Routine Assessment of Nutritional, Functional and Inflammatory Criteria in Patients with Cancer: A systematic review

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## 19 Abstract

20 21

Background: The review discusses the significant impact of cancer on patients, particularly
focusing on cachexia - a condition marked by weight and lean tissue loss. This condition critically
affects the nutritional status, quality of life, and treatment outcomes of cancer patients.

25 Research Question: The review seeks to understand the effectiveness and necessity of routine
26 clinical monitoring of cancer cachexia, and how it can aid in better therapeutic interventions.

Methods: The systematic review followed a pre-defined protocol based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)statement. A systematic search using specific keywords was conducted in PubMed and EMBASE databases on October 24, 2023, supplemented by citations from the original papers. The selection process involved screening titles and abstracts for relevance.

32 Results: The review finds varying levels of effectiveness in the different measurement criteria 33 used for monitoring cachexia. It highlights the potential of the Global Leadership Initiative on 34 Malnutrition (GLIM) framework in defining and managing cancer cachexia, though noting some 35 challenges in standardisation and implementation of measurements.

36 **Conclusion:** The present systematic review highlights the variability and lack of standardization 37 in the application of GLIM criteria for monitoring cachexia in cancer patients. Despite these 38 challenges, it will be important to determine the most efficacious clinically routine nutritional and 39 inflammation assessments in the routine application of GLIM criteria assessment.

## 40 Keywords

41 Cancer, Cachexia, Routine assessment, Malnutrition, Systematic inflammatory, Weight loss

## 42 Introduction

43 44

45 Of all of the effects of cancer on the host the most obvious is cachexia, characterized by 46 progressive involuntary loss of weight and lean tissue. This is a prevalent syndrome as the cancer 47 progresses and, in addition to nutritional status, impacts on functional status, quality of life and 48 treatment outcomes. This complex condition transcends the simple perception that this is a 49 nutritional problem since nutritional interventions have not been successful (1, 2). The syndrome's 50 complex pathophysiology involves negative energy and protein balance (3) and systemic 51 inflammation (2, 4). In particular, systemic inflammation, however measured, has been considered as tip of the tumour/ host iceberg alerting to changes in host metabolism, catabolism and quality 52 53 of life (5). Patients with aggressive cancer, such as lung and pancreatic cancer, often exhibit 54 systemic inflammation at diagnosis, complicating their prognosis and potential benefit from 55 conventional nutritional interventions (1, 6).

Therefore, there is a need to clinically monitor the syndrome of cancer cachexia (similar to that of tumour progression) on a routine basis to provide longitudinal knowledge of the condition and landmarks for therapeutic intervention. The aim of the present review was to examine which measurements best captured this syndrome for routine clinical monitoring of the host.

60

## 61 Nutritional status

The importance of nutritional status in the definition of cancer cachexia is emphasised in the Fearon definition (3) which proposed a diagnosis of cachexia if any one of these conditions regarding weight loss was met: a minimum of 5% weight loss in the past six months, excluding straightforward starvation causes; or at least a 2% weight loss in the those patients with a BMI <20

kg/m2 or the presence of sarcopenia. Indeed, these criteria have formed the cornerstones of clinical 66 67 research in cancer cachexia in the past 3 decades. From this definition a Body Mass Index (BMI) 68 -adjusted weight loss grading system has been shown to have prognostic value (7, 8) and was 69 found to be associated with quality of life in patients with advanced cancer (8, 9). However, there 70 have been long established malnutrition screening tools such as Malnutrition Universal Screening 71 Tool (MUST), Malnutrition Screening Tool (MST) and Nutritional Risk Screening 2002 (NRS-72 2002) and of these MUST would appear most closely aligned with the Fearon definition (10). This 73 is perhaps not surprising since weight loss and BMI are integral to the MUST score. The Fearon 74 definition also included the presence of sarcopenia as an indicator of cachexia in patients with 75 cancer. In the past decade of so with the advent of Computed Tomography (CT)-derived body 76 composition and a reliable assessment of low muscle mass, the relationship between a low muscle 77 mass and global quality of life (11) and its prognostic importance has been confirmed (12-14).

78

### 79 Functional status

In addition to being defined as part of the syndrome of cancer cachexia, sarcopenia has, in 80 81 turn, been defined as a syndrome characterized by progressive and generalized loss of skeletal 82 muscle mass and strength that is associated with physical disability, poor quality of life and death. 83 From the above it is clear that muscle mass can be routinely measured by CT-derived body 84 composition analysis. In contrast, muscle strength and its relationship with the ability to carry out 85 daily living activities is less well defined. In oncology, such Eastern Cooperative Oncology Group 86 Performance Status (ECOG-PS) has been recognised to be associated with quality of life (15) and 87 survival (16). Similarly, a direct method of muscle strength, hand grip strength has been shown to 88 be associated with quality of life (17) and survival (18).

# 89 Systemic inflammation

90	Although not included in the Fearon criteria for diagnosis of cancer cachexia, inflammation
91	plays a pivotal role in cancer growth and progression and is considered a hallmark of cancer (19).
92	Indeed, the prognostic importance of systemic inflammation had led to its inclusion in a number
93	of consensus frameworks for defining cancer cachexia (2). The main systemic inflammation based
94	prognostic scores used in this context are the Glasgow Prognostic Score (GPS) (20) and the
95	neutrophil lymphocyte ratio (21, 22). Furthermore, the systemic inflammatory response (SIR), as
96	evidenced by the modified Glasgow Prognostic Score (mGPS), has been shown to be associated
97	with quality of life (15, 23, 24).
98	
99	Proposed combinations of criteria
100 101	Over the past two decades attempts to clinically identify the syndrome of cancer cachexia
102	have evolved. Presently, initiatives like the Global Leadership Initiative on malnutrition (GLIM)
103	criteria consider cancer cachexia to be "disease related malnutrition with inflammation" (2) and
104	consider both phenotypic criteria (weight loss, BMI and low muscle mass) and aetiologic criteria
105	(low food intake/assimilation and disease burden/inflammation). However, the measurements to
106	be used for criteria of low muscle mass, low food intake and inflammation remain to be defined
107	and linked to routine clinical practice.
108	Patton and coworkers introduced the Routine EValuatiOn of people LivIng with cancer
109	protocol (REVOLUTION) (25), designed to provide continuous assessment of patients with
110	advanced cancer. For body composition evaluation bioelectrical impedance measurement and CT
111	scans were proposed. For physical function Karnofsky Performance Status (KPS) and the use of

112 an eight-day continuous physical activity monitoring were proposed. For appraising the SIR full 113 white cell count, urea and electrolytes, albumin, and lactate dehydrogenase were proposed tests. Lastly, for quality of life European Organization for the Research and Treatment of Cancer Quality 114 115 of Life Questionnaire (EORTC-QLQ-C30), Edmonton Symptom Assessment System (ESAS), the 116 Functional Assessment of Anorexia/ Cachexia Therapy Scale (FAACT), Patient-Generated 117 Subjective Global Assessment (PGSGA), the Hospital Anxiety and Depression Scale (HADS), and 118 the Eating Assessment Tool-10 (EAT-10) were proposed (25). Upon closely examining the details 119 of REVOLUTION certain concerns arise. Although Revolution study covers all aspects of the 120 cancer cachexia patients, it does not clearly define the best method or sequence in which to conduct 121 these assessments.

122 Vigano and colleagues (26) outlined routinely available clinical, nutritional, and functional 123 criteria for staging cachexia in advanced cancer patients. Beginning with the four-stage 124 classification system proposed for cachexia namely non-cachexia (NCa), pre-cachexia (PCa), 125 cachexia (Ca) and refractory cachexia (RCa), patients were assigned to these cachexia stages 126 according to five classification criteria available in clinical practice: 1) biochemistry (high C-127 reactive protein or leukocytes, or hypoalbuminemia, or anemia), 2) food intake 128 (normal/decreased), weight loss: 3) moderate ( $\leq$ 5%) or 4) significant ( $\geq$ 5%/past six months) and 129 5) ECOG-PS  $\geq$  3. They then determined if symptom severity, body composition changes, 130 functional levels, hospitalizations and survival rates varied significantly across cachexia stages. 131 There were significant differences across the cachexia stages for most of the outcome measures 132 including symptoms, body composition, hand-grip strength, clinical outcomes and survival. They 133 concluded that the above 5 clinical criteria can be used to stage cachexia in cancer patients and 134 predict important clinical, nutritional and functional outcomes.

## 135 Methods

## 136 - Search strategy

The current systematic review of the published literature was conducted following a predefined protocol as articulated in the PRISMA statement. A systematic search was conducted using keywords "(Cancer) AND (The Global Leadership Initiative on Malnutrition)" Two databases, PubMed and EMBASE, were extensively explored to retrieve relevant articles on 24th October 2023. Moreover, citations from the original assessment paper were followed to ensure comprehensive inclusion of relevant studies. Titles and abstracts of these articles were screened to determine their relevance for full-text review.

## 144 - Data Extraction:

For papers shortlisted for full-text review, key data points were extracted and tabulated. This included the study objective, population demographics, study design, results, and conclusions.

148 - Analysis:

After close consideration of details from the Revolution and Vigano framework papers, specific concerns related to methodology and outcomes were noted. Based on these observations, the primary focus of this review was directed towards the GLIM framework. The analysis of the framework and its implications in clinical practice formed the crux of our analysis.

## 153 **Results**

The systematic literature search found 2,801 studies (**Figure 1**). A total of 993 studies were excluded before the title and abstract screening and 1,681 studies were excluded after the title and abstract screening. Additionally, 33 studies measured outcomes using GLIM criteria to assess the efficacy of treatment or its impact without specifying which particular GLIM assessment model was implemented were excluded after full text articles were assessed for eligibility. Reasons for exclusion are shown in **Figure 1**. Analysis of 94 pertinent studies revealed a consistent application of GLIM assessment, The summary of characteristics of the 94 studies was shown in **Table 1**.

161

## Phenotypic Criteria

162 It was consistently observed that all studies recorded weight loss, patients' weight and 163 height (BMI). The lower muscle mass criterion was absent from 11 studies (27-37). Twenty-eight 164 studies used CT scans at the L3 vertebral level, with this method being the sole assessment tool in 165 21 studies (38-58). Only a minority of six studies used this method in conjunction with muscle strength assessments (59-64), and one study used Bioelectrical Impedance Analysis (BIA) (65). 166 167 Anthropometry was the most common assessment method, implemented in 38 studies, measuring 168 parameters such as mid-arm muscle circumference (MAMC), mid-upper arm circumference 169 (MUAC), muscle arm circumference (MAC), arm muscle circumference (AMC), appendicular 170 skeletal muscle index (ASMI), calf circumference (CC), and triceps skin fold (TSF) thickness. 171 Fifteen studies exclusively relied on anthropometry (66-80), while 21 studies integrated it with 172 muscle strength assessments (81-101), 1 study combined anthropometry with BIA (102), and 1 173 study combined both BIA and muscle strength assessments (103). The utilization of BIA devices, 174 despite being the simplest and quickest method, was the least frequent, appearing in only 15

9

studies. Of these, BIA was the sole assessment tool in 9 studies (104-112), was combined with muscle strength assessments in 3 studies (113-115), with CT scans in 1 study, with anthropometry in 1 study, and with both anthropometry and muscle strength assessments in 1 study. Nearly all of the 36 studies assessing muscle strength utilized Handgrip Strength (HGS). This method was the sole assessment tool in 5 studies (116-120).

180 Etiologic criteria

181 The reduced food intake or assimilation component, there was notable variability, with 15 182 studies (30, 31, 37, 38, 42, 43, 48, 65, 70, 77, 79, 100, 107, 115, 119) omitting this aspect altogether. 183 Thirty-three studies utilized patient-reported assessments. A diverse range of tools was used across 184 46 studies for the final assessment approach, including NRS-2002 in 22 studies (29, 32, 39, 45, 185 46, 51, 56, 57, 60-62, 64, 69, 72, 78, 85, 90, 95, 98, 108, 111, 117), MUST in 7 studies (28, 36, 49, 186 55, 58, 71, 88), PG-SGA in 5 studies (40, 44, 53, 101, 113), and MST in 2 studies (59, 66). Several 187 studies combined assessment tools, with NRS-2002 and PG-SGA used in 5 studies (33, 82-84, 86), 188 MUST and Mini Nutritional Assessment (MNA) in 2 studies (68, 73), MST and PG-SGA in 1 189 study (63), and the MD Anderson Symptom Inventory Gastrointestinal (MDASI-GI) with Cancer 190 Appetite and Symptom Questionnaire (CASCO) in 1 study (35). Moreover, there was one study 191 that compared three tools MUST, NRS-2002 and PG-SGA in GLIM (74).

In the context of assessing disease burden and inflammatory conditions, 20 studies did not include this evaluation (32, 36, 50, 51, 54, 56, 60, 63, 68, 73-76, 78, 82, 87, 88, 95, 98, 102) and there were 30 studies predicated their assessments on the assumption that the study population consisted solely of cancer patients. There were 44 studies based on laboratory values, within the laboratory value-based studies, the most measured markers were C-Reactive Protein (CRP),

197 recorded in 14 studies (28, 31, 34, 35, 40, 53, 71, 80, 93, 105, 109, 111, 112, 116), and Albumin 198 levels, noted in 4 studies (57, 59, 62, 85). Eleven studies conducted a broader analysis 199 incorporating more than one laboratory value, commonly CRP in conjunction with Albumin levels 200 (33, 58, 90, 92, 103, 113). Fifteen studies used this assessment tool to analyses the laboratory 201 results, the most frequently utilized predefined models were mGPS and GPS, implemented in 5 202 studies (55, 91, 110, 118, 119). The Neutrophil-to-Lymphocyte Ratio (NLR) appearing alone in 3 203 study (84, 89, 101). One study use both of mGPS and NLR (43). Additionally, 5 studies employed 204 a composite approach, integrating mGPS/GPS or NLR with other indicators, including the 205 Albumin-Lymphocyte Index (ALI) (29), the Systemic Immune-Inflammation Index (SII) (29, 206 115), the inflammatory burden index (IBI) (52), the Monocyte-to-Lymphocyte Ratio (MLR) (49), 207 the Prognostic Nutritional Index (PNI) (30), the Controlling Nutritional Status (CONUT) (30), and 208 the Lymphocyte-to-Monocyte Ratio (LMR) (115). Moreover, a study used unique markers namely 209 the fat-age-inflammation (FAIN) index (86).

## 210 Discussion

211 The results of the present systematic review show that the comprehensive assessment of 212 nutritional, functional and inflammatory criteria to date are most commonly reported within the 213 GLIM framework (n=94). Within this framework phenotypic criteria are most commonly reported, 214 especially weight loss and BMI and there is agreement on how they should be measured. In 215 contrast, etiologic criteria are less commonly reported and there is little agreement on the 216 individual criteria and how they should be measured. The current ESMO guidelines (121) 217 recommend that cachexia is defined "as disease-related malnutrition with inflammation" as per the 218 GLIM definition of malnutrition. This proposes that phenotypic nutritional criteria (including 219 weight loss) should take precedent over etiologic criteria (including inflammation). This may be 220 because the measures of the phenotypic criteria are well defined by the GLIM group. However, 221 the GLIM group have recently defined the measure of inflammation as a raised CRP (122). 222 Therefore, as previously proposed (2) it may be that cachexia should be defined as disease related 223 inflammation with malnutrition with consequent implications for the reversal of the order of measurements (etiological criteria first followed by phenotypic criteria). 224

225 The phenotypic criteria, which encompasses unintentional weight loss and low BMI, are 226 largely pre-defined by the GLIM criteria. These stipulate a weight loss exceeding 5% within three 227 months, or beyond 10% over six months, and delineate a Low BMI as under 20 kg/m<sup>2</sup> for patients 228 younger than 70 years, or less than  $22 \text{ kg/m}^2$  for those aged 70 and above (123). Demonstrating 229 precision in determining the reduced muscle mass criterion, CT scans at the L3 vertebral level 230 were used in the majority of studies. Nevertheless, HGS and anthropometry could also be utilised, 231 as they have been employed to ascertain lower muscle mass criterion in numerous studies. 232 Moreover, HGS can be used to assess muscle strength, the dominant diagnostic feature of

sarcopenia (124) and a critical aspect of concern in cancer patients suffering from cachexia (25).
Recently, in a systematic review of randomised clinical trials in cancer cachexia MacDonald and
coworkers (17) concluded that among the objective measures of physical function hand grip
strength (HGS) was the most commonly used physical function endpoint. However, heterogeneity
in study design, populations, intervention and endpoint selection made it difficult to recommend
the optimal physical function endpoint and how to measure this.

239 In evaluating the etiological criterion, most studies did not reliably report on this aspect. 240 Although there are various tools that have been used to determine the reduced food Intake 241 component (125), the assimilation component is less well defined. Also, as an etiologic factor, 242 disease burden and inflammation are both considered as one criteria where it has not been 243 established whether they have the same effect on outcome. Furthermore, if the sensitivity of the 244 current GLIM framework is dependent on whether disease burden/inflammation is utilized as a diagnostic criterion, given their differential association between SIR and low skeletal muscle mass 245 246 (14, 126), then it is crucial to distinguish between these factors. Given that the GLIM framework requires just one phenotypic and one etiological criterion; many studies have only considered 247 248 disease burden and not inflammation in patients with cancer. However, systemic inflammation is 249 increasingly recognized as central to defining, diagnosing, and treating cancer cachexia (6, 127). 250 The origin of the SIR in cancer patients is not fully understood, but it is believed to be a general 251 reaction to tumor-induced hypoxia/necrosis or local tissue damage (2, 128). With regard to 252 defining cancer associated inflammation both GPS/ mGPS and NLR have extensively validated 253 prognostic value and may be employed to measure this criterion (2).

Our analysis illuminated the considerable variability in GLIM criteria application across clinical cancer research, echoing the urgent call for standardized practices. This variability not

256 only complicates the interpretation of nutritional assessments but also hampers the comprehensive 257 management of cancer cachexia. The present analysis highlights the considerable variability in the 258 application of GLIM criteria application and thus pressing need for standardisation of criteria to 259 be used. Recently resting energy expenditure has been proposed as useful measurement to 260 characterize cachexia in patients with NSCLC (129, 130). However, the complexity and variability 261 of such measurements may be difficult to incorporate into routine clinical practice (131). Furthermore, the present study, given the variable measurements for phenotypic and aetiologic 262 263 criteria, was not able to differentiate GLIM effects of different cancer types. With the 264 standardisation of GLIM criteria measurements, it may be able to better understand its clinical 265 utility across different cancer populations.

### 266 Conclusion

Therefore, despite increasing consensus in what should be measured to define cancer cachexia, the present systematic review highlights the variability and lack of standardization in the application of GLIM criteria for monitoring cachexia in cancer patients. Despite these challenges, it will be important to determine the most efficacious clinically routine nutritional and inflammation assessments in the routine application of GLIM criteria assessment. Further studies are required to test the relative prognostic value of the various GLIM components.

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## 279 Author contribution

280 **Chattarin Pumtako** initiated and was involved in conceptualization, formal analysis, contributed 281 to specifically in methodology, analysis and interpretation of data, wrote the original and revision 282 of the manuscript for important intellectual content and approved the final version of the 283 manuscript.

Ross D Dolan involved in conceptualization, contributed to specifically in methodology, analysis
and interpretation of data, revision of the manuscript for important intellectual content and
approved the final version of the manuscript.

Josh McGovern involved in conceptualization, analysis and interpretation of results, revised
versions of the manuscript and approved the final version of the manuscript.

289 **Donald C McMillan** initiated and was involved in conceptualization, formal analysis, 290 investigation, analysis and interpretation of data, wrote the original and revision of the manuscript 291 for important intellectual content and approved the final version of the manuscript. Merker M, Felder M, Gueissaz L, Bolliger R, Tribolet P, Kagi-Braun N, et al.

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 Table 1. Key characteristics of eligible studies

Author (Reference)	Year	Sample size	Study design	Cancer type	Intervention	Reduce food intake	Inflammatory	Reduce muscle mass	Other tools
Wongdama, S., et al. (27)	2023	350	Cross-sectional study	All type without breast or prostate cancer	radiotherapy	quartiles of the previous 7-14 days	Blood test	-	NRS2002, SPENT, PG-SGA
Molfino, A., et al. (28)	2022	102	Prospective study	gastrointestinal or lung cancers	non-interventional	MUST	CRP	-	-
Zhang, K. P., et al. (29)	2022	1431	Cohort study	cancer	non-interventional	NRS2002	ALI/ mGPS/ SII	-	EORTC
Takamizawa, Y., et al. (30)	2020	1030	Cohort study	colorectal cancer	curative resection		mGPS/ PNI/ CONUT	-	-
Einarsson, S., et al. (31) <sup>-</sup>	2020	229	Observational study	head and neck cancer	anti-cancer treatment	-	CRP	-	-
Chen, W. Z., et al. (32)	2023	1359	Retrospective study	gastric cancer	gastrectomy	NRS2002	-	-	-
Ozorio, G. A., et al. (33) <sup>+</sup>	2023	885	Retrospective study	cancer	chemotherapy, radiotherapy, or surgery	NRS2002, SGA	Albumin CRP	-	-
Okada, G., et al. (34)	2021	117	Randomized controlled trial	esophageal cancer	postoperative	quartiles of the previous 7-14 days	CRP	-	-
Tan, S., et al. (35) <sup>+</sup>	2022	1115	Observational study	gastric, colorectal, pancreatic, or biliary cancer	cancer treatment	MDASI-GI/ CASCO	CRP	-	-
Gascon-Ruiz, M., et al. (36)	2021	165	Cross-sectional study	upper gastrointestinal tract, colorectal, and of the head and neck area	active oncological treatment	MUST	-	-	ESPEN
Przekop, Z., et al. (37) <sup>+</sup>	2022	237	Retrospective study	Head and Neck Cancer		-	Disease*	-	-
Murnane, L. C., et al. (38)	2023	108	Cohort Study	oesophago-Gastric cancer	surgery	-	Disease*, Blood test	СТ	-
Liu, Y., et al. (39) <sup>+</sup>	2023	182	Cohort study	adenocarcinoma and squamous cell carcinoma	surgery	NRS2002	Disease	СТ	PG-SGA
Matsui, R., et al. (40)	2023	512	Retrospective cohort study	gastric cancer	gastrectomy	SGA	CRP	CT	-
Menozzi, R., et al. (41)	2023	103	Retrospective study	carcinoma	Surgery	energy requirement	Disease	СТ	-
Korczak, J., et al. (42)	2023	64	Observational study	prostate adenocarcinoma	androgen deprivation therapy	-	Disease	СТ	NRS2002
McGovern, J., et al. (43)	2023	436	Retrospective cohort study	advanced cancer	anti-cancer therapy with palliative intent	-	NRL/ mGPS	СТ	-

Author (Reference)	Year	Sample size	Study design	Cancer type	Intervention	Reduce food intake	Inflammatory	Reduce muscle mass	Other tools
da Silva Couto, A., et al. (44) <sup>+</sup>	2023	191	Retrospective cohort study	colorectal cancer	routine abdominal CT scan	PG-SGA	Disease	СТ	-
Zhang, Y., et al. (45)	2022	182	Retrospective cohort study	gastric cancer	radical surgery after neoadjuvant treatment	NRS2002	Disease*	СТ	-
Cai, W., et al. (46)	2022	1007	Propensity Score- Matched Analysis	gastric cancer	radical gastrectomy	NRS2002	Disease*	СТ	-
Huang, Y., et al. (47)	2022	488	Cohort study	gastrointestinal cancer	non-interventional	quartiles of the previous 7-14 days	Disease	СТ	NRS 2002, GNRI, MNA-S
Xu, L. B., et al. (48)	2022	1188	Retrospective cohort study	gastric cancer	gastrectomy	-	Disease*	СТ	-
Xu, L. B., et al. (49) <sup>+</sup>	2022	1020	Retrospective study	gastric cancer	gastrectomy	MUST	NLR/ MLR	СТ	-
Findlay, M., et al. (50)	2021	359	Retrospective cohort study	head and neck cancer	adjuvant	food diary	-	CT	-
Huang, D. D., et al. (51)	2021	587	Observational study	gastric cancer	radical gastrectomy	NRS 2002	-	CT	-
Xie, H., et al. (52)	2023	5700	Prospective study	cancer	noninterventional	self-reported	IBI/CRP/NLR /ALB	CT	ECOG
Matsui, R., et al. (53) <sup>+</sup>	2023	281	Retrospective cohort study	gastric cancer	adjuvant chemotherapy	BWL, SGA	CRP	СТ	-
Zhang, F. M., et al. (54)	2021	1315	Random resampling	gastric cancer	curative surgery	quartiles of the previous 7-14 days	-	СТ	-
Abbass, T., et al. (55)	2020	647	Cohort study	lung cancer	radiotherapy	MUST	mGPS	СТ	ECOG
Zhou, C. J., et al. (56)	2023	624	Cohort study	rectal cancer	proctectomy	NRS-2002	-	СТ	-
Chen, X. Y., et al. (57)	2022	636	Cohort study	rectal cancer patients	proctectomy	NRS-2002	Albumin	СТ	-
Almasaudi, A. S., et al. (58)	2020	795	Retrospective cohort study	colorectal Cancer	surgery	MUST	Albumin CRP	СТ	-
Tolonen, A., et al. (59)	2023	80	Retrospective- cohort study	upper GI, lower GI, and other cancers	CT scan	MST	Albumin	CT, Handgrip	Sit to Stand
Caccialanza, R., et al. (60)	2022	180	Randomized clinical trial	head and neck cancer	immunonutrition	NRS-2002	-	CT, Handgrip	-
Huang, D. D., et al. (61) <sup>+</sup>	2022	1359	Cohort study	gastric cancer	gastrectomy	NRS2002	Disease*	CT, Handgrip	-

Author (Reference)	Year	Sample size	Study design	Cancer type	Intervention	Reduce food intake	Inflammatory	Reduce muscle mass	Other tools
Chen, W. Z., et al. (62)	2022	742	Observational study	gastric cancer	gastrectomy	NRS2002	Albumin	CT, Handgrip	-
Djordjevic, A., et al. (63)	2022	57	Exploratory study	colorectal cancer	surgery	MST/ PG-SGA	-	CT, Handgrip	-
Zhou, L. P., et al. (64)	2021	2209	Cohort study	gastrointestinal cancers	cancer treatment	NRS2002	Disease*	CT, Handgrip	-
Qin, L., et al. (65) <sup>+</sup>	2021	217	Cross-sectional study	gastric Cancer	cancer treatment	5	Disease*	CT/ BIA	ECOG, KPS, PG- SGA
Kiss, N., et al. (66) <sup>+</sup>	2023	2801	Cohort Study	cancer	radiotherapy, intravenous chemotherapy or immunotherapy	MST	Disease	MMT	PG-SGA
Gounitsioti, I. S., et al. (67)	2022	53	Two-time points study	gynecological Cancer	Surgery	dietary recall	Disease*	Anthropometry	SGA
Srinivasaragh avan, N., et al. (68)	2022	107	Cross-sectional	cancer	noninterventional	MUST/ MNA-SF	-	CC	-
Yin, L., et al. (69)	2022	2672	Cohort study	lung cancer	noninterventional	NRS2002	Disease*	Anthropometry	EORTC
Yin, L., et al. (70)	2021	4025	Cohort study	cancer	cancer treatment	-	Disease	CC	-
Wang, Y., et al. (71)	2021	686	Cross-sectional	cancer	noninterventional	MUST	CRP	CC	PG-SGA
Yin, L., et al. (72) <sup>+</sup>	2021	360	Cohort study	esophageal cancer	Esophagectomy	NRS2002	Disease*	CC	PG-SGA, ESPEN
Lopez- Gomez, J. J., et al. (73)	2023	149	Longitudinal, retrospective study	cancer	cancer treatment	MUST/ MNA	-	ASMI/ CC	-
Zhang, Z., et al. (74)	2021	637	Observational study	cancer	radiation therapy	NRS2002, MUST, PG-SGA	-	MAC/ CC	-
Zheng, H. L., et al. (75) <sup>+</sup>	2023	1121	Retrospective study	gastric adenocarcinoma	radical gastrectomy	quartiles of the previous 7-14 days	-	validated body composition measuring techniques.	-
Zhang, Z., et al. (76) <sup>+</sup>	2022	468	Randomized clinical trial	cancer	radiotherapy	quartiles of the previous 7-14 days	-	CC/ MAC	PG-SGA
Huo, Ż., et al. (77) <sup>–</sup>	2023	6697	Rohort study	lung cancer	anticancer therapies	-	Disease*	CC	PG-SGA

Author (Reference)	Year	Sample size	Study design	Cancer type	Intervention	Reduce food intake	Inflammatory	Reduce muscle mass	Other tools
	2021		Deference etime			NRS 2002			10015
Zhang, X., et al. (78) <sup>+</sup>		1281	Retrospective cohort study	cancers	noninterventional	NRS 2002	-	Anthropometric	-
Zhuang, C. L., et al. (79)	2022	17597	Retrospective study	cancers	noninterventional	-	Disease*	MUAC/ CC	PG-SGA
Cioce, M., et al. (80)	2022	36	Observational study	myeloma, lymphoma, leukemia	allogeneic hematopoietic stem cell transplantation	quartiles of the previous 7-14 days	CRP	PA	NRS-2002
Crestani, M. S., et al. (81)	2023	183	Cohort study	gastrointestinal, head and neck, and lung cancer	cancer therapy	self-reported	Disease*	Handgrip, CC	-
Wu, T., et al. (82) <sup>+</sup>	2022	10214	Cohort study	colorectal cancer	reduced muscle mass assessment	NRS2002/ PG-SGA	-	Handgrip, MAMC/ CC	-
Song, M., et al. (83) <sup>+</sup>	2022	8478	Cohort study	16 types of locally or metastatic malignant solid tumors.	cancer therapy	NRS2002/ PG-SGA	Routine blood tests	Handgrip, MAMC/ CC/ TSF	KPS
Wang, Y., et al. (84)	2022	1637	Cohort study	colorectal cancer	surgery	NRS2002/ PG-SGA	NLR	Handgrip, Anthropometry	EORTC
Liu, C., et al. (85) <sup>+</sup>	2021	2388	Retrospective study	cancer	cancer therapy	NRS2002	Albumin	Handgrip, Anthropometry	-
Yin, L., et al. (86)	2022	14134	Cohort study	cancer	anti-cancer treatment	NRS2002/ PG-SGA	FAIN	Handgrip, Anthropometry	-
Lopez- Gomez, J. J., et al. (87)	2022	43	Cross-sectional study	cancer	noninterventional	food diary	-	Handgrip, Anthropometry	-
de Sousa, I. M., et al. (88)	2022	178	Cohort study	gastric and colorectal cancer	noninterventional	MUST	-	Handgrip, CC	PG-SGA
Yin, L., et al. (89)	2021	4025	Cohort study	cancer	noninterventional	quartiles of the previous 7-14 days	CPR/ NLR	Handgrip, MAC/ TSF/ MAMC/ CC	-
Yilmaz, M., et al. (90)	2020	135	Randomized controlled trials	hematologic malignancy	noninterventional	NRS2002	Albumin CRP	Handgrip, MUAC/ CC	-
Contreras- Bolivar, V., et al. (91) <sup>+</sup>	2019	351	Observational study	cancer	noninterventional	food diary	GPS	Handgrip, AMC/ CC	MUST, SGA
Ruan, X., et al. (92) <sup>-</sup>	2022	1,358	Retrospective cohort study	colorectal cancer	cancer treatment	food diary	Albumin CRP	Handgrip, CC/ MAC/ MAMC	-
Landgrebe, M., et al.(93) <sup>+</sup>	2023	120	Observational study	non-small cell lung cancer	first line anti-neoplastic treatment	percentile	CRP	Handgrip, MMC/ CC	-

Table 1. Key characteristics of eligible studies (	(continue)	)
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Author (Reference)	Year	Sample size	Study design	Cancer type	Intervention	Reduce food intake	Inflammatory	Reduce muscle mass	Other tools
Yin, L., et al. (94) <sup>+</sup>	2021	1238	Cohort study	lung cancer	noninterventional	interview	laboratory indices	Handgrip, CC	-
Yin, L., et al. (95)	2022	2529	Retrospective cohort study	cancer	cancer treatment	NRS2002	-	Handgrip, CC/ MAC/ TSF	-
Li, Q., et al. (96) <sup>+</sup>	2021	219	Cohort study	gastric cancer	noninterventional	self-reported	Disease*	Handgrip, MAC/ CC	NRS 2002
Yin, L., et al. (97)	2021	1219	Cohort study	lung cancer	noninterventional	Nutrition interview	laboratory indices	Handgrip, CC	-
Santos, I., et al. (98)	2021	41	Cohort study	pancreatic cancer	noninterventional	NRS-2002	-	Handgrip, Anthropometry	-
Zhang, Q., et al. (99)	2021	3547	Cohort study	cancer	cancer treatment	self-reported	Disease*	Handgrip, AMC/ MAC/ CC	-
Zou, Y., et al. (100) <sup>+</sup>	2023	963	Cohort study	non-hodgkin's lymphoma	cancer treatment	-	Disease*	Handgrip, MAMC/ MAC/ CC	PG-SGA
Yin, L., et al. (101)	2021	4025	Cohort study	cancers	noninterventional	PGSGA	CRP/ NLR	Handgrip, CC	-
Artero, A., et al. (102)	2023	53	Cross-sectional study	cancer	cancer therapy	the fasting and non- fasting	-	Anthropometry, BIA	-
Movahed, S., et al. (103)	2020	71	Cross-sectional survey study	esophageal Cancer	chemoradiation	24 Hours food recall	Albumin CRP	Handgrip, BIA/ MUAC	-
Wang, Y., et al. (104)	2023	537	Prospective longitudinal study	head and neck cancer	radiotherapy	quartiles of the previous 7-14 days	Disease	BIA	NRS2002
Curtis, A. R., et al. (105)	2023	2415	Cross-sectional study	cancer	non-interventional	dietary recall	CRP	BIA	-
Gascon-Ruiz, M., et al. (106) <sup>+</sup>	2022	165	Observational prospective study	head and neck, upper digestive tract, and/or colorectal	non-interventional	quartiles of the previous 7-14 days	Disease	BIA	-
Takimoto, M., et al. (107)	2022	660	Retrospective observational study	gastrointestinal and hepatobiliary–pancreatic cancers	digestive surgery and transplantation	-	Disease*	BIA	-
Wan, M., et al. (108) <sup>+</sup>	2022	113	Retrospective study	nasopharyngeal carcinoma	radiotherapy	NRS2002	Disease*	BIA	-
Einarsson, S., et al. (109) <sup>+</sup>	2020	210	Observational study	head and neck cancer	nutritional treatment	food diary	CRP	BIA	-
Amiri Khosroshahi, R., et al. (110)	2023	98	Longitudinal study	acute leukemia	hematopoietic stem cell transplantation	dietary recall	mGPS/ CRP	BIA	-

Author (Reference)	Year	Sample size	Study design	Cancer type	Intervention	Reduce food intake	Inflammatory	Reduce muscle mass	Other tools
Guo, F., et al. (111)	2022	98	Cohort study	leukemias, lymphomas, cancer of plasma cells	hematopoietic stem cell transplant	NRS-2002	CRP	BIA	PG-SGA
Orell, H. K., et al. (112) <sup>+</sup>	2022	65	Randomized controlled study	head and neck cancer	curative	quartiles of the previous 7-14 days	CRP	BIA	PG–SGA
Balci, C., et al. (113) <sup>+</sup>	2023	267	Longitudinal, multicenter observational study	newly diagnosed with different types of cancer	non-interventional study	PG-SGA	Albumin CRP	Handgrip, BIA	
Muresan, B. T., et al. (114)	2022	107	Observational Study	cancer	cancer treatment	quartiles of the previous 7-14 days	Disease	Handgrip, BIA	-
Huang, C. H., et al. (115)	2023	61	Prospective longitudinal study	oral cancer	curative treatment	-	LMR/ NLR/ SII	Handgrip, BIA	5-CST
Harimoto, N., et al. (116) <sup>+</sup>	2023	254	Retrospective cohort study	hepatocellular carcinoma	hepatic resection	quartiles of the previous 7-14 days	CRP	Handgrip	CONUT
Song, H. N., et al. (117) <sup>+</sup>	2022	918	Cohort study	colorectal cancer	surgery	NRS2002	Disease*	Handgrip	-
Sanchez- Torralvo, F. J., et al. (118)	2022	351	Observational prospective study	cancer	cancer treatment	quartiles of the previous 7-14 days	GPS	Handgrip	-
Perrier, M., et al. (119)	2022	879	Cohort study	digestive cancer	chemotherapy or biotherapy	-	mGPS	Handgrip	-
Steer, B., et al. (120) <sup>+</sup>	2020	188	Retrospective study	head and neck cancer	Radiotherapy and chemotherapy	Nutrution interview	Disease	subjective assessment (PG- SGA)	-

Disease<sup>\*</sup> = the study that exclude the etiologic criteria because the disease, += the study that test the validly or quality of GLIM and the result was positive, and -= result is negative

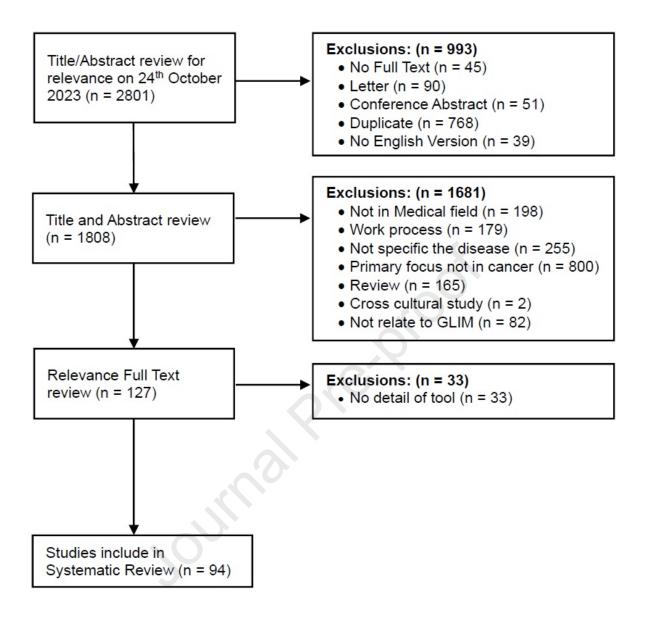


Figure 1 PRISMA flowchart demonstrating study selection.