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Original article

Agreement between GLIM and PG-SGA for diagnosis of malnutrition depends on the screening tool used in GLIM

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SUMMARY

Background & aim: The Global Leadership Initiative on Malnutrition (GLIM) has suggested a process for the diagnosis of malnutrition. The process consists of applying an existing screening tool for malnutrition screening, followed by malnutrition diagnostics, and finally categorization of malnutrition severity (moderate or severe) according to specific GLIM criteria. However, it is not known how well the GLIM process agrees with other diagnostic tools used in the current clinical practice. The aim of this study was to validate the GLIM process against the Patient Generated-Subjective Global Assessment (PG-SGA) when different screening tools were applied in the screening step of the GLIM process.

Methods: Colorectal cancer (CRC) patients from the ongoing CRC-NORDIET study were included. For the GLIM process, the patients were first screened for malnutrition using either 1) Nutritional risk screening, first 4 questions (NRS-2002-4Q), 2) Malnutrition Screening Tool (MST), 3) Malnutrition Universal Screening Tool (MUST) or 4) the PG-SGA short form (PG-SGA-SF). The GLIM malnutrition diagnosis was then based on combining the result from each of the screening methods with the etiological and phenotypic GLIM-criteria including weight loss, BMI and fat free mass. In parallel, the patients were diagnosed using the PG-SGA methodology categorizing the patients into either A: well nourished, B: moderately malnourished or C: severely malnourished. The four different GLIM based diagnoses were then validated against the diagnosis obtained by the PG-SGA tool. Sensitivity, specificity and positive predictive value (PPV) were calculated to evaluate validity.

Results: In total, 426 patients were included (mean age: 66, ±8 years) at a mean time of 166 (±56) days after surgery. The GLIM diagnosis based on the four different screening tools identified 10–24% of the patients to be malnourished, of which 3–8% were severely malnourished. The PG-SGA method categorized 15% as moderately malnourished (PG-SGA: category B) and no patients as severely malnourished (PG-SGA: category C). The agreement between the PG-SGA and GLIM process was in general low, but differed according to the tools: PG-SGA SF (sensitivity 47%, PPV 71%), MST (sensitivity 56%, PPV 47%), NRS-2002-4Q (sensitivity 63%, PPV 53%) and MUST (sensitivity 53%, PPV 34%).

Conclusion: In this cross-sectional study of patients with CRC, the concordance between the GLIM-criteria and PG-SGA depended on the screening tool used in the GLIM process. Malnutrition frequency based on the GLIM process schould be reported with and without the use of a screening tool.

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1. Introduction

Malnutrition, which frequently occurs in patients with cancer diagnoses, is associated with increased morbidity and mortality [1–3]. There is currently no gold standard for the diagnosis of malnutrition, and numerous methods are applied in clinical- and research settings. The lack of consensus on diagnostic criteria makes it problematic to compare results from different studies around the world. Therefore, based on a consensus process the Global Leadership Initiative on Malnutrition (GLIM) has suggested a method, hereafter termed the GLIM-process, for diagnosing malnutrition including diagnostic criteria [4]. However the operational criteria of the GLIM-process need to be validated [5].

The GLIM-process suggests a step-wise approach for diagnosing malnutrition [4]. Step 0 is screening for the risk of malnutrition, for which GLIM suggests to use one of the existing, validated screening tools. In step 1, GLIM introduces the new criteria for malnutrition diagnostics in which both etiology (reduced intake, malabsorption and increased energy needs) and symptoms/signs (low BMI, weight loss and low muscle mass) are included. In the final step, step 2, the severity of malnutrition is determined based on two sets of cut-off values for the GLIM-criteria in step 1. However, it is not known how well the GLIM method agrees with the current clinical practice.

The Patient Generated-Subjective Global Assessment (PG-SGA) [6,7] is a nutritional assessment tool recommended for oncology practice and research [8]. The PG-SGA is one of only few nutritional assessment tools that cover all domains of the definition of malnutrition [9]. The PG-SGA form includes two pages, in which the patient completes the first page and the health care professionals completes the second page. The first page includes four patient-generated components (weight history, food intake, nutritional impact symptoms and activity level and function) and the second page three professional components (diagnosis and age, metabolic stress and nutrition focused physical examination). The physical examination, (part of page 2) performed by the health care professionals, consists of visual inspection and palpation of muscles, subcutaneous fat and edema. Based on an evaluation of the patient-generated components and the physical examination, the patients are categorized as well-nourished (PG-SGA A), moderately malnourished (PG-SGA B) or severely malnourished (PG-SGA C). The first page can be used as a stand-alone screening tool and is then referred to as "PG-SGA short-form" (PG-SGA SF).

The evaluation of weight loss, energy intake, altered energy needs and muscle mass is included in both GLIM and PG-SGA. It is well recognized that the loss of fat-free mass (FFM) is linked to adverse outcomes in cancer patients. Progressive loss of skeletal muscle, the major constituent of FFM, is shown to be an independent predictor of chemotherapy toxicity [10], post-operative complications [11] and mortality [12–14] in cancer patients. Depletion of FFM may occur with or without loss of fat mass, and may therefore be masked by obesity or a stable body weight [15]. The clinical consequences of low FFM overlap with the consequences of malnutrition [16], and thus low FFM seem to be a key component for the malnutrition diagnosis.

According to the GLIM-process, any existing, validated screening tool could be applied in order to screen for the risk of malnutrition. Several screening tools are recommended and used in clinical practice [17], e.g. Malnutrition Screening Tool (MST), Malnutrition Universal Screening Tool (MUST), and Nutritional Risk Screening (NRS-2002) in which the first four questions (NRS-2002-4Q) have also been suggested as a separate screening tool [18–21]. The short form of PG-SGA (PG-SGA SF), including only the first page completed by the patient, can also be used as screening tool. In previous publications using the GLIM process, malnutrition prevalence is presented with or without initial screening. It is, however, not known how the use of different screening tools affects the result of the GLIM process.

The aim of the present study was to investigate the agreement between the GLIM process and PG-SGA for diagnosing malnutrition in patients with colorectal cancer (CRC) when different screening tools are applied in step 0 of the GLIM process.

2. Subjects and methods

2.1. Participants

The participants included in this cross-sectional study were recruited from the ongoing randomized clinical trial (RCT) "The Norwegian Dietary Guidelines and Colorectal Cancer Survival study" (CRC-NORDIET) [22]. Detailed information on the CRC-NORDIET study including recruitment, measurements, methods, exclusion and inclusion criteria have been published elsewhere [22,23]. Briefly, eligible participants were women and men (50–80 years) with a confirmed primary CRC (ICD-10 C18-20), and staged I–III according to the tumor node staging (TNM) system [24]. All patients had undergone surgery at Oslo University Hospital or Akershus University Hospital in Norway, and were enrolled between 2012 and 2020. The current study is a cross-sectional study from the inclusion time point (baseline), 2–9 months after curative surgery, meaning that all measurements were performed prior to the one-year intensive dietary intervention of the CRC-NORDIET study. Information about site and classification of the malignant tumors (TNM stage) were obtained from electronic patient records.

2.2. Ethics

The CRC-NORDIET study was carried out in accordance to the Helsinki Declaration and informed consent was obtained from all participants. The study was approved by the Regional Committees for Medical and Health Research Ethics in Norway (REC Protocol Approval 2011/836) and by the data protection officials at Oslo University Hospital and Akershus University Hospital. The CRC-NORDIET study is registered at the National Institutes of Health Clinical Trials (www.ClinicalTrials.gov; Identifier: NCT01570010).

2.3. The GLIM approach

In step 0 of the GLIM approach (Fig. 1), we used four different tools to screen for risk of malnutrition; 1) Malnutrition Universal Screening tool (MUST), 2) Malnutrition Screening Tool (MST), 3) NRS-2002-4Q or 4) the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF). Screening with NRS-2002, MST and MUST were conducted retrospectively, based on data collected at the study visit.

Nutritional risk screening (NRS 2002) was developed in Denmark [17,18]. The procedure has two steps and is more complex compared to the other mentioned tools, as the patient has to be scored in different components: malnutrition and disease severity [18]. The NRS first 4 questions (NRS-2002-4Q) have however been used as a separate screening tool, and have shown to predict morbidity and mortality [19]. Malnutrition risk was defined as $\geq$1 (out of 4) for NRS-2002-4Q in the present study.

MST was originally developed in Australia, and consists of only two questions regarding appetite and recent unintentional weight loss [20]. In the present study, this information was self-reported. MST scores $\geq$2 (out of 5) was defined as malnutrition risk, according to the developer's guidelines.

MUST is a risk screening tool developed by The British Association for Parenteral and Enteral Nutrition (BAPEN) [21]. In the present study, MUST scores were calculated from anthropometric

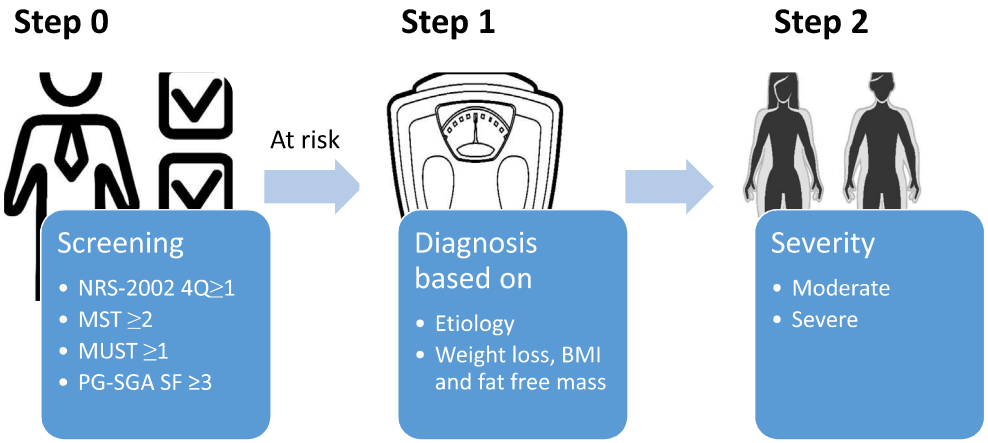

Fig. 1. Overview of the GLIM process. In Step 0 of the GLIM approach, we used four different screening tools 1) Nutrition Risk screening first 4Q (NRS-2002-4Q), 2) Malnutrition Screening tool (MST), 3) Malnutrition Universal Screening Tool (MUST) or 4) the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF). In step 1 diagnosis was performed based on ethology and phenotype, and step 2 the severity was graded into severe malnutrition or moderate malnutrition.

measurements performed at the center and weight loss was self-reported by the patient on the first page of PG-SGA. Malnutrition risk was defined by MUST score ≥1 out of 3, as recommended [21].

PG-SGA SF consists of four patient generated items: weight history, nutrition impact symptoms, food intake and activity level, and is the first page of the full PG-SGA [7]. As the PG-SGA SF is designed to be completed by the patient, most patients manage to do this without problems [25]. However, in the present study, a dietitian or master student provided assistance if needed. As there are currently no official guidelines for how to define risk of malnutrition based on the PG-SGA SF, we selected a cut-off value of ≥3 based on own receiver operating characteristic curve (ROC curve) analyses with PG-SGA category as outcome variable in a subsample of the CRC-NORDIET study (data not shown).

For step 1 and 2 of the GLIM process; diagnosis and severity grading of malnutrition, the GLIM criteria as defined by the consensus report from the global clinical nutrition community [4] were applied.

Anthropometric measurements as part of step 1, were performed as previously described [22]. In short, body weight was measured on a Marsden M-420 Digital Portable Floor Scale (Marsden, Rotherham, South Yorkshire, United Kingdom) or a digital wireless measuring station for height and weight, Seca 285 (Seca, Birmingham, United Kingdom). Height (cm) was measured with a mechanical height rod (Kern MSF- 200) or a digital wireless stadiometer (Seca 285). For the phenotypic criteria of step 1, BMI was calculated based on measured values, and categorized as: moderately low if BMI <20 kg/m^2 (<22 if more than 70 years) and severely low if BMI <18.5 kg/m^2 (<20 if more than 70 years). Weight loss the last six months were self-reported, and the cut off 10% were used.

Bioelectrical impedance analysis (BIA) was used for assessment of FFM. A single frequency whole-body BIA (BIA 101, SMT Medical, Würzburg, Germany) was used from 2012 to 2018. The device applies a current of 400 μA at a constant frequency of 50 kHz. From 2018, this device was replaced by a multi-frequency, segmental Seca mBCA515 (Seca, Birmingham, United Kingdom). Both instruments have previously been validated against Dual-energy X-ray Absorptiometry (Lunar iDXA, GE Healthcare software enCORE version 16) in a subgroup of CRC patients included in the CRC-NORDIET study [26]. All measurements were performed under standardized conditions according to the manufacturer's protocol and FFM was calculated by the included regression equations incorporated in the BIA software. Cut-off values for low muscle mass were set to FFMI (FFM (kg)/height (m^2)) <15 kg/m^2 for women and <17 kg/m^2 for men for moderate malnutrition, according to cut-off values for FFMI proposed for sarcopenia by ESPEN [27,28]. No additional cut-offs for FFMI were used for defining severe malnutrition, as this is not specified in the original GLIM publication [4].

All participants were a priori defined as having at least one etiologic criteria (chronic disease), because of their recent cancer diagnosis. Other etiological criteria were self-reported by the PG-SGA SF (information on dietary intake, diarrhea or vomiting).

For step 2 of the GLIM process the severity of malnutrition was categorized as moderate if BMI <20 kg/m^2 (<22 if more than 70 years) and/or weight loss 5–10%. Participants were graded as severely malnourished if BMI <18.5 kg/m^2 (<20 if more than 70 years) and/or weight loss >10%. No additional cut-offs for FFMI were used for defining severe malnutrition, as this is not specified in the original GLIM publication [4].

2.4. The PG-SGA

A validated Norwegian version of the scored PG-SGA (15-004 v10.13.16) was used as a reference method for malnutrition assessment [29]. A detailed description of the PG-SGA procedure has been published previously [23]. Briefly, the PG-SGA assessment was carried out by either registered clinical dietitians or trained master students in clinical nutrition in accordance with the guidelines [30]. All personnel underwent training in the PG-SGA procedure, as training has been shown to increase comprehensibility [31]. Permission for use was obtained by the copyright holder of the instrument. The results are presented both as total score and the global rating. According to the procedures for global rating, the patients were classified as well-nourished (PG-SGA A), moderately malnourished (PG-SGA B) or severely malnourished (PG-SGA C) based on the first page of the PG-SGA form and the physical examination [7].

2.5. Statistical analyses

The statistical analyses recommended by van der Schueren for validation of the GLIM criteria were used [5]. For the malnutrition diagnosis according to GLIM, we used subjects with any combinations of phenotype and etiologic criteria. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each combination of screening tool with the

GLIM criteria against PG-SGA (global rating) as reference method as follows:

$$\text{Sensitivity} = \text{malnourished}_{\text{both methods}}/\text{malnourished}_{\text{PG-SGA}}$$

$$\text{Specificity} = \text{not malnourished}_{\text{both methods}}/\text{not malnourished}_{\text{PG-SGA}}$$

$$\text{PPV} = \text{malnourished}_{\text{both methods}/}\text{malnourished}_{\text{GLIM}}$$

$$\text{NPV} = \text{not malnourished}_{\text{both methods}/}\text{not malnourished}_{\text{GLIM}}$$

In accordance with the recommendations for validation of the GLIM criteria [5] sensitivity and specificity of >80% was interpreted as acceptable for the diagnosis of malnutrition. Since PG-SGA is a "semi-gold standard" for malnutrition, we also calculated the agreement between the tools using Cohens kappa. Level of agreement was interpreted as almost perfect if Cohens kappa (k) was >0.91, strong if k = 0.81–0.90, moderate if k = 0.60–0.80, week if k = 0.40–0.59 and minimal if k < 0.40 [32]. All statistical analyses were performed using SPSS (IBM SPSS Statistic v.27).

2.6. Sample size calculation

A post hoc sample size calculation was performed on sensitivity and specificity as recommended by de van der Schureren [5] using the method described by Jones [33]. Using a sensitivity and specificity of 70%, and a malnutrition rate of 36% (corresponding to the actual results in the present study) we are 95% confident that the value of sensitivity obtained from our sample was within a distance of ±5 percent points from the true value, and the specificity within a distance of ±4 percent points from the true value.

3. Results

Five hundred and three patients were included in the study. Of these, 77 patients were excluded from the current analysis due to missing PG-SGA or lack of data needed to determine FFMI. Characteristics of the 426 eligible patients are described in Table 1. The mean age was 66 years and mean BMI was 26.9 kg/m^2. Sixty-one percent of the patients had colon cancer, 34% had rectum cancer and 5% patients had rectosigmoid cancer. The median time from CRC surgery to assessments was 166 days.

The results of the screening tools to be applied in step 0 of the GLIM assessment is described in Table 2. Depending on the screening tool, 22–37% of patients were found to be at risk of malnutrition. NRS-2002-4Q detected more subjects at risk of malnutrition compared to the other screening tools.

The number of patients fulfilling the GLIM criteria in step 1 and 2 of the GLIM process (without applying step 0) is shown in Table 3. The GLIM criteria in step 1 and 2 identified 36% as malnourished, whereof 28% were moderately malnourished and 8% severely malnourished. The different combinations of etiology and phenotype leading to the malnutrition diagnoses sums up to more than 100% because one person can fullfit several of the six combinations of criteria. Low FFMI and inflammation was the most frequent combination leading to the malnutrition diagnosis, followed by weight loss and inflammation. The combination of low BMI with reduced food intake was least frequent.

The result of the total GLIM process is described in Fig. 2. Depending on the screening tool in step 0, the GLIM process identified 10–24% as malnourished. In step 2, no cut-off values for FFMI for severe malnutrition are suggested by GLIM. Thus, cut-off values for FFM were only applied for moderate malnutrition, and the commonly used 15 kg/m^2 for women and 17 kg/m^2 for men was used. Again, depending on the screening tool applied in step 0, 7–16% of the participants were categorized as moderately malnourished and 3–8% of the participants were categorized as severely malnourished.

The results of the PG-SGA assessment are described in Table 4. According to PG-SGA, 15% were categorized as moderately malnourished (PG-SGA B) and no patients were severely malnourished (PG-SGA C).

The agreement between GLIM and PG-SGA is shown in Table 5. The GLIM process identified more subjects compared to PG-SGA for 3 out of 4 screening tools applied in step 0 of GLIM. When considering the PG-SGA as the reference method, the sensitivity of GLIM did not reach acceptable levels, neither with nor without screening, irrespective of the tool used. The specificity increased to an acceptable level with all screening tools compared to without screening. The agreement between the PG-SGA and GLIM criteria was minimal using MUST (kappa 0.28), weak using the MST (kappa

Table 1
Baseline characteristics of the study population.

	All subjects	Women	Men
	n = 426	n = 195	n = 231
Age, years, mean (SD)	65.9 (7.6)	65.4 (7.7)	66.3 (7.5)
Anthropometric measures, mean (SD)			
Height, cm	172.9 (8.7)	166.1 (5.8)	178.6 (6.2)
Body weight, kg	80.5 (16.3)	71.8 (14.6)	87.9 (13.9)
Body composition (BIA), mean (SD)			
FFM, kg	53.7 (11.3)	44.1 (5.1)	61.9 (8.3)
FM, kg	26.3 (9.6)	27.2 (10.9)	25.5 (8.3)
BMI, kg/m^2, mean (SD)	26.9 (4.7)	26.1 (5.3)	27.5 (4.0)
Time since surgery, days, mean (SD)	166 (56)	166 (57)	167 (55)
Tumor localization, n (%)			
C 18 Colon	260 (61)	132 (68)	128 (56)
C 19 Rectosigmoid	22 (5)	10 (5)	12 (4)
C 20 Rectum	144 (34)	53 (27)	91 (40)
TNM-stage, n (%)			
I	116 (27)	47 (24)	69 (30)
II	143 (34)	68 (35)	75 (32)
III	118 (28)	63 (32)	55 (24)
Not specified	49 (12)	17 (9)	32 (14)
Treatment, n (%)			
Neoadjuvant	40 (9)	15 (8)	25 (11)
Adjuvant	99 (23)	49 (25)	50 (22)
Number of comorbidities, n (%)			
0	151 (35)	58 (30)	93 (40)
1	144 (34)	70 (36)	74 (32)
≥2	131 (31)	67 (34)	64 (28)
Highest completed education, n (%)			
Primary school	42 (10)	17 (9)	25 (11)
Vocational school	122 (30)	51 (27)	71 (32)
Secondary school	47 (11)	26 (13)	21 (10)
University or college	202 (49)	98 (50)	104 (47)
Other/not answered	13 (3)		
Ability to work, n (%)			
Working (fulltime or parttime)	126 (30)	47 (24)	79 (34)
Not working	71 (17)	38 (19)	33 (14)
Retired	218 (51)	108 (55)	110 (48)
Other/not answered	11 (3)	2 (1)	9 (4)

BIA: Bioelectrical impedance analysis, SD: Standard deviation, TNM: Tumor Nodes Metastasis Classification of Malignant Tumors.

Table 2
The results for the screening tools to be applied in step 0 of GLIM.

Step of the GLIM process	Positive screening by:	n	%
Step 0	NRS-2002-4Q (≥1 point)	157	37
	MST (≥2 points)	113	27
	MUST (≥1 point)	101	24
	PG-SGA SF (≥3 points)	94	22

N = 426. NRS-2002-4Q: Nutritional risk screening (NRS 2002) first four questions, MST: Malnutrition Screening Tool, MUST: Malnutrition Universal Screening Tool. PG-SGA SF: The short form of Patient Generated-Subjective Global Assessment.

Table 3
The results for step 1 and 2 of the GLIM process without applying step 0.

Step of the GLIM process	Criteria	n	%
	Malnourished, any combination:	**154**	**36**
Step 1: Diagnosis	Weight loss >5% last 6 months and reduced food intake/assimilation	38	25
	Weight loss >5% last 6 months and inflammation	88	57
	BMI <20 kg/m^2 and reduced food intake/assimilation	9	6
	BMI <20 kg/m^2 and reduced food intake/assimilation	31	20
	Low FFMI and reduced food intake/assimilation	23	15
	Low FFMI and inflammation	84	55
Step 2: Severity	**Moderately malnourished, total:**	**121**	**28**
	BMI 18.5–20 kg/m^2	22	5
	Weight loss 5–10% last 6 months	62	15
	Low FFMI	84	20
	Severe malnourished, total:	**33**	**8**
	KMI <18.5 kg/m^2	9	2
	Weight loss >10% last 6 months	26	6

N = 426. FFMI: Fat free mass index. BMI: Body Mass Index. GLIM: Global Leadership Initiative on Malnutrition.

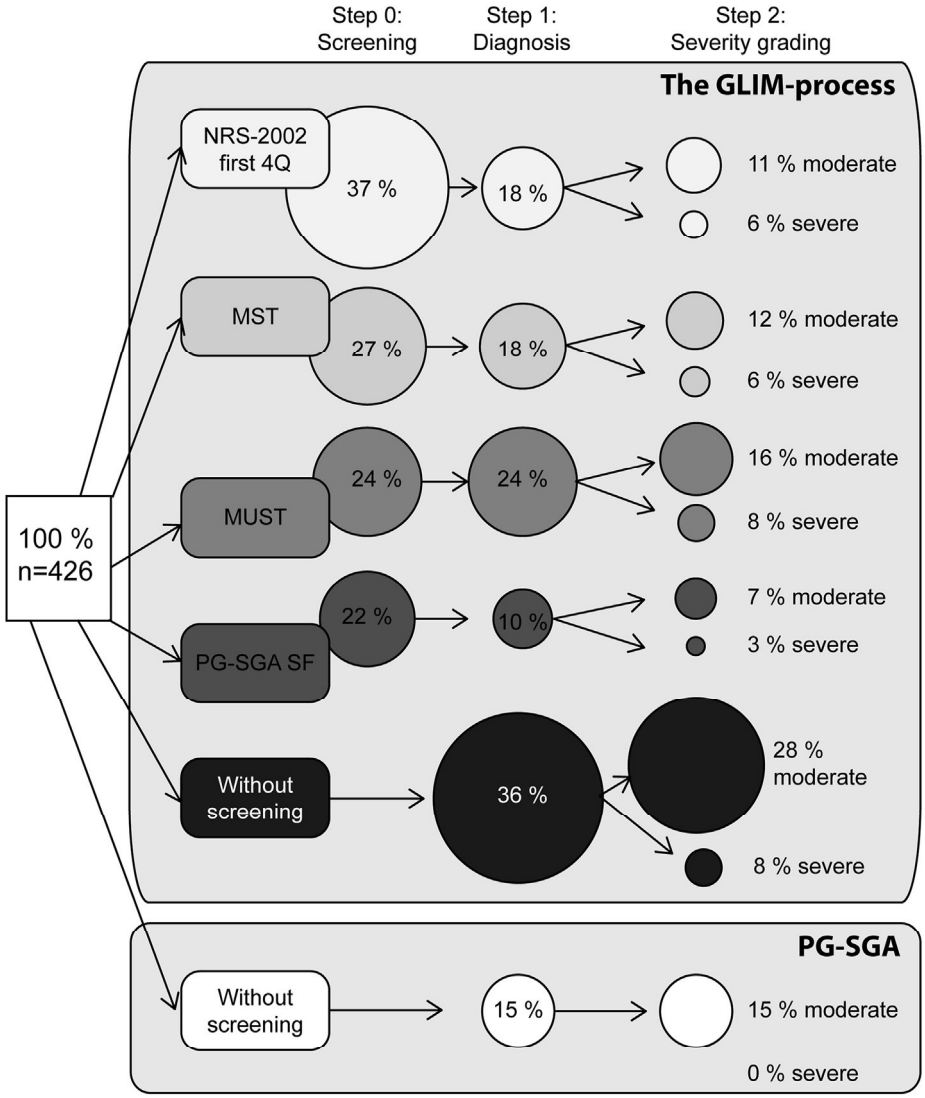

Fig. 2. Result of the total GLIM process showing the amount of patients diagnosed with malnutrition when different screening tools were used in step 0 of the GLIM process. The amount of patients diagnosed with malnutrition without applying any screening tool and by PG-SGA is shown for comparison. NRS-2002-4Q: Nutritional risk screening (NRS 2002) first four questions, MST: Malnutrition Screening Tool, MUST: Malnutrition Universal Screening Tool. PG-SGA SF: The short form of Patient Generated-Subjective Global Assessment.

Table 4
Malnutrition based on PG-SGA.

	n	%
Global rating*, n (%)		
Well nourished (A)	362	85
Moderately malnourished (B)	64	15
Severely malnourished (C)	0	0
Total PG-SGA score		
PG-SGA score <4, n (%)	271	64
PG-SGA score 4–8, n (%)	127	30
PG-SGA score ≥9, (%)	28	6
Median (range)	3	(1–20)

N = 426. PG-SGA: Patient Generated-Subjective Global Assessment *Based on page 1 of PG-SGA and the physical examination.

0.42) and NRS-2002 first 4 questions (kappa 0.49) and moderate using PG-SGA SF (kappa 0.60). Negative predictive values (NPV) were acceptable for all screening tools.

4. Discussion

This cross-sectional study, conducted in CRC patients about 5 months after surgery, shows that the percentage of patients with malnutrition varied from 10 to 24% depending on which screening tool used during the step 0 of the GLIM process. When applying the GLIM process without the use of screening, as many as 36% were identified as malnourished. In comparison, the PG-SGA detected only 15% as malnourished and did not identify any patients to be severely malnourished. The agreement between the PG-SGA and GLIM methods was in general low, but varied according to the screening tool used in step 0.

4.1. Agreement between GLIM and PG-SGA

Few other studies have compared the GLIM process with that of PG-SGA. We found that GLIM, without previous screening as step 0, identified more than twice the number of malnourished participants (36%) compared to PG-SGA (15%). The results are in accordance with an Australian study by De Groot et al. [34] who reported 35% malnourished patients with GLIM compared to 16% with PG-SGA in patients with mixed cancer diagnosis (breast, gynecological and colorectal). Compared to our study, this study did not use fat-free mass as a GLIM criteria. In contrast to the findings by De Groot et al. [34], Zhang et al. [35] reported that the malnutrition prevalence was lower with GLIM (28%) compared to PG-SGA (43%) in a Chinese adults with cancer stage I–IV (gastrointestinal-, head & neck and lung cancer). This was also the case in a recent Norwegian study from a nutrition outpatient clinic, where the malnutrition prevalence was 36% by GLIM and 69% by PG-SGA [36]. The discrepancy may partly be explained by different populations, as these studies included patients with higher risk of malnutrition because of a high number of nutrition impact symptoms and high severity of the disease. PG-SGA weigh symptoms high compared to phenotypic changes and BMI is not included at all. The subjects with low FFMI contributed to about 30% of those diagnosed as malnourished by GLIM. We recognize that the GLIM criteria include low FFMI as an aspect of malnutrition — but of course, one can discuss if these subjects are truly malnourished. If not, this can explain why the GLIM process identifies more subject as malnourished compared to the PG-SGA in our patient group. Another explanation may be that the PG-SGA is not sensitive enough for identifying low muscle mass because of the subjective aspect of the physical examination and that obesity can mask low muscle mass. Because of the conceptual differences between the GLIM criteria and the PGS-SGA, a 100% agreement cannot be expected, but the agreement need to be acceptable, for GLIM to fullfit its purpose.

In contrast to our finding, Allard et al. [37] detected a lower proportion of malnutrition by GLIM, without step 0 screening, (33%) than using SGA (45%) (a previous version of the PG-SGA) in a retrospective study of 784 patients with mixed diagnosis in Canadian hospitals. However, because Allard et al. did not measure and include fat-free mass as part of the GLIM process, the studies might not be directly comparable. Also, different populations of cancer patients may also have contributed to the discrepancies in prevalence of malnutrition, as the participants in the present study only included patients with CRC stage 1–3.

In the present study, the sensitivity of GLIM was 69% without step 0 screening and reduced to 47–63%, when a screening tool was applied as recommended in the full GLIM process. The sensitivity, without previous screening, was in between the results from Allard (sensitivity of 61%) and De Groot (sensitivity of 76%) [34,37]. In the present study, the PPV was only 29%, also in line with the De Groot study (PPV: 34%), but surprisingly low compared to the PPV of 83% reported by Allard. Our result cannot be directly compared with the Zhang study, as they used the GLIM process as a reference method for the other screening and assessment tools (i.e. did the opposite calculations for sensitivity and specificity). The kappa value for GLIM step 1 and 2 only in the present study (0.24) indicated a minimal agreement between GLIM and PG-SGA, which also was the case in the De Groot study (kappa: 0.32). Zhang found kappa: 0.45, and noted that the agreement increased in subgroups with higher malnutrition prevalence [35].

4.2. Effect of screening tool

In the present study, the specificity, PPV and kappa value when comparing the GLIM process to that of PG-SGA increased when a screening tool was applied as step 0. The kappa value was only 0.24 when comparing the PG-SGA method to the GLIM method without screening as part of step 0. Our findings demonstrate that screening reduces the number of patients in need of a full assessment, and

Table 5
Agreement between GLIM and PG-SGA.

	Malnourished					Specific agreement	
	PG-SGA	GLIM	Sensitivity	Specificity	Kappa	PPV %	NPV %
Screening tool used in step 0 of GLIM	n	n	%	%	(95% CI)	%	%
Without screening	64	154	69	70	0.24 (0.16–0.33)	29	93
MST	64	77	56	89	0.42 (0.30–0.53)	47	92
MUST	64	101	53	81	0.28 (0.17–0.39)	34	91
NRS-2002-4Q	64	75	63	90	0.49 (0.38–0.60)	53	93
PG-SGA SF	64	42	47	97	0.60 (0.49–0.70)	71	91

N = 426. NRS-2002-4Q: Nutritional risk screening (NRS 2002) first four questions, MST: Malnutrition Screening Tool, MUST: Malnutrition Universal Screening Tool. PG-SGA SF: The short form of Patient Generated-Subjective Global Assessment, PPV: positive predictive value, NPV: negative predictive value.

increases the agreement with the reference method (PG-SGA). The sensitivity of the GLIM process, however decreased as a result of the screening. With the low sensitivity, we are worried that the screening process may eliminate patients that are truly malnourished. This may be supported by the fact that none of the existing screening tools are capable of detecting low muscle mass, as described in an earlier publication from a subsample of the present study population [23].

We have showed that both absolute prevalence and the accordance with a reference method, depends upon the screening tool used in step 0 of GLIM. As expected, the best agreement was observed when the PG-SGA SF was used as the screening tool, however even with this screening tool, the sensitivity was rather low. NRS-2002-4Q, on the other hand, identified a relatively high proportion of patients "at risk of malnutrition", while at the same time having the highest sensitivity and showing fair agreement with PG-SGA. Taken together, this is pointing to PG-SGA SF and NRS-2002-4Q being the most suitable as step 0 screening tool in the GLIM process. Still, using any of those two screening tools, implicates that a high number of malnourished patients will not be identified, as recently also illustrated at a nutrition outpatient clinic [36]. We speculate that the high proportion of malnourished patients not detected by the screening in our population is due to the presence of many overweight and obese patients. MUST differed from the other screening tools and gave similar result for screening and assessment. This can be explained by the fact that MUST uses the same questions and cut-off points as the GLIM diagnose step 1. These results indicate that screening with MUST may be interchangeable with the diagnostic step 1 of GLIM even though the sensitivity towards PG-SGA is low in our population. For choosing a specific screening tool to a clinical or research setting, resources for training and conducting the screening, available dietitian resources for doing full assessments as well as the characteristics of the specific patient group have to be considered.

4.3. Strengths & limitations

The strength of the present study is that we have followed the GLIM process, exact as described by Cederholm [4] and used the recommendations for validation of the GLIM-process suggested by van der Schueren [5]. In contrast to other publications, we have tested several commonly used screening tools, and included measurement of fat-free mass by bioimpedance. The population includes participants with a range of BMI values, weight loss and gain, in a post therapy situation were monitoring of malnutrition is especially important and relevant. A possible limitation is the double use of the PG-SGA first page (both as a screening tool and included in the reference method) and use of two different BIA-devices, but they are both validated and found suitable to classify subjects as having low vs normal fat free mass [26]. Another limitation is that the global PG-SGA = B can be interpreted as both "moderately malnourished" as well as "risk of malnutrition". Consequently, interpreting PG-SGA B as "malnutrition" may therefor may overestimate the true malnutrition prevalence.

4.4. Implications

Caution should be used when comparing the results from studies using different screening tools as step 0 of the GLIM process, as both the proportion of malnourished as well as the agreement with the reference method depend on the choice of screening tool. Since different screening tools will continue to exist, it is important for clinicians and researchers to be aware of this fact, and malnutrition frequency by GLIM should be reported with and without previous screening procedures. One of the intentions with GLIM was to enable comparison of malnutrition rates in different studies. To achieve this goal, it is essential to further standardize the GLIM process. In our opinion, the screening should be part of good clinical nutrition practice, but should be kept out of the diagnostic procedure in GLIM. This would be more in line with other medical diagnosis were screening is often performed, but in not mandatory for diagnosis.

The agreement between GLIM and PG-SGA was not very strong, and one explanation could be that the PG-SGA does not detect low fat free mass in the same way as the full GLIM process when a measurement of body composition is included. Although PG-SGA is suitable for cancer patients with nutrition impact symptoms and ongoing weight reduction, the GLIM process may be better to detect hidden malnutrition, such as obesity sarcopenia.

5. Conclusion

In this cross-sectional study of patients with CRC, 10–24% were malnourished depending on the screening tool used as step 0 of the GLIM process. The agreement between the GLIM and PG-SGA method was low. Our results indicate that PG-SGA SF and NRS-2002-4Q are the most suitable screening tools, but this may vary according to patient group. The discrepancies between the GLIM criteria and PG-SGA with all screening tools tested, call for further standardization of the diagnostic criteria for malnutrition. PG-SGA and GLIM are not interchangeable as diagnostic criteria, as they probably detect different aspects of malnutrition. Malnutrition frequency based on the GLIM criteria should be reported with and without the use of a screening tool.

Authors contributions

CH: Conceptualization, Methodology, Formal analysis, Writing - Original Draft. **IP**: Conceptualization, Methodology, Visualization, Writing - Original Draft. **AP, ASK, HR, HBH & SKB**: Investigation, Review & Editing. **GW**: Resources, Review & Editing. **RB**: Conceptualization, Methodology, Supervision and Funding acquisition. All authors contributed to analysis and interpretation, and approved the final version to be published.

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Conflict of interest

The authors declare that there have no conflicts of interest.

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References

[1] Torbahn G, Strauss T, Sieber CC, Kiesswetter E, Volkert D. Nutritional status according to the mini nutritional assessment (MNA)(R) as potential prognostic factor for health and treatment outcomes in patients with cancer - a systematic review. BMC Cancer 2020;20(1):594.

[2] Zhang X, Tang T, Pang L, Sharma SV, Li R, Nyitray AG, et al. Malnutrition and overall survival in older adults with cancer: a systematic review and meta-analysis. J Geriatr Oncol 2019;10(6):874–83.
[3] Efthymiou A, Hersberger L, Reber E, Schonenberger KA, Kagi-Braun N, Tribolet P, et al. Nutritional risk is a predictor for long-term mortality: 5-year follow-up of the EFFORT trial. Clin Nutr 2021;40(4):1546–54.
[4] Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition - a consensus report from the global clinical nutrition community. Clin Nutr 2019;38(1):1–9.
[5] de van der Schueren MAE, Keller H, Consortium G, Cederholm T, Barazzoni R, Compher C, et al. Global Leadership Initiative on Malnutrition (GLIM): Guidance on validation of the operational criteria for the diagnosis of protein-energy malnutrition in adults. Clin Nutr 2020;39(9):2872–80.
[6] Paulsen MM, Hagen MLL, Froyen MH, Foss-Pedersen RJ, Bergsager D, Tangvik RJ, et al. A dietary assessment app for hospitalized patients at nutritional risk: development and evaluation of the MyFood app. JMIR Mhealth Uhealth 2018;6(9):e175.
[7] Jager-Wittenaar H, Ottery FD. Assessing nutritional status in cancer: role of the Patient-Generated Subjective Global Assessment. Curr Opin Clin Nutr Metab Care 2017;20(5):322–9.
[8] Thompson KL, Elliott L, Fuchs-Tarlovsky V, Levin RM, Voss AC, Piemonte T. Oncology evidence-based nutrition practice guideline for adults. J Acad Nutr Diet 2017;117(2):297–310. e47.
[9] Sealy MJ, Nijholt W, Stuiver MM, van der Berg MM, Roodenburg JL, van der Schans CP, et al. Content validity across methods of malnutrition assessment in patients with cancer is limited. J Clin Epidemiol 2016;76:125–36.
[10] Prado CM, Baracos VE, McCargar LJ, Reiman T, Mourtzakis M, Tonkin K, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clin Cancer Res 2009;15(8):2920–6.
[11] Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer 2012;107(6):931–6.
[12] Martin L, Birdsell L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. J Clin Oncol 2013;31(12):1539–47.
[13] Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol 2008;9(7):629–35.
[14] de van der Schueren MAE, de Smoker M, Leistra E, Kruizenga HM. The association of weight loss with one-year mortality in hospital patients, stratified by BMI and FFMI subgroups. Clin Nutr 2018;37(5):1518–25.
[15] Prado CM, Siervo M, Mire E, Heymsfield SB, Stephan BC, Broyles S, et al. A population-based approach to define body-composition phenotypes. Am J Clin Nutr 2014;99(6):1369–77.
[16] Mareschal J, Achamrah N, Norman K, Genton L. Clinical value of muscle mass assessment in clinical conditions associated with malnutrition. J Clin Med 2019;8(7).
[17] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22(4):415–21.
[18] Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003;22(3):321–36.
[19] Tangvik RJ, Tell GS, Eisman JA, Guttormsen AB, Henriksen A, Nilsen RM, et al. The nutritional strategy: four questions predict morbidity, mortality and health care costs. Clin Nutr 2014;33(4):634–41.
[20] Ferguson M, Capra S, Bauer J, Banks M. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. Nutrition (Burbank, Los Angeles County, Calif) 1999;15(6):458–64.
[21] M. E. The 'MUST' report. Nutritional screening of adults: a multidisciplinary responsibility. BAPEN, (MAG); 2003.
[22] Henriksen HB, Raeder H, Bohn SK, Paur I, Kvaerner AS, Billington SA, et al. The Norwegian dietary guidelines and colorectal cancer survival (CRC-NORDIET) study: a food-based multicentre randomized controlled trial. BMC Cancer 2017;17(1):83.
[23] Raeder H, Henriksen C, Bohn SK, de Fey Vilbo ARO, Henriksen HB, Kvaerner AS, et al. Agreement between PG-SGA category and fat-free mass in colorectal cancer patients. Clin Nutr ESPEN 2018;27:24–31.
[24] Schulze KV, Swaminathan S, Howell S, Jajoo A, Lie NC, Brown O, et al. Edematous severe acute malnutrition is characterized by hypomethylation of DNA. Nat Commun 2019;10(1):5791.
[25] Balstad TR, Bye A, Jenssen CR, Solheim TS, Thoresen L, Sand K. Patient interpretation of the Patient-Generated Subjective Global Assessment (PG-SGA) Short Form. Patient Prefer Adherence 2019;13:1391–400.
[26] Raeder H, Kvaerner AS, Henriksen C, Florholmen G, Henriksen HB, Bohn SK, et al. Validity of bioelectrical impedance analysis in estimation of fat-free mass in colorectal cancer patients. Clin Nutr 2017;37(1):298–300.
[27] Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition - an ESPEN consensus statement. Clin Nutr 2015;34(3):335–40.
[28] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. Age Ageing 2010;39(4):412–23.
[29] Henriksen C, Thoresen L, Fjoseide B, Lorentzen SS, Balstad TR, Ottery FD, et al. Linguistic and content validation of the translated and culturally adapted PG-SGA, as perceived by Norwegian cancer patients and healthcare professionals. Clin Nutr ESPEN 2020;38:178–84.
[30] MPDaP CG, editor. The clinical guide to oncology nutrition. Chicago, Illinois: The American Dietetic Association; 2000.
[31] Sealy MJ, Ottery FD, van der Schans CP, Roodenburg JLN, Jager-Wittenaar H. Evaluation of change in dietitians' perceived comprehensibility and difficulty of the Patient-Generated Subjective Global Assessment (PG-SGA) after a single training in the use of the instrument. J Hum Nutr Diet 2017;31(1):58–66.
[32] McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb) 2012;22(3):276–82.
[33] Jones JM. Validity of nutritional screening and assessment tools. Nutrition 2004;20(3):312–7.
[34] De Groot LM, Lee G, Ackerie A, van der Meij BS. Malnutrition screening and assessment in the cancer care ambulatory setting: mortality predictability and validity of the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) and the GLIM criteria. Nutrients 2020;12(8).
[35] Zhang Z, Wan Z, Zhu Y, Zhang L, Zhang L, Wan H. Prevalence of malnutrition comparing NRS2002, MUST, and PG-SGA with the GLIM criteria in adults with cancer: a multi-center study. Nutrition 2021;83:111072.
[36] Rosnes KS, Henriksen C, Hoidalen A, Paur I. Agreement between the GLIM criteria and PG-SGA in a mixed patient population at a nutrition outpatient clinic. Clin Nutr 2021;40(8):5030–7.
[37] Allard JP, Keller H, Gramlich L, Jeejeebhoy KN, Laporte M, Duerksen DR. GLIM criteria has fair sensitivity and specificity for diagnosing malnutrition when using SGA as comparator. Clin Nutr 2020;39(9):2771–7.