Effectiveness of GLIM and SGA for diagnosing malnutrition and predicting wound healing in patients with diabetic foot ulcers

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Abstract

Malnutrition significantly hampers wound healing processes. This study aimed to compare the effectiveness of the Global Leadership Initiative on Malnutrition (GLIM) and Subjective Global Assessment (SGA) in diagnosing malnutrition and predicting wound healing in patients with diabetic foot ulcers (DFU). GLIM criteria were evaluated for sensitivity (SE), specificity (SP), positive predictive value (PPV), negative PV (NPV), and kappa (κ) against SGA as the reference. Modified Poisson regression model and the DeLong test investigated the association between malnutrition and non-healing ulcers over six months. This retrospective cohort study included 398 patients with DFU, with a mean age of 66.3 ± 11.9 years. According to SGA and GLIM criteria, malnutrition rates were 50.8% and 42.7%, respectively. GLIM criteria showed a SE of 67.3% (95% CI: 60.4%, 73.7%) and SP of 82.7% (95% CI: 76.6%, 87.7%) in identifying malnutrition, with a PPV of 80.0% and an NPV of 71.1% (κ = 0.50) compared to SGA. Multivariate analysis demonstrated that malnutrition, as assessed by SGA, was an independent risk factor for non-healing (relative risk [RR] 1.84, 95% CI: 1.45, 2.34), whereas GLIM criteria were associated with poorer ulcer healing in patients with estimated glomerular filtration rate ≥60mL/min/1.73m^2 (RR: 1.46, 95% CI: 1.10, 1.94). SGA demonstrated a superior AUROC for predicting non-healing compared to GLIM criteria [0.70 (0.65–0.75) vs. 0.63 (0.58–0.65), *P* <0.01]. These findings suggest that both nutritional assessment tools effectively identify patients with DFU at increased risk, with SGA showing superior performance in predicting non-healing ulcers.

Keywords: Global Leadership Initiative on Malnutrition; Subjective Global Assessment; nutritional assessment; diabetes; wound healing

1. Introduction

The prevalence of diabetes has been on the rise in China over the past decades, resulting in an increased prevalence of diabetic foot ulcers (DFU) [1]. The lifetime risk of developing a foot ulcer in individuals with diabetes is estimated to be as high as 25%. Globally, a lower limb is lost to diabetes-related complications every 30 seconds [2]. Risk factors contributing to foot diseases, such as peripheral neuropathy and vascular disease, are present in over 10% of patients at the time of diabetes diagnosis. Moreover, the first year following a diagnosis of diabetes poses a heightened risk period for foot ulcers and subsequent amputations [3]. The prolonged non-healing and deterioration of ulcers significantly increase the risk of major amputations and mortality, imposing significant economic burdens on families and society [4]. Among the various factors influencing the prognosis of DFU, malnutrition stands out as a considerable concern, frequently leading to delayed wound healing [5]. Nutritional intervention is vital to DFU treatment, potentially reducing hospital stays, controlling inflammation, and enhancing healing outcomes [6; 7; 8]. Consequently, early identification and diagnosis of malnutrition are crucial. However, the optimal method for assessing the nutritional status of patients with DFU remains uncertain.

Traditional nutritional assessments frequently rely on indicators such as body weight, body mass index (BMI), and biochemical parameters. A low BMI (<18.5 kg/m^2) is a strong predictor of non-healing and mortality in patients with DFU [3]. Weight loss, particularly involving skeletal muscle reduction, is independently associated with amputations [9]. Decreased serum albumin levels elevate the risk of treatment failure in osteomyelitis [10] and mortality in patients with DFU [11]. However, relying solely on a single parameter or index may not effectively identify adult malnutrition.

Internationally, multidimensional nutritional assessment tools such as the Subjective Global Assessment (SGA) and the recently introduced Global Leadership Initiative on Malnutrition (GLIM) criteria are commonly utilized to evaluate malnutrition. SGA incorporates eight semi-quantitative indicators, including medical history and physical examination, allowing for a swift and reproducible assessment of nutritional status [12; 13]. It is preferred as a nutritional

assessment and prognostic tool for inpatients in various fields, such as internal medicine and general surgery [14], and specific clinical contexts, such as renal disease [15], liver transplantation [16], and critical care [13]. While SGA is considered a "semi-gold standard," only one study has established the association between malnutrition assessed by SGA and short-term non-healing in patients with DFU [5].

The GLIM consensus was developed to establish standardized diagnostic criteria for adult malnutrition, aiming to facilitate international comparisons of malnutrition prevalence and the effectiveness of nutritional interventions. This diagnostic framework involves two steps: identifying nutritional risk status and conducting a nutritional assessment, followed by severity grading based on phenotype and etiology indicators. Although applicable across diverse settings and patient groups, further validation through retrospective or prospective studies is necessary to establish its clinical validity [17]. Only two small-scale studies have incorporated GLIM into the nutritional assessment of patients with DFU, providing limited predictive value concerning ulcer outcomes [18; 19]. There is a lack of data regarding the application of GLIM among Chinese patients with DFU.

Therefore, our study aimed to compare the prevalence of malnutrition in middle-aged and older Chinese patients with DFU using the GLIM criteria and SGA. Furthermore, a modified Poisson regression model was used to investigate the relationship between malnutrition and the non-healing of ulcers over six months.

2. Methods

2.1. Study population

A single-center, retrospective cohort study was conducted at the Endocrinology Department of Sun Yat-sen Memorial Hospital, Sun Yat-sen University, involving patients hospitalized for the first time with DFU between October 2016 and June 2021. Inclusion criteria comprised a diagnosis of type 2 diabetes (T2D) and DFU, and age ≥18 years. Exclusion criteria included pregnancy or lactation, presence of Charcot's foot without ulcers, acute pancreatitis, severe liver disease, active malignancy, ongoing immunosuppressive therapy, history of radiation therapy at

the ulcer site, additional ulcers such as pressure ulcers and non-healing wounds after significant amputation, and those cases with incomplete medical data. The study was approved by the Medical Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University (SYSKY-2023-883-01), which waived the requirement for written consent following the China legislation governing the ethical review of biomedical research involving human subjects. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline (Supplementary Table 1).

2.2. Baseline information collection

A standardized data collection form was employed to gather patient information, including date of birth, sex, smoking status, history of foot ulcers, lower limb amputation, duration of diabetes, associated complications, and characteristics of foot lesions. Smoking status was categorized as active or ceased within the preceding month. Samples of wound secretions were obtained during the initial debridement for pathogen culture and drug sensitivity testing. The ulcer's area (cm^2) was calculated as the product of the longest measurement in length and the width perpendicular to it [(20)]. Within 24 hours of admission, standard procedures were utilized to measure white blood cell (WBC) count, hemoglobin, albumin, creatinine, triglycerides, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, glycated hemoglobin (HbA_{1c}), and urinary protein. Moreover, some patients were evaluated for C-reactive protein (CRP) and procalcitonin levels. Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft–Gault formula for women (eGFR = body weight *0.85*(140- age)/72/ creatinine) and for men (eGFR= body weight *(140- age)/72/creatinine) [(21)]. Lower limb arterial disease encompasses acute or severe limb ischemia, intermittent claudication, rest pain, or a history of peripheral vascular reconstruction [(22)]. It is characterized by reduced or absent distal arterial pulsations, ankle-brachial index (ABI) <0.9, toe-brachial index (TBI) <0.75, or evidence of lower limb arterial stenosis or occlusion determined through Doppler ultrasound or arteriography. Diabetic neuropathy was defined as two or more abnormalities among the following five tests: abnormal temperature sensation, diminished or absent sensation upon nylon filament testing,

abnormal vibration perception, absence of ankle reflex, and slowing nerve conduction in two or more nerves. Diabetic foot infections were evaluated using the classification developed by the Infectious Diseases Society of America [23]. Various classification systems have been employed to describe the severity of DFU, such as Wagner's grading and the SINBAD system [20]. Among these, the SINBAD system is widely regarded as the preferred framework for communication among healthcare professionals, characterizing the severity of DFU. In our study, the SINBAD system was utilized to assign a score of 0 or 1 based on ulcer site (S), ischemia (I), neuropathy (N), bacterial infection (B), and ulcer depth (D), where a total score of SINBAD ≥4 indicated severe DFU.

2.3. Nutritional evaluation

Within 48 hours of admission, a proficient nutritionist conducted routine nutritional assessments. Patient data were gathered concerning dietary intake the week before admission or over an extended period, self-reported weight changes, gastrointestinal symptoms, and activity levels. Height, weight, non-dominant calf circumference (CC), triceps skinfold thickness (TSF), and mid-arm circumference (MAC) were measured using established methods [24; 25]. For patients unable to stand, knee length was used to estimate height [26], while a wheelchair scale measured weight. BMI and mid-upper arm muscle circumference (MAMC) were calculated as follows: BMI (kg/m^2) = weight (kg) / height (m^2) and MAMC (cm) = MAC (cm) - π * TSF (cm).

Nutritional risk screening-2002 (NRS-2002) scores ≥3 indicate nutritional risk presence [27]. SGA assesses weight fluctuations, dietary intake, functional capacity, gastrointestinal symptoms, metabolic stress, subcutaneous fat loss, muscle wasting, and ankle or sacral edema. Nutritional status is categorized as A for well-nourished, B for moderately malnourished, or C for severely malnourished [12]. In this study, moderate and severe malnutrition were combined and designated as malnutrition.

The GLIM criteria were applied for post hoc routine nutritional assessment data analysis. As DFU meets the etiology criterion for disease/inflammation, CRP (>10 mg/L) or WBC (>$10.0*10^9$/L) [28] were utilized as inflammation-supporting indicators. Malnutrition was

diagnosed when patients with NRS-2002 scores ≥3 satisfied at least one phenotype criterion: unintentional weight loss of ≥5% within the past 6 months or ≥10% for >6 months [17]; low BMI: <18.5 kg/m^2 if <70 years or <20 kg/m^2 if ≥70 years [17]; reduced muscle mass: CC serves as a surrogate indicator, with a CC ≤30 cm for men and ≤29 cm for women [29].

2.4. DFU treatment and outcomes

Following the guidelines established by the International Working Group on the Diabetic Foot, a multidisciplinary team provided personalized care to all patients. Malnourished individuals received systematic dietary advice and, when necessary, oral or intravenous nutritional supplementation. Decisions regarding blood flow reconstruction or major amputation were made based on guidelines and team consensus.

Post-discharge wound care was facilitated through WeChat communication, allowing for sharing media files, such as photos and videos of the DFU, to instruct family members in wound management. Patients attended foot clinics monthly for dressing changes, and those with deteriorating wounds were readmitted for further intervention. A six-month follow-up ensued after enrollment, with the primary outcome being complete wound healing, defined as complete epithelialization of the lesion over two consecutive follow-up visits, encompassing the foot and ankle distal recovery to the amputation site. Details regarding major amputations and fatalities were obtained through medical record inquiries or phone communications.

2.5. Statistical analysis

MedCalc Statistical Software was used to determine an appropriate sample size based on a significance level of 0.05 and an allowable error of 0.10 (90% Power). This calculation resulted in a minimum expected area under the curve (AUC) of 0.70, a null hypothesis value of 0.5, and a ratio of well-nourished to malnourished of 3.237, based on a previous study conducted using the GLIM to determine nutritional status in patients with DFU [18]. The minimum sample size required was 119. Anticipating a response rate of 90% would result in a total sample size of 132. With these assumptions, 398 cases had sufficient power to detect the effect size.

Data were analyzed using SPSS version 24.0 software. The Kolmogorov-Smirnov normality

test was applied to continuous data. Normally distributed data were expressed as means ± standard deviations (SD), while non-parametric data were presented as medians and interquartile ranges (IQR). Inter-group comparisons were conducted using non-paired t-tests or Mann–Whitney U tests. Categorical data were presented as frequencies (n) and percentages (%), with inter-group comparisons performed using the $\chi 2$ test.

Cohen's kappa (κ) coefficient was employed to assess the consistency between SGA and GLIM criteria in diagnosing malnutrition. The κ values were interpreted as follows: 0–0.20 for slight agreement, 0.21–0.40 for fair agreement, 0.41–0.60 for moderate agreement, 0.61–0.80 for substantial agreement, and 0.81–1.00 for almost perfect agreement [30]. The receiver's operating characteristic (ROC) curve analysis was employed to assess the concurrent validity of the GLIM criteria, using SGA as the reference. Sensitivity (SE), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) were calculated, with values >80% classified as good, values <80% and >50% regarded as fair, and values <50% considered poor [31]. Modified Poisson regression analysis was conducted to estimate relative risk (RR) and 95% confidence intervals (CIs) for the association between malnutrition and ulcer healing. Covariates with P <0.1 in univariate analysis were included in the multivariate regression analysis. Given the inclusion of BMI in the GLIM criteria, it was omitted from the multivariate regression analysis for outcome prediction. Subgroup analysis was conducted to detect significant interactions. The DeLong test, performed using MedCalc software, compared the area under the ROC curve (AUROC) to predict non-healing between the two nutritional assessment methods. Statistical significance was set at a two-sided P-value of 0.05.

3. Results

3.1. Baseline characteristics

In our study, out of 500 patients admitted to the hospital with DFU, 398 were included in the analysis. Figure 1 illustrates the flowchart of the research and the selection of eligible participants. Baseline characteristics are summarized in Table 1. The mean age was 66.3 ± 11.9 years, with men comprising 64.6% of the sample. The median duration of T2D was 10.0 (IQR 5.0, 20.0) years, with 38.9% having concurrent cardiovascular disease (CVD), approximately half of whom also had diabetic kidney disease (DKD). Among them, 51 cases (12.8%) had ulcers on both feet, and the analysis focused on the more severe foot condition based on the SINBAD score. The duration of DFU was 2.0 (0.8, 4.0) months, with 268 cases (67.3%) classified as neuro-ischemic ulcers, 67 (16.8%) as ischemic ulcers, and 39 (9.8%) as neuropathic ulcers. Patients with moderate to severe infections accounted for 333 cases (83.7%) and 67 (16.8%) underwent minor amputations.

A total of 297 patients (74.6%) were identified as having nutritional risk. The patients had a median BMI of 22.9 kg/m², and based on the GLIM criteria, 43 cases (10.8%) had a low BMI, while 81 (20.4%) experienced weight loss of ≥5%. Compared to well-nourished individuals, patients with malnutrition were older and more likely to have comorbidities such as stroke. They also exhibited more severe foot lesions and infections, displaying lower BMI, CC, MAMC, albumin, hemoglobin, and serum lipid levels (all P <0.05). However, there were no significant differences between the two groups regarding the duration of T2D, types of foot ulcers, HbA1c levels, and eGFR (all P >0.05).

3.2. Diagnosing malnutrition using two assessment tools

With SGA, 191 cases (48.0%) were categorized as moderately malnourished and 11 (2.8%) as severely malnourished, resulting in an overall malnutrition rate of 50.8%. According to the GLIM criteria, the malnutrition rate was 42.7%. The agreement between the two assessment tools for diagnosing malnutrition was moderate (κ = 0.50, P = 0.043). Using SGA as the reference, the GLIM criteria exhibited an AUROC of 0.75 (95% CI: 0.70, 0.79), with a SE of

67.3% (95% CI: 60.4%, 73.7%) and SP of 82.7% (95% CI: 76.6%, 87.7%). The PPV was 80.0%, and the NPV was 71.1%. As depicted in Figure 2, among the 136 patients diagnosed with malnutrition by both assessment tools, 34 were not classified as malnourished by SGA, and 66 were not classified as malnourished by the GLIM criteria.

3.3. Malnutrition and adverse outcomes of DFU

Within 6 months, 205 cases of ulcers did not heal (51.5%), including 44 that underwent significant amputation and 19 resulting in death. The non-healing rate of ulcers in patients with malnutrition was significantly higher than in well-nourished patients (SGA: 71.3% vs. 31.1%; GLIM: 66.5% vs. 40.4%, both P <0.001). After adjusting for confounding factors such as age, sex, smoker, comorbidities, SINBAD score, gangrene, BMI, and levels of HbA1c, eGFR, and albumin, modified Poisson regression analysis revealed that malnutrition, as assessed by SGA, was an independent risk factor for non-healing ulcers (RR: 1.84; 95% CI: 1.45, 2.34) (Table 2). Similarly, patients identified as malnourished by GLIM had a 1.28 times higher risk of non-healing ulcers than well-nourished individuals (RR: 1.28; 95% CI: 1.05, 1.56). Furthermore, the analysis of predictive values for non-healing indicated that SGA exhibited a higher AUROC compared to the GLIM criteria (0.70 [0.65–0.75] vs. 0.63 [0.58–0.65], P <0.01) (Figure 3).

Subgroup analysis further revealed an interaction between malnutrition, as assessed by SGA, and albumin levels on non-healing outcomes (P = 0.034) (Table 3). In the subgroup with albumin levels ≥30 g/L (190 cases), the non-healing rate was higher in patients with malnutrition compared to those well-nourished (67.8% vs 22.1%, P <0.001). After adjusting for potential confounders, malnutrition significantly increased the risk of non-healing (RR: 2.67; 95% CI: 1.80, 3.97, P <0.001). In the subgroup with albumin levels <30 g/L (208 cases), this association remained significant after adjusting for multiple variables (RR: 1.32; 95% CI: 1.02, 1.72, P = 0.036). This observation suggests a substantial correlation between malnutrition and adverse outcomes regardless of albumin levels.

Furthermore, an interaction was observed between malnutrition identified by the GLIM criteria and the eGFR regarding non-healing outcomes (P = 0.046) (Table 3). Among patients

with eGFR ≥60 mL/min/1.73m^2 (260 cases), those with malnutrition exhibited a significantly higher non-healing rate compared to individuals who were well-nourished (67.0% vs 33.1%, *P* <0.001). The modified Poisson regression analysis revealed that malnutrition increased the risk of non-healing (RR: 1.46; 95% CI: 1.10, 1.94, *P* = 0.009). However, among patients with eGFR <60 ml/min/1.73m^2 (138 cases), the association between malnutrition and healing was not substantial (RR: 1.13; 95% CI: 0.86, 1.48, *P* = 0.376).

4. Discussion

To the best of our knowledge, this study makes the first attempt to assess the efficacy of the GLIM criteria and SGA in identifying malnutrition among patients with DFU. Our findings revealed a malnutrition prevalence of approximately 51% according to SGA and around 43% according to the GLIM criteria, with a moderate level of agreement between the tools. SGA exhibited superior predictive ability for the non-healing outcomes of DFU compared to the GLIM criteria. Furthermore, our modified Poisson regression analysis indicated that malnutrition assessed by SGA independently increased the risk of non-healing. However, GLIM criteria were associated with poorer ulcer healing, specifically in patients with eGFR ≥60mL/min/1.73m^2.

SGA is a widely utilized multidimensional nutritional assessment tool in clinical settings, offering a rapid means of determining nutritional status with sensitivity, reliability, and predictive potential for various disease outcomes [13; 14; 15; 16]. It further demonstrates substantial agreement with other assessment methods [32]. According to SGA, over half of patients with DFU experience malnutrition, likely due to reduced nutrient intake, elevated energy and protein requirements, heightened losses, and inflammation, all of which render patients with DFU susceptible to malnutrition [5]. As anticipated, we found that malnutrition, as determined by SGA, increased the risk of non-healing ulcers, aligning with the findings of Zhang SS et al., who reported that 69% of patients with malnutrition failed to achieve healing within 6 months [5].

The GLIM consensus introduces a novel approach to diagnosing adult malnutrition, endorsing validation using "semi-gold standard" methods such as SGA [17]. Brito JE et al. [33]reported that the GLIM criteria effectively identified malnutrition in hospitalized patients.

Moreover, the GLIM criteria have demonstrated applicability for nutritional assessment in acute and critically ill patients [34; 35; 36]. However, a retrospective study indicated good SP (>80%) and reduced SE (<80%) for the GLIM criteria when omitting "low muscle mass" as a phenotype criterion for malnutrition diagnosis [37]. Furthermore, the accuracy of GLIM diagnosis varies depending on the screening methods used. In a large-scale prospective study involving patients with cancer undergoing major abdominal surgery, GLIM diagnosis utilizing the mini nutritional assessment short-form (MNA-SF) screening demonstrated the highest consistency with SGA (κ= 0.56) compared to NRS-2002, with good SP (83%), fair SE (72%), and an NPV of 82% [38]. A recent meta-analysis of subgroup data from seven eligible studies involving 2137 hospitalized patients revealed the superior diagnostic value of GLIM criteria over SGA (SE 81%, SP 80%, AUROC 0.87) [39].

Only two small-sample studies have employed the GLIM criteria to evaluate the nutritional status of patients with DFU. In a prospective study involving 77 patients with ischemic foot ulcers, muscle mass was assessed using arm circumference, revealing a malnutrition prevalence of 71.4% (the nutritional screening method was unreported) [19]. Another study with 110 individuals with DFU employed bioelectrical impedance analysis (BIA) to assess diminished muscle mass, identifying a malnutrition rate of 23.6% (screened using NRS-2002) [18]. However, neither study observed a correlation between malnutrition and outcomes (such as non-healing ulcers or death), nor did they validate diagnostic accuracy. In our research, malnutrition was diagnosed in 42.7% of patients, consistent with findings from a meta-analysis (44.2%) [39]. Discrepancies in malnutrition rates can be attributed to variations in patient characteristics, different criteria for assessing "low muscle mass," the potential impact of edema on measurement of fat-free mass (FFM) and CC obtained through BIA, or diverse nutritional screening methods [40; 41].

Moreover, GLIM criteria exhibited good SP and fair SE in identifying malnutrition in patients with DFU compared to SGA. Based on expert consensus, the GLIM criteria aim to establish a diagnostic framework for protein-energy malnutrition. They share core assessment

indicators with SGA (such as reduced food intake, gastrointestinal symptoms, weight and body composition changes, and stress). This similarity explains the moderate agreement between the two tools ($\kappa = 0.50$). Our study findings indicate that the GLIM criteria demonstrate reasonable specificity (82.7%) but lower sensitivity (67.3%) in assessing malnutrition among patients with DFU. This observation suggests that while the GLIM criteria may effectively identify a more significant number of well-nourished patients with DFU, they may still overlook some cases of malnutrition. Several potential reasons account for this discrepancy. One reason is the limited accuracy of BMI in distinguishing body composition and malnutrition according to GLIM guidelines [17]. For instance, edema could overestimate BMI, although SGA might still categorize these patients as malnourished. Ascites or edema in patients with liver cirrhosis could impede agreement between GLIM and SGA [42]. In addition, the methods used by the two tools to measure muscle mass are different. GLIM recommends sophisticated techniques such as using dual-energy X-ray absorptiometry (DEXA), BIA, computed tomography (CT), or magnetic resonance imaging (MRI) for assessing muscle mass, or cost-effective and accessible physical examinations or body measurements such as CC, especially considering Asian standards [17]. Given the likelihood of low CC in patients with DFU and its superior predictability of functional and frailty indicators over MAC [43], CC was chosen to gauge muscle mass. However, the presence of edema and severe obesity could impact its effectiveness. SGA assesses muscle mass loss across various muscle groups (temporal, clavicular, shoulder, scapular, interosseous muscles, knees, quadriceps, and gastrocnemius), possibly offering a more suitable approach for well-trained healthcare professionals. Furthermore, SGA's focus on recent weight fluctuations enhances its ability to identify early-stage malnutrition compared to the GLIM criteria.

In our analysis of the clinical effectiveness of nutritional assessment tools, SGA and GLIM criteria for diagnosing malnutrition were independently associated with short-term non-healing of DFU. We further demonstrated that SGA exhibited superior predictive capability for non-healing compared to the GLIM criteria. SGA effectively predicted prognosis across all patients with DFU, while the GLIM criteria showed limited performance in predicting ulcer

healing among those with impaired kidney function (eGFR <60 mL/min/1.73m^2). It is worth noting that subgroup analysis with relatively wide CIs hinted at a trend of heightened non-healing associated with malnutrition. Moreover, patients with impaired kidney function frequently experience microvascular damage, an increased risk of neuropathy, and compromised vascular function, all of which were correlated with suboptimal wound healing and survival rates [11].

Notable strengths of our study include the pioneering evaluation of the performance of the GLIM criteria in patients with DFU and its comparison with the semi-gold standard SGA, a widely accepted nutritional assessment method. Moreover, data collection and nutritional assessment were executed by well-trained, dedicated nutritionists. However, several limitations warrant comment. Firstly, the study's single-center and retrospective design may limit generalizability, although comprehensive data on GLIM criteria and confounding factors, such as comorbidities and biochemical markers, were obtained. Secondly, the primary muscle mass assessment methods recommended by the GLIM consensus were not feasible; however, obtaining DEXA, BIA, CT, or MRI is frequently challenging. Further research could explore combining CC with other indicators, such as MAMC and muscle functions [44]. Thirdly, reliance on self-reported data for food intake and weight changes may introduce bias. Fourthly, focusing on baseline nutritional status without tracking dynamic indicators and the relatively brief follow-up duration may not accurately capture long-term effects. Fifthly, including cases with bilateral and multiple ulcers contributes to heterogeneity and reflects genuine characteristics of the DFU population. Finally, the lack of information regarding edema and obesity in the population may lead to an underestimation of malnutrition due to their impact on body measurements such as CC and MAC.

5. Conclusions

Malnutrition is prevalent among hospitalized patients with DFU. While both nutritional assessment tools could identify patients with DFU at risk, SGA demonstrated superior capability in predicting non-healing ulcers. The GLIM criteria could be a better independent prognostic indicator for patients with eGFR ≥60 mL/min/1.73m^2. These findings emphasize the significance of employing appropriate assessment tools for malnutrition detection, facilitating timely nutritional intervention, and optimizing clinical outcomes.

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Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Z.M.Y., J.C.J., and P.Z. conceived and designed the study; Z.M.Y., J.G.L., and C.Z.W. wrote and revised the manuscript; Y.Z. and C.Y.W. performed the collection of data; Z.M.Y. and Y.Y.Z. carried out the statistical analysis and interpretation of data; C.Z.W., C.G.C., P.Z., and J.M.R. supervised the data analysis and interpretation; C.Z.W. and P.Z. were responsibility for the integrity and accuracy of the data; All authors critically reviewed and approved the final manuscript.

Abbreviations: ABI, ankle-brachial index; AUC, area under the curve; BMI, body mass index; CC, calf circumference; CI, confidence interval; CRP, C-reactive protein; DFU, diabetic foot ulcers; eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition; IQR, interquartile ranges; MAC, mid-arm circumference; MAMC, mid-upper arm muscle circumference; NPV, negative predictive value; NRS-2002, nutritional risk screening-2002; PPV, positive predictive value; ROC, receiver's operating characteristic; RR, relative risk; SD, standard deviations; SGA, Subjective Global Assessment; T2D, type 2 diabetes; TBI, toe-brachial index; TSF, triceps skinfold thickness; WBC, white blood cell

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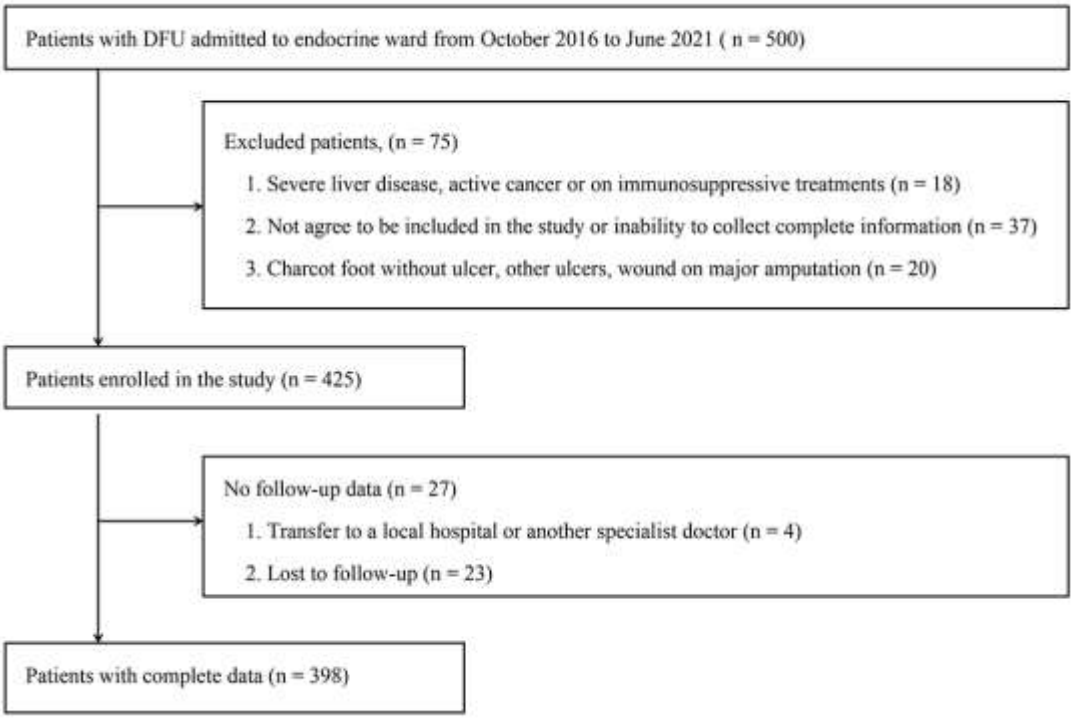

Figure 1. Flowchart showing the selection of eligible participants with diabetic foot ulcers.

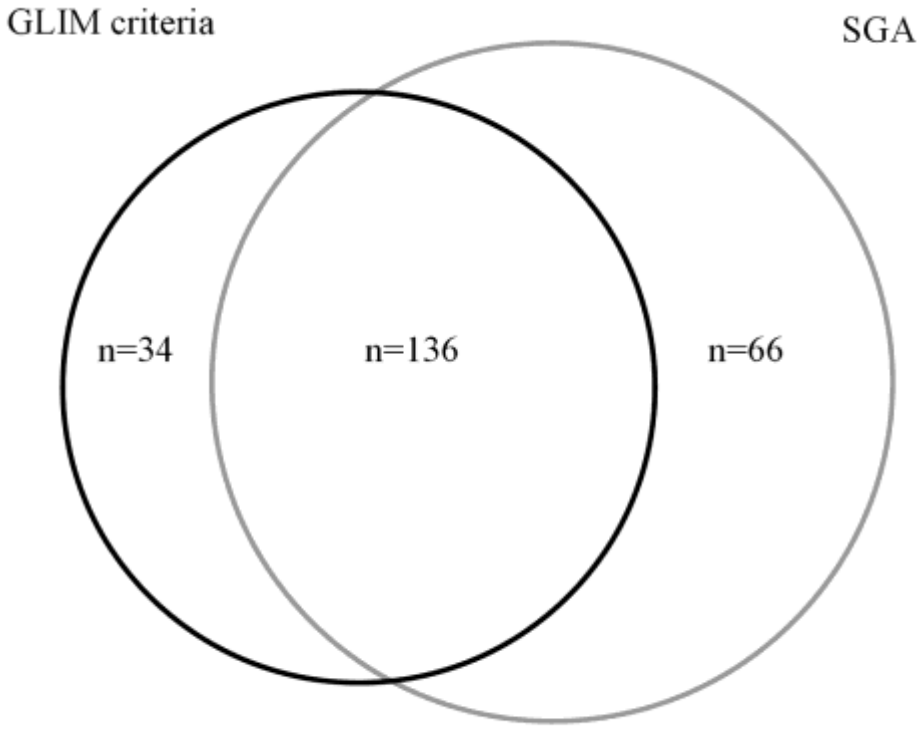

Figure 2. Overlap of patients with malnutrition between the GLIM criteria and SGA for 398 hospitalized patients with diabetic foot ulcers included in a post hoc analysis on the validity of the GLIM criteria compared with SGA.

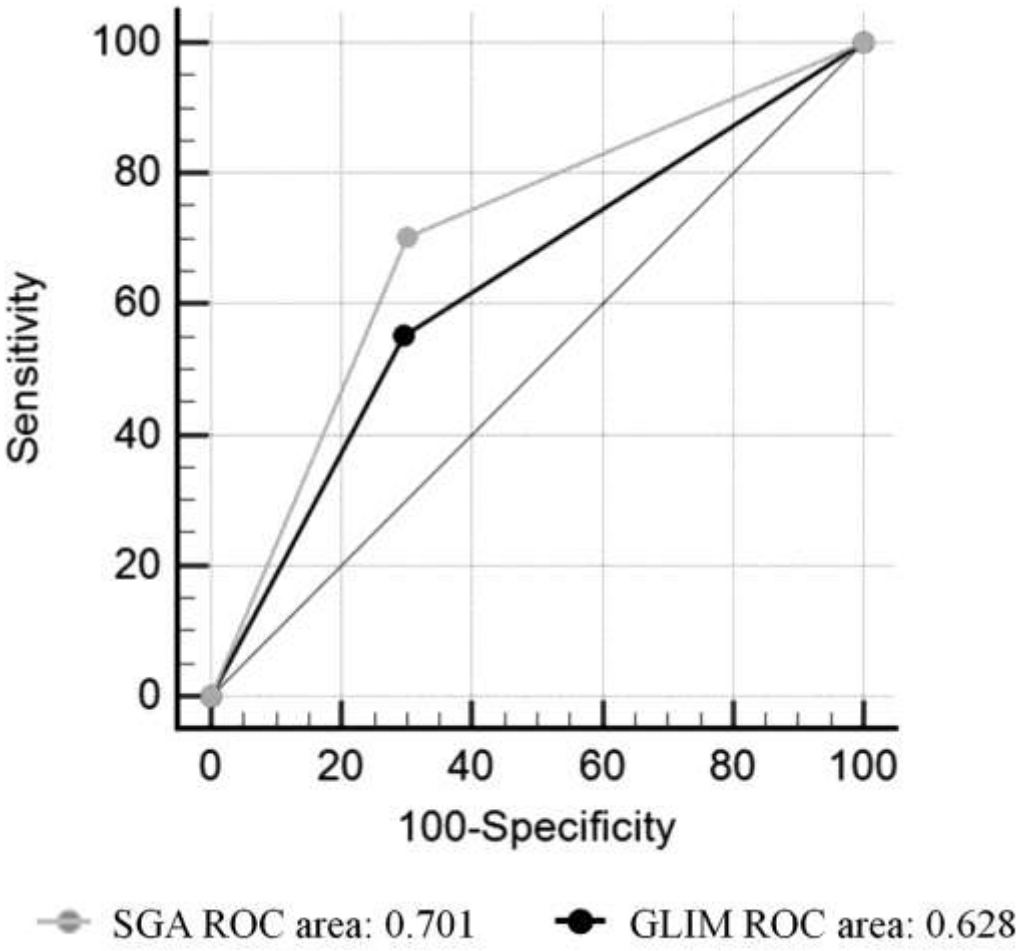

Figure 3. Sensitivity and specificity by ROC curve for the predictive value of clinical outcomes based on malnutrition obtained by the GLIM criteria and SGA among patients with diabetic foot ulcers.

Table 1. Baseline characteristics of patients with DFU by nutritional status

Variables		**GLIM criteria**			**SGA**		
	Total (N = 398)	**Well-nourished (N = 228)**	**Malnutrition (N = 170)**	***P* value**	**Well-nourished (N = 196)**	**Malnutrition (N = 202)**	***P* value**
Age (years)	66.3 ± 11.9	64.0 ± 12.4	69.4 ± 10.5	**<0.001**	65.1 ± 12.5	67.5 ± 11.2	0.051
Men [*N* (%)]	257 (64.6)	153 (67.1)	104 (61.2)	0.221	136 (69.4)	121 (59.9)	**0.048**
Smoking [*N* (%)]	106 (26.6)	60 (26.3)	46 (27.1)	0.868	55 (28.1)	51 (25.2)	0.526
Duration of DM (years)	10.0 (5.0, 20.0)	10.0 (5.3, 18.8)	10.0 (5.0, 20.0)	0.922	10.0 (5.0, 20.0)	10.0 (5.8, 19.3)	0.607
DPN [*N* (%)]	307 (77.1)	180 (78.9)	127 (74.7)	0.319	155 (79.1)	152 (75.2)	0.363
PAD [*N* (%)]	335 (84.2)	186 (81.6)	149 (87.6)	0.101	161 (82.1)	174 (86.1)	0.275
IHD [*N* (%)]	102 (25.6)	53 (23.2)	49 (28.8)	0.207	40 (20.4)	62 (30.7)	**0.019**
Stroke [*N* (%)]	78 (19.6)	32 (14.0)	46 (27.1)	**0.001**	28 (14.3)	50 (24.8)	**0.009**
DKD [*N* (%)]	198 (49.7)	118 (51.8)	80 (47.1)	0.354	100 (51.0)	98 (48.5)	0.617
Duration of DFU (months)	2.0 (0.8, 4.0)	1.0 (0.7, 4.0)	2.0 (1.0, 4.3)	**0.004**	1.0 (0.7, 3.4)	2.0 (1.0, 4.0)	0.053
SINBAD sore	4 (4, 5)	4 (4, 5)	5 (4, 5)	**0.007**	4 (3, 5)	5 (4, 5)	**<0.001**
Moderate to severe infected [*N* (%)]	333 (83.7)	182 (79.8)	151 (88.8)	**0.016**	147 (75.0)	186 (92.1)	**<0.001**
MDR [*N* (%)]	89 (22.4)	38 (16.7)	51 (30.0)	**0.002**	36 (18.4)	53 (26.2)	0.060
Gangrene [*N* (%)]	163 (41.0)	73 (32.0)	90 (52.9)	**<0.001**	59 (30.1)	104 (51.5)	**<0.001**
BMI (kg/m^2)	22.9 (20.9, 25.6)	24.2 (22.5, 27.0)	21.2 (19.0, 22.9)	**<0.001**	23.9 (22.1, 26.7)	21.8 (19.8, 24.2)	**<0.001**
CC (cm)	31.4 ± 4.1	33.7 ± 3.1	28.3 ± 3.1	**<0.0**	33.0 ± 3.4	29.9 ± 4.1	**<0.00**

				01			**1**
MAMC (cm)	23.4 ± 2.5	24.2 ± 2.4	22.3 ± 2.3	**<0.0**	24.2 ± 2.2	22.6 ± 2.5	**<0.00**
				01			**1**
Albumin (g/L)	29.2 ± 6.3	30.1 ± 6.4	28.1 ± 6.0	**0.002**	31.9 ± 5.8	26.6 ± 5.7	**<0.00**
							1
Hemoglobin (g/L)	106.4 ± 21.9	109.5 ± 21.1	102.2 ± 22.5	**0.001**	114.0 ± 20.2	99.0 ± 21.2	**<0.00**
							1
TG (mmol/L)	1.2 (0.9, 1.6)	1.2 (0.9, 1.7)	1.1 (0.8, 1.4)	**0.006**	1.2 (0.9, 1.7)	1.1 (0.8, 1.5)	**0.032**
TC (mmol/L)	3.8 ± 1.3	3.9 ± 1.3	3.8 ± 1.3	0.491	4.1 ± 1.3	3.6 ± 1.3	**0.001**
HDL-C (mmol/L)	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.2	0.873	0.9 ± 0.2	0.8 ± 0.3	**0.008**
LDL-C (mmol/L)	2.4 ± 0.9	2.4 ± 0.9	2.4 ± 0.9	0.535	2.6 ± 0.9	2.3 ± 0.9	**0.001**
WBC ($\times 10^9$/L)	10.0 (7.5, 13.5)	9.8 (7.3, 12.9)	10.6 (8.0, 14.5)	0.071	8.96 (7.2, 12.2)	11.48 (8.2, 15.3)	**<0.00**
							1
HbA1c >8.0% [*N* (%)]	221 (54.4)	124 (54.4)	91 (53.5)	0.865	105 (53.6)	110 (54.5)	0.860
eGFR (ml/min/1.73m^2)	73.5 ± 32.4	71.3 ± 31.2	75.2 ± 33.5	0.425	73.3 ± 29.2	72.7 ± 34.5	0.747

Values presented as mean ± SD or the median (25–75th quartiles). Abbreviate: BMI, body mass index; CC, calf-circumference; DFU, diabetic foot ulcers; DKD, diabetic kidney disease; DPN, diabetic peripheral neuropathy; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL-C high-density lipoprotein cholesterol; IHD, ischemic heart disease; LDL-C, low-density lipoprotein cholesterol; MDR, multidrug resistant; PAD, peripheral arterial disease; SINBAD, site, ischemia, neuropathy, bacterial infection, area, and depth; TC, total cholesterol; TG, triglycerides; WBC, white blood cell.

Table 2 Modified Poisson regression analyses of risk factors for six-month wound unhealing among patients with DFU

Characteristics	GLIM criteria[c]		SGA[d]	
	RR (95% CI)	***P* value**	**RR (95% CI)**	***P* value**
Malnutrition[a]	1.28 (1.05-1.56)	**0.016**	NA	NA
Malnutrition[b]	NA	NA	1.84 (1.45-2.34)	**<0.001**
Age	1.00 (0.99-1.01)	0.671	1.00 (0.99-1.01)	0.626
Men	1.00 (0.82-1.22)	0.998	1.05 (0.86-1.28)	0.666
Current smoker	1.21 (0.99-1.48)	0.062	1.21 (0.99-1.48)	0.063
Previous DFU	1.08 (0.91-1.29)	0.375	1.10 (0.93-1.31)	0.264
Hypertension	0.85 (0.70-1.04)	0.118	0.90 (0.74-1.10)	0.313
IHD	1.10 (0.92-1.31)	0.303	1.09 (0.92-1.30)	0.332
Stroke	1.08 (0.88-1.32)	0.487	1.07 (0.87-1.30)	0.530
Lung disease	1.18 (0.99-1.42)	0.070	1.16 (0.97-1.38)	0.115
Duration of DFU ≥2 months	1.30 (1.06-1.60)	**0.013**	1.32 (1.08-1.62)	**0.006**
SINBAD score ≥4	0.87 (0.66-1.14)	0.309	0.84 (0.65-1.09)	0.186
MDR	1.17 (0.96-1.41)	0.115	1.19 (0.99-1.42)	0.058
Gangrene	1.55 (1.26-1.91)	**<0.001**	1.55 (1.27-1.90)	**<0.001**

BMI <18.5kg/m^2		NA	NA	0.97 (0.77-1.23)	0.812
Albumin <30g/L		1.45 (1.15-1.84)	**0.002**	1.26 (1.00-1.58)	**0.047**
Hemoglobin <100g/L		1.06 (0.86-1.31)	0.599	0.99 (0.80-1.22)	0.933
HDL-C <1.03mmol/L		1.01 (0.80-1.29)	0.918	1.03 (0.82-1.28)	0.826
HbA1c ≥8.0%		0.91 (0.75-1.10)	0.325	0.93 (0.77-1.12)	0.396
eGFR ml/min/1.73m^2	<60	1.03 (0.86-1.25)	0.723	1.06 (0.89-1.27)	0.513
Albuminuria		1.05 (0.84-1.32)	0.670	1.01 (0.81-1.25)	0.951

a. Moderate to severe malnutrition defined by GLIM criteria.

b. Moderate to severe malnutrition defined by SGA.

c. Adjusted by age, sex, smoker, IHD, stroke, lung disease, ulcers duration, Gangrene, SINBAD score, Hemoglobin, HDL-C, Albumin, HbA1c, eGFR, Albuminuria, and MDR.

d. Adjusted by age, sex, smoker, IHD, stroke, lung disease, ulcers duration, Gangrene, SINBAD score, Hemoglobin, HDL-C, Albumin, HbA1c, eGFR, Albuminuria, MDR, and BMI.

Abbreviate: BMI, body mass index; DFU, diabetic foot ulcers; eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein-cholesterol; IHD, ischemic heart disease; MDR, multidrug resistant; NA, not available; SINBAD, site, ischemia, neuropathy, bacterial infection, area, and depth; SGA, global subjective assessment. Boldface type indicates P <0.05.

Table 3. Relative risk (95% CI) for six-month wound unhealing according to nutritional status stratified by potential risk factors among patients with DFU

Subgroup	N	GLIM criteria			SGA		
		RR (95% CI)	***P* Value**	***P* interaction**	**RR (95% CI)**	***P* Value**	***P* interaction**
Age, years				0.572			0.157
<65	169	1.47 (1.05-2.06)	**0.026**		1.57 (1.12-2.20)	**0.009**	
≥65	229	1.19 (0.93-1.53)	0.165		2.04 (1.46-2.86)	**<0.001**	
Sex				0.127			0.372
Men	257	1.08 (0.84-1.38)	0.555		1.69 (1.30-2.19)	**<0.001**	
Women	141	1.73 (1.20-2.49)	**0.004**		2.27 (1.39-3.73)	**0.001**	
Current smoking				0.820			0.694
Yes	106	1.15 (0.78-1.71)	0.483		1.62 (1.10-2.40)	**0.015**	
No	292	1.33 (1.05-1.68)	**0.017**		1.94 (1.43-2.63)	**<0.001**	
BMI, kg/m^2				NA			0.988
<22.89 (median)	196	NA	NA		1.83 (1.26-2.66)	**0.002**	
≥22.89	202	NA	NA		1.86 (1.32-2.62)	**<0.001**	
HbA1c, %				0.592			0.749
<8.0	182	1.16 (0.89-1.51)	0.275		1.46 (1.05-2.02)	**0.023**	
≥8.0	216	1.32 (0.99-1.77)	0.058		2.15 (1.52-3.04)	**<0.001**	
eGFR, $ml/min/1.73m^2$				**0.046**			0.575
<60	138	1.13 (0.86-1.48)	0.376		1.58 (1.12-2.22)	**0.009**	
≥60	260	1.46 (1.10-1.94)	**0.009**		2.01 (1.45-2.80)	**<0.001**	
Albumin, g/L				0.356			**0.034**
<30	208	1.10 (0.88-1.36)	0.415		1.32 (1.02-1.72)	**0.036**	
≥30	190	1.55 (1.06-2.28)	**0.025**		2.67 (1.80-3.97)	**<0.001**	

Gangrene				0.897			0.746
Yes	163	1.16 (0.93-1.45)	0.200		1.57 (1.19-2.07)	**0.001**	
No	235	1.37 (0.95-1.96)	0.088		2.19 (1.46-3.27)	**<0.001**	
Duration of DM, years				0.063			0.178
<10	144	0.86 (0.60-1.25)	0.430		1.55 (1.03-2.34)	**0.036**	
≥10	254	1.56 (1.22-2.01)	**0.001**		2.12 (1.55-2.89)	**<0.001**	

Adjusted by age, sex, smoker, IHD, stroke, lung disease, ulcers duration, Gangrene, SINBAD score, Hemoglobin, HDL-C, Albumin, HbA1c, eGFR, Albuminuria, MDR, and BMI except for the corresponding subgroup variables. Abbreviate: BMI, body mass index; DFU, diabetic foot ulcers; eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein-cholesterol; IHD, ischemic heart disease; NA, not available; SINBAD, site, ischemia, neuropathy, bacterial infection, area, and depth; SGA, global subjective assessment. Boldface type indicates P <0.05.