.

BMI (*n* = 11, 14.1%). Most patients met one (*n* = 37, 47.4%) or two (*n* = 37, 47.4%) of the phenotypic criteria, with 4 patients (5.1%) meeting all three criteria. Figure 2 demonstrates the relationship between the phenotypic criteria. For overweight and obese patients with GLIM-defined malnutrition (*n* = 31), most were in the low SMI-only category (*n* = 15, 48.3%), followed by low SMI and weight loss (*n* = 12, 38.7%) and weight loss only (*n* = 4, 12.9%). The GLIM etiologic criteria were confirmed for all patients, as cancer is considered a chronic inflammatory condition.

Further categorization of patients with low SMI was required to establish the severity of muscle loss for GLIM-defined malnutrition. The SMI thresholds for men were 39.1–52.3 cm^2/m^2 for mild to moderately low SMI, and <39.1 cm^2/m^2 for severely low SMI; and for women were 34.2–38.4 cm^2/m^2 for mild to moderately low SMI, and <34.2 cm^2/m^2 severely low SMI.

3.3 | Postoperative complications

The overall postoperative complication rate was 52.8% (*n* = 57), with 18.5% (*n* = 20) graded as severe (Clavien–Dindo grade ≥3). The most prevalent postoperative complications were pneumonia (*n* = 23, 21.3%), pleural effusion (*n* = 10, 9.3%), atelectasis (*n* = 10, 9.3%), and anastomotic leak (*n* = 10, 9.3%).

Data in Table 3 show no difference in the number of postoperative complications between well-nourished and malnourished patients when using the ICD-10 definition. However, malnutrition identified using the GLIM criteria demonstrated a higher incidence of pleural effusions (12.8% vs. 0%, *p* = 0.029) and pneumonia (26.9% vs. 6.7%, *p* = 0.010) compared to well-nourished patients.

Results from logistic regression analysis to determine variables that predict pneumonia are shown in Table 4. Variables associated with pneumonia at univariate analysis are age (OR: 1.06, 95% CI: 1.01–1.12, *p* = 0.023) male gender (OR: 9.7, 95% CI: 1.24–75.79, *p* = 0.03), low SMI (OR: 5.6, 95% CI: 1.56–20.46, *p* = 0.008), cardiac disease (OR: 3.79, 95% CI: 1.45–9.94, *p* = 0.007), ASA score (OR: 2.32, 95% CI: 1.04–5.19, *p* = 0.040), and malnutrition (GLIM criteria) (OR: 5.17, 95% CI: 1.13–23.57, *p* = 0.034) (Table 4a). Three multivariate analysis models were required to account for multicollinearity, as BMI and low SMI are components of the GLIM diagnostic criteria (Table 4b). Model 2 demonstrates that a lower BMI is associated with an increased risk of postoperative pneumonia (OR: 0.86, 95% CI: 0.75–98, *p* = 0.025). In model 3, low SMI (OR: 4.8, 95% CI: 1.11–20.86, *p* = 0.036) is independently associated with pneumonia. Malnutrition defined by GLIM was not associated with pneumonia after accounting for confounding variables (Table 4b, model 1).

3.4 | Postoperative outcomes

The overall 90-day mortality rate was 4.6% (*n* = 5), including an in-hospital mortality rate of 2.8% (*n* = 3). The median postoperative LOS was 14 days (IQR 9). Most patients were discharged home (*n* = 78, 72.2%) or to a rehabilitation facility (*n* = 19, 17.6%). The 90-day hospital readmission rate was 35.2% (*n* = 38). There were no differences in these postoperative outcomes between well-nourished and malnourished patients when using the ICD-10 or GLIM diagnostic criteria (Table 3).

3.5 | Long-term survival

3.5.1 | Overall survival

The 5-year OS rate was 64.8%. Survival analysis showed that the survival trajectory for each group differed depending on the malnutrition definition. When assessed as a dichotomous variable, patients with ICD-10 malnutrition had poorer overall 5-year survival compared to well-nourished patients (50.0% malnourished vs. 75.0%, *p* = 0.013), whereas there was no difference in survival between the GLIM-defined malnourished and well-nourished group (61.5% malnourished vs. 73.3%, *p* = 0.088). Subgroup analysis of severity groups (well-nourished, mild-moderate, and severe malnutrition) within ICD-10 and GLIM-defined malnutrition groups was undertaken.

TABLE 2 Anthropometric and body composition characteristics of malnourished compared to well-nourished patients using ICD-10 and GLIM criteria.

	ICD-10 criteria			GLIM criteria		
	Well nourished (*n* = 64)	Malnourished (*n* = 44)	*p* Value	Well nourished (*n* = 30)	Malnourished (*n* = 78)	*p* Value
Anthropometric characteristics						
Body weight (kg)[a]	81.6 (19.7)	70.2 (16.6)	0.002*	86.3 (23.3)	73.4 (16.2)	0.002*
BMI (kg/m)[2a]	27.8 (5.5)	24.3 (4.8)	<0.001**	30.3 (6.4)	24.8 (4.2)	<0.001*
BMI categories (kg/m)[2] *n* (%)			0.004*			<0.001**
Underweight (BMI < 18.5)	0 (0)	2 (4.5)		0 (0)	2 (2.6)	
Healthy (BMI 18.5–24.9)	22 (34.4)	28 (63.6)		5 (16.7)	45 (57.7)	
Overweight (BMI 25–29.9)	26 (40.6)	8 (18.2)		12 (40)	22 (28.2)	
Obese (BMI ≥ 30)	16 (25)	6 (13.6)		13 (43.3)	9 (11.5)	
Preoperative (%) LOW[a]	2.1 (3.9)	10.1 (4.9)	<0.001*	1.6 (2.6)	6.9 (6.1)	<0.001*
Body composition						
Skeletal muscle CSA (cm)[2a]	144.5 (32.1)	130.5 (30.4)	0.026*	151.0 (38.9)	134.1 (27.8)	0.014*
Skeletal muscle index (cm^2/m)[2a]	49.2 (8.8)	45.5 (10.0)	0.008*	52.9 (9.9)	45.8 (8.5)	<0.001*
Intramuscular adipose tissue CSA (cm)[2a]	13.8 (12.9)	11.1 (10.4)	0.042*	13 (7.9)	12.5 (13.1)	0.158
Visceral adipose tissue CSA (cm)[2a]	166.2 (100.2)	157.4 (125.9)	0.354	179.3 (103.8)	156.0 (113.8)	0.232
Subcutaneous adipose tissue CSA (cm)[2a]	163.7 (82.4)	138.9 (75.1)	0.141	194.0 (97.8)	140.2 (69.5)	0.013*
Total adipose tissue CSA (cm)[2a]	343.2 (174.3)	283.0 (162.1)	0.110	377.8 (183.8)	298.2 (163.5)	0.115

Note: Preoperative % LOW: percentage of weight loss from baseline.

Abbreviations: BMI, body mass index, CSA, cross-sectional area; GLIM, global leadership initiative on malnutrition; LOW, loss of weight; SMI, skeletal muscle index (cm^2/m^2).

[a]Mean (standard deviation).

*Statistical significance ($p < 0.05$), independent *T*/Mann–Whitney *U* test.

**Statistical significance ($p < 0.05$), χ^2/Fisher's exact test.

Univariate Kaplan–Meyer 5-year OS analysis data for malnutrition severity categories are shown in Figure 3.

Results from multivariate Cox-regression analysis used to determine predictors of 5-year OS are shown in Supporting Information: Table 1. Several regression models were required to account for multicollinearity as BMI and preoperative LOW are components of malnutrition definitions. Along with age, stage 4 disease, and severe complications, preoperative LOW (HR: 1.08, 95% CI: 1.02–1.15, $p = 0.012$) (model 1), severe GLIM-defined malnutrition (HR: 2.51, 95% CI: 1.20–5.24, $p = 0.014$) (model 3), and ICD-10 malnutrition (HR: 2.15, 95% CI: 1.04–4.47, $p = 0.039$) (model 4) were independently associated with poorer OS at 5-years.

3.5.2 | Disease-freesurvival

Comparison of DFS at 5 years showed no difference between the well-nourished and malnourished groups for ICD-10 (17.2% well-nourished vs. 11.4%, $p = 0.33$) and GLIM definitions (18.2% well-nourished vs. 13.3%, $p = 0.19$). There was also no difference in DFS between malnutrition severity groups for ICD-10 ($p = 0.507$) or GLIM criteria ($p = 0.200$).

4 | DISCUSSION

This study demonstrates that malnutrition defined using the GLIM criteria was associated with postoperative pleural effusions and pneumonia, whereas malnutrition defined using the ICD-10 criteria lacked the discriminating power for association with complications. Furthermore, severe GLIM-defined malnutrition had the most significant impact on poorer OS at 5 years. The GLIM criteria identified a significantly higher proportion of patients with malnutrition than the ICD-10 definition.

GLIM-defined malnutrition has been linked to increased postoperative complications in a mixed cohort of surgical patients[13] and,

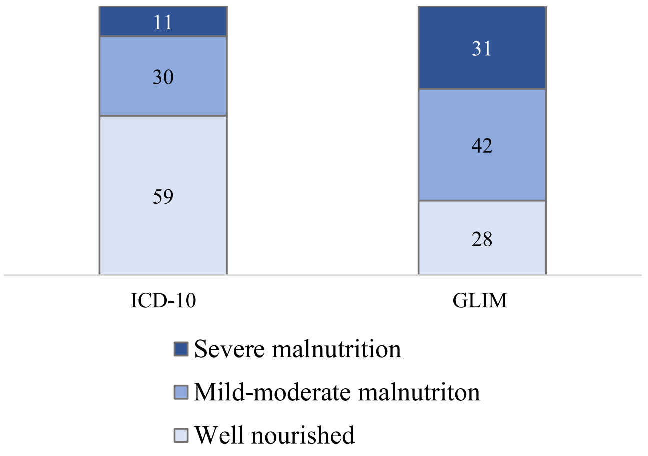

FIGURE 1 The proportion of patients in each category using the ICD-10 and GLIM criteria to detect malnutrition. GLIM, global leadership initiative on malnutrition; ICD-10, International Classification of Diseases, 10th Edition.

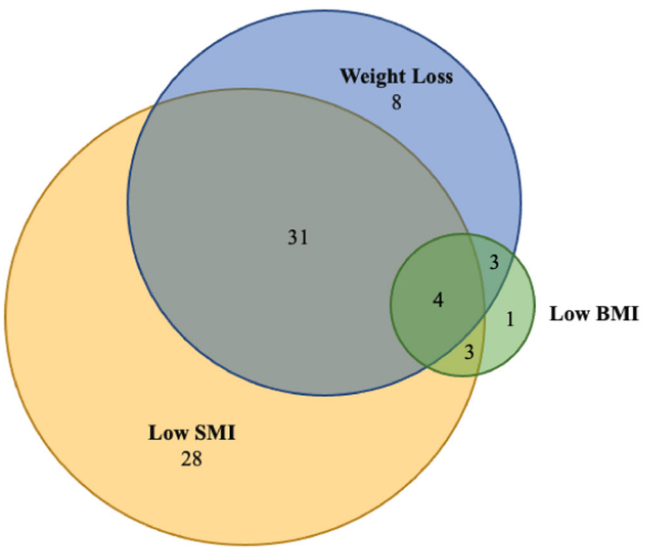

FIGURE 2 A Venn diagram demonstrating the relationship between the phenotypic criteria met for patients with GLIM-defined malnutrition (n = 78). GLIM, global leadership initiative on malnutrition.

more specifically, pulmonary complications.[23–25] The low muscle mass component of the GLIM criteria likely contributes significantly to the higher incidence of postoperative pneumonia in the GLIM-defined malnourished group, given the previously reported independent association with low SMI.[26] In addition, pulmonary complications negatively impact patient recovery, and overall and DFS,[3,4,27] highlighting the need to consider malnutrition and low muscle mass as modifiable surgical risk factors.

In addition to advanced disease stage and higher age, increased preoperative LOW, ICD-10 malnutrition, and severe GLIM-defined malnutrition were independent negative prognostic indicators of 5-year OS. The differences in survival between malnutrition severity categories may be explained by the higher number of severely malnourished patients in the GLIM group (31%) compared to ICD-10, where only 11% met severe malnutrition criteria. Despite ICD-10 being less sensitive than GLIM at detecting malnutrition, ICD-10 was associated with poorer OS at the univariate level, whereas no difference was observed with GLIM. The ICD-10 definition of malnutrition lacks an objective measure of muscle stores; therefore, significant weight loss is a key diagnostic criterion for ICD-10 malnutrition which may result in identifying patients with more significant or acute nutritional deficits and overall poorer physical condition, negatively impacting long-term survival outcomes. Conversely, 36% of patients were malnourished using the GLIM criteria based on low SM stores without weight loss. Furthermore, this study was not powered to predict differences in survival between malnourished groups. However, data from Asian cohorts confirm that GLIM-defined malnutrition is independently associated with reduced OS,[28,29] although larger studies in Western populations are required to validate these findings.

The objective assessment of low SM mass using CT imaging was a key criterion contributing to the high detection of GLIM-defined malnutrition (72.2%) compared to the ICD-10 definition (40.7%). Our data show that over one-third of all patients, and 43% who were overweight or obese, met the GLIM criteria due to having low SMI alone without a low BMI or significant weight loss. These findings indicate that without an objective assessment of SM mass, a significant proportion of patients may not be recognized as malnourished, and the required nutrition intervention may be delayed or not received.

Few studies have compared the prevalence of malnutrition identified using the ICD-10 and GLIM definitions. Poulter et al.[30] showed that GLIM-defined malnutrition (23%) was more significant than ICD-10 malnutrition (12.3%) in a mixed group of cancer patients using a subjective measure of muscle (Patient Generated-Subjective Global Assessment). Similarly, malnutrition diagnosed with GLIM detected approximately twice the rate of malnutrition defined using the ICD-10 criteria in a study of lung transplant candidates who had muscle mass assessed using bioelectrical impedance analysis.[31]

The prevalence of GLIM-defined malnutrition in patients with cancer varies considerably (23%–87.9%).[24,25,28,30,32,33] Comparisons between published studies that assess the prevalence of GLIM-defined malnutrition and its impact on surgical outcomes are challenging due to the heterogeneity of cancer types, various methods of muscle mass assessment and the multiple combinations of phenotypic and etiologic criteria used.[34] Yin et al.[25] assessed the impact of malnutrition, comparing several definitions, on complications in 360 patients after oesophagectomy. According to GLIM, 120 patients (33.3%) were diagnosed with malnutrition with muscle mass determined by measuring calf circumference. Although calf circumference is an accepted method for assessing muscle mass in the absence of technology-based methods (e.g., CT, DXA scanning, bioelectrical impedance),[35] low calf circumference is not an adequate surrogate for low SMI using CT.[36] These differences in muscle assessment methods may partly account for variances in GLIM-

TABLE 3 Postoperative complications and outcomes of malnourished compared to well-nourished patients using ICD-10 and GLIM criteria.

	ICD-10 criteria			GLIM criteria		
	Well nourished (n = 64)	Malnourished (n = 44)	p Value	Well nourished (n = 30)	Malnourished (n = 78)	p Value
Postoperative complications n (%)						
Any complication	31 (48.4)	22 (50)	0.425	18 (60)	39 (50)	0.818
Bleeding	35 (54.7)	22 (50)	0.777	1 (3.3)	1 (1.3)	0.097
Pleural effusion	4 (6.3)	6 (13.6)	0.311	0 (0)	10 (12.8)	0.029**
Cardiac ischemia	1 (1.6)	0 (0)	1.000	0 (0)	1 (1.3)	1.000
Anastomotic leak	6 (9.4)	4 (9.1)	1.000	2 (6.7)	8 (10.3)	0.500
Atelectasis	4 (6.3)	6 (13.6)	0.311	1 (3.3)	9 (11.5)	0.16a6
Wound infection	4 (6.3)	5 (11.4)	0.482	4 (13.3)	5 (6.4)	0.485
Cardiac arrhythmia	4 (6.3)	4 (9.1)	0.713	4 (13.3)	4 (5.1)	0.257
Pneumonia	12 (18.8)	11 (25)	0.479	2 (6.7)	21 (26.9)	0.010**
Vocal cord palsy	0 (0)	1 (2.3)	0.407	0 (0)	1 (1.3)	1.000
Chyle leak	2 (3.1)	1 (2.3)	1.000	0 (0)	3 (3.8)	0.550
Pneumothorax	2 (3.1)	2 (4.5)	1.000	2 (6.7)	2 (2.6)	0.589
Bacteraemia/septicemia	4 (6.3)	1 (2.3)	0.646	2 (6.7)	3 (3.8)	0.649
Other complication	13 (20.3)	5 (11.4)	0.296	6 (20)	12 (15.4)	1.000
Severe complication	14 (21.9)	6 (13.6)	0.556	4 (13.3)	16 (20.5)	0.599
Postoperative outcomes						
In-hospital mortality n (%)	2 (3.1)	1 (2.3)	1.000	0 (0)	3 (3.8)	0.550
90-day mortality n (%)	2 (3.1)	0 (0)	0.513	1 (3.3)	4 (5.1)	0.550
LOS days median[a]	13 (7)	14 (11)	0.885	15 (5)	13 (8)	0.705
Hospital readmission n (%) (days)						
<28	13 (20.3)	4 (9.1)	0.212	7 (23.3)	10 (12.8)	0.274
28–90	9 (14.1)	12 (27.3)	0.207	12 (40)	23 (29.5)	0.194

Abbreviations: GLIM, global leadership initiative on malnutrition; LOS, length of stay.

[a]Median (interquartile range).

**Statistical significance (p < 0.05), χ^2/Fisher's exact test.

defined malnutrition prevalence between the studies. Sanchez-Torralvo et al., using CT body composition analysis to assess muscle, found 87.9% of patients with solid (13% OG) and hematological cancers had GLIM-defined malnutrition.[33] The higher prevalence of malnutrition is likely explained by the greater proportion of patients with stage 4 disease (74%) compared to our study (5%), as the cancer stage is known to correlate positively with malnutrition severity.[37]

A key strength of our study is the objective and quantitative assessment of muscle mass using CT images, with contrast in the portal venous phase, to limit potential variability in measurements. CT muscle assessment is strongly recommended in consensus guidelines,[35] cannot be predicted using other surrogate measures such as calf-circumference,[36] and the inclusion of muscle mass assessment in the GLIM criteria improves its validity in detecting malnutrition.[32] Our study also considered the use of the GLIM criteria in clinical outcome prediction, as recommended by the GLIM consensus group.[38] Furthermore, our database of surgical complications is prospectively maintained, with real-time grading of complications, providing robust data to determine predictors of meaningful short and long-term surgical outcomes.

Our study has several limitations. First, the retrospective study design restricted access to reliable information to assess the GLIM etiologic criteria, including detailed, quantifiable dietary assessments, and objective markers of inflammation. The GLIM consensus report recognizes malignant disease as a chronic inflammatory condition.[9] All patients in our study met the disease burden or inflammation criterion, as was applied in similar studies.[25,28] However, future studies may benefit from additional proxy measures to confirm the presence or severity of inflammation and to identify the contribution that reduced food intake, or assimilation makes to malnutrition diagnosis. Second, there is currently no consensus on optimal SMI cut-points used to determine the severity of muscle loss for GLIM-

TABLE 4 (a) Univariate logistic regression analysis for variables associated with pneumonia; and (b) multivariate logistic regression analysis with separate models for variables with multicollinearity, including malnourished (GLIM) (model 1), BMI (model 2), and low SMI (model 3).

(a)

	Univariate OR	95% CI	*p*
Age (years)	1.06	1.10–1.12	0.023*
Gender (male)	9.70	1.24–75.8	0.03*
BMI (kg/m^2)	0.91	0.82–1.01	0.091
Preoperative LOW (%)	1.01	0.93–1.09	0.887
Low SMI	5.65	1.56–20.46	0.008
Myosteatosis	1.00	0.40–2.54	0.996
Malnourished (GLIM)	5.17	1.13–23.57	0.034
Malnourished (ICD-10)	1.44	0.57–3.65	0.437
Comorbidities			
Smoking (current/ex)	2.29	0.82–6.38	0.113
Cardiac disease	3.79	1.45–9.94	0.007*
Respiratory disease	2.39	0.89–6.41	0.083
Diabetes	1.42	0.41–4.95	0.585
Renal disease	2.67	0.78–9.14	0.188
ASA score	2.32	1.04–5.19	0.040*
Surgery type (oesophagectomy)	0.43	0.17–1.13	0.085

(b)

	Multivariate Model 1			Multivariate Model 2			Multivariate Model 3		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Age (years)	1.06	0.99–1.13	0.062	1.06	0.99–1.13	0.081	1.05	0.99–1.12	0.127
Gender (male)	4.46	0.50–40.13	0.182	7.55	0.84–67.63	0.071	3.97	0.44–35.87	0.219
BMI (kg/m^2)	-	-	-	0.86	0.75–0.98	0.025*	-	-	-
Preoperative LOW (%)	-	-	-	-	-	-	-	-	-
Low SMI	-	-	-	-	-	-	4.80	1.11–20.86	0.036*
Myosteatosis	-	-	-	-	-	-	-	-	-
Malnourished (GLIM)	3.99	0.78–20.44	0.096	-	-	-	-	-	-
Malnourished (ICD-10)	-	-	-	-	-	-	-	-	-
Comorbidities							-	-	-
Smoking (current/ex)	-	-	-	-	-	-	-	-	-
Cardiac disease	1.84	0.54–6.27	0.330	2.02	0.58–3.92	0.270	1.91	0.55–6.60	0.308
Respiratory disease	1.43	0.40–5.16	0.583	1.06	0.71–5.18	0.928	1.57	0.42–5.84	0.502
Diabetes	-	-	-	-	-	-	-	-	-
Renal disease	-	-	-	-	-	-	-	-	-
ASA score	1.57	0.62–3.95	0.339	1.91	0.71–5.18	0.203	1.78	0.67–4.71	0.248
Surgery type (oesophagectomy)	2.28	0.72–7.30	0.164	2.83	0.87–9.22	0.083	1.93	0.60–6.21	0.27

Abbreviations: ASA, American Society of Anaesthesiology; BMI, body mass index; GLIM, global leadership initiative on malnutrition; ICD-10, International Classification of Diseases, 10th edition; LOW, loss of weight; SMI, skeletal muscle index.

*Statistical significance ($p < 0.05$).

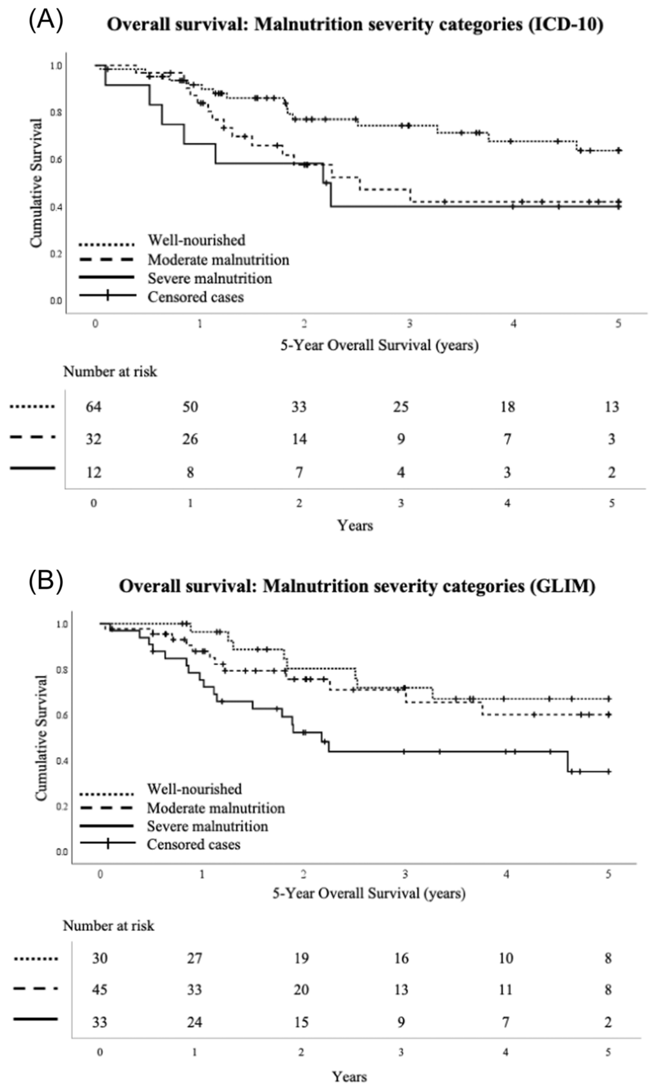

FIGURE 3 Kaplan–Meier univariate survival analysis comparing cumulative overall survival rates at 5 years for (A) ICD-10 definition groups: well-nourished (75.0%), mild-moderate malnutrition (53.1%), and severe malnutrition (41.7%) (Log-rank $p = 0.038$); and (B) GLIM definition groups: well-nourished (73.3%), moderate malnutrition (73.3%), and severe malnutrition (45.5%) (Log-rank $p = 0.022$). GLIM, global leadership initiative on malnutrition; ICD-10, International Classification of Diseases, 10th Edition.

defined malnutrition. Therefore, patients were grouped based on SMI tertiles; however, larger validation studies from multiple institutions are required to establish a consensus for muscle mass thresholds using CT. Third, the study cohort included patients with oesophageal and gastric cancer and various neoadjuvant therapies and surgical techniques were utilized. Although this is representative of the cohort managed in clinical practice, more cases are required to undertake subgroup analysis based on cancer or surgery type. Finally, the assessment of SM area using CT image analysis software has yet to be widely utilized in clinical practice, which may limit the generalizability of our findings to other centers.

5 | CONCLUSION

GLIM-defined malnutrition before OG cancer surgery is highly prevalent, and GLIM detects more malnutrition cases than ICD-10. Including an objective measure of muscle mass in malnutrition diagnostic tools may enable more timely and effective interventions that can potentially reduce the risk of pulmonary complications and improve rates of long-term survival. The opportunistic use of CT images to conduct body composition assessment should be utilized in settings where CT images are routinely taken. Future endeavors would benefit from implementing CT body composition assessment into routine image analysis processes to accurately identify malnutrition and initiate the required nutrition management as part of cancer care pathways.

AUTHOR CONTRIBUTIONS

Lisa C. Murnane, Paul R. Burton, Audrey C. Tierney, and Wendy A. Brown contributed to the conception and design of research. Wendy A. Brown, Kalai Shaw, Lisa C. Murnane, Marina Mourtzakis, and Jim Koukounaras contributed to the acquisition of data. Lisa C. Murnane, Paul R. Burton, Audrey C. Tierney, Adrienne K. Forsyth, and Susannah King contributed to data analysis and interpretation. Lisa C. Murnane drafted the manuscript. All authors provided a critical appraisal of the manuscript and provided approval for publication of the final version.

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CONFLICTS OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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