UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE MEDICINA

PROGRAMA DE PÓS-GRADUAÇÃO EM ALIMENTAÇÃO, NUTRIÇÃO E SAÚDE

MALNUTRITION ASSESSMENT IN INPATIENTS WITH CANCER: VALIDITY OF THE GLOBAL LEADERSHIP INITIATIVE ON MALNUTRITION DIAGNOSIS USING HANDGRIP STRENGTH AND CALF CIRCUMFERENCE COMPARED TO SUBJECTIVE GLOBAL ASSESSMENT (SGA) AND PATIENT-GENERATED SGA (PG-SGA).

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Mariana Scortegagna Crestani

Orientadora: Profª. Drª. Thais Steemburgo

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Formato da dissertação

Essa dissertação segue o formato proposto pelo Programa de Pós-Graduação em Alimentação, Nutrição e Saúde da Universidade Federal do Rio Grande do Sul:

1. Revisão da literatura relacionada ao tema da dissertação;

2. Artigo original;

3. Anexo

Sumário

Lista de abreviaturas

3MinNS	3-Minute Nutrition Screening
AMC	Arm Muscle Circumference
ASG	Avaliação Subjetiva Global
ASG-PPP	Avaliação Subjetiva Global - Produzida pelo Paciente
AUC	Area Under the Curve
BMI	Body Mass Index
CC	Calf Circunference
CI	Confidence Interval
CRP	C-reactive Protein
ECOG-PS	Eastern Cooperative Oncology Group Performance Status
ESPEN	European Society for Clinical Nutrition and Metabolism
FFMI	Fat-Free Mass Index
FMI	Fat Mass Index
GLIM	Global Leadership Initiative on Malnutrition
GMS	Graz Malnutrition Screening
HGS	Handgrip Strength
IMC	Índice de Massa Corporal
INST	Innsbruck Nutrition Screening Tool

KPS	Karnofsky Performance Status
LOS	Length of Stay
MAC	Mid-arm Circunferemce
MNA	Mini Nutritional Assessment
MST	Malnutrition Screening Tool
MUST	Malnutrition Universal Screening Tool
NIS	Nutrition Impact Symptoms
NRI	Nutritional Risk Index
NRS-2002	Nutritional Risk Screening- 2002
PG-SGA	Patient-Generated Subjective Global Assessment
PG-SGA SF	Patient-Generated Subjective Global Assessment Short Form
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RMNST	Royal Marsden Nutrition Screening Tool
ROC	Receiver Operating Characteristic
SGA	Subjective Global Assessment
SNAQ	Short Nutritional Assessment Questionnaire

Lista de tabelas e figuras

Capítulo I

Revisão Sistemática:

Methods of nutritional assessment and functional capacity in the identification of unfavorable clinical outcomes in hospitalized patients with cancer: a systematic review

Capítulo II

Artigo Original

Malnutrition assessment in inpatients with cancer: Validity of the Global Leadership Initiative on Malnutrition diagnosis using handgrip strength and calf circumference compared to Subjective Global Assessment (SGA) and Patient-generated SGA (PG-SGA).

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INTRODUÇÃO

O câncer é uma doença crônica não transmissível que afeta uma proporção significativa da população mundial. Segundo o *Global Cancer Statistics*, no ano de 2020, em nível mundial, ocorreram 19,3 milhões de novos casos de câncer e aproximadamente 10 milhões de pessoas morreram pela doença. Já no Brasil, estima-se que para cada ano do triênio 2020 - 2022 ocorrerão 625 mil casos novos de câncer. O câncer ocasiona um grande número de alterações clínicas, decorrentes do estresse causado pela própria doença e do tratamento aplicado, o que torna os pacientes especialmente suscetíveis ao risco de desnutrição. A etiologia da desnutrição em indivíduos com câncer é complexa e multifatorial, podendo ser influenciada pela localização e tipo de tumor, estágio da doença, efeitos colaterais do tratamento, condição socioeconômica, capacidade funcional e sintomas de impacto nutricional. A presença da desnutrição associada a esses fatores pode resultar em menor tolerância ao tratamento, maior tempo de hospitalização, pior qualidade de vida e taxas aumentadas de morbidade e mortalidade. Nessa perspectiva, o principal objetivo da terapia nutricional no paciente oncológico é evitar a progressão para o quadro de desnutrição, prevenindo e/ou revertendo o declínio do estado nutricional garantindo melhor qualidade de vida para o paciente. Para isso, a avaliação precoce do estado nutricional a qual inclua medidas de consumo alimentar, sintomas de impacto nutricional, massa muscular, desempenho físico e o grau de inflamação sistêmica - são essenciais para embasar as intervenções nutricionais e garantir cuidados adequados e individualizados para os pacientes com câncer. Os principais instrumentos de avaliação nutricional validados para os pacientes oncológicos são a Avaliação Subjetiva Global (ASG) e a Avaliação Subjetiva Global - Produzida pelo Paciente (ASG-PPP). Mais recentemente, o *Global Leadership Initiative on Malnutrition* (GLIM) propôs um consenso a respeito de critérios destinados ao diagnóstico de desnutrição do adulto no

cenário clínico. O objetivo desta avaliação é identificar critérios fenotípicos [perda de peso, índice de massa corporal (IMC) e massa muscular reduzida] e etiológicos (redução da ingestão alimentar e inflamação ou gravidade da doença). Sendo necessário para diagnosticar a desnutrição a presença de pelo menos um critério fenotípico e um critério etiológico.

Evidências cientificas vem demonstrando a validade e concordância do GLIM com os instrumentos utilizados na avaliação do estado nutricional. Em pacientes hospitalizados, com diferentes diagnósticos, o critério GLIM demonstrou validade satisfatória com as ferramentas ASG e a ASG-PPP. Em pacientes oncológicos hospitalizados e ambulatoriais o GLIM apresentou concordância moderada e razoável com a ASG-PPP, respectivamente. Também em indivíduos com câncer a presença da desnutrição, avaliada pelo critério GLIM, demonstrou associação positiva a desfechos como o maior tempo de internação e mortalidade em seis meses.

Considerando que mau estado nutricional é capaz de aumentar as chances de desfechos clínicos desfavoráveis, identificar os melhores instrumentos de avaliação nutricional é de grande importância em pacientes oncológicos. Em vista disso, o critério GLIM tem se mostrado promissor para avaliar a desnutrição e, a análise de sua validade, comparado aos instrumentos já validados e amplamente utilizados na prática clínica, bem como sua capacidade preditiva de prever desfechos clínicos pode colaborar para consolidar a utilização do GLIM na avaliação nutricional de pacientes com câncer hospitalizados.

Neste sentido, os objetivos dessa dissertação foram: (1) através de uma revisão sistemática da literatura avaliar e sumarizar os principais instrumentos de avaliação nutricional utilizados em pacientes oncológicos hospitalizados e sua associação com desfechos clínicos e, (2) por meio de um estudo transversal analisar a validade dos

critérios GLIM, para diagnóstico da desnutrição, considerando como referência os instrumentos ASG e ASG-PPP, e a associação da desnutrição com o maior tempo de internação em pacientes com câncer.

CAPÍTULO I

REVISÃO DA SISTEMÁTICA DA LITERATURA

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Nutritional instruments in cancer patients: a systematic review

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ABSTRACT

Context: Malnutrition has a negative impact on clinical outcomes and mortality in cancer patients. Identifying risk, nutritional status and functional capacity can contribute to an adequate and early nutritional therapy, which can reduce unfavorable clinical outcomes in this group of patients.

Objective: To evaluate the scientific evidence on the main instruments for nutritional screening, nutritional assessment and functional capacity and present the best tools to assess the risks and predict relevant clinical outcomes hospitalized cancer patients.

Data sources: PubMed/MEDLINE, Embase, SciELO and LiLACS databases were searched to identify relevant publications up to January 31, 2021.

Study selection: The studies included compared the following instruments: (1) nutritional screening, (2) nutritional screening based on laboratory parameters, (3) nutritional assessment, (4) nutritional diagnosis and, (5) functional capacity.

Data extraction: Data were extracted by 2 independent reviewers (Kappa = 0.813).

Results: A total of 28 studies met the inclusion criteria. The highest nutritional risk, worst nutritional status and low functional capacity assessed by the Nutritional Risk Screening 2002, Patient- Generated Subjective Global Assessment (PG-SGA) and lower handgrip strength (HGS) instruments, respectively, were associated with longer hospital stay (LOS). Also, the Global Leadership Initiative on Malnutrition (GLIM) criteria for diagnosing malnutrition was useful to predict six-month mortality when using HGS and free fat mass index.

Conclusions: The PG-SGA is an effective tool for assessing the nutritional status of cancer patients. The combination of the methods might be recommended for a complete assessment of the nutritional status of hospitalized cancer patients.

Keywords: *cancer; nutritional screening; nutritional assessment; functional capacity*.

INTRODUCTION

Cancer patients present the highest prevalence of malnutrition, with 30–50% of hospitalized cancer patients found to be malnourished or at risk of malnutrition.[1] Malnutrition has a negative impact on clinical outcomes and mortality in cancer patients due to the physical and metabolic effects of the disease and the therapies applied to its treatment, which can result in decreased response to cancer treatment and quality of life, with greater risks of postoperative complications, increased morbidity and mortality, prolong the length of stay (LOS) and hospital cost.[2] In addition, malnutrition and muscle loss are frequently seen in these patients due to increased energy and protein needs, inadequate food intake and decreased physical activity.[2]

Access to nutritional screening and functional capacity of patients allows the identification of nutritional status, contributing to early and appropriate nutritional therapy.[2] Currently, several screening and nutritional assessment tools have been developed and are widely used in clinical practice.[3-15] The National Consensus of Oncological Nutrition of 2015 and 2016 recommends the use of Nutritional Risk Screening 2002 (NRS-2002), Subjective Global Assessment (SGA) or Patient Generated-Subjective Global Assessment (PG-SGA) and the Hand Grip Strength (HGS) for screening, nutritional assessment and functional capacity of cancer patients, respectively.[16] Recently, the Global Leadership Initiative on Malnutrition (GLIM), suggested a more accurate and complete for nutritional diagnosis in hospitalized patients with and without cancer.[6] However, it is recognized that none of them are specific to oncological patients.[2] Thus, several studies have compared these tools in different types of cancer.[17-44]

Although numerous nutritional screening assessment tools are in use, their levels of validity, reliability, generalization and agreement vary.[45] These tools present

nutritional variables that evaluate different clinical aspects of patients with objective measures that include recent weight loss, changes in food intake, presence of physical diseases related to decreased nutrient intake or malabsorption, biochemical markers and severity of the disease.[46] Thus, they assign a score that allows classifying patients according to the risk of malnutrition.[46]

Considering that the deficit in nutritional status is closely related to the decreased response to cancer treatment and quality of life, it is important to identify the nutritional risk in cancer patients in order to offer an appropriate nutritional approach minimizing malnutrition as well as the side effects of therapy. Thus, the objective of the present study was to systematically review the main nutritional risk screening, nutritional assessment and functional capacity instruments used in hospitalized cancer patients and to present the best methods to assess risks and predict relevant clinical outcomes in this group of patients.

METHODS

We systematically searched the PubMed/MEDLINE, Embase, SciELO and LiLACS electronic databases to identify studies that report differences between nutritional screening methods in cancer patients, through January 31, 2021. This review was performed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement, checklist presented in the Supplementary Material. [49]

The search strategy was defined by keywords related to cancer patients (Neoplasms, Tumor, Cancer, Oncology), associated with the assessment of nutritional risk, nutritional status and functional status terms (Nutrition Assessment, Nutrition screening, Handgrip strength, Performance status, Functional capacity) in the hospital

setting (Hospital, Inpatients). We also added MeSH terms related to the study design to perform a more comprehensive search (Prevalence, Epidemiology, Cohort, Longitudinal, Prospective, Retrospective, Cross-sectional.). The complete search strategy is available at Supplementary Material. Reference lists of identified articles were checked for additional relevant publications. MEDLINE and EMBASE databases were searched for relevant publications in the peer-reviewed literature. PICOS (Population, Intervention, Comparison, Outcomes, and Study design) criteria were used to define the research question (Table 1).

Were considered original studies, written in english, spanish or portuguese, carried out with hospitalized cancer patients (whether or not they underwent surgical treatment, chemotherapy, and radiotherapy), adults and/or elderly patients (aged over 18 years) that compared the performance of nutritional screening, nutritional assessment and functional capacity assessment instruments. We excluded studies performed in children, adolescents, pregnant women, outpatients, emergency patients, palliative care, critically ill, hematologic cancer patients and randomized clinical trials and validation studies due to not compare different tools. Since conference abstracts were also excluded, we contacted the authors to inquire if there was full text available.

Studies were assessed independently by two investigators (M.C. and T.G.). After initial search titles and abstracts were evaluated to identify potentially eligible studies. Studies that did not meet the inclusion criteria were excluded. The full text of the remaining papers was obtained for further examination. Data were extracted independently by the same two investigators with an excellent agreement between them ($k = 0.813$). The other author (T.S.) resolved divergences.

Data extraction was performed in Google Forms (Google, Mountain View, CA) and exported to Microsoft Office Excel (Microsoft, Redmond, WA). This was guided by a standardized electronic form, performed independently by 2 reviewers (M.C and T.G). Disagreements were discussed, analyzed and resolved through the arbitration of a third reviewer (T.S). The extracted data, in addition to the assessment of nutritional status, as a primary or secondary outcome, included: name of the author, year of publication, study design, number of participants and patient characteristics (age), type of nutritional risk assessment tool used and purpose of the study. Information on the type of cancer and assessment of functional capacity was extracted when available. The methodological quality of each included study was assessed using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, available at the Supplementary Material.[50]

RESULTS

Selection and general characteristics of included studies

A total of 3,753 articles were initially identified through database searches. The full text of 109 studies was assessed for eligibility and 83 articles were excluded based on the title / abstract. Twenty-six articles met the inclusion criteria and two articles were added through manual search. In total, 28 studies were included in the present review.[17-44] The flow diagram for the search strategy is shown in Figure 1. Regarding study designs, 17 were cross-sectional studies, 6 were prospective observational, 3 were retrospective observational and 2 were retrospective cohort studies. The year of publication varied from 2012 to 2020.[17,44] The sample size ranged from 49 to 11,324 cancer patients.[31,32]

Twenty-two instruments for assessing nutritional risk and status and functional capacity were described. The results of the studies showed correlations and concordances

between the tools evaluated. Also, the outcomes observed in the studies included malnutrition, infectious and noninfectious complications, psychological stress, LOS, morbidity and mortality. The methodological quality was classified as Good in 5[20,25,36-38] studies, Fair in 11[18,19,22-24,34,39,41-44] and Poor in 12.[17,21,26-33,35,40] The inferior quality was mainly related to cross-sectional studies, which provide weaker evidence regarding a potential causal relationship between exposures and outcomes. Other biases present in studies classified as Poor were the absence of uniform eligibility criteria for the population and lack of adjustment for the confounding variables in multivariate analysis. In addition, the components of each nutritional instrument are described in Table 5.

The NRS-2002 was the most common nutritional risk assessment tool used in studies (n = 16),[17,19,20-23,26-28,31,35,39,40,41,43,44] other instruments as Malnutrition Universal Screening Tool (MUST),[18,25,31,36,41,44] Malnutrition Screening Tool (MST),[24,37,41] Nutritional Risk Index (NRI),[18,39] Innsbruck nutrition screening tool (INST),[17] Royal Marsden Nutrition Screening Tool (RMNST),[24] Short Nutritional Assessment Questionnaire (SNAQ),[25] Graz Malnutrition Screening (GMS)[33] and, 3 Minute Nutrition Screening (3minNS)[37] also were observed (Table 2).

The nutritional status assessed by the PG-SGA was the most frequent in the studies (n = 15),[19,20,23,24,26,30,32-35,37,39,40,42,44] followed by the SGA (n = 8)[18,22,27,28,29,30,36,38] while the Mini Nutritional Assessment-Short Form (MNA-SF),[19,23,31,33] Mini Nutritional Assessment Full Version (MNA)[28] and GLIM[36,43,44] tools were used in a smaller number of studies (Table 3). Eight studies evaluated the functional capacity by the HGS[20,21,26,32,34,36,40,42] and four studies by Eastern Cooperative Oncology Group Performance Status (ECOG-PS)[30,34,38,43] and Karnofsky Performance Status Scale (KPS),[29,30,32,40] respectively (Table 4).

Nutritional risk screening tools

The analysis of studies that assessed nutritional risk showed that the risk of malnutrition ranged from 4.6% (MST) to 88.0% (MUST).[41,18] Twenty studies used several nutritional screening instruments to categorize patients into categories of low, moderate and high nutritional risk.[17,18,20-28,31,33,35,37,39,41,43,44] NRS-2002 was the most commonly used (16 studies) showing a prevalence that ranged from 14.7% to 92.2% of nutritional risk.[41,31]

Seven studies associated nutritional risk with clinical outcomes.[18,20,22,27,35,37,41] The instruments used in these studies included NRS-2002, MUST, NRI, MST and 3MinNS. LOS,[20,22,27,41] psychological stress[35] and mortality[27] were significantly associated with the risk of malnutrition detected by NRS-2002. Unlike the risk of malnutrition by the MST and MUST, which did not present a significant association with the LOS.[41] The nutritional risk detected by MUST, NRI and 3MinNS showed good agreement in the prediction of mortality and excellent agreement in the prediction of post-surgical complications and LOS.[18,37] Using albumin as a blood biomarker for the diagnosis of malnutrition and comparing it with the nutritional risk assessed by NRS-2002 resulted in a slight but significant agreement.[26]

Regarding to the agreement between instruments in screening the nutritional risk, NRS-2002 presented moderate agreement related to MUST,[41] slight agreement related to MST[41] and PG-SGA,[19,23] fair[28] or moderate[22] agreement compared to SGA and moderate agreement compared to MNA-SF.[28] The GLIM criteria presented an excellent agreement with NRS-2002 and moderate with MUST.[44]

Some of the instruments were included in only one or two studies, such as 3MinNS, RMNST, MST, GMS, NRI, SNAQ and INST. The performances of the RMNST and MST in predicting nutritional risk, compared to the PG-SGA, were

excellent.[24] The nutritional risk screening by GMS, presented moderate and substantial agreement with PG-SGA and MNA-SF, respectively.[33] In addition, a study demonstrated better accuracy of NRI than NRS-2002 in predicting nutritional risk.[39]

Nutritional assessment tools

Twenty-four studies included nutritional assessment instruments,[18-20,22-24,26-41,43,44] and characterized the nutritional status of patients in: well-nourished, moderately malnourished or severely malnourished. The prevalence of malnutrition ranged from 18.2% (SGA) to 97.1% (PG-SGA).[27,39]

PG-SGA was the most commonly used instrument. Four studies used the nutritional status by PG-SGA as a parameter to assess the performance of other instruments such as NRS,[19,40] RMNST and MST[24] and to propose new cutoff points for HGS.[41] One study demonstrated a fair agreement between PG-SGA and albumin, and a moderate correlation with NRS-2002 in detecting malnutrition.[26]

Eight studies associated nutritional status with clinical outcomes.[20,22,27,35-37,40,43] The instruments used in these studies included PG-SGA, SGA and GLIM. A longer LOS was significantly associated with malnutrition detected by the PG-SGA[20] and SGA instruments.[22,27] Postoperative complications were associated with worse nutritional status according to the SGA,[27] but not with the PG-SGA,[37] which was associated with greater psychological distress[35] and worsening in quality of life parameters.[40] Higher mortality was observed in malnourished patients according to the SGA[22,27,36] and GLIM.[36,43]

Functional capacity tools

A total of 12 studies assessed functional capacity and demonstrated a good correlation with nutritional status assessment.[20,21,26,29,30,32,34,36,38,40,42,43] Malnutrition by PG-SGA was correlated with worse functional capacity by HGS,[26,32,40,42] ECOG-PS[30] and KPS[26,30] and malnutrition by SGA correlated to ECOG-PS[30,38] and KPS[29,30]. The nutritional risk by NRS-2002 was associated with lower HGS.[26]

In comparison with malnourished patients assessed by other tools (NRS-2002 and PG-SGA), low HGS was associated with a greater reduction in the probability of patients being discharged.[20] Nutritional intake was negatively affected by symptoms of nutritional impact in patients with low HGS.[21] And functional capacity assessment by HGS and ECOG-PS demonstrated moderate and significant agreement.[34]

The different methods used to assess reduced functional capacity were determinant for the diagnosis of malnutrition by the GLIM criteria. When using HGS and free-fat mass index (FFMI) as measures of reduced muscle mass, malnutrition by GLIM was associated with higher mortality among patients, the use of mid-arm circumference (MAC) and arm muscle circumference (AMC) did not present the same effect.[34]

DISCUSSION

The present study aimed to review the literature on the main instruments for screening nutritional risk, assessing malnutrition and functional capacity in hospitalized cancer patients and present the best methods to assess the risks and predict relevant clinical outcomes in this group of patients.

Malnutrition in cancer patients, when not identified, is not treated and, consequently, leads to a worse prognosis with increased clinical complications, length of hospital stay and mortality, as well as decreased response and tolerance to treatment.

Several studies in this review demonstrated an association between clinical outcomes and nutritional risk[18,20,22,27,35,37,41] and patients nutritional status. [20,22,27,35-37,40,43]

In our review, malnutrition risk according to NRS-2002 was associated with prediction of a longer LOS, with similar performance as PG-SGA[20,27] and better performance than MUST and MST.[41] Stating that there is no consensus regarding nutritional screening tools for this population, the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline for cancer patients recommends the use of tools that evaluate Body Mass index (BMI) , weight loss, and an index of food intake, such as NRS-2002, MUST or MST.[2] On the contrary, a review conducted with the intent to identify validated nutritional screening tools for patients with cancer, did not find studies that aimed at validating the NRS-2002.[47]

According to the Academy of Nutrition and Dietetics (AND) adult oncology patients could be screened using MST or MUST.[51] Contrariwise, in our review, we did not find enough evidence to support this statement. Nutritional risk assessed by MST presented excellent performance compared with PG-SGA,[24] but was not a good predictor of postoperative complications.[37] Neither MST nor MUST were efficient in identifying patients at risk for longer LOS.[41] An important difference in results might be related to the assessment of the reduced food intake in each questionnaire. The reduction in food intake accessed by the MST is linked to loss of appetite, while the NRS-2002 option "less food intake in the last week" is not required to be caused by decreased appetite, while MUST does not include a question regarding this matter at all.[41]

In cancer patients serum albumin is considered as a good marker of nutritional status, and higher serum albumin levels are associated with better survival. [52] However, when comparing PG-SGA and NRS-2002 against albumin, one study found that the

agreement of both methods was low, indicating poor consistency of malnutrition identification.[26]

Patients identified as at-risk should be assessed regarding dietary intake, body composition, physical activity and metabolic stress, in order to guide adequate nutritional intervention. There is also no consensus on the individual methods to assess these parameters. Both ESPEN[2] and AND[51], point out the PG-SGA and SGA as valid and reliable tools for a comprehensive nutritional assessment of cancer patients.

In this review, we found that SGA and PG-SGA were the tools for assessment of nutritional status that best determined important clinical outcomes among cancer patients, such as LOS, postoperative complications and mortality.[20,22,27,35,36,40] Another systematic review concluded that malnutrition according to these instruments was a better predictor of LOS in gastrointestinal cancer patients.[53] Compared with the original version, the PG-SGA allows for a more objective nutritional assessment and the identification of nutritional impact symptoms. Its score-based assessment model can be used to demonstrate subtle changes in nutritional status, unlike the SGA, which only classifies patients into categories.

GLIM criteria diagnosis of malnutrition also demonstrated efficacy in predicting overall survival,[36,43] while using NRS-2002 as the nutritional screening tool in the first step of the assessment. A study revealed that among the criteria, unintentional weight loss was the most determining factor acting upon mortality, while reduced muscle mass and reduced food intake showed a moderate impact on survival.[54]

In the present review, both nutritional risk and malnutrition were associated with worse functional capacity accessed by ECOG-PS, KPS and HGS. These findings are in line with the recommendations of ESPEN, which advises the use of ECOG-PS or KPS

for classification of functional capacity, and the use of HGS as a method for monitoring the muscular function of patients.[2] Besides, the three methods are validated, non-invasive and easy to apply.

Implications for clinical practice and research

In order to offer adequate and early nutritional therapy to hospitalized oncological patients, it is important to first know their nutritional status. For such, knowing the instrument of nutritional screening, nutritional assessment and functional capacity that best predict outcomes in this population is essential. Although there is no consensus on a specific and exclusive tool for cancer patients, our findings consent with current guidelines and support the use of PG-SGA to assess patients' nutritional status. Besides, we reinforce the importance of validating NRS-2002 as a screening tool for cancer patients, since its use is widespread. In addition, we encourage the conduct of studies that evaluate the performance of GLIM, with viable alternatives for measuring the reduction of muscle mass, given the promising results of this review.

Limitations

The limitations were some, due to the heterogeneity in the comparison of instruments, cancer diagnosis, cancer treatment and study design, meta-analysis of extracted data was not possible. Since our search strategy was not designed to capture markers of malnutrition, but nutritional evaluating instruments instead, we might have missed studies of biomarkers commonly related to malnutrition, such as Albumin, Hemoglobin and C-Reactive Protein. Also, quality assessment of individual studies presented the majority of the studies as with poor quality.

Our research was limited to instruments applied for the adult and elderly hospitalized cancer population. A strength of this study was the broad inclusion criteria of patients with any oncologic treatment (chemotherapy, radiotherapy e/or surgery) and multiple outcomes. We excluded studies performed in children, adolescents, pregnant women, outpatients, emergency patients, palliative care, critically ill and hematologic cancer patients.

CONCLUSION

PG-SGA is an effective tool for assessing the nutritional status of cancer patients, in accordance with the practices recommended by guidelines in several countries. NRS-2002 as a part of GLIM diagnostic criteria, associated with measures of reduced muscle mass might be an option, but require further studies evaluating representative samples to support the use of these instruments among oncological inpatients. Therefore, the combination of methods such as nutritional screening, nutritional assessment and functional capacity measures are helpful to define the best nutritional therapy for cancer patients.

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Declaration of interest

The authors have no relevant interests to declare.

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Table 1 **PICOS criteria for inclusion of studies**

Parameter	**Criteria**
Population	Hospitalized cancer patients age ≥ 18years, affected by solid tumours, submitted to cancer treatment (chemotherapy,radiation therapy or surgery).
Intervention	-
Comparison	Nutritional risk screening tools, nutritional status and functional capacity assessment tools assessment instruments
Outcomes	Nutritional impact symptoms, length of hospital stay (LOS), infectious and non-infectious complications, morbidity and mortality.
Study design	Cross-sectional, prospective and retrospective observational studies

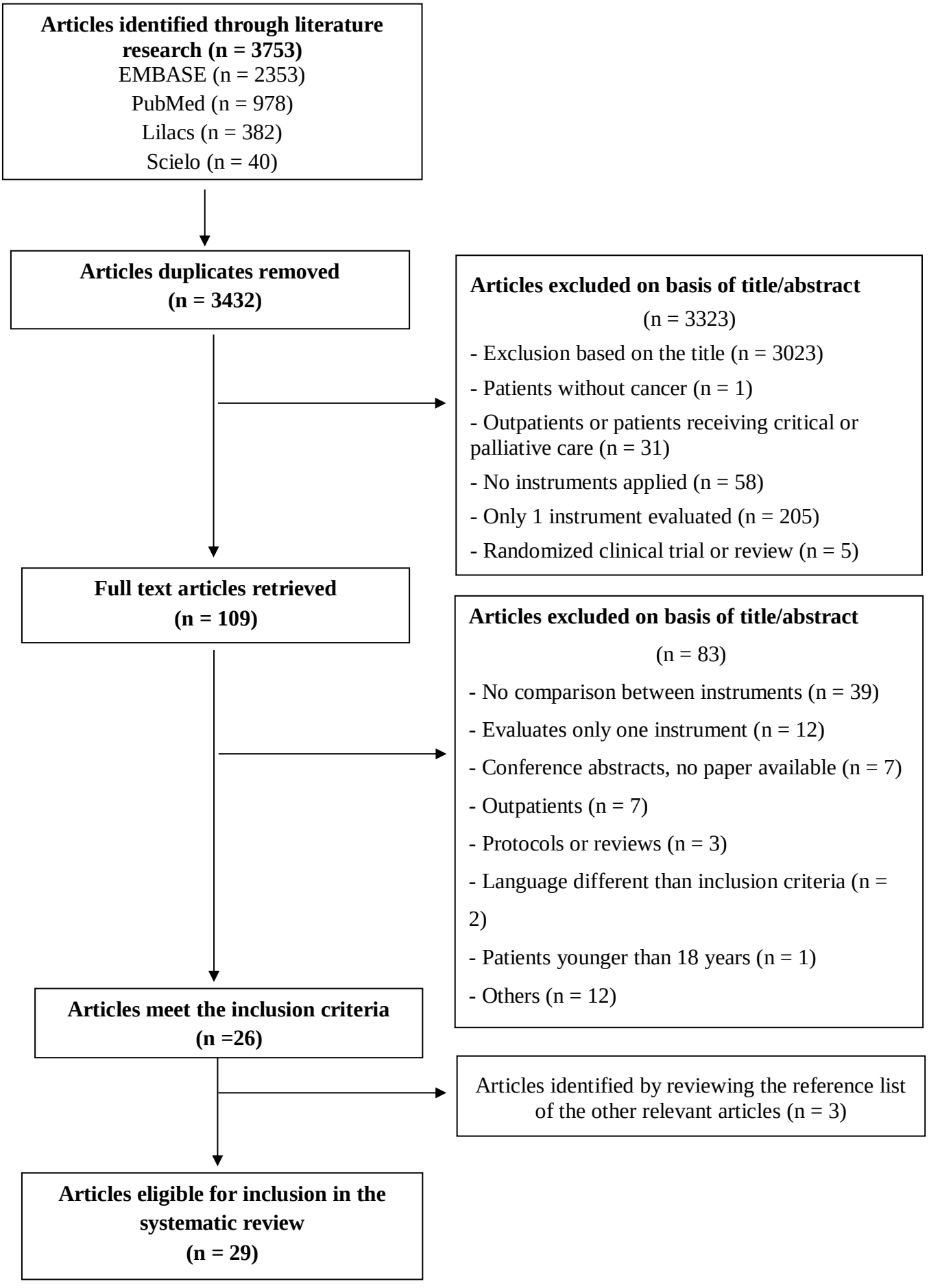

Figure 1 **Flow chart illustrating the literature search and study selection process.**

Table 2. **Characteristics of studies included according to nutritional risk tools**

Reference	Design	Studied population	Cancer diagnosis	Nutritional Tools	Study Objective	Main Results
Haid et al (2012)[17]	Prospective	n = 634 21.8% cancer 57.4 ± 16.3 years old	Malignoma: 120 (18.9%) Gastrointestinal Malignoma: 19 (2.9%)	NRS-2002 INST	Assess the frequency of malnutrition and compare two nutritional screening instruments.	Malignoma* **NRS- 2002:** 31.60 % **INST:** 33.30% Gastrointestinal Malignoma* **NRS-2002:** 63.10% **INST:** 36.80% Agreement: NA Correlations: NA *P value: NA
La Torre et al (2013)[18]	Retrospective Cohort	n = 143 100% cancer 67 (31– 86) years old	Periampullary and Pancreatic carcinoma	NRI MUST	Evaluate the prevalence of malnutrition, by means of screening instruments and to analyze the role of malnutrition in predicting postoperative complications.	NRI† **Mild risk:** 17% **Moderate risk:** 42% **Severe risk:** 41% MUST† **Low risk:** 12% **Medium risk:** 34% **High risk:** 54% Agreement: **MUST and NRI** Overall morbidity — kappa = 0.83** Mortality — kappa = 0.48* SSI — kappa = 0.77** LOS — kappa = 0.89** Correlations: NA

						†P value: NA * kappa between 0.400 and 0.750: fair–good agreement **kappa > 0.750: excellent agreement beyond chance
López et al (2014)[19]	Cross-sectional	n = 277 22.02% cancer 67.71±17.03	-	NRS-2002	Determine the prevalence of hospital malnutrition both at admission and at discharge.	NRS-2002 (Admission)† **Risk of Malnutrition**: 31.15% NRS-2002 (Discharge)† **Risk of Malnutrition**: 60.71% Agreement: **NRS-2002 vs PG-SGA** (Admission) kappa = 0.17 **NRS-2002 vs PG-SGA** (Discharge) kappa = 0.48 Correlations: NA †P value: NA
Mendes et al (2014)[20]	Prospective	n = 130 100% cancer 61.6 ± 14.1 years old	Multiple	NRS-2002	Quantify and compare the association between nutritional status and handgrip strength at hospital admission with time to discharge in cancer patients.	NRS-2002† **Without nutritional risk:** 46.9% **With nutritional risk:** 53.1% NRS-2002 and LOS* **Without nutritional risk:** 7 (4.0 – 11.0) **With nutritional risk:** 13 (8.0 – 25.0) Agreement: NA Correlations: NA †P value: NA *P < 0.0001
Knudsen et al (2015)[21]	Cross-sectional	n = 126 10% cancer 52.0 ± 17.0 years old	-	NRS-2002	Assess the prevalence of NIS among hospitalized patients with gastrointestinal and liver diseases and the relation between NIS and NRS-2002 or nutritional status as	NRS* Without nutritional risk: 60% With nutritional risk: 40% Agreement: NA Correlations: NA *P value: NA

					determined by HGS or BMI.	
Leandro-Merhi et al (2015)[22]	Cross-sectional	n = 500 58% cancer 59 (19– 81) years old	-	NRS-2002	Investigate and compare the efficacy of different nutritional status assessment methods in patients with neoplasms and digestive tract diseases and to determine which instrument best predicts clinical outcomes.	NRS-2002† **Not at Risk:** 63.7% **At Risk:** 37.2% NRS-2002 at Risk **Death:** 63.6%* **LOS:** 9.7 ± 7.2** **Complications:** 36.4%* Agreement: **SGA and NRS-2002** kappa = 0.5262 **NRS-2002 and Anthropometry** kappa = 0.3993 Correlations: NA †P value: NA *P value > 0.05 ** P value < 0.05
López et al (2015)[23]	Cross-sectional	n = 174 total 23.56% cancer 78.43 ± 7.89 years old	-	NRS-2002	Determine the prevalence of malnutrition among >65-year-old patients admitted to our center, both in admission and discharge	NRS-2002 (Admission)† **Risk of Malnutrition**: 34.14% NRS-2002 (Discharge)† **Risk of Malnutrition**: 57.89% Agreement: **NRS-2002 vs PG-SGA (Admission)** kappa = 0.16 **NRS-2002 vs PG-SGA (Discharge)** kappa = NA Correlations: NA †P value: NA
Shaw et al (2015)[24]	Cross-sectional	n = 126 100% cancer 59 (19– 81) years old	Multiple	RMNST MST	Evaluate the sensitivity of the RMNST and the	RMNST† **Well Nourished:** 20% **Moderate Nourished:** 26%

					MST against the PG-SGA.	**Malnourished:** NA **Severely Malnourished:** 54% MST† **Well Nourished:** 48% **Moderate Nourished:** NA **Malnourished:** 52% **Severely Malnourished:** NA Agreement: NA Correlations (AUROC): **RMNST** 0.84 **MST** 0.83 †P value: NA
Badosa et al (2017)[25]	Prospective	N = 409 20.1% cancer 61.8 ± 16.9 years old	-	MUST SNAQ	Assess the risk of malnutrition in patients recently admitted to a third-level hospital and to estimate the associations between risk of malnutrition and comorbidities, LOS and mortality.	MUST* **Not undernourished:** 82.5% **Undernourished:** 17.5% SNAQ** **Not Undernourished:** 71.6% **Undernourished:** 28.4% Agreement: NA Correlations: NA *P value > 0.05 **P value < 0.001
Du et al (2017)[26]	Cross-sectional	n = 927 100% cancer 61 years (52-78) years old	Multiple	NRS-2002	Analyze the potential relationship of the PG-SGA with nutritional status assessed by NRS-2002, anthropometry and biochemical indicators to determine its value	NRS-2002† **At nutritional risk:** 30.7% Agreement: **NRS-2002 vs Albumin** kappa = 0.160* **PG-SGA vs Albumin** kappa = 0.251*

					as a clinical tool for integration in the assessment of patients with cancer.	Correlations: **NRS-2002 *vs* PG-SGA** Women r = 0.575** Men r = 0.543** †P value: NA *P value < 0.05 **P value < 0.001
Leandro-Merhi et al (2017)[27]	Cross-sectional	n = 600 50% cancer 52.6% (< 60 years old) 47.3% (≥ 60 years old)	Multiple	NRS-2002	Determine the relationship between nutritional status and the clinical outcomes of patients with and without neoplasms during hospital stay.	NRS-2002: With and without complications* **At risk:** 53.8% and 38.3% **Not at risk:** 46.2% and 61.7% NRS-2002: No death and death** **At Risk:** 39.1% and 72.7% **Not At Risk:** 60.9% and 27.3% NRS-2002: Length of stay ≤ 6 days and ≥ 7 days** **At Risk:** 30.8% and 49.0% **Not at risk:** 69.2% and 51.0% Agreement: NA Correlations: NA *P value > 0.05 **P value < 0.05
Leandro-Merhi, et al (2017)[28]	Cross-sectional	n = 79 100% cancer 71.5 ± 5.8 years old	Multiple	NRS-2002	Investigate the nutritional indicators that best predict nutritional risk according to the NRS-2002, to verify the agreement between the nutritional assessment methods.	NRS-2002† **At nutritional risk:** 43.04% **No nutritional risk:** 56.96% Agreement: **SGA *vs* NRS-2002** kappa = 0.2386 **MNA-SF *vs* NRS-2002** kappa = 0.5281 Correlations: NA †P value: NA

Doundoulakis, et al (2018)[31]	Cross-sectional	n = 2970 49 oncologic patients 67.6 ± 12.6 years old	-	NRS-2002 MUST	Evaluate the nutrition risk.	NRS-2002† **Low/Medium Nutritional Risk:** 76.2% **High Nutritional Risk:** 16.7% MUST† **Medium Nutritional Risk:** 38.3% **High Nutritional Risk:** 23.4% Adjusted OR for malnutrition: **NRS-2002** 2.28 (95% CI: 1.52-3.40)* **MUST** 2.39 (95% CI: 1.69-3.37)* Agreement: NA Correlations: NA †P value: NA *P value: < 0.001
Lima et al (2018)[33]	Cross-sectional	n = 87 70% cancer 64.2 ± 12.0 years	-	GMS	Evaluate the agreement of the GMS with subjective methods of nutritional evaluation in hospitalized patients.	GMS† **Nutritional Risk:** 64.4% Agreement: **GMS *vs* MNA-SF** kappa = 0.602* **GMS *vs* PG-SGA** kappa = 0.648* Correlations: **GMS *vs* MNA-SF** r = - 0.674* **GMS *vs* PG-SGA** r = 0.767* †P value: NA *P value < 0.001
Zhu et al (2018)[35]	Cross-sectional	n = 466 100% cancer 50.6 ± 11.9 years old	Multiple	NRS-2002	Investigate the prevalence of malnutrition and distress in cancer patients and to examine	NRS-2002† **Nutritional risk:** 25.8% Agreement: NA Correlations with Psychological Distress:

					the relationship between them.	**NRS-2002** r = 0.142* †P value: NA *P value < 0.001
Eu et al, (2019)[37]	Prospective	n = 85 100% cancer 20 - 80 years old	Bone sarcoma	MST 3MinNS	Determine the prevalence of malnutrition during preoperative period.	MST† **Malnutrition:** 29.41% 3MinNS† **Malnutrition:** 23.53% Adjusted OR for precision of tools and postoperative complications: Infectious **MST** 1.49 (95% CI: 0.74 – 3.00)† **3MinNS** 1.69 (95% CI: 1.31 – 2.17)** Non infectious **MST** 1.50 (95% CI: 0.663 – 0.330)† **3MinNS** 1.503 (95% CI: 1.069 – 0.019)* Agreement: NA Correlations: NA †P value: NA *P value > 0.05 **P value < 0.001
Wen Dong, et al (2020)[39]	Prospective	n = 138 100% cancer 60.59 ± 7.775 years old	Esophageal	NRS-2002 NRI	Determine the most appropriate nutritional risk screening system for esophageal cancer patients in China.	NRS-2002 † **No risk:** 43.5% **Mildly:** 35.5% **Severely:** 21.0% NRI † **No risk:** 58.0% **Mildly:** 39.1% **Severely:** 2.9% Agreement: NA

						Correlations (AUROC): **NRS-2002** 0.722 **NRI** 0.796 †P value: NA
Ma, et al (2020)[41]	Cross-sectional	n = 197 100% cancer 61.82 (8.77) years old	Laryngeal	NRS-2002 MUST MST	Compare NRS-2002, MUST and MST in inpatients with laryngeal cancer, and identify which is the most accurate.	NRS-2002† **Admission nutritional risk:** 14.7% **Discharge nutritional risk:** 27.9% MUST† **Admission nutritional risk:** 22.3% **Discharge nutritional risk:** 26.9% MST† **Admission nutritional risk:** 4.6% **Discharge nutritional risk:** 11.2% Adjusted OR for association between malnutrition and long LOS (≥15 days): NRS-2002 5.59 (95% CI: 1.86–16.81)* MUST 2.05 (95% CI: 0.96–4.39) MST 3.39 (95% CI: 0.63–18.13) Agreement: Admission **MUST vs NRS-2002** kappa = 0.584 **MST vs NRS-2002** kappa = 0.208 Discharge **MUST vs NRS-2002** kappa = 0.413 **MST vs NRS-2002** kappa = 0.243

						Correlations: NA †P value: NA *P value <0.05	
Zhang, et al (2021)[43]	Retrospective Cohort	N = 1492 100% cancer ≥ 65 years old	Multiple	NRS-2002	Investigate the application of the GLIM criteria in nutrition assessment and survival prediction.	Primary Cohort† NRS-2002 **Nutritional Risk:** 64.8% Validation Cohort NRS-2002† **Nutritional Risk:** 67.3% Agreement: NA Correlations: NA †P value: NA	
Zhang, et al (2021)[44]	Cross-sectional	n = 637 100% cancer 56.8 ± 14.4 years old	Multiple	NRS-2002 MUST	Evaluate the diagnostic capacity of the NRS 2002, MUST, PG-SGA in light of the GLIM criteria.	NRS-2002† **Nutritonal Risk:** 24.8% MUST† **Nutritional Risk:** 15.4% Agreement: **GLIM vs NRS-2002** **GLIM vs MUST** Correlations: NA †P value: NA *P value < 0.001	 kappa = 0.823* kappa = 0.596*

Abbreviations: 3MinNS, 3-minute nutritional screening; GLIM, global leadership initiative on malnutrition; GMS, graz malnutrition screening; INST, innsbruck nutrition screening tool; LOS, length of stay; MNA, mini nutritional assessment full version; MNA-SF, mini nutritional assessment–short form; MST, malnutrition screening tool; MUST, malnutrition universal screening ool; NR, not reported, NA, not applicable; NIS, nutrition impact symptoms; NRI, nutritional risk index; NRS, nutritional risk screening; PG-SGA, patient generated subjective global assessment; RMNST, royal marsden nutrition screening tool; ROC, receiver operator curve; SGA, subjective global Assessment; SNAQ, short nutritional assessment questionnaire.

Table 3. **Characteristics of studies included according to nutritional assessment tools**

Reference	Design	Studied population	Cancer diagnosis	Nutritional Tools	Study Objective	Main Results
La Torre, et al (2013)[18]	Retrospective Cohort	n = 143 100% cancer 67 (31– 86) years old	Periampullary and Pancreatic carcinoma	SGA	Evaluate the prevalence of malnutrition, by means of screening instruments and to analyze the role of malnutrition in predicting postoperative complications.	SGA† **Well Nourished:** 48% **Moderately Undernourished:** 37% **Severely Undernourished:** 15% Agreement: **MUST and SGA** Overall morbidity kappa = 0.68* Mortality kappa = 0.39 SSI kappa = 0.79** LOS kappa = 0.52* Correlations: NA †P value: NA * kappa between 0.400 and 0.750: fair–good agreement **kappa > 0.750: excellent agreement beyond chance
López, et al (2014)[19]	Cross-sectional	n = 277 22.02% cancer 67.71±17.03	-	PG-SGA	Determine the prevalence of hospital malnutrition both at admission and at discharge.	PG-SGA (Admission)† **Moderate Malnutrition:** 38.98% **Severe Malnutrition:** 13.56% Agreement: **NRS-2002 vs PG-SGA** (Admission) kappa = 0.17 **NRS-2002 vs PG-SGA** (Discharge) kappa = 0.48 Correlations: NA †P value: NA
Mendes, et al (2014)[20]	Prospective	n = 130 100% cancer 61.6 ± 14.1 years old	Multiple	PG-SGA	Quantify and compare the association between nutritional status and handgrip	PG-SGA† **Well nourished:** 35.4% **Moderate undernutrition:** 42.3%

					strength at hospital admission with time to discharge in cancer patients.	**Severe undernutrition:** 22.3% PG-SGA and LOS* **Well nourished:** 7 (4.0 – 13.8) **Moderate undernutrition:** 9 (5.0 – 15.5) **Severe undernutrition:** 17 (12.0 – 31.5) Agreement: NA Correlations: NA †P value: NA *P value < 0.0001
Leandro-Merhi, et al (2015)[22]	Cross-sectional	n = 500 58% cancer 59 (19– 81) years old	-	SGA	Investigate and compare the efficacy of different nutritional status assessment methods in patients with neoplasms and digestive tract diseases and to determine which instrument best predicts clinical outcomes.	SGA† **Well nourished:** 62.4% **Malnourished:** 37.5% SGA Malnourished: **Death:** 72.7%** **LOS:** 10.9 ± 8.9*** **Complications:** 40.9%* Agreement: **SGA and NRS-2002** kappa = 0.5262 **SGA and Anthropometry** kappa = 0.3931 Correlations: NA †P value: NA *P value > 0.05 **P value < 0.05 ***P value < 0.0001
López, et al (2015)[23]	Cross-sectional	n = 174 total 23.56% cancer 78.43 ± 7.89 years old	-	PG-SGA MNA-SF	Determine the prevalence of malnutrition among >65-year-old patients admitted to our center, both in	PG-SGA (Admission)† **Moderate Malnutrition:** 46.15% **Severe malnutrition:** 10.26% MNA-SF (Admission)† **Nutritional Risk:** 44.59%

					admission and discharge	**Malnutrition:** 23.07% Agreement: **NRS-2002 vs PG-SGA (Admission)** kappa = 0.16 **NRS-2002 vs PG-SGA (Discharge)** kappa = NA **MNA-SF vs PG-SGA (Admission)** kappa = 0.16 **MNA-SF vs PG-SGA (Discharge)** kappa = NA Correlations: NA †P value: NA
Shaw, et al (2015)[24]	Cross-sectional	n = 126 100% cancer 59 (19– 81) years old	Multiple	PG-SGA	Evaluate the sensitivity of the RMNST and the MST against the PG-SGA.	PG-SGA* **Well-nourished:** 29% **Moderately nourished:** 50% **Malnourished:** NA **Severely malnourished:** 21% Agreement: NA Correlations: NA *P value: NA
Du, et al (2017)[26]	Cross-sectional	n = 927 100% cancer 61 years (52-78) years old	Multiple	PG-SGA	Analyze the potential relationship of the PG-SGA with nutritional status assessed by NRS-2002, anthropometry and biochemical indicators to determine its value as a clinical tool for integration in the assessment of patients with cancer.	PG-SGA† **Well-nourished:** 13.7% **Moderately malnourished:** 57.8% **Severely malnourished:** 28.5% Agreement: **PG-SGA vs Albumin** kappa = 0.251* Correlations: **NRS-2002 *vs* PG-SGA** Women r = 0.575** Men r = 0.543** †P value: NA

						*P value < 0.05 **P value < 0.001
Leandro-Merhi, et al (2017)[27]	Cross-sectional	n = 600 50% cancer 52.6% (< 60 years old) 47.3% (≥ 60 years old)	Multiple	SGA	Determine the relationship between nutritional status and the clinical outcomes of patients with and without neoplasms during hospital stay.	SGA: With and without complications** **Malnourished:** 46.2% and 23.8% **Well Nourished:** 53.8% and 76.2% SGA: No death and death** **Malnourished:** 25.3% and 63.6% **Well Nourished:** 74.7% and 36.4% SGA Length of stay ≤ 6 days and ≥ 7 days** **Malnourished**: 18.2% and 34.4% **Well nourished**: 81.8% and 65.6% Agreement: NA Correlations: NA *P value > 0.05 **P value < 0.05
Leandro-Merhi, et al (2017)[28]	Cross-sectional	n = 79 100% cancer 71.5 ± 5.8 years old	Multiple	SGA MNA long form	Investigate the nutritional indicators that best predict nutritional risk according to the NRS-2002, to verify the agreement between the nutritional assessment methods.	SGA† **Malnourished:** 20.51% **Well nourished:** 79.49% MNA† **Malnourished:** 13.92% **Risk of malnutrition:** 43.04% **Nourished:** 43.04% Agreement: **SGA *vs* NRS-2002** kappa = 0.2386 **MNA *vs* NRS-2002** kappa = 0.5281 Correlations: NA †P value: NA

Péres-Cruz, et al (2017)[29]	Retrospective	n = 57 100% cancer 57.8 ± 14.5 years old	Digestive Tract	SGA	Determine the nutritional status and its association with functional capacity.	SGA† **Moderate Malnourished:** 21% **Severe Malnourished:** 61.5% Association between SGA and KPS of the patients who showed malnourishment: **Activity limitations:** 78.7% $x^2 = 1.56$* Agreement: NA †P value: NA *P value > 0.05
Quyen, et al (2017)[30]	Cross-sectional	n = 64 patients 100% cancer 54.9 ± 6.52 years old	Esophageal	SGA PG-SGA	Determine the nutritional status of patients with esophageal cancer, and to investigate its relationship with performance status and prognosis.	SGA† **Well Nourished:** 50% **Moderate Malnourished:** 43.8% **Severe Malnourished:** 6.2% PG-SGA† **Well nourished or anabolic:** 4.7% **Moderate undernutrition:** 40.6% **Severe undernutrition:** 54.7% Agreement: NA Correlations: **SGA vs KPS** r = - 0.632* **SGA vs ECOG-PS** r = 0.626* **PG-SGA vs KPS** r = - 0.717* **PG-SGA vs ECOG-PS** r = 0.672* †P value: NA *P value < 0.001
Doundoulakis, et al (2018)[31]	Cross-sectional	n = 2970 49 oncologic patients 67.6 ± 12.6 years old	-	MNA-SF	Evaluate the nutrition risk.	MNA-SF† **Medium Nutritional Risk:** 45.5% **High Nutritional Risk:** 48.5%

						Adjusted OR for malnutrition: **MNA-SF** 1.42 (95% CI: 0.94-2.16)* Agreement: NA Correlations: NA †P value: NA *P value > 0.05 **P value < 0.001
Hu, et al (2018)[32]	Retrospective	n = 11314 100% cancer (18-90) years old	Multiple	PG-SGA	Explore the nutritional assessment value and determinants of HGS in patients hospitalized with cancer.	PG-SGA† Adults **Moderate or suspected malnutrition:** 30.3% **Severely malnourished:** 22.3% Elderly **Moderate or suspected malnutrition:** 36.4% **Severely malnourished:** 37.8% Agreement: NA Correlations: **PG-SGA vs HGS** Adult Men r = - 0.215* Adult Women r = - 0.244* Elderly Men r = - 0.253* Elderly Women r = - 0.259* †P value: NA *P value < 0.001
Lima, et al (2018)[33]	Cross-sectional	n = 87 70% cancer 64.2 ± 12.0 years	-	PG-SGA MNA-SF	Evaluate the agreement of the GMS with subjective methods of nutritional evaluation in hospitalized patients.	PG-SGA† **Moderate or Severe Malnourished:** 47.1% MNA-SF† **Nutritional Risk or Malnourished:** 49.4%

						†P value: NA
Steemburgo, et al (2018)[34]	Cross-sectional	n = 76 patients 100% cancer 56.0±17.0 years old	Multiple	PG-SGA	Assess nutritional status through the PG-SGA and functional capacity through HGS and ECOG-PS; and associate HGS and nutritional status according to PG-SGA.	PG-SGA† **Malnutrition:** 53.9% Significant association between the worst nutritional status (severely malnourished): **PG-SGA vs HGS** 24.0 ± 10.4kg* **PG-SGA vs ECOG-PS** 3.0 (1.0-3.0)* †P value: NA *P value < 0.05
Zhu, et al (2018)[35]	Cross-sectional	n = 466 100% cancer 50.6 ± 11.9 years old	Multiple	PG-SGA	Investigate the prevalence of malnutrition and distress in cancer patients and to examine the relationship between them.	PG-SGA† **Nutritional risk:** 39.1% Agreement: NA Correlations with Psychological Distress: **PG-SGPA** r = 0.148* †P value: NA *P value < 0.001
Contreras-Bolívar, et al (2019)[36]	Prospective	n = 282 100% cancer 60.4 ± 12.6 years old	Multiple	SGA GLIM	Determine the prevalence of malnutrition according to SGA and GLIM criteria and to determine which nutrition-related classification better predicts six-month mortality.	SGA† **Normally Nourished:** 18.4% **Moderate malnutrition:** 25.5% **Severe malnutrition:** 56.1% GLIM criteria using MAC† **Normally Nourished:** 27.8% **Moderate malnutrition:** 72.2% GLIM criteria using AMC† **Normally Nourished:** 28.2% **Moderate malnutrition:** 71.8% GLIM criteria using FFMI† **Normally Nourished:** 22.0%

Moderate malnutrition: 77.6%

GLIM criteria using HGS†
Normally Nourished: 20.0%
Moderate malnutrition: 80.0%

Adjusted OR for association between malnutrition and mortality (six-month mortality risk):

SGA
Normally nourished *vs* Moderate Malnutrition
1.65 (95% CI: 0.78 – 3.5)*

Normally nourished *vs* Severe Malnutrition
2.87 (95% CI: 1.47 – 5.6)**

Normally nourished *vs* Malnutrition
2.41 (95% CI: 1.27 – 4.6)**

GLIM criteria using MAC
1.72 (95% CI: 0.99 – 3.01)*

GLIM criteria using AMC
1.61 (95% CI: 0.93 – 2.75)*

GLIM criteria using FFMI
1.94 (95% CI: 1.08 – 3.48)**

GLIM criteria using HGS
1.61 (95% CI: 0.93 – 2.75)**

Agreement: NA

Correlations: NA

						†P value: NA *P value > 0.05 **P value < 0.05
Eu, et al (2019)[37]	Prospective	n = 85 100% cancer 20 - 80 years old	Bone sarcoma	PG-SGA	Determine the prevalence of malnutrition during preoperative period.	PG-SGA† **Moderate Malnutrition:** 32.94% **Severe Malnutrition:** 12.94% Adjusted OR for precision of tools and post-operative complications: Infectious **PG-SGA** 1.99 (95% CI: 0.21 – 18.52)† Non infectious **PG-SGA** 1.56×10^9 (95% CI: 0.000)† Agreement: NA Correlations: NA †P value: NA
Yanaranop, et al (2019)[38]	Prospective	n = 200 100% cancer	Gynecologic	SGA	Determine the prevalence of malnutrition in Thai women with gynecologic cancer undergoing surgery and to identify malnutrition-associated risk factors for adverse surgical outcomes.	SGA† **Well Nourished:** 79.5% **Modetated Malnourished:** 20.5% ECOG-PS *vs* SGA (Well Nourished and Moderated Malnourished)* **Score 0**: 44.7% and 2.2% **Score 1:** 51.6% and 63.4% **Score2:** 3.8% and 24.2% Agreement: NA Correlations: NA †P value: NA *P value < 0.001

Wen Dong, et al (2020)[39]	Prospective	n = 138 100% cancer 60.59 ± 7.775 years old	Esophageal	PG-SGA	Determine the most appropriate nutritional risk screening system for esophageal cancer patients in China.	PG-SGA† **No risk:** 2.9% **Mildly:** 19.6% **Severely:** 77.5% Agreement: NA Correlations: AUROC **PG-SGA** 0.515 †P value: NA
Guo, et al (2020)[40]	Cross-sectional	n = 2322 100% cancer 62 (25 - 90) years old	Gastric	PG-SGA	Evaluate the nutritional status of hospitalized patients and to analyze the influence of their nutritional status on their quality of life.	PG-SGA† **Moderate Malnutrition:** 35.3% **Severe Malnutrition:** 45.1% Association between the PG-SGA and nutritional parameters: NRS-2002 3.41 ± 1.26* HGS 21.6 ± 11.2* KPS 77.1 ± 16.86* Agreement: NA Correlations: **PG-SGA *vs* NRS-2002** r = 0.455* **PG-SGA *vs* HGS** r = -0.165* **PG-SGA vs KPS** r = -0.380* † P value: NA *P value < 0.001
Mendes, et al (2020)[41]	Retrospective	n = 76 100% cancer 56.8 ± 16.6 years old	Multiple	PG-SGA	Compare HGS with objective methods of nutritional assessment and to propose a cut-off point for its use as a	PG-SGA† **Malnourished:** 53.9% Agreement: NA Correlations:

					predictor of malnutrition.	**PG-SGA *vs* HGS**	r = 0.332* †P value: NA *P value < 0.05
Zhang, et al (2021)[43]	Retrospective Cohort	n = 1492 100% cancer ≥ 65 years old	Multiple	GLIM	Investigate the application of the GLIM criteria in nutrition assessment and survival prediction.	Primary Cohort GLIM† **Malnourished:** 48.8% Validation Cohort GLIM† **Malnourished:** 46.0% Agreement: NA Correlations: GLIM and Overall Survival **Moderate malnutrition** HR 1.35 (95% CI: 1.09 - 1.66)* **Severe malnutrition:** HR 1.71 (95% CI: 1.37 - 2.14)** †P value: NA *P value: <0.005 **P value: < 0.001	
Zhang et al, (2021)[44]	Cross-sectional	n = 637 100% cancer 56.8 ± 14.4 years old	Multiple	PG-SGA GLIM	Evaluate the diagnostic capacity of the NRS 2002, MUST, PG-SGA in light of the GLIM criteria.	PG-SGA† **Well-Nourished:** 56.7% **Malnourished:** 43.3% GLIM† **Malnourished:** 28.3% Agreement: **GLIM vs NRS-2002** **GLIM vs PG-SGA** **GLIM vs MUST**	 kappa = 0.823* kappa = 0.453* kappa = 0.596*

	Correlations: NA
	†P value: NA
	*P value < 0.001

Abbreviations: NRS-2002: Nutritional Risk Screening; INST: Innsbruck Nutrition Screening Tool; NA: Not Available; MUST: Malnutrition Universal Screening Tool; SNAQ: Short Nutritional Assessment Questionnaire; LOS: Length Of Hospital Stay; SGA: Subjective Global Assessment; NRI: Nutritional Risk Index; PG-SGA: Patient Generated Subjective Global Assessment; MNA-SF: Mini Nutritional Assessment Short Form; HGS: Hand Grip Strength; RMNST: Royal Marsden Nutrition Screening Tool; NIS: Nutrition Impact Symptoms; MST: Malnutrition Screening Tool; KPS: Karnofsky Performance Status Score; ECOG-PS: Eastern Cooperative Oncology Group Performance Scores; GMS: Graz Malnutrition Screening; AWGS: Working Group for Sarcopenia; GLIM: Global Leadership Initiative on Malnutrition; MAC: Mid-Arm Circumference; AMC: Arm Muscle Circumference; FFMI: Fat-Free Mass Index; 3MinNS: 3-minute Nutritional Screening; AUROC: area under receiver operating characteristic; SSI: Surgical site infection.

Table 4. **Characteristics of studies included according to functional capacity tools**

Reference	Design	Studied population	Cancer diagnosis	Nutritional Tools	Study Objective	Main Results
Mendes, et al (2014)[20]	Prospective	n = 130 100% cancer 61.6 ± 14.1 years old	Multiple	HGS	Quantify and compare the association between nutritional status and handgrip strength at hospital admission with time to discharge in cancer patients.	HGS† **Women:** 17.8 ± 6.2 **Men:** 30.0 ± 8.2 HGS and LOS* **High:** 6 (4.0 -11.0) **Intermediate:** 12 (7.3 - 23.3) **Low:** 17 (7.0 - 32.0) Agreement: NA Correlations: NA †P value: NA *P value < 0.0001
Knudsen, et al (2015)[21]	Cross-sectional	n = 126 10% cancer 52.0 ± 17.0 years old	-	HGS	Assess the prevalence of NIS among hospitalized patients with gastrointestinal and liver diseases and the relation between NIS and NRS-2002 or nutritional status as determined by HGS or BMI.	HGS* Normal: 31% Low: 69% Agreement: NA Correlations: NA †P value: NA *P value: <0.001
Du, et al (2017)[26]	Cross-sectional	n = 927 100% cancer 61 years (52-78) years old	Multiple	HGS	Analyze the potential relationship of the PG-SGA with nutritional status assessed by NRS-2002, anthropometry and biochemical indicators to determine its value as a clinical tool for	HGS* Men: 20.00 (12-27.93) kg Women: 4.05 (10-20) kg Agreement: NA Correlations: Man

					integration in the assessment of patients with cancer.	**HGS *vs* PG-SGA** **HGS *vs* NRS-2002** Woman **HGS *vs* PG-SGA** **HGS *vs* NRS-2002** †P value: NA *P value < 0.001	r = -0.333* r = -0.324* r = -0.219* r = -0.239*
Péres-Cruz, et al (2017)[29]	Retrospective	n = 57 100% cancer 57.8 ± 14.5 years old	Digestive Tract	KPS	Determine the nutritional status and its association with functional capacity.	KPS† **Normal:** 24.5% **Activity limitations**: 75.5% Association between SGA and KPS of the patients who showed malnourishment: **Activity limitations:** 78.7% Agreement: NA Correlations: **KPS *vs* Cancer Stage** †P value: NA *P value > 0.05 **P value = 0.001	 x^2 = 1.56* r = 0.489**
Quyen, et al (2017)[30]	Cross-sectional	n = 64 patients 100% cancer 54.9 ± 6.52 years old	Esophageal	ECOG-PS KPS	Determine the nutritional status of patients with esophageal cancer, and to investigate its relationship with performance status and prognosis.	ECOG-PS: 1.47±0.67 KPS: 77.5±15.1 Agreement: NA Correlations: **SGA vs KPS** **SGA vs ECOG-PS** **PG-SGA vs KPS**	 r = - 0.632* r = 0.626* r = - 0.717*

						PG-SGA vs ECOG-PS r = 0.672* *P value < 0.001
Hu, et al (2018)[32]	Retrospective	n = 11314 100% cancer (18-90) years old	Multiple	HGS KPS	Explore the nutritional assessment value and determinants of HGS in patients hospitalized with cancer.	HGS † Adults **Men:** 31.4±11.9 kg **Women:** 20.0±7.6 kg Agreement: NA Correlations: **PG-SGA vs HGS** Adult Men r = - 0.215* Adult Women r = - 0.244* Elderly Men r = - 0.253* Elderly Women r = - 0.259* †P value: NA *P value < 0.001
Steemburgo, et al (2018)[34]	Cross-sectional	N = 76 patients 100% cancer 56.0±17.0 years old	Multiple	HGS ECOG-PS	Assess nutritional status through the PG-SGA and functional capacity through HGS and ECOG-PS; and associate HGS and nutritional status according to PG-SGA.	HGS† **Low Functional Capacity:** 81.3% ECOG-PS† **Limitations:** 39.2% Significant association between the worst nutritional status (severely malnourished): **PG-SGA vs HGS** 24.0 ± 10.4kg* **PG-SGA vs ECOG-PS** 3.0 (1.0-3.0)* Agreement: **HGS vs ECOG-PS** kappa = 0.427** Correlation: **HGS vs ECOG-PS** r = 0.136* †P value: NA

						*P value < 0.05 **P value < 0.001
Contreras-Bolívar, et al (2019)[36]	Prospective	n = 282 100% cancer 60.4 ± 12.6 years old	Multiple	HGS	Determine the prevalence of malnutrition according to SGA and GLIM criteria and to determine which nutrition-related classification better predicts six-month mortality.	GLIM criteria using HGS† **Normally Nourished:** 20.0% **Moderate malnutrition:** 80.0% GLIM criteria using FFMI† **Normally Nourished:** 22.0% **Moderate malnutrition:** 77.6% Adjusted OR for association between malnutrition and mortality (six-month mortality risk): GLIM criteria using MAC 1.72 (95% CI: 0.99 – 3.01)* GLIM criteria using AMC 1.61 (95% CI: 0.93 – 2.75)* GLIM criteria using FFMI 1.94 (95% CI: 1.08 – 3.48)** GLIM criteria using HGS 1.61 (95% CI: 0.93 – 2.75)** Agreement: NA Correlations: NA †P value: NA *P value > 0.05 **P value < 0.05
Yanaranop, et al (2019)[38]	Prospective	n = 200 100% cancer	Gynecologic	ECOG-PS	Determine the prevalence of malnutrition in Thai women with gynecologic cancer	ECOG-PS *vs* SGA (Well Nourished and Moderate Malnourished* **Score 0**: 44.7% and 2.2% **Score 1:** 51.6% and 63.4% **Score2:** 3.8% and 24.2%

					undergoing surgery and to identify malnutrition-associated risk factors for adverse surgical outcomes.	Agreement: NA Correlations: NA *P value < 0.001
Guo, et al (2020)[40]	Cross-sectional	n = 2322 100% cancer 62 (25 - 90) years old	Gastric	HGS KPS	Evaluate the nutritional status of hospitalized patients and to analyze the influence of their nutritional status on their quality of life.	Association between the PG-SGA and functional capacity: HGS: 21.6 ± 11.2* KPS: 77.1 ± 16.86* Agreement: NA Correlations: **PG-SGA *vs* HGS** r = -0.165* **PG-SGA vs KPS** r = -0.380* *P value < 0.001
Mendes, et al (2020)[42]	Retrospective	n = 76 100% cancer 56.8 ± 16.6 years old	Multiple	HGS	Compare HGS with objective methods of nutritional assessment and to propose a cut-off point for its use as a predictor of malnutrition.	HGS† **Malnourished:** 81.6% Agreement: NA Correlations: **PG-SGA *vs* HGS** r = 0.332* †P value: NA *P value < 0.05
Zhang, et al (2021) China[43]	Retrospective Cohort	n = 1492 100% cancer ≥ 65 years old	Multiple	ECOG-PS	Investigate the application of the GLIM criteria in nutrition assessment and survival prediction.	Primary Cohort† ECOG-PS in malnourished patients: **33.3% poor ECOG-PS (>1)** Validation Cohort† ECOG-PS in malnourished patients:

		31.7% poor ECOG-PS (>1) Agreement: NA Correlations: **ECOG-PS *vs* Malnutrition** 1.73 (95% CI: 1.40 – 2.14)* †P value: NA *P value <0.001

Abbreviations: NRS-2002: Nutritional Risk Screening; INST: Innsbruck Nutrition Screening Tool; NA: Not Available; MUST: Malnutrition Universal Screening Tool; SNAQ: Short Nutritional Assessment Questionnaire; LOS: Length Of Hospital Stay; SGA: Subjective Global Assessment; NRI: Nutritional Risk Index; PG-SGA: Patient Generated Subjective Global Assessment; MNA-SF: Mini Nutritional Assessment Short Form; HGS: Hand Grip Strength; RMNST: Royal Marsden Nutrition Screening Tool; NIS: Nutrition Impact Symptoms; MST: Malnutrition Screening Tool; KPS: Karnofsky Performance Status Score; ECOG-PS: Eastern Cooperative Oncology Group Performance Scores; GMS: Graz Malnutrition Screening; AWGS: Working Group for Sarcopenia; GLIM: Global Leadership Initiative on Malnutrition; MAC: Mid-Arm Circumference; AMC: Arm Muscle Circumference; FFMI: Fat-Free Mass Índex; 3MinNS: 3-minute Nutritional Screening; AUROC: area under receiver operating characteristic; SSI: Surgical site infection.

Table 5 **Characteristics of the malnutrition instruments**

	Anthropometrics					**Dietary intake and symptoms**				**Age / Metabolic stress**			**Biochemical**
Tools	Weight Loss	BMI	Muscle Mass	Physical exam	Functional Capacity	Food intake	Appetite	Supplementation or Tube Feeding	NIS	Age	Severity of the disease / Metabolic stress	Psychological stress / Neuropsychological problems	Albumin
GMS	**x**	**x**				**x**				**x**	**x**		
NRS 2002	**x**	**x**				**x**				**x**	**x**		
RMNST	**x**			**x**		**x**			**x**				
MST	**x**					**x**							
3-MinNS	**x**			**x**		**x**							
MUST	**x**	**x**									**x**		
INST	**x**	**x**				**x**				**x**			
NRI	**x**												**x**
MNA	**x**	**x**	**x**		**x**	**x**				**x**	**x**	**x**	
MNA-SF	**x**	**x**	**x**		**x**	**x**					**x**	**x**	
SGA	**x**			**x**	**x**	**x**			**x**		**x**		
PG-SGA	**x**			**x**	**x**	**x**			**x**	**x**	**x**		
SNAQ	**x**						**x**	**x**					
GLIM	**x**	**x**	**x**			**x**					**x**		

Abbreviations: NRS-2002: Nutritional Risk Screening; INST: Innsbruck Nutrition Screening Tool; MUST: Malnutrition Universal Screening Tool; SNAQ: Short Nutritional Assessment Questionnaire; SGA: Subjective Global Assessment; NRI: Nutritional Risk Index; PG-SGA: Patient Generated Subjective Global Assessment; MNA: Mini Nutritional assessment Full Version; MNA-SF: Mini Nutritional Assessment Short Form; RMNST: Royal Marsden Nutrition Screening Tool; NIS: Nutrition Impact Symptoms; MST: Malnutrition Screening Tool; GMS: Graz Malnutrition Screening; GLIM: Global Leadership Initiative on Malnutrition; 3MinNS: 3-minute Nutritional Screening; BMI: Body Mass Index.

CAPÍTULO II

ARTIGO ORIGINAL

Artigo submetido à revista

Clinical Nutrition

(FI 7.324; Qualis A1, Capes)

Malnutrition assessment in inpatients with cancer: Validity of the Global Leadership Initiative on Malnutrition diagnosis using handgrip strength and calf circumference compared to Subjective Global Assessment (SGA) and Patient-generated SGA (PG-SGA).

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Abstract

Background & aims: Malnutrition is a prevalent condition among hospitalized cancer patients and is associated with poor outcomes including a longer length hospital stay (LOS). Tools such as the Subjective Global Assessment (SGA) and Subjective Global Assessment - Patient Generated (PG-SGA) are essential for early detection of malnutrition. Recently, the Global Leadership Initiative on Malnutrition (GLIM) proposed a new framework for diagnosing malnutrition and, so far, evidence on its validity in cancer patients is still being explored. This study aimed to analyze the validity of GLIM using evaluations of the muscle function by handgrip strength (HGS) and muscle mass by calf circumference (CC) criteria for malnutrition considering SGA and PG-SGA as references, and the association between malnutrition with LOS in patients with cancer.

Methods: We conducted a prospective cohort study in cancer inpatients from May 2021 to March 2022. The presence of malnutrition was assessed within the first 48 hours of admission by SGA, PG-SGA and GLIM criteria. Clinical data and LOS were obtained from electronic medical records. Accuracy tests, agreement, linear and logistic regression analysis were performed for testing criterion validity of the GLIM criteria for the malnutrition diagnosis.

Results: 276 inpatients with cancer were evaluated [61.1 ± 14.3 years, 57% were male, 26% had gastrointestinal cancer, 26% with advanced stage tumors (III/IV) and 24% with metastasis]. The median LOS was 5 (3–9) days and 45% of patients were hospitalized >5 days. The malnutrition was diagnosed in 49% (SGA), 81% (PG-SGA), 62% ($GLIM_{HGS}$) and 72% ($GLIM_{CC}$) of the patients with cancer. The $GLIM_{HGS}$ and $GLIM_{CC}$ presented satisfactory sensitivity (> 80%) compared to SGA. The best and moderate agreement was observed between $GLIM_{HGS}$ with the SGA, kappa = 0.503. In the linear regression model, malnourished patients, by $GLIM_{HGS}$ and $GLIM_{CC,}$ remained hospitalized 2.8 and 1.6 days more than well-nourished patients, respectively. In the logistic regression model, the presence of malnutrition in relation to the SGA increased the chance of LOS > 5 days 2.56 times.

Conclusion: In patients with cancer the malnutrition diagnosed by $GLIM_{HGS}$ and $GLIM_{CC}$ presents adequate sensitivity compared to SGA and can be applied during clinical practice.

Keywords: Nutrition Assessment; GLIM criteria; Malnutrition; Length of stay; Cancer; Inpatients.

1. Introduction

Malnutrition is a prevalent condition among hospitalized cancer patients [1], and it is associated with several factors, such as patient age, type of cancer, stage of the disease and type of treatment [2]. Also, in individuals with cancer, malnutrition is associated with lower treatment tolerance, prolonged hospitalizations, worse quality of life, and higher rates of morbidity and mortality [3].

According to the European Society for Clinical Nutrition and Metabolism (ESPEN) expert group, early nutritional risk screening and nutritional assessment practices that include measures of nutritional intake, nutrition impact symptoms, muscle mass, physical performance, and the degree of systemic inflammation, are key to adequate nutritional care for people with cancer [1, 4]. The Subjective Global Assessment (SGA) and Subjective Global Assessment - Patient Generated (PG-SGA) are validated nutritional assessment tools that early identify the presence of malnutrition, enabling an adequate and specialized nutritional intervention.

The SGA [5] is considered the reference method in the assessment of nutritional status due to its effectiveness as a diagnostic and prognostic tool [6]. In cancer patients its diagnosis was associated with longer length of hospital stay (LOS) [7, 8], postoperative complications, [8] and higher mortality rate [7, 8, 9]. The PG-SGA was adapted from the SGA and developed specifically for individuals with cancer [10]. It includes additional questions regarding the presence of nutritional symptoms and short-term weight loss. The scored PG-SGA, unlike SGA, which is categorical, is a continuous measure. The higher the score the greater the risk for malnutrition. In addition, PG-SGA presents satisfactory sensitivity and specificity at predicting SGA classification in cancer patients [11]. Also, the malnutrition according to PG-SGA was significantly associated with longer LOS [12, 13]. More recently, a systematic review of 29 studies showed that PG-SGA is an effective tool in assessing unfavorable clinical outcomes in hospitalized cancer patients [14].

Lately, the Global Leadership Initiative on Malnutrition (GLIM) proposed a new framework for diagnosing malnutrition [18]. The classification criteria for malnutrition are divided into phenotypic [weight loss, body mass index (BMI) and reduced muscle mass] and etiological (reduced food intake and inflammation or disease severity). The presence of at least one phenotypic criterion and one etiological criterion is required for the diagnosis of

malnutrition. In a study with hospitalized patients with different diseases, the GLIM demonstrated validity for the diagnosis of malnutrition [19]. In patients with cancer, the GLIM was an effective tool to assess nutrition status and predict survival [20, 21] and six-month mortality [9].

Furthermore, it is important to emphasize the assessment of muscle mass in identifying the presence of malnutrition. Techniques for muscle functional assessment like hand grip strength (HGS) could be considered as a supportive measure [9], and the calf circumference (CC) is a proposed measure that has been used to assess muscle mass as alternative when imaging technologies are not available [18]. In individuals with cancer, the diagnosis of malnutrition according to GLIM, using CC and HGS, was associated with hospitalization costs and LOS [22], and an inverse association between HGS values and mortality was also observed [9].

Considering that malnutrition and loss of muscle mass are frequently reported in cancer patients and that studies regarding the GLIM criteria in this group of individuals are still being explored, this study aimed to analyze the validity of GLIM criteria, using evaluations of the muscle function by HGS and muscle mass by CC, for malnutrition diagnosis considering SGA and PG-SGA as references, and the association between malnutrition, identify by these tools, with LOS in cancer inpatients.

2. Methods

2.1 Study design and subjects

A prospective cohort study was conducted in subjects with cancer admitted to the Southern Brazil University Hospital, between May 2021 to March 2022. This study was approved by the Hospital Ethics Committee (number 2019.0708) and all participants provided an informed consent form before the collection of data. We considered the following inclusion criteria: patients of both sexes, aged 18 years with solid tumor, lucid, oriented, coherent, able to communicate and perform HGS test or CC measure. Individuals in the emergency, intensive care unit, palliative care, and with COVID-19 were not included. The flowchart of patients' selection was described in Figure 1.

2.2 Data collection

Data collection was conducted within 48 hours after the hospital admission at the patient's bedside, by trained researchers.

2.2.1 General and clinical collection

General and clinical features, such as type and stage of cancer, treatment, chronic diseases, and laboratory measurements of albumin and C-reactive protein (CRP), when available, were collected from the electronic records. Patients were followed up until hospital discharge to assess the length of hospital stay (LOS) and in-hospital mortality.

2.2.2 Nutritional features and assessment of the presence of malnutrition

The patients were weighed at admission. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m^2). At the time of the interview, the patient was asked about weight loss prior to hospitalization. The usual weight was questioned and subtracted from the current weight. The nutritional screening was assessed using Nutritional Risk Screening 2002 (NRS-2002): scores 3 indicate nutritional risk and <3 no risk [23].
The muscle function was measured by hydraulic dynamometer (Jamar®), three consecutive HGS measurements were obtained using the dominant hand while in a seated position, elbow bent at a 90º angle. The highest of the three measures was recorded and a HGS ≤16 Kg for women and ≤27 Kg for men was considered a low muscle function [24]. The CC was evaluated using an inextensible tape measure (Cescorf®, Brazil), with the patient seated, with the foot supported, and the leg flexed at an angle of 90°. The measurement was taken at the point of greatest horizontal circumference of the calf on the right leg. The CC values were adjusted by patient's BMI, in order to help to remove the confounding effects of adiposity, as follows: decrease the measured value by 3 cm (BMI, 25- 30 kg/m²) or 7 cm (BMI, 30 – 40 kgm²) [25]. Finally, CC of ≤34 cm (men) and ≤33 cm (women) was indicative of low muscle mass [26].

The presence of malnutrition was detected using three tools: SGA, PG-SGA, and GLIM criteria (Figure 2). All patients were evaluated regardless of the nutritional screening result.

The SGA classified the patients regarding weight loss, reduced food intake, gastrointestinal symptoms, functional capacity, and muscle and subcutaneous fat loss, those who had SGA A were considered well nourished, SGA B were moderately or suspected of being malnourished, and SGA C were severely malnourished [5].

The PG-SGA is an instrument specific for subjects with cancer. It relies on patients' history (weight history, dietary intake, nutrition impact symptoms, physical function, metabolic stress), and physical assessment (body fat, muscle mass, fluid retention). The patients completed the patient component of PG-SGA, while the professional component was completed by the researchers. The individuals were categorized as well-nourished (category A), moderately malnourished or suspected malnourished (category B) or severely malnourished (category C) [10,15].

The GLIM criteria were applied, and malnutrition identified by combining at least one of three phenotypic criterion: (1) weight loss >5% within past 6 months or >10% beyond 6 months; (2) BMI <20kg/m² if <70 years, or <22kg/m² if >70 years; and (3) low muscle mass defined by reduced CC or low muscle function defined by reduced HGS according to previously described cut-off points [24, 26]; and at least one of the two etiological criterion: (1) reduced food intake or assimilation, identified by self-reported percent of actual food intake compared to the usual intake and/or presence of gastrointestinal symptoms that impact food intake or absorption (nausea, vomiting, diarrhea); and (2) inflammation and disease burden, in this study, all patients classified due to cancer diagnosis. The remaining participants were classified as well-nourished [18]. (Table 2).

2.3 Statistical analysis

Continuous variables were expressed as mean and standard deviation, or median (p25 - p75). Categorical variables were expressed as absolute (n) and relative (%) frequencies. The comparisons between patients with and without malnutrition according to the $GLIM_{HGS}$ and/or $GLIM_{CC}$ were made using the Student's t-test, Mann- Whitney, Chi-square and Fisher's exact tests. Moderate and severe malnutrition were grouped as with malnutrition for analysis.

The agreement between GLIM criteria and SGA and PG-SGA for malnutrition diagnosis was analyzed using the kappa coefficient (k). The values used to assess agreement were: 0.01-0.20 (poor); 0.21–0.40 (fair); 0.41–0.60 (moderate); 0.61–0.80 as substantial; 0.81–0.99 (almost perfect); and 1.00 as perfect [27].

The receiver operating characteristic (ROC) curves with a confidence interval (CI) of 95%, Area Under the Curve (AUC), sensitivity, specificity and positive and negative predictive values were calculated to compare the validity of the GLIM criteria (using HGS

and CC) for malnutrition diagnosis considering SGA and PG-SGA as references. The AUC values were: 0.5-0.6 as very bad; 0.6-0.7 as poor; 0.7-0.8 as moderate; 0.8-0.9 as good; and > 0.9 as excellent [28]. In addition, sensitivity and specificity values >80% were considered satisfactory concurrent validity [29].

Linear regression was used to calculate the difference between the mean LOS and respective 95% CIs of well-nourished and malnourished patients according to GLIM criteria. And multiple logistic regression analysis was used to calculate odds ratio (OR) and respective 95% CIs, considering prolonged LOS (> 5 days) as the dependent variable. All models were adjusted for sex, age and presence of metastasis as a marker of advanced disease.

Data analysis was completed using IBM SPSS (Statistical Package for the Social Sciences, Chicago, Illinois, United States) software V. 20.0 for Windows, and a significance level of 0.05 was considered statistically significant.

3. Results

3.1 General, clinical features, and clinical outcomes

Table 1 describes the sociodemographic and main clinical characteristics of the 276 inpatients evaluated. The mean age was 61.1 ± 14.3 years, 57% were male (n = 159), 85%, white (n = 234), and 55% had ≤8 years of schooling (n = 151). Older patients had greater malnutrition according to $GLIM_{HGS}$ and $GLIM_{CC}$. Regarding the patient's lifestyle, 34% reported alcohol consumption (n = 94), 10% were smokers (n = 28) and 76% were sedentary (n = 210). The most frequent types of cancer were gastrointestinal (26%), head and neck (18.5%) and hepatic (9%), 26% of the patients were diagnosed with advanced cancer (stage III and IV) and 24% presented metastatic tumor. Regarding cancer treatment, 59% of the patients were submitted to surgery, 8% chemotherapy, and 2% radiotherapy.

The mean albumin was 3.5 ± 0.7g/dl and was available only for 58 patients. However, patients diagnosed as malnourished according to $GLIM_{HGS}$ had significantly lower values than well-nourished patients (3.4 ± 0.7 vs. 3.8 ± 0.5 g/dl; p = 0.009). Already, the CRP was available for 51 patients and the median value was 74 (24–128) mg/dL. We observed no significant differences between the groups.

When the clinical outcomes were evaluated, all patients had a median LOS of 5 (3 - 9) days, 45% remained hospitalized for >5 days, 17% were readmitted, and hospital death rate was observed in 3% of the subjects. In addition, patients diagnosed as malnourished according to $GLIM_{HGS}$ had longer LOS when compared to well-nourished [5.5 (3.0-10.75) vs. 4 (2 -7) days; p = 0.001].

3.2 Nutritional features

Table 2 describes nutritional features of the inpatients with cancer according to the presence of malnutrition diagnosed by GLIM criteria. In all individuals the mean weight was 61.1 ± 14.3 kg, BMI of 26.8 ± 5.3 kg/m^2, and 33% (n = 90) of patients had weight loss > 5%. Also, 33% (n = 90) of the subjects were considered at high nutritional risk by NRS-2002. As expected, the malnourished patients diagnosed by $GLIM_{HGS}$ and $GLIM_{CC}$ showed lower values of weight, BMI, weight loss, and higher nutritional risk (NRS-2002 ≥ 3) in comparison to well-nourished patients.

In relation the assessment of function and muscle mass, the mean of the HGS and CC were 31.8 ± 10.2 kg and 33.4 ± 3.1 cm for men, and 16.1 ± 6.7 kg and 32.3 ± 3.5 cm for women, respectively. Among them, 30% of male patients had low HGS and 61% reduced CC. In the female group, 54% of the patients had reduced values of the HGS and 60% of the CC. In addition, malnourished individuals evaluated by GLIM (using HGS and CC) showed reduced values of both measures when compared to well-nourished individuals.

Regarding phenotypic criteria for diagnosing malnutrition by GLIM, the results identified low BMI in 12% of patients, weight loss in 33%, low muscle function in 40% and 60.5% of the patients had low muscle mass.

Among the etiological criteria, we verified the presence of inflammation in 100% of the patients, while reduced food consumption/impaired nutrients assimilation was found in 37% of the total patients evaluated.

In addition, when we evaluated the main symptoms that have a nutritional impact on cancer patients, we observed a prevalence of changes in appetite (28%), inappetence (22%), xerostomia (20%), and nausea (20%). And these rates were significantly higher when malnutrition was present by evaluation GLIM criteria.

3.2 Prevalence of malnutrition

Figure 2 demonstrates malnutrition according to the tool used. The prevalence of malnutrition detected by SGA and PG-SGA, 36% (n = 100) and 38.5% (n = 106) of the patients were diagnosed as moderately malnourished, while 13% (n = 35) and 42.5% (n = 117) were diagnosed as severely malnourished, respectively. When evaluated by GLIM, malnutrition was identified in 62%, n = 172 (using HGS) and 72%, n = 199 (using CC) of the inpatients with cancer.

3.3 Validity of GLIM criteria for malnutrition diagnosis

Table 3 shows the validity of GLIM criteria for malnutrition diagnosis considering SGA and PG-SGA as references.

The $GLIM_{HGS}$ criteria in identifying malnutrition demonstrated satisfactory validity with sensitivity ≥ 80% for SGA (88%) but not with PG-SGA (72%). The agreement was moderate with SGA (kappa = 0.503; p <0.001) and fair with PG-SGA (kappa = 0.359; p <0.001). The use of the $GLIM_{HGS}$ demonstrated moderate values to predict malnutrition compared to SGA (AUC ROC: 0.753) and PG-SGA (AUC ROC: 0.746).

$GLIM_{CC}$ also demonstrated satisfactory validity to assess malnutrition in patients with cancer compared to SGA (88%) but not with PG-SGA (77%). Differently, we observed poor values in the AUC ROC curve to identify malnutrition in relation to SGA (AUC ROC: 0.657) and PG-SGA (AUC ROC: 0.631). The agreement was fair with SGA (kappa = 0.311; p <0.001) and PG-SGA (kappa = 0.223; p <0.001).

3.4 Association between malnutrition and hospitalization in the cancer inpatients

According to the linear regression model (Table 4), adjusted for sex, age and presence of metastasis, malnourished patients diagnosed with $GLIM_{HGS}$ and $GLIM_{CC}$ remained hospitalized approximately 2.8 and 1.64 days longer than well-nourished patients, respectively. The malnutrition identified by SGA (2.02 days) and PG-SGA (3.18 days) also was associated with the LOS in patients with cancer. In addition, when developed a logistic regression model, the malnutrition diagnosed by SGA was positively and significantly associated with a LOS >5 days (OR 2.56; 95%CI 1.55 - 4.23; p<0.001). No associations were observed with the other tools (Table 5).

4. Discussion

The current study in patients with cancer demonstrated that GLIM criteria using evaluations of the muscle function by HGS and muscle mass by CC demonstrated satisfactory sensitivity (>80%) compared to SGA, but not with PG-SGA. The best and moderate accuracy value was observed between $GLIM_{HGS}$ and SGA (AUC = 0.753). We also observed moderate agreement between $GLIM_{HGS}$ and SGA (kappa = 0.503) and fair agreement between $GLIM_{CC}$ and SGA (kappa = 0.311). According to the linear regression model, malnourished patients, diagnosed using $GLIM_{HGS}$, remained hospitalized 2.8 days longer than well-nourished patients, and according to the $GLIM_{CC}$, malnourished patients remained hospitalized 1.6 days longer than well-nourished patients. Also, malnutrition diagnosed by the SGA increased the chance of prolonged hospitalization (> 5 days) by 2.56 times.

Prevalence of malnutrition according to GLIM

In our record, the frequency of malnutrition identified by the $GLIM_{HGS}$ was 62% and by $GLIM_{CC}$ was 72%. In other studies, involving hospitalized cancer patients, the prevalence of malnutrition ranged from 26.5% to 80.0% diagnosed with malnutrition by GLIM [9, 20, 21, 22, 30]. In our sample, some factors might have influenced the high prevalence of malnutrition, such as the cancer type and age. In fact, in a multicenter study the highest rates of malnutrition occurred within gastrointestinal (47.3%) and head and neck cancer patients (25.9%) [30]. In our group of patients, we also observed a higher prevalence of these two types of cancer, around 45%. In addition, in a retrospective cohort study in cancer patients aged ≥ 65 years the prevalence of malnutrition according to the GLIM ranged from 48.4% - 46.0% [20]. In our sample, the individuals had a mean age of 61.1 ± 14.3 years and 42% ≥ 65 years, which may also have influenced the prevalence of malnutrition.

Moreover, malnutrition rates can also be influenced by the different methods used to assess muscle mass. The consensus of the GLIM group recommends the use of imaging (i.e., computed tomography or magnetic resonance imaging) or bioelectrical bioimpedance methods to assess muscle mass, when these techniques are unavailable, anthropometric measures and physical examination are proposed as alternatives [18, 32]. In addition, the original GLIM guideline described muscle function assessment as an appropriate alternative

in situations where muscle mass cannot be assessed [18]. More recently published guideline stated that remains under debate the role of muscle function as a potential surrogate for muscle mass, recommending the use of HGS as a complementary measure [32]. Among the measures already investigated to assess the phenotypic criterion of reduced muscle mass of GLIM in the context of cancer inpatients, there are CC [20, 21, 22, 30], arm muscle circumference (AMC) [9, 20], fat-free mass index (FFMI) [9, 31], and HGS to asses muscle function [9, 22].

In our research, we used HGS and CC as alternative measures in assessing muscle function and muscle mass. Using these measurements according to sex-specific cut-off points (24, 26), we observed that 40% and 60.5% of cancer patients had reduced of muscle function and mass, according to HGS and CC, respectively. Therefore, the presence of malnutrition by $GLIM_{CC}$ was higher than $GLIM_{HGS}$ (72 *vs.* 62%). Regarding the phenotypic criteria described by GLIM, in our inpatients the most frequent criteria were weight loss (33%), low muscle function (40%) and low muscle mass (60.5%). Recently, a study involving 210 cancer patients compared different combinations of GLIM criteria and demonstrated that the highest prevalence of malnutrition (32.4% of patients) was observed combining weight loss > 5% as phenotypic criterion and CRP > 5 mg/L as etiological criterion [31]. Also, in a multicentered study, multivariable analysis revealed that unintentional weight loss was the most determining factor acting upon mortality in cancer patients, followed by reduced muscle mass and reduced food intake or assimilation that showed a moderate impact on survival [21].

Finally, we observed that the prevalence of malnutrition, assessed by the GLIM, may have been influenced because we applied the GLIM in all patients, regardless of the previous nutritional risk. Although we found that 33% of our patients were at nutritional risk according to NRS-2002. These data collaborate with a study that evaluated the agreement between GLIM and PG-SGA criteria in a mixed population of patients, which demonstrated that when the NRS-2002 was used, the malnutrition rate was lower (36%) than GLIM performed without prior screening (59%) [33]. On the other hand, in our cancer patients, the prevalence of severe malnutrition was also observed when we used other tools, such as the SGA (13%) and PG-SGA (42.5%) (Figure 2).

Criterion validity of GLIM criteria for malnutrition diagnosis

Research regarding the concurrent validity of GLIM criteria is still being investigated for hospitalized cancer patients. Our study observed satisfactory sensitivity (>80%) of $GLIM_{HGS}$ and $GLIM_{CC}$, considering SGA as the reference method. Compared to PG-SGA, the concurrent validity criteria were unsatisfactory (<80%) for $GLIM_{HGS}$ and $GLIM_{CC}$. In a cross-sectional observational study including 246 adult ambulatory patients with cancer, the validation of GLIM against the PG-SGA showed a sensitivity of 76%, specificity of 73%, and a fair agreement (kappa = 0.323). When was added the HGS to the GLIM, the sensitivity and specificity were 19% and 96%, respectively, and a poor agreement was observed (kappa = 0.186) [34]. The authors attributed the difference in malnutrition rates between PG-SGA and GLIM criteria to the different time frames for assessing weight loss percentage [34].
In our group of cancer inpatients, the $GLIM_{CC}$ criteria demonstrated a fair agreement (kappa = 0.223), poor AUC value (0.631), and unsatisfactory sensitivity and specificity (<80%) with PG-SGA. When we evaluated the validity of $GLIM_{HGS}$ with PG-SGA, the agreement (kappa = 0.359) and AUC values (0.746) improved, but sensitivity reduced to 72%. Collaborating with our data in an observational cohort study with cancer patients, the PG-SGA also showed poor agreement with GLIM using CC (kappa = 0.136), and CC + HGS (kappa = 0.127) [22]. Already, in a multi-center study in adults with cancer the PG-SGA demonstrated a moderate agreement with GLIM criteria (kappa = 0.453) [30]. In our analyses, the best agreement was observed between $GLIM_{HGS}$ with SGA, the reference method for assessing nutritional status (kappa = 0.503, moderate).

Association between malnutrition and clinical outcomes in the cancer patients

In our study, the predictive validity of GLIM, using CC and HGS, was confirmed, since it was a predictor of longer LOS. Moreover, we demonstrated that the difference in mean LOS between well-nourished and malnourished was greater when diagnosed by $GLIM_{HGS}$ (2.79 additional days) than by GLI_{CC} (1.64 additional days). In agreement with our results, a study conducted in 282 cancer patients demonstrated that malnourished patients, according to GLIM criteria using HGS and SGA, had a significantly higher LOS, in-hospital mortality and six-month mortality as compared to well-nourished patients [9]. Also, we observed a positive and significant association between malnourished patients, identified by SGA, with LOS > 5 days (2.56 times).

The CC is measures proposed as an alternative to assess muscle mass, while HGS is recommended as a complementary measure to identify muscle function [18, 32]. As expected, some studies showed disparities regarding the use of these measures when evaluated with the GLIM [22, 34, 35]. A multicenter observational cohort study including 3998 cancer patients showed that CC appears to be adequate to evaluate the reduced muscle under GLIM framework [22]. Moreover, the supportive value of the HGS was limited and using it in combination with CC may increase the risk of a missed diagnosis [22]. This observation collaborates with a study in ambulatory cancer patients where the addition of HGS in GLIM criteria did not improve the recognition of malnutrition or mortality risk [34]. In addition, a recent study in cancer patients demonstrated that the combination of fat mass index (FMI) by bioelectrical impedance plus GLIM has the maximal prognostic value among the dual factor combinations of the FMI, HGS, and malnutrition [35].

Implications for clinical practice

The findings of our study suggest that the GLIM criteria, using HGS and CC, might be considered as an appropriate alternative for the diagnosis of malnutrition in hospitalized cancer patients. $GLIM_{HGS}$ seems to be sensible and moderately concordant compared to the reference tool in nutritional assessment, SGA (Sensibility = 88%; kappa = 0.503). In addition, we found that patients with malnutrition, evaluated by $GLIM_{HGS}$, experienced more symptoms that impacted nutrition than patients without malnutrition, which presented as most common symptoms appetite change (37%), inappetence (31%), xerostomia (27%) and nausea (24%).

This record also demonstrated that, in the absence of imaging techniques to assess the muscle mass of patients, it is possible to use more accessible techniques, such as CC measurement with different cut-off points [26]. In addition, HGS is a supportive measure, which complements nutritional assessment, and is indicated only when muscle mass cannot be assessed [32]. In this sense, these assessments can be incorporated into clinical practice to identify nutritional status in hospitalized cancer patients.

Our study has some limitation such as the heterogeneity of the sample regarding the type and treatment of cancer and incomplete data on biochemical markers, such as CRP and albumin values. To minimize their effects on the main results, the linear and logistic regression analyzes were adjusted for sex, age and presence of metastasis. Unfortunately,

adjustment for laboratory parameters was not possible since they were not collected in some patients. In addition, it would be interesting to follow these patients for a complete assessment of changes in nutritional status, muscle mass and muscle function during the period of hospitalization. However, this study presents important data related to the high prevalence of malnutrition in individuals with cancer at their hospital admission and reinforces the importance of nutritional assessment for early nutritional intervention aimed at reducing unfavorable clinical outcomes such as prolonged LOS.

5. Conclusion

In the cancer inpatients, GLIM criteria using muscle function by HGS and muscle mass by CC identified approximately 60 - 70% cases of malnutrition, presented a satisfactory sensitivity, and moderate agreement when compared with the reference criteria, SGA. Furthermore, its validity was confirmed since malnutrition was associated with a longer LOS.

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Authorship

TS and MSC conceived and designed the study. MSC, GPS and LMS contributed with data acquisition. MSC and TS did the analysis and interpretation of the data. MSC and TS drafted the initial manuscript. All authors critically revised the manuscript and approved the final version. TS is the guarantor and attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Conflict of interest

The authors declare no conflicts of interest.

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Figures and Tables

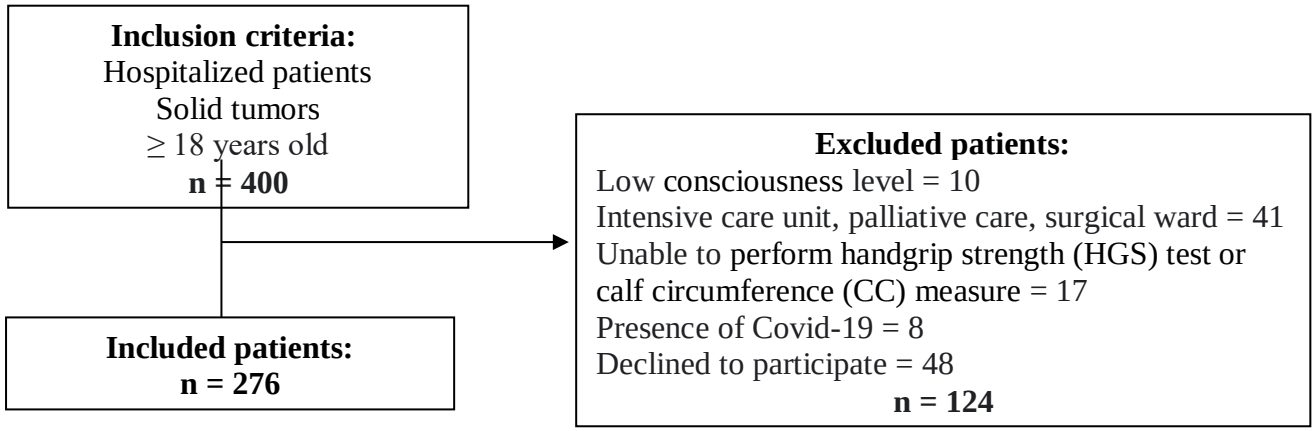

Figure 1. Flowchart of patient selection

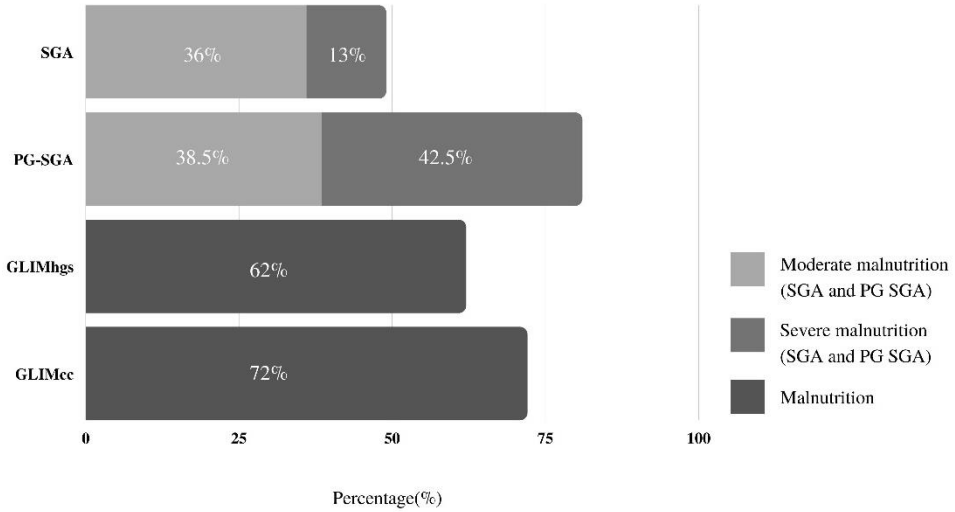

Figure 2. Malnutrition in cancer patients according to the tool used. SGA = Subjective Global Assessment; PG SGA = Patient Generated Subjective Global Assessment; GLIM = Global Leadership Initiative on Malnutrition; HGS = handgrip strength; CC = calf circumference.

Table 1. Features of the inpatients with cancer grouped according to the presence of malnutrition diagnosed by the GLIM criteria.

Variables	All sample (n = 276)	$GLIM_{HGS}$			$GLIM_{CC}$		
		Well-nourished (n = 104)	Malnutrition (n = 172)	P-value	Well-nourished (n = 77)	Malnutrition (n = 199)	P-value
General features							
Age (years)	61.1 ± 14.3	58.5 ± 14.1	62.7 ± 14.2	**0.017**	57.2 ± 15.1	62.7 ± 13.7	**0.004**
Sex (male)	159 (57%)	71 (68%)	88 (51%)	**0.008**	45 (58%)	114 (57%)	0.969
Ethnicity (white)	234 (85%)	88 (85%)	146 (85%)	0.079	65 (85%)	169 (85%)	**0.010**
Education ≤8 years (%)	151 (55%)	49 (47%)	102 (60%)	0.065	33 (43%)	118 (59%)	**0.020**
Alcohol intake (yes)	94 (34%)	40 (38%)	54 (31%)	0.477	31 (40%)	63 (32%)	0.285
Smoking (yes)	28 (10%)	9 (9%)	19 (11%)	0.573	6 (8%)	22 (11%)	0.477
Sedentary (yes)	210 (76%)	74 (71%)	136 (79%)	0.178	58 (75%)	152 (76%)	0.978
Clinical features							
Cancer type							
Gastrointestinal	72 (26%)	19 (18%)	53 (31%)		16 (21%)	56 (28%)	
Head and neck	51 (18.5%)	18 (17%)	33 (19%)	**0.012**	12 (16%)	39 (20%)	**0.040**
Hepatic	26 (9%)	12 (11%)	14 (8%)		9 (12%)	17 (8%)	
Cancer Stage							
I - II	52 (19%)	18 (17%)	34 (20%)		15 (19%)	37 (19%)	
III-IV	72 (26%)	25 (24%)	47 (27%)	0.649	25 (32%)	47 (24%)	0.266

Unknown	152 (55%)	61 (59%)	91 (53%)		37 (48%)	115 (58%)	
Cancer treatment							
Surgery	162 (59%)	69 (66%)	93 (54%)		51 (66%)	111 (56%)	
Chemotherapy	22 (8%)	4 (6%)	16 (9%)	0.060	4 (5%)	18 (9%)	0.320
Radiotherapy	6 (2%)	1 (1%)	5 (3%)		1 (1%)	5 (2%)	
Chronic diseases							
Diabetes	58 (21%)	17 (16%)	41 (24%)	0.184	8 (10%)	50 (25%)	0.011
Hypertension	143 (52%)	48 (46%)	95 (55%)	0.181	36 (47%)	107 (54%)	0.362
Albumin (g/dl) *	3.5 ± 0.7	3.8 ± 0.5	3.4 ± 0.7	**0.009**	3.7 ± 0.6	3.5 ± 0.7	0.186
CRP (mg/dl) **	74 (24 – 128)	54 (22 - 116)	82 (25 - 135)	0.230	63 (20 - 130)	82 (24 - 124)	0.592
Metastasis	65 (24%)	20 (20%)	45 (26%)	0.242	20 (26%)	45 (23%)	0.666
Clinical outcomes							
Hospital LOS (days)	5 (3 - 9)	4 (2 - 7)	5.5 (3 – 10.75)	**0.001**	4 (3 – 7.5)	5 (3 - 10)	0.084
Hospital LOS (>5 day)	125 (45%)	39 (37%)	86 (50%)	0.058	31 (40%)	94 (47%)	0.363
Hospital readmission	48 (17%)	17 (16%)	31 (18%)	0.847	10 (13%)	38 (19%)	0.306
Hospital death	9 (3%)	0 (0%)	9 (5%)	**0.015**	0 (0%)	9 (4.5%)	0.066

Data are presented as number (%), mean ± standard deviation or median (p25-p75); p value with Chi-square test, Fisher's exact test, Student's t-test and Mann-Whitney test.

GLIM = Global Leadership Initiative on Malnutrition; HGS= hand grip strength; CC = calf circumference; LOS = length of hospital stay; CRP = C-Reactive Protein.

*n = 58; **n = 51.

Table 2. Nutritional features of the inpatients with cancer grouped according to the presence of malnutrition diagnosed by GLIM criteria.

Variables	All sample (n = 276)	$GLIM_{HGS}$			$GLIM_{CC}$		
		Well-nourished (n = 104)	Malnutrition (n = 276)	P-value	Well-nourished (n = 77)	Malnutrition (n = 199)	P-value
Nutritional features							
Current weight (kg)	61.1 ± 14.3	80.9 ± 15.6	69.5 ± 17.7	**<0.001**	81.9 ± 16.6	70.7 ± 17.4	**<0.001**
BMI (kg/m^2)	26.8 ± 5.3	28.5 ± 4.6	25.7 ± 5.4	**<0.001**	28.9 ± 5.1	25.9 ± 5.1	**<0.001**
Low BMI (kg/m^2)*	31 (11%)	1 (1%)	30 (17%)	**<0.001**	0 (0%)	31 (16%)	**<0.001**
High BMI (kg/m^2)**	138 (50%)	69 (66%)	69 (40%)	**<0.001**	49 (64%)	89 (45%)	**<0.001**
GLIM Low BMI (kg/m^2)***	33 (12%)	0 (0%)	33 (19%)	**<0.001**	0 (0%)	33 (17%)	**<0.001**
Body weight loss > 5%	90 (33%)	0 (0%)	90 (52%)	**<0.001**	0 (0%)	90 (45%)	**<0.001**
High nutritional risk (NRS-2002 ≥ 3)	90 (33%)	6 (6%)	84 (49%)	**<0.001**	6 (8%)	84 (42%)	**<0.001**
HGS (kg)							
Men	31.8 ± 10.2	37.0 ± 7.9	27.5 ± 9.9	**<0.001**	34.8 ± 10.8	30.6 ± 9.8	**0.018**
Low HGS (%)	47 (30%)	0 (0%)	47 (53%)	**<0.001**	11 (24%)	36 (32%)	0.487
Women	16.1 ± 6.7	21.8 ± 3.8	14.0 ± 6.4	**<0.001**	18.0 ± 6.8	15.4 ± 6.6	0.061
Low HGS (%)	63 (54%)	0 (0%)	63 (75%)	**<0.001**	12 (37%)	51 (60%)	0.049
CC (cm)							
Men	33.4 ± 3.1	34.1 ± 2.6	32.9 ± 3.3	0.013	36.3 ± 1.5	32.3 ± 2.8	**<0.001**
Low CC (%)	97 (61%)	37 (52%)	60 (68%)	0.057	0 (0%)	97 (85%)	**<0.001**

Women	32.3 ± 3.5	34.3 ± 3.3	31.6 ± 3.3	**<0.001**	35.7 ± 2.0	31.1 ± 3.1	**<0.001**
Low CC (%)	70 (60%)	13 (39%)	57 (68%)	0.009	0 (0%)	70 (82%)	**<0.001**
Inflammation	200 (100%)	104 (100%)	172 (100%)	-	77 (100%)	199 (100%)	-
Reduced FI/impaired nutrients assimilation	102 (37%)	16 (15%)	86 (50%)	**<0.001**	15 (19%)	87 (44%)	**<0.001**
Phenotypic criteria (number)	1 (1 - 2)	0 (0 - 0)	2 (1 - 2)	**<0.001**	0 (0 - 0)	1 (1 - 2)	**<0.001**
Etiologic criteria (number)	1 (1 - 2)	1 (1 - 1)	1.5 (1 - 2)	**<0.001**	0 (0 - 0)	1 (1 - 2)	**<0.001**
Nutritional impact symptoms							
Appetite change	78 (28%)	14 (13.5%)	64 (37%)	**<0.001**	7 (9%)	71 (36%)	**<0.001**
Inappetence	61 (22%)	8 (8%)	53 (31%)	**<0.001**	6 (8%)	55 (28%)	**0.001**
Xerostomia	55 (20%)	11 (11%)	44 (27%)	**0.004**	12 (16%)	43 (22%)	0.339
Nausea	54 (20%)	12 (11%)	42 (24%)	**0.014**	13 (17%)	41 (21%)	0.592

Data are presented as number (%), mean ± standard deviation or median (p25-p75). p value with Chi-square test, Fisher's exact test, Student's t-test and Mann-Whitney test.

GLIM = Global Leadership Initiative on Malnutrition; BMI = body mass index; HGS= hand grip strength; CC = calf circumference; FI = food intake.

* Low BMI (kg/m^2) = adults <18.5 kg/m^2 and older adults <22 kg/m^2; ** High BMI (kg/m^2) = adults > 25 kg/m^2 and older adults >27 kg/m^2; *** GLIM Low BMI (kg/m^2) = adults <20 kg/m^2 and older adults (>70 years) <22 kg/m^2.

Table 3. Validity of GLIM using HGS and CC criteria for malnutrition diagnosis considering SGA and PG-SGA as references.

Parameters of validity ($GLIM_{HGS}$)	**SGA**	**PG-SGA**
Kappa (P-value)*	0.503 (<0.001)	0.359 (<0.001)
AUC ROC (CI 95%)**	0.753 (0.694 - 0.811)	0.746 (0.672 - 0.819)
Sensitivity (%)***	**88%**	72%
Specificity (%)***	62%	77%
Positive predictive value (%)	69%	**93%**
Negative predictive value (%)	85%	39%
Parameters of validity ($GLIM_{CC}$)	**SGA**	**PG-SGA**
Kappa (P-value)*	0.311 (<0.001)	0.223 (<0.001)
AUC ROC (CI 95%)**	0.657 (0.592 - 0.722)	0.631 (0.543 - 0.718)
Sensitivity (%)***	**88%**	77%
Specificity (%)***	43%	49%
Positive predictive value	60%	**86%**
Negative predictive value	79%	34%

GLIM = Global Leadership Initiative on Malnutrition; HGS = hand grip strength; CC = calf circumference; SGA = Subjective Global Assessment; PG-SGA = Patient- Generated Subjective Global Assessment. AUC = area under the curve; ROC = receiver operating characteristics CI = confidence interval. *Kappa values = 0.20 (poor), 0.21 and 0.40 (fair), 0.41 and 0.60 (moderate), 0.61 and 0.80 (substantial), 0.81 and 0. 99 (almost perfect) and (1.00 perfect); ** AUC values = 0.5-0.6 (very bad), 0.6-0.7 (poor), 0.7-0.8 (moderate) 0.8-0.9 (good), > 0.9 (excellent); *** Sensitivity and specificity values ≥ 80% (satisfactory).

Table 4. Linear regression model: Association between malnutrition and days of hospitalization in the cancer patients.

	Difference in mean LOS between well-nourished and malnourished (95%CI)	**P-value**	***B* (95%CI)**	**P-value**
LOS				
$GLIM_{HGS}$	2.79 days (1.42 – 4.17)	**<0.001**	-0.394 (-0.592 – -0.196)	**<0.001**
$GLIM_{CC}$	1.64 days (0.16 – 3.12)	**0.030**	-0.227 (-0.440 – -0.015)	**0.036**
SGA (moderately and severely malnourished)	2.02 days (0.55 – 3.48)	**0.007**	-0.267 (-0.458 – -0.076)	**0.006**
PG-SGA (moderately and severely malnourished)	3.18 days (1.79 – 4.57)	**<0.001**	-0.493 (-0.735 – -0.251)	**<0.001**

Model adjusted for sex, age and metastasis.

CI = confidence interval; LOS = length of hospital stay; GLIM = Global Leadership Initiative on Malnutrition; HGS= hand grip strength; CC = calf circumference; SGA = Subjective Global Assessment; PG-SGA = Patient- Generated Subjective Global Assessment.

Table 5. Logistic regression model: Association between malnutrition and hospitalization >5 days in the cancer patients.

	Odds Ratio (95%CI)	**P-value**
LOS > 5 days		
$GLIM_{HGS}$	1.52 (0.909 - 2.55)	0.110
$GLIM_{CC}$	1.32 (0.76 - 2.29)	0.318
SGA (moderately and severely malnourished)	2.56 (1.55 - 4.23)	**<0.001**
PG-SGA (moderately and severely malnourished)	1.86 (0.97 - 3.57)	0.060

Model adjusted for sex, age and metastasis.

OR = Odds Ratio; CI = confidence interval; LOS = length of hospital stay; GLIM = Global Leadership Initiative on Malnutrition; HGS= hand grip strength; CC = calf circumference; SGA = Subjective Global Assessment; PG-SGA = Patient- Generated Subjective Global Assessment.

ANEXOS

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Language: English

Document: Assessment in the cancer inpatients: Validity of the Global Leadership Initiative on Malnutrition using handgrip strength and calf circumference criteria for the diagnosis of malnutrition compared to Subjective Global Assessment, Patient-Generated SGA and PG-SGA short form.

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