Classification of Cancer Cachexia

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and wellbeing; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the ESP website. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

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Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

Katherine Petersen, MS, RD, CSO, CNSC
Chair, Oncology Nutrition Clinical Subcommittee
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Technical Expert Panel

To ensure robust, scientifically relevant work, the technical expert panel (TEP) guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members included:

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Disclosures

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The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. The final research questions, methodology, and/or conclusions may not necessarily represent the views of contributing operational and content experts. No investigators have affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

Executive Summary

KEY FINDINGS

- The most frequently evaluated algorithms included the Fearon 2011 algorithm, the Cachexia Index (CXI), and Evans 2008 algorithm.
- Twenty-two algorithms were compared against either clinical exam or another cachexia algorithm in 23 studies. Fearon 2011 was used as a comparison algorithm in 17 of these studies.
- Fearon 2011, CXI, and Evans 2008 algorithms found worse survival outcomes for people with cachexia compared to those without cachexia. Among other algorithms, the majority found worse survival in cachectic compared to noncachectic patients.
- The cachexia algorithms that categorized patients by severity, including the Glasgow Prognostic Score, Cancer Cachexia Score, Cancer Cachexia Staging Index, Vigano 2017 algorithm, Cachexia Staging System, and Cachexia Staging Score, found worse survival outcomes in those with more severe cachexia compared to less severe cachexia.
- Patients with cachexia based on the Fearon 2011 algorithm had longer hospital and intensive care unit stays.
- There may not be a difference in survival outcomes between precachectic and noncachectic populations.
- There was sparse reporting of outcomes relating to physical functioning, hospitalization, and cachexia symptom burden, and no studies reported outcomes of cachexia progression or feeding tube placement.
- Worse overall mortality is predicted by the Evans 2008 algorithm, Fearon 2006 algorithm, or CXI compared to the Fearon 2011 algorithm.

INTRODUCTION

Cachexia is a progressive wasting syndrome characterized by loss of weight and muscle mass, and changes in inflammatory and metabolic processes. Cachexia in patients with cancer is associated with poor outcomes including mortality, reduced quality of life, decreased physical and psychological functioning, and increased hospital length of stay. There are a variety of proposed algorithms to diagnosis and stage cancer cachexia; however, some include components that are not easily obtained in all settings and some algorithms may not distinguish cachexia from other related conditions such as malnutrition. Although multiple cancer cachexia diagnostic and staging algorithms are available, the effect of these strategies on clinical and patient-important outcomes remains unclear.

The VA Evidence Synthesis Program (ESP) was asked by the Veterans Health Administration (VHA) Nutrition Field Advisory Board for an evidence review on classification systems for staging cancer cachexia and the outcomes associated with cachexia stages. In this review, we first describe published classification strategies, their performance measures (*eg,* sensitivity and specificity), and then synthesize the association between cachexia and cachexia staging with clinical and patient-important outcomes. The following Key Questions (KQs) were developed in collaboration with VA partners:

KQ1: What cancer cachexia classification systems have been described and what criteria have been used to develop these?

KQ2: What are their performance characteristics?

KQ3: What are the short- and long-term outcomes for patients following cachexia classification with the tools identified in KQ1?

METHODS

We searched for peer-reviewed articles in Medline, Embase, Cochrane library, and ClinicalTrials.gov from inception to August 1, 2023. Eligible studies included patients ≥18 years of age with any cancer. Only studies that explicitly examined cachexia were included. Studies had to include an algorithm with multiple components with the intent to identify or stage cachexia. For KQ1 and KQ2, we extracted the algorithm components, scoring or classification functions, and performance characteristics. Studies for KQ1 and KQ2 could be comparative or noncomparative. For KQ3, we included KQ1 and KQ2 studies that compared either cachexia stages or cachexia versus no cachexia. For this KQ, we only included studies that controlled for confounding (*eg*, multivariable regression) between groups. We extracted information on study design, baseline population characteristics, cachexia assessment, and outcomes of interest, which included survival, function, hospitalization, cachexia progression, symptom burden, and feeding tube placement. Risk of bias was assessed for all KQ3 studies. Studies had low risk of bias if they used propensity scores as their method of adjustment domain, moderate if they used multivariable regression, and high if there were concerns about the adjusted analysis. Where there were at least 3 studies reporting results from comparable analyses, we conducted meta-analyses using random-effects models. Using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology, we determined certainty of evidence for algorithms with 3 or more comparative studies. Other results were narratively summarized. The review protocol was registered in PROSPERO (CRD42023458540).

RESULTS

Description of Algorithms

We identified 114 eligible studies for KQ1 which described a total of 137 (32 unique) cancer cachexia algorithms. Two studies were conducted within the VA. Most studies described algorithms with a dichotomous definition of cachexia ($N = 99$), 19 studies described a 3-category definition, and 15 studies described a 4-category definition. The Fearon 2011 algorithm, or a modification of it, was the most frequently reported algorithm ($N = 68$), followed by the Cachexia Index (CXI) ($N = 16$), the Evans 2008 algorithm ($N = 8$), and the Glasgow Prognostic Score or a modification of it ($N = 6$). All other classification algorithms were reported in fewer than 5 studies, including algorithms originally designed to measure other aspects of health, such as malnutrition.

Across all studies, the 32 unique algorithms used more than 20 different components. The most frequently used components across algorithms included anorexia, appetite loss, or nutrition measures ($N = 18$); sarcopenia or skeletal muscle index ($N = 15$); weight loss ($N = 15$); body mass index ($N = 15$); albumin ($N = 14$); and performance, function, or muscle strength ($N = 13$). Additional components included C-reactive protein, hemoglobin, white blood cell count fatigue, neutrophil to lymphocyte ratio, quality of life, or some other component. The cutoffs for components and definitions of cachexia varied across studies and algorithms.

Algorithm Performance

Twenty-two of the identified algorithms (in 49 of 114 studies) were compared to either clinical exam or to another cachexia algorithm, with the majority of studies comparing algorithms to the Fearon 2011 algorithm. In summary, 1 study found slight agreement between the Fearon 2011 algorithm and a clinical assessment of cachexia based on oncologists' opinion. Three studies compared the CXI to the Fearon 2011 algorithm. Two of the 3 studies found that a greater proportion of patients in the low-CXI group were classified as cachectic using the Fearon 2011 algorithm compared to the high-CXI group; the third study found no difference between groups. More patients were classified as cachectic using the Evans 2008 compared to Fearon 2011 (in 2 of 3 studies). Eleven studies found similar proportions of people were classified as cachectic between the Fearon 2006 algorithm (1 study), Cancer Cachexia Staging Index (1 study), Patient-Generated Subjective Global Assessment (2 studies), modified Glasgow Prognostic Score (2 studies), Global Leadership Initiative on Malnutrition with and without additional nutrition screening (1 study), Malnutrition Universal Screening Tool (1 study), Nutritional Risk Screening 2002 (1 study), Malnutrition Screening Tool (1 study), Short Nutritional Assessment Questionnaire (1 study), nomograms (4 studies), and Fearon 2011, with some of these studies comparing multiple algorithms to the Fearon 2011 algorithm.

Outcomes for Patients Following Cachexia Classification

Forty-nine studies reported the adjusted association between cachexia as determined by an algorithm and a prioritized outcome. The majority of studies were from Japan ($N = 13$), China ($N = 9$), and Korea ($N = 5$), with 3 conducted in the US. The studies were conducted between 1991 and 2002 and with a wide range of follow-up durations (10 days to 12 years). A total of 31,317 patients were included. The mean age of patients in 24 studies ranged from 57.8 to 75.6 years; the median age in 22 studies was between 57 and 83 years. In 2 studies, the majority of patients were ≤65 years old, and 1 study reported that the majority of patients were ≥60 years old. Males made up 40.5% to 100% of patients. The studies included patients with a variety of cancer types and stages.

ES Table shows summary results by algorithm. Overall survival was the most commonly reported outcome (reported on 50 times in 44 studies), followed by progression-free survival ($N = 11$), disease-free survival ($N = 8$), and relapse-free survival ($N = 2$). Other outcomes included function ($N = 2$), hospitalization ($N = 2$), or cachexia relevant burden or severity ($N = 2$). No study evaluated cachexia progression or feeding tube placement.

ES Table. Associations Between Cachexia Diagnosis or Severity and Outcomes for Each Algorithm

Algorithm Outcome	N[a]	Comparison Groups	Overall Confidence	Summary of Association
Fearon 2011				
Overall survival	13	Cachexia vs no cachexia	Moderate	Worse overall mortality (pooled HR = 1.59; 95% CI [1.36, 1.86]).
	1	Cachexia vs no cachexia using a modified algorithm		• Worse overall mortality; • No significant difference between precachexia and no cachexia.
	1	3 cachexia criteria vs <3		Worse overall mortality.
Cancer progression-free survival	4	Cachexia vs no cachexia	Moderate	Worse cancer progression-free survival (pooled HR = 2.05; 95% CI [1.40, 3.02]).
Other outcomes	4	Cachexia vs no cachexia	Low or No Evidence	Worse disease-free survival, longer length of stay in the hospital and ICU, and worse self-perception of dysphagia.
Cachexia Index (CXI)				
Overall survival	15	Cachexia vs no cachexia[b]	Low	• Worse overall mortality (pooled HR = 2.32; 95% CI [1.98, 2.71]). • No significant differences between intermediate-CXI to high-CXI groups
	1	Cachexia vs no cachexia using a modified algorithm		Worse overall mortality.
Progression-free survival	5	Low CXI vs high CXI; cachexia vs no cachexia	Moderate	Worse disease-free survival (pooled HR= 1.91, 95% CI [1.57, 2.33]).
Disease-free survival	5	Low CXI vs high CXI; intermediate CXI vs high CXI; stage II cachexia vs stage I cachexia; cachexia vs no cachexia	Moderate	• Worse disease-free survival (pooled HR=1.89; 95% CI [1.46, 2.44]). • No significant difference in survival between intermediate-CXI to high-CXI groups.
Relapse-free survival	1	Low CXI vs high CXI	Low	Worse relapse-free survival.
Evans 2008				
Overall survival	4	Cachexia vs no cachexia[c,d]	Moderate	Worse overall mortality (pooled HR= 4.24; 95% CI [2.60, 6.90]).

Algorithm Outcome	N[a]	Comparison Groups	Overall Confidence	Summary of Association
Other Algorithms				
Overall survival	15	Cachexia vs no cachexia[e]	Not Assessed	• Worse overall mortality between patients with and without cachexia and people with more severe stages (13/15 studies). • No significant difference in overall mortality in 1 of 3 studies comparing precachexia to no cachexia. • No significant differences in overall mortality between meeting 2 of 3 or 3 of 3 Fearon 2006 vs not in subgroup of patients with stage IV cancer.
Other outcomes	8	Cachexia vs no cachexia[f]	Not Assessed	• Worse disease-free, relapse-free, and progression-free survival. • Results from functional outcomes were inconsistent. • One study reported significantly worse disease burden in people with refractory cachexia vs those without cachexia, but no differences were seen when comparing precachectic patients to those without cachexia.

Notes. [a] Based on number of times this outcome was reported; [b] Defined as low CXI vs high CXI, intermediate CXI vs high CXI, stage II cachexia vs stage I cachexia; [c] One study compared patients with cachexia at pretreatment or immediately after treatment but not thereafter vs patients without cachexia at all time periods, patients with no cachexia at pretreatment or immediately after treatment but newly developed cachexia at 6- or 12-months post-treatment vs patients without cachexia at all time periods, patients with sustained cachexia both before and after treatment vs patients without cachexia at all time periods. [d] One study reported no significant differences were seen between those with cachexia at pretreatment or immediately following treatment but not thereafter vs patients without cachexia at any time point; [e] Definitions of cachexia classifications varied by algorithm and included: well-nourished, precachexia vs no cachexia, refractory cachexia vs no cachexia, severe cachexia vs mild or moderate cachexia, high vs low cancer cachexia risk, mild or moderate cachexia vs no cachexia, severe cachexia vs no cachexia, cachexia vs no cachexia, cachexia vs precachexia, refractory cachexia vs precachexia, met all 3 components of cachexia profile vs did not meet all 3 components, met ≥ 2 of 3 components of cachexia profile vs did not meet ≥ 2 of 3 components, cachexia within 6 mo of treatment vs no cachexia within 6 mo of treatment, low H-CXI vs high H-CXI. [f] Severe cancer cachexia vs no cachexia, high vs low cancer cachexia risk, cachexia vs well-nourished, noncachexia vs refractory cachexia, malnourished vs refractory cachexia, cachexia vs refractory cachexia.

Abbreviations. CI=confidence interval; HR=hazard ratio; ICU=intensive care unit.

Fearon 2011 Algorithm

Fifteen comparative studies reported overall survival for patients with and without cachexia based on the Fearon 2011 algorithm or some modification of this. One of these studies classified patients by the number of Fearon 2011 algorithm criteria met. Another study used a modified version of the Fearon 2011 algorithm. Overall, 1 study was low risk of bias, 15 studies used multivariable regression and had no additional concerns (moderate risk of bias), and 3 studies controlled for multiple algorithms of cachexia in their final models (therefore, high risk of bias).

In summary (ES Table), there was significantly worse overall mortality (12 of 15 studies), worse progression-free survival (in 3 of 4 studies) (moderate confidence) and worse disease-free survival (1 study) for people with cachexia compared to people without cachexia (low confidence). Cachectic patients also had greater hospital and ICU length of stay (low confidence) and greater perception of dysphagia (insufficient evidence). No study assessed function, cachexia progression, or feeding tube placement.

Cachexia Index

Sixteen studies evaluated overall survival based on the Cachexia Index (CXI) or a modification of this algorithm. One of these studies evaluated a modified version of the CXI using handgrip strength. One study was low risk of bias, 12 studies used multivariable regression and had no other concerns (moderate risk of bias), and 3 studies were high risk of bias due to controlling for multiple algorithms of cachexia in their final models.

In summary (ES Table), there was significantly worse overall mortality (16 of 16 studies) (low confidence), progression-free (4 of 5 studies), disease-free survival (5 of 5 studies) (moderate confidence), or relapse-free survival (1 study) (low confidence) in people identified as cachectic, having low CXI, or stage II cachexia compared to those who were not. No study reported cachexia symptom burden, function, hospitalization outcomes, cachexia progression, or feeding tube placement.

Evans 2008 Algorithm

Four studies compared overall survival by cachexia based on the Evans 2008 algorithm. All 4 studies used multivariable regression to account for confounding and had no other concerns (therefore, moderate risk of bias).

In summary (ES Table), there was significantly worse overall survival among those classified as cachectic (in 4 of 4 studies; moderate confidence). No study reported cachexia symptom burden, functional levels, hospitalization outcomes, cachexia progression, and feeding tube placement.

Fearon 2006 Algorithm

Two studies used the Fearon 2006 algorithm. One of these studies adjusted for multiple definitions of cachexia in the same model (therefore, high risk of bias). The other had moderate risk of bias due to using multivariable regression to account for confounding.

In summary (ES Table), there was significantly worse overall survival among those classified as cachectic compared to people without cachexia (2 of 2 studies). One study reported worse mortality among patients with stage II or III cancer with cachexia; however, there was no significant difference

in mortality in patients with stage IV cancer with and without cachexia. No study reported cachexia symptom burden, function, hospitalization outcomes, cachexia progression, or feeding tube placement.

Glasgow Prognostic Score

Two studies used the Glasgow Prognostic Score (GPS) to classify patients as cachectic. Both studies used multivariable regression to account for confounding and had no other concerns (therefore, moderate risk of bias).

In summary (ES Table), there was significantly worse overall survival among patients with precachexia or refractory cachexia compared to no cachexia (1 study). There was no significant difference in hyporexia (decrease in appetite) between those with precachexia no cachexia (1 study). There was significantly greater hyporexia, nausea, intestinal constipation, xerostomia, dysgeusia, and fatigue for patients with refractory cachexia (1 study). Karnofsky Performance Status improved or stabilized for those classified as noncachectic compared to those classified as having refractory cachexia (1 study). There was no significant difference in quality of life between those classified as cachectic and those with refractory cachexia (1 study). No study used the GPS to assess hospitalization outcomes, cachexia progression, or feeding tube placement.

Other Assessments

Eleven other studies reported 12 different algorithms to classify patients as cachectic. Nine studies used multivariable regression to account for confounding and had no other concerns (moderate risk of bias), and 2 studies were high risk of bias due to unclear reporting or because the multivariable models controlled for a variable that was also included as part of the cachexia assessment variable.

In summary (ES Table), there was significantly worse overall survival (9 of 11 studies), progression-free (in 2 of 2 studies), and disease-free survival (2 of 2 studies) for people with cachexia. There was significantly worse disease-free survival (1 study) and relapse-free survival (1 study) for patients with severe or high risk cachexia compared to those with moderate, mild, or low risk cachexia. There was significantly worse health-related quality of life in patients classified with cachexia (1 study). No study evaluated cachexia progression, hospitalization outcomes, or feeding tube placement.

Comparisons Between Algorithms

Six studies compared survival outcomes between algorithms. Four of these studies were rated as having moderate risk of bias because they used multivariable regression but had no additional concerns, while 2 were rated as high risk of bias because studies controlled for multiple algorithms of cachexia in their final models.

In summary, there was worse overall mortality for patients identified as cachectic using the Evans 2008 algorithm compared to the Fearon 2011 algorithm (3 of 3 studies), CXI algorithm compared to Fearon 2011 (1 study), and Fearon 2006 algorithm compared to Fearon 2011 (1 study). There was no difference in mortality between the Vigano and Wallengren algorithms (1 study).

DISCUSSION

We identified 114 studies that described 32 unique algorithms to diagnose or stage cachexia. Of the 32 algorithms, 22 were compared to the clinical exam or against the Fearon 2011 algorithm, 5 compared results to another cachexia algorithm, and 1 compared the developed algorithm to several existing

algorithms (including Fearon 2011). Forty-nine studies evaluated the adjusted association between cachexia and a prioritized outcome. Some studies adjusted for individual components of the cachexia algorithm which raised concerns of collinearity, and some studies adjusted for multiple definitions of cachexia in the same model. Few studies reported on function, hospitalization, or cachexia symptom burden. No study reported feeding tube placement or cachexia progression. The sparse reporting of outcomes of interest to the operational partners is a limitation of the literature.

There is great clinical interest in being able to prospectively identify people at high risk of developing cachexia or in the early stages of the disorder. Early identification can lead to quicker intervention and better characterize the disorder to inform future research. Complicating practice are multiple cachexia definitions and algorithms described in the medical literature. To improve measurement of cachexia requires a consensus definition with algorithms that are easy to implement in practice. Recent guidelines from the European Society for Medical Oncology state that a comprehensive cachexia assessment should include information about nutritional, metabolic, and functional status; nutritional barriers; gastrointestinal dysfunction; distress and quality of life; and cancer-related factors. However, we found the algorithms of cachexia described in the literature included only some of these criteria. Further, while there have been recent efforts to distinguish cachexia from malnutrition or sarcopenia alone, the nuanced relationship between these syndromes was not consistent in the identified algorithms.

The lack of a singular method to identify cachexia makes understanding its impact on cancer patients challenging. Further, variation in measures or tools to assess individual components also made it challenging to evaluate algorithms. For example, across studies that used the Fearon 2011 algorithm, sarcopenia was measured by CT, BIA, MUAMA, DEXA, SARC-F, and other tools, and cutoffs of these varied. While cost, burden, and availability of tools for measuring components are important considerations, the lack of consistency adds further complication to the identification of cachexia and evaluation of algorithms.

Strengths and Limitations of the Systematic Review Process

The detailed coding of algorithm components, scoring functions, and definitions is a strength of our review. Our approach to evaluating algorithms provides a foundation to understand nuanced scoring criteria beyond face level labels of the individual algorithm components (*eg,* BMI or weight loss). For example, sarcopenia was commonly included in the algorithms and our coding allows readers to understand how this measure was collected and incorporated within and across algorithms.

In the literature, the term cachexia was sometimes used interchangeably with related syndromes, such as malnutrition or anorexia. We included only studies that explicitly used the term “cachexia” to avoid incorrectly including studies that were not specific to cachexia. Therefore, it is possible that we excluded studies that assessed cachexia but used a different term or have included studies that did not explicitly distinguish between cachexia and other related conditions. This review was intended to focus on classification algorithms that used >1 component, such as weight measures, to identify cachexia. However, for the Fearon 2011 algorithm, cachexia could be defined by either weight measures alone or weight loss in combination with sarcopenia. It is possible that patients included in these studies were identified as cachectic based solely on weight measures. Further, for some assessment tools, such as the CXI, we used study-specific cutoffs for cachexia classifications, which may make these definitions less applicable to other external samples. Additionally, our choice to only include studies that adjusted for confounding limited the number of studies and type of outcomes included in our analyses of the

association between algorithms and outcomes, but by doing so, we excluded studies with clear confounder bias.

Implications for VA Policy and Practice

VA diagnoses over 50,000 Veterans with cancer annually and has made significant investments to deliver the "most effective" treatment to Veterans regardless of their location through cancer genomics, tele-oncology, and clinical trials. Although only 2 studies were conducted within the VA, the components of described cachexia algorithms can be measured in Veterans with cancer (*eg*, weight loss, sarcopenia, anorexia). However, it is important to note that nearly 40% of the available studies were conducted in China or Japan, which may limit the generalizability of evidence on the contribution of each component to algorithm performance.

Systematic collection of cachexia-related data is a necessary but complex task in a busy clinical environment, with implications for both front-line health care staff and VA's data infrastructure. Thus, implementation of a standardized cachexia measure would require VA leadership support, development of the collection infrastructure, education of the oncology field, and the monitoring/re-enforcement of the importance of collection. Alongside these steps, it will likely be valuable to implement predictive analytics to identify those Veterans most at risk for cachexia and focus assessments on them.

Effective management of cachexia requires timely identification. The importance of identifying cachexia early and by severity is also highlighted by the role of emerging therapeutics. Few studies reported on patient quality of life or function, which are measures that may be sensitive to health system features. Again, this represents an opportunity for VA, which has the capability of collecting patient-reported outcomes and other measures. Being able to uniformly collect these data points could help improve understanding and identification of cachexia.

Future Research

While a variety of cachexia algorithms have been reported, few studies directly compared cachexia algorithms. Direct comparisons are needed to understand the settings and situations specific algorithms perform best. Future studies should be explicitly designed to compare algorithms and evaluate outcomes using propensity score or regression adjustment methods that control for known and potential sources of confounding. There is also a need to compare algorithms against, at minimum, an agreed-upon reference standard (*eg,* Fearon 2011), and to validate these within specific populations, such as Veterans. This includes validation of biomarkers and other surrogate end points. Most cachexia classification algorithms included only 2 stages (presence or absence of cachexia), and there is a need to expand research on algorithms that more finely characterize cachexia severity and outcomes associated with cachexia severity, and for cachexia definitions to assess more clinically relevant outcomes, such as patient or caregiver experiences and patient functioning. Few studies reported prioritized outcomes of interest. While survival outcomes based on cachexia status are of interest, other more modifiable outcomes such as quality of life or function should be included in future studies to clarify the impact of cachexia and cachexia interventions on these outcomes. Newly developed algorithms should focus on comprehensive assessments of cachexia and should consider clinically meaningful outcomes beyond survival.

CONCLUSIONS

Standardizing the identification of cancer cachexia can improve practice and support targeted interventions. Health systems aiming to implement an algorithm in routine practice should focus on feasibility and ease of use. The Fearon 2011, Cachexia Index, and Evans 2008 algorithms were the most frequently described. While many of the identified algorithms incorporate components for anorexia, appetite, or nutrition, albumin, sarcopenia, and/or weight loss to assess cachexia, the overall literature base included more than 20 different components in a variety of combinations. In 5 studies that used Fearon 2011 and another algorithm to assess outcomes of interest in this report, effect sizes were greater for patients identified as cachectic using the Evans 2008, CXI, and Fearon 2006 criteria, though these were not significantly different from Fearon 2011 estimates. Studies are needed to identify optimal cachexia algorithms and to better understand the relationship between cachexia severity and outcomes such as function or quality of life.

Main Report

Evidence Synthesis Program

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ABBREVIATIONS TABLE

Abbreviation	Definition
AUC	Area under the curve
BMI	Body mass index
CAS	Cachexia assessment scale
CASCO	Cachexia score
CRP	C-reactive protein
CT	Computed tomography
CI	Confidence interval
CXI	Cachexia Index
CCSG	Cancer cachexia study group
CSS	Cachexia staging score
CCSI	Cancer Cachexia Staging Index
ECOG-PS	Eastern Cooperative Oncology Group Performance Status
ECOG	Eastern Cooperative Oncology Group
EORTC	European Organization for Research and Treatment of Cancer
ESAS	Edmonton Symptom Assessment System
ESP	Evidence Synthesis Program
GLIM	Global Leadership Initiative on Malnutrition
GNRI	Geriatric nutritional risk index
GPS	Glasgow Prognostic Score
HR	Hazard ratio
KQ	Key questions
L3-SMI	L3 skeletal muscle index
MeSH	Medical subject headings
MUST	Malnutrition universal screening tool
MST	Malnutrition screening tool
NRCS	Nonrandomized comparative studies
NLR	Neutrophil to lymphocyte ratio
NRS	Nutritional risk screening
NS	Nutrition screening
OR	Odds ratio
PG-SGA	Patient-generated subject global assessment
PM-SMI	PM skeletal muscle index
QLQ-C30	Quality of life questionnaire C30
REML	Restricted maximum-likelihood estimation
R-CSS	Radiotherapy cachexia staging score
RCT	Randomized controlled trial
SARC-F	Strength, assistance walking, rising from a chair, climbing stairs, and falls
SNAQ	Short nutritional assessment questionnaire

Abbreviation	Definition
SMI	Skeletal muscle index
SRDR+	Systematic Review Data Repository
WBC	White blood cell
VA	Veterans Affairs
VAS	Visual analogue scale
VHA	Veterans Health Administration
US	United States
TEP	Technical expert panel

BACKGROUND

Cachexia is a progressive wasting syndrome characterized by loss of weight and muscle mass,[1] as well as accompanying changes in inflammatory and metabolic processes.[2-4] A recent systematic review estimated that more than half of cancer patients in the United States (US) develop cachexia.[5] Cancer cachexia is associated with poor outcomes including mortality, reduced quality of life, and decreased physical and psychological functioning.[6-8] Cancer cachexia is also associated with increased hospital length of stay and health care costs.[8, 9] Generally, the prevalence of cachexia is higher in more advanced stages of cancer.[10, 11] More advanced cancer cachexia stages may be associated with worse clinical, person-centered, and health care utilization outcomes.[12,13] There may, therefore, be a benefit to understanding the different cachexia staging tools available in order to identify people who may be at risk for worse outcomes. Cachexia management generally focuses on appetite improvement through nutritional interventions; however, this does not address all aspects of the disorder. Other interventions may include medications for anorexia or physical activity, but there are currently no proven management strategies for cachexia.[2]

There are multiple proposed tools or algorithms to diagnose and stage cancer cachexia.[14] These algorithms use a variety of criteria or measures, some of which may not be easily obtained in routine clinical settings.[15] For example, a computed tomography (CT) scan for sarcopenia might require an additional scan beyond what is ordered for the underlying cancer, or these images may be obtained for other clinical purposes but not evaluated for sarcopenia. In addition, some strategies use only a limited number of components or stages to define cachexia, which may oversimplify staging of these patients by assuming equal risk of poor outcomes within these groups.[15] Malnutrition screening tools are sometimes used to stage cachexia, despite malnutrition and cachexia being separate diagnoses.[16] While weight loss, malnutrition, and sarcopenia are all intertwined with cachexia, they do not individually encompass the diagnosis of cancer cachexia. For example, patients may experience muscle loss without loss of adipose tissue or may experience fluid accumulation (and thus weight gain) related to cancer or its treatments.[1, 4] In these situations, weight change alone may not detect cachexia. More recent literature has highlighted the potential for biomarkers to help identify cachexia before clinical signs appear;[17] although, to date, no biomarker has been validated for cachexia diagnosis.

Although multiple cancer cachexia diagnostic and staging algorithms are available, it remains unclear whether classifying patients based on any of the algorithms is associated with clinical and patient-important outcomes. There is also little guidance available for diagnosing the severity of cancer cachexia. As an integrated health system for 9 million Veterans, the Department of Veterans Affairs (VA) diagnoses over 50,000 Veterans with cancer annually[18] and is committed to the whole health of Veterans.[19, 20] Because cachexia may impact cancer outcomes, VA is interested in systematic ways to diagnose, treat, and mitigate cancer cachexia. The Veterans Health Administration (VHA) Nutrition Field Advisory Board requested the present review of evidence on classification systems for staging cancer cachexia among adults and the short- and long-term outcomes associated with cachexia stages using the classification systems. We first describe the classification algorithms that have been published and the performance of these algorithms, then synthesize available evidence on the association between cachexia and clinical and patient-important outcomes. The Nutrition Field Advisory Board intends to use the findings of this review to inform guidance on strategies to identify and stage patients with cancer cachexia across the VA.

METHODS

TOPIC DEVELOPMENT

We worked with representatives from the VHA Nutrition Field Advisory Board and our technical expert panel (TEP), which included individuals from the VHA Nutrition & Food Services and Geriatrics & Extended Care, to refine the key questions (KQ). We focus on studies that report classification or staging algorithms for cancer cachexia, their performance metrics, and the clinical and patient-important health outcomes based on these classification algorithms. We define classification or staging algorithms as those that use more than 1 criterion or variable to classify cancer cachexia and that use measures beyond weight. We excluded cancer cachexia algorithms that used only single predictors or variables, including single laboratory measures or imaging techniques.

KEY QUESTIONS AND PROTOCOL

The following key questions were the focus of this review:

Key Question 1	What cancer cachexia classification algorithms have been described and what criteria have been used to develop these?
Key Question 2	What are their performance characteristics?
Key Question 3	What are the short- and long-term outcomes for patients following cachexia classification with the tools identified in KQ1?

A preregistered protocol for this review can be found on the PROSPERO international prospective register of systematic reviews (CRD42023458540).

SEARCHING AND STUDY SELECTION

We conducted a preliminary search in Medline (via PubMed) that was focused on Medical Subject Headings (MeSH) terms specific to cachexia, cancer, classification, and measures, with confirmation that several known relevant publications were captured. We also explored and adopted aspects of search strategies from several existing systematic reviews relating to the terms specified as appropriate.[5, 21-36]

For our final searches, we searched Medline, Embase, the Cochrane library, and ClinicalTrials.gov from dates of inception to August 1, 2023 (see Appendix for complete search strategies). For the final searches, we used MeSH and free text terms for *cachexia*, *emaciation*, and *wasting syndrome*; terms specific to cancer, including *neoplasm*, *carcinoma*, and *tumor*; and terms relating to classification systems, including *severity assessment*, *prognostic factor*, or *staging*. Additional citations were identified from hand-searching reference lists of relevant systematic reviews and consultation with experts.

Citations were entered into EndNote where duplicates were removed. Remaining citations were screened in Systematic Review Data Repository (SRDR+) (https://srdrplus.ahrq.gov/). To ensure common understanding of the eligibility criteria, we ran 3 pilot rounds of 100 citations each, where all team members screened the same citations, until we achieved acceptable agreement. After the pilot rounds, we screened citations in duplicate. Conflicts that arose between screeners were adjudicated by discussion with the research team or by the lead researcher. Abstracts were excluded if they used the term cachexia (to describe presence or absence) but did not name the cachexia tool used or describe the

components used to define cachexia. We also excluded abstracts that did not mention any outcomes of interest. Accepted abstracts underwent full-text review by 2 independent reviewers; an additional team member was consulted to resolve conflicts as necessary. A list of studies extracted at full-text review, along with the reason for their exclusion, can be found in Appendix.

Study eligibility criteria are listed in Table 1. For all KQs, eligible studies included people ≥18 years of age with any type of cancer. Studies had to evaluate cancer cachexia diagnostic or classification algorithms that included multiple predictors or variables to define or stage cachexia. Evaluations of single measures (*eg,* weight loss, laboratory values, imaging findings) were excluded.

For KQs 1 and 2, our focus was on reporting the components (*eg,* weight and albumin) and performance characteristics (*eg,* sensitivity and specificity) of cancer cachexia classification algorithms. We included any study design, including validation studies, randomized controlled trials (RCTs), nonrandomized comparative studies (NRCSs), and single group studies.

For KQ3, eligible studies reported the association between cachexia stage using a classification algorithm described for KQ1 that compared either cachexia stages or cachexia diagnosis (*ie,* versus no cachexia). For KQ 3, the study could be of any design, but the study had to report on analyses that compared cachexia stages or cachexia to no cachexia (as defined by the evaluated algorithm). We excluded studies that describe cachexia algorithms that included outcomes of interest as part of their classification algorithm (*eg,* if a quality of life measure was included in the cachexia algorithm and then also assessed the same quality of life measure in the outcomes). Finally, studies had to use an analytic method to account for confounding between cancer cachexia and the prioritized outcomes (*eg,* inclusion of potential confounders in multivariable regression).

Table 1. Eligibility Criteria

	Inclusion Criteria	Exclusion Criteria
Population	KQ1, 2, & 3: Adults (≥18 years) with any type of cancer at risk for cachexia or with cachexia.	• Non-cancer populations • Non-humans • Studies in children
Exposure (Algorithm)	KQ1 & 2: • Cancer cachexia diagnostic strategies, screening, and classification/severity scoring algorithms (including modified algorithms) • Studies that identify patients as having cachexia using a multicriteria classification algorithm but only use weight to determine stage are included if they meet all other inclusion/exclusion criteria. • Studies that use multiple laboratory measurements or biomarkers but do not include any other clinical information for classification are included if they meet all other inclusion/exclusion criteria. KQ 3: • Cachexia stage or diagnosis as determined by a described algorithms eligible for KQ1	• Studies evaluating only individual predictors/variables, individual laboratory tests, strategies that solely rely on weight measures (*eg,* weight change, BMI, serum albumin) • Studies evaluating sarcopenia or malnutrition classification algorithms without mention of cachexia (in title or abstract at screening level) • Classification algorithms using single imaging or single lab techniques without any other accompanying classification criteria • Studies that analyze cachexia as present/absent but do not provide criteria for this definition in the abstract and did not report outcomes interest in the abstract • Undefined cachexia classification system (*eg*, ICD code, use of the term “cachexia” without naming a tool/algorithm or description of components) • Tools that use outcomes as part of their staging/classification definitions

	Inclusion Criteria	Exclusion Criteria
Comparator	KQ1 & 2: None, reference standard, alternate classification algorithms. KQ3: Lower cachexia stage or classification of no cachexia.	
Outcomes	KQ1 & 2 • Components for classification • Performance measures KQ3 • Survival (overall, cancer specific, *etc*) • Cachexia symptom burden/severity (anorexia, nausea, vomiting) • Functional levels (quality of life, Eastern Cooperative Oncology Group Score, Karnofsky Performance Scale Index, Activities of Daily Living, measures of mobility, exercise tolerance, fatigue, *etc*) • Hospitalizations • Feeding tube placement (including location and type) • Cachexia progression	
Timing	KQ1, 2, & 3: Any	
Setting	KQ1, 2, & 3: Any	
Study Design	KQ1, 2, & 3 • Validation • RCT • NRCS • Single group studies KQ1 & 2 • N ≥ 10 KQ3 • Studies that evaluate the association between cachexia tools and eligible outcomes in multivariable regression models, and that explicitly report the association between the tool and the outcome • N ≥ 10 per cachexia group	KQ1 & 2 • Protocols • Conference abstracts or other non-peer-reviewed sources KQ3 • Unadjusted associations between tools and outcomes

Abbreviations. KQ=key question; NRCS=non-randomized comparative study; RCT=randomized controlled trial.

DATA EXTRACTION AND RISK OF BIAS ASSESSMENT

For all KQs, we extracted details about the study design, total sample size, and the cachexia assessment algorithm used. For KQs 1 and 2, we extracted details on the components of the cancer cachexia classification algorithm, coding or scoring scheme, and cutoffs used. Performance characteristics were collected for studies that compared algorithms against a reference standard of either clinical exam or another cachexia algorithm, including sensitivity, specificity, positive and negative predictive values, and interrater reliability and correlation measures. For KQ3, we extracted details on study design, baseline population characteristics, and prioritized outcomes (survival, function, hospitalization, cachexia progression and symptom burden, and feeding tube placement). For all KQs, all data extraction was first completed by 1 reviewer and then confirmed by a second reviewer, with consultation from other team members as needed to resolve conflicts.

For KQ3, study risk of bias was independently assessed by 1 reviewer using questions derived from the Risk of Bias In Non-randomized Studies – of Interventions tool (see Appendix). We additionally evaluated whether the article was free of discrepancies and adequately reported patient eligibility criteria, protocols, setting, and outcome assessments. Studies had low risk of bias if they used propensity score adjustment and had ≤1 other concern. Studies had moderate risk if they used a multivariable regression to adjust for confounding and had ≤1 other concern or if they used propensity score adjustment and had 2 concerns for bias in other domains. Studies were high risk of bias if there were concerns about the adjustment used, used a propensity score but had ≥2 other concerns, or used multivariable regression and had ≥2 concerns for bias in other domains.

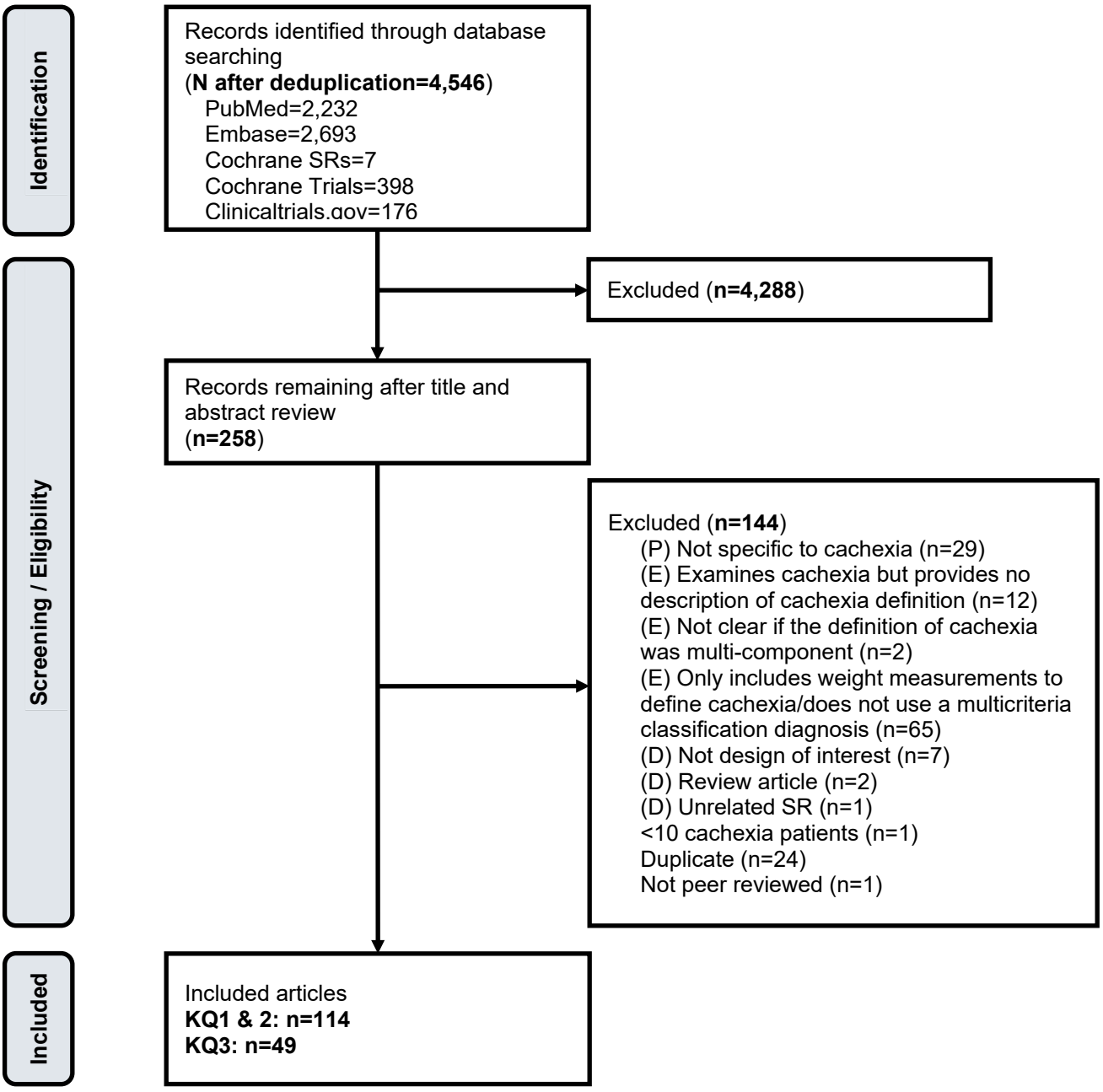
SYNTHESIS

For KQ1 and 2, we described the features of the classification algorithm including their scoring and performance characteristics. For KQ3, we extracted results data from reported multivariable regression models including odds ratios (OR), risk ratios (RR), hazard ratios (HR), or beta coefficients. Where there were at least 3 studies reporting results from sufficiently similar analyses (based on population, interventions, comparators, and outcomes), we conducted random-effects meta-analyses using the *meta* package for R version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria).[37] Statistical heterogeneity was estimated using restricted maximum-likelihood estimation (REML) and is reported using the I^2 statistic, which is the proportion of all variability in effects (within and between studies) that is attributable to between-study variation (*ie*, heterogeneity). We used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology to determine certainty of evidence for cachexia algorithms that had 3 or more comparative studies.

RESULTS

LITERATURE FLOW AND OVERVIEW

Of 4,546 records screened, 258 were accepted for full-text review. After reviewing these, 114 were eligible for KQ1 and 2, and 49 (a subset of the 114) were eligible for KQ3. The most common reasons for exclusion included not reporting a multicriteria classification algorithm ($N = 65$) and not being specific to cancer cachexia ($N = 29$).



CLASSIFICATION ALGORITHMS TO DIAGNOSE AND STAGE CACHEXIA

For KQ1, 114 studies described 137 (32 unique) cancer cachexia algorithms. These studies were conducted mostly in Europe (*N* = 36), China (*N* = 23), and Japan (*N* = 21); 11 studies were conducted in the US. The included studies were published between 2006 and 2023. Two studies were conducted within the VA. Most studies (*N* = 99) described algorithms that had a dichotomous definition of cachexia (*ie,* present or absent), 19 studies described a 3-category definition (*eg,* no cachexia, mild cachexia, severe cachexia), and 15 studies described a 4-category definition (*eg,* no cachexia, precachexia, cachexia, refractory cachexia). Four described a continuous risk score. Table 2 shows the 32 different cancer cachexia classification algorithms and their components (see Appendices for full definitions of cachexia algorithms and their components). The Fearon 2011 algorithm, or a modification of it, was the most frequently reported algorithm (*N* = 68), followed by the Cachexia Index (CXI) (*N* = 16), the Evans 2008 algorithm (*N* = 8), and the Glasgow Prognostic Score (GPS) or a modification of it (*N* = 6). All other classification algorithms were reported in fewer than 5 studies. Eleven studies described an unnamed investigator-developed algorithm. Eight studies, including the 6 that used GPS, described algorithms originally designed to measure other aspects of health, such as malnutrition or inflammation.

Studies described cancer cachexia classification algorithms with a diverse range of components. The individual components included: anorexia, appetite loss, or nutrition measures (*N* = 18); sarcopenia or skeletal muscle index (SMI) (*N* = 15); weight loss (*N* = 15); body mass index (BMI) (*N* = 15); albumin (*N* = 14); performance, function, or muscle strength (*N* = 13); C-reactive protein (CRP) (*N* = 12); hemoglobin (Hb) (*N* = 11); white blood cell (WBC) count (*N* = 4); fatigue (*N* = 4); neutrophil to lymphocyte ratio (NLR) (*N* = 3); quality of life (*N* = 2); dysphagia (*N* = 1); stomatitis (*N* = 1); edema (*N* = 1); ascites (*N* = 1); serum creatinine (*N* = 1); or some other component (*N* = 19), which included: impaired glucose tolerance, diarrhea, nausea, vomiting, abdominal pain, other gastrointestinal symptoms (unspecified), plasma IL-6, plasma pre-albumin, plasma lactate, plasma triglycerides, plasma urea, ROS plasma levels, tumor volume, test/HOMA index altered, absolute lymphocyte number, PG-SGA, GNRI, MUST, MST, SNAQ, NRS-2002, age, cancer site and stage, advanced lung cancer inflammation index, time from symptom onset to hospitalization, platelets, direct bilirubin, dinking (yes/no), total protein, <3 months expected survival, combined or other inflammatory markers (not specified), and underlying chronic disease (not specified). See component details in Appendix for a detailed description of the heterogeneous measures used to evaluate these components. For example, 14 algorithms included physical function measured by the Patient Generated Subjective Global Assessment (PG-SGA), hand grip strength, Karnofsky performance score, Eastern Cooperative Oncology Group (ECOG) scale, or other undefined functional or physical status scores. There were no temporal relationships identified in parameters included in the algorithms; however, several of the more recent algorithms identified developed nomograms as part of their assessment for cachexia. The component details table (see Appendix) also provides a detailed description of the different cutoffs for each measure. For example, weight loss was a component in 15 studies with cutoffs ranging from <2% to >20%.

In summary, 114 studies described 32 unique cancer cachexia algorithms. The most frequently evaluated algorithms included the Fearon 2011 algorithm, the Cachexia Index, and the Evans 2008 algorithm.

Table 2. Components Included in Identified Algorithms

Algorithm	Number of Cachexia Classifications/Stages	Weight Loss	Body Mass Index	Sarcopenia or Skeletal Muscle Index	C-Reactive Protein	Albumin	Neutrophil to Lymphocyte Ratio (NLR)	Anorexia or Appetite Loss or Nutrition	Performance/Function/ Muscle Strength[c]	White Blood Cell Count	Hemoglobin (Hb)	Dysphagia	Stomatitis	Edema	Ascites	Creatinine	Quality of Life	Fatigue	Other	Number of Studies
Fearon 2011 (without modification)[a,b]	2	X	X	X																53
Fearon 2011 (with modification or staging)[a,b]	2-4	X	X	X	X			X	X										X	15
Cachexia Index (CXI)[a,b]	Continuous, 2			X		X	X													16
Cachexia Staging Score (CSS)[a]	3	X		X		X		X	X	X	X									2
Radiotherapy Cachexia Staging Score (R-CSS)	3	X	X	X		X		X	X	X	X								X	1
Cachexia Assessment Scale (CAS)[b]	4	X	X			X		X	X		X	X	X	X	X	X			X	1
Evans 2008[a,b]	2	X	X	X	X	X		X	X		X							X	X	8
Cancer Cachexia Score (CCS)[a]	3		X	X				X											X	1
Cancer Cachexia Staging Index (CCSI)[a,b]	3	X	X	X		X		X	X										X	1
Cancer Cachexia Study Group (CCSG)/Fearon 2006[a,b]	2	X			X			X												4
Cachexia SCOre (CASCO) and miniCASCO[b]	3-4	X			X	X		X	X		X						X	X	X	3

Algorithm	Number of Cachexia Classifications/Stages	Weight Loss	Body Mass Index	Sarcopenia or Skeletal Muscle Index	C-Reactive Protein	Albumin	Neutrophil to Lymphocyte Ratio (NLR)	Anorexia or Appetite Loss or Nutrition	Performance/Function/ Muscle Strength[c]	White Blood Cell Count	Hemoglobin (Hb)	Dysphagia	Stomatitis	Edema	Ascites	Creatinine	Quality of Life	Fatigue	Other	Number of Studies
Glasgow Prognostic Score or modified Glasglow Prognostic Score[a,b]	3 or 4				X	X														6
Patient-Generated Subjective Global Assessment (PG-SGA)[b]	2 or 3																		X	3
Fearon 2011 and Evans 2008 combined[a]	2 - 4	X	X	X	X	X		X	X	X	X									4
Hand Grip Strength Cachexia Index (H-CXI)[a,b]	2					X	X		X											1
Wallengren 2013[a,b]	2	X			X													X		2
Nutritional Status Algorithm[a]	4	X	X	X	X	X		X	X		X							X	X	1
Orell-Kotikangas 2017[a]	2			X					X											1
Solheim 2011	3		X		X			X	X											1
Go 2020[a]	2			X															X	1
Namikawa 2022[a]	2	X	X		X	X		X			X									1
Huo 2022[b]	Continuous							X									X		X	1
Liu 2022[b]	Continuous					X					X								X	1
Tan 2023[a,b]	Continuous		X	X			X	X											X	1
Yin 2022[b]	Continuous		X		X			X			X								X	1
Vigano 2017[a,b]	4	X			X	X		X	X	X	X									1

Algorithm	Number of Cachexia Classifications/Stages	Weight Loss	Body Mass Index	Sarcopenia or Skeletal Muscle Index	C-Reactive Protein	Albumin	Neutrophil to Lymphocyte Ratio (NLR)	Anorexia or Appetite Loss or Nutrition	Performance/Function/ Muscle Strength[c]	White Blood Cell Count	Hemoglobin (Hb)	Dysphagia	Stomatitis	Edema	Ascites	Creatinine	Quality of Life	Fatigue	Other	Number of Studies
Wiegert 2021[a]	3		X	X																1
Global Leadership Initiative on Malnutrition (GLIM)[b]	2	X	X	X				X											X	1
Malnutrition Universal Screening Tool (MUST)[b]	2																		X	1
Nutritional Risk Screening (NRS)-2002[b]	2																		X	1
Malnutrition Screening Tool (MST)[b]	2																		X	1
Short Nutritional Assessment Questionnaire (SNAQ)[b]	2																		X	1
Number of Algorithms Using Each Component		**15**	**15**	**15**	**12**	**14**	**3**	**18**	**13**	**4**	**11**	**1**	**1**	**1**	**1**	**1**	**2**	**4**	**19**	**137**

Notes. [a] Included in KQ 3; [b] Compared against clinical exam or compared to another cachexia algorithm; [c] Measures of muscle strength were included with physical function or performance.

Fearon 2011 and Its Modifications

Sixty-eight studies described the Fearon 2011 algorithm ($N = 53$)[7, 16, 38-88] or some modification of this ($N = 15$).[8, 89-102] Both of the studies conducted within the VA used the Fearon 2011 algorithm. The main definition of Fearon 2011 consisted of either weight loss, a combination of weight loss and low BMI, or a combination of weight loss and sarcopenia. Generally, cutoffs for weight loss were ≥5% for weight loss alone and ≥2% when combined with BMI or sarcopenia; although these thresholds and the timing of measurement varied by study (see Appendix). BMI cutoffs included <20 kg/m^2 and <18.5 kg/m^2 depending on the study population. Measurements for sarcopenia varied widely and included CT; dual x-ray absorptiometry (DEXA) scan; mid-upper arm mass area (MUAMA); bioelectrical impedance (BIA); strength, assistance walking, rising from a chair, climbing stairs, and falls screening tool (SARC-F); European working group on sarcopenia in older people (EWGSOP) criteria; and other methods. Fifteen studies included modifications ($N = 5$) or additional staging ($N = 10$) to the Fearon 2011 algorithm. Additional components used in these studies included CRP measurements ($N = 3$), appetite, anorexia, or nutritional assessments ($N = 4$), function, performance, or muscle strength measures ($N = 3$), impaired glucose tolerance measures ($N = 1$), unresponsiveness to treatment ($N = 1$), and expected survival estimates ($N = 1$). Three studies described modifications with 4 stages, 6 studies with 3 stages, and 1 with 2 stages. Stages included no cachexia or normal status, precachexia, cachexia, and refractory cachexia. Weight loss thresholds for modified and staged versions for the Fearon 2011 algorithm ranged from no weight loss for precachexia to ≥15% weight loss for refractory stage cachexia. BMI thresholds for modified or staged Fearon 2011 algorithm ranged from <20 to ≥22 kg/m^2. Again, definitions of sarcopenia varied across studies (see Appendix).

Cachexia Index and Its Modifications

Sixteen studies describe the CXI,[49, 80, 103-116] which was used in most studies to classify patients as either low CXI or stage II (*ie*, cachectic) or high CXI or stage I (*ie*, noncachectic). One study classified patients into 3 stages based on SMI using both the L3 vertebral muscles and the pectoralis muscles (PM) at the T4 vertebral level. High CXI had both high L3-CXI and high PM-CXI, intermediate had high L3-CXI and low PM-CXI, and low-CXI groups had low L3-CXI and low PM-CXI, with CXI cutoffs based on the Youden index.[107] Components for the CXI include measurements of SMI, albumin, and NLR. The CXI was calculated as (SMI × albumin)/NLR, with cutoffs for cachexia varying by sex, measurement of SMI used, and unit of measurement for albumin. Generally, cutoffs were determined by the Youden index or median CXI value for the study sample. One study described a modified version of the CXI that incorporated hand grip strength (H-CXI) as an additional component.[84] Similar to the original CXI, the H-CXI was calculated as [hand grip strength (kg)/height (m)^2 × serum albumin (g/L)]/NLR, and cutoffs for cachexia were 175 for males and 113 for females.

Evans 2008

Eight studies[60, 78, 79, 88, 102, 117-119] described the Evans 2008 algorithm, which defined cachexia as weight loss or low BMI, plus any 3 of the following: fatigue, anorexia, decreased muscle strength, low fat-free mass index, abnormal serum biochemistry (including increased inflammatory markers, anemia, and low serum albumin).[14] All 8 studies reported weight loss cutoffs ≥5% over 6-12 months and BMI cutoffs from 18.5-22 kg/m^2. When specified, sarcopenia was measured using fat-free mass index (measuring low muscle), low muscle mass assessed by appendicular skeletal muscle index or mid-arm muscle circumference, or lean muscle depletion measured by bioelectrical impedance analysis. Decreased muscle strength was measured by hand grip strength, and anorexia was assessed by visual analog scale (VAS), energy intake, or European Organization for Research and Treatment of Cancer

(EORTC) questionnaire appetite loss score. Fatigue was measured by the EORTC or VAS. Cutoffs for albumin were <32 g/L or <35 g/L for serum albumin, >5 mg/L for CRP, and Hb cutoffs were <120 g/L or <117 g/L. Other components included unspecified inflammatory markers, IL-6 >4pg/ml, and underlying chronic disease.

Combined Evans and Fearon

Four studies described a combined Evans 2008 and Fearon 2011 algorithm, which was attributed to Vigano et al.[120-123] One study included a 2-stage definition of cachexia (*eg,* yes/no) that was based on weight loss or weight loss and BMI, in conjunction with abnormal laboratory values (CRP, albumin, or Hb)[120]. Two studies included a four-stage definition of cachexia defined as no cachexia, precachexia, cachexia, and refractory cachexia groups, with both subdividing the stage of cachexia as either "cachexia" or "cachexia caused by low BMI or sarcopenia." The classifications were based on a combination of abnormal laboratory values (CRP, albumin, WBC, or Hb), anorexia or decreased food intake based on the Edmonton Symptom Assessment System (ESAS) or PG-SGA, physical function or muscle strength based on PG-SGA or hand grip strength, and a combination of BMI, weight loss, or sarcopenia measures. A fourth study classified patients into precachexia, cachexia, and refractory cachexia groups, with the refractory cachexia category incorporating the physical function measures.[123]

Cancer Cachexia Study Group (CCSG)/Fearon 2006

Four studies described the Cancer Cachexia Study Group (CCSG) criteria, which is sometimes called the Fearon 2006 algorithm.[76, 79, 81, 124] The CCSG classifies patients as cachectic if they meet 2 of the following criteria: CRP ≥10 mg/L, weight loss ≥10%, or caloric intake of ≤1500 kcal/d. One study applied 2 different approaches to classify patients: 1) patients who met 2 criteria and 2) patients who met all 3 criteria.[79]

Cachexia Score (CASCO) and Mini Cachexia Score (miniCASCO)

Three studies describe the cachexia score (CASCO) and miniCASCO.[61, 125, 126] The CASCO uses body weight loss and lean body mass; inflammation, metabolic disturbances, fatigue, anemia, immunosuppression; physical performance; anorexia; and quality of life to generate a composite score for cachexia. For the CASCO, 40% of the summary score is based on weight loss or body composition, 20% on inflammatory or metabolic disturbances or immunosuppression, 15% on performance assessed through 5 questions about physical activity, 15% on anorexia assessed by the SNAQ, and 10% on quality of life assessed by the QLQ-C30.[127] The miniCASCO is an abbreviated version of this tool that uses investigator-developed questions to assess performance, anorexia, and quality of life rather than formal tools, like the SNAQ, and also includes fewer blood components. In the included studies, both the CASCO and miniCASCO used a numeric scale from 0-100 to classify patients into 4 groups: no cachexia (≤14), mild (15–28), moderate (29–46), and severe (>46) cachexia. However, 1 identified study used the CASCO to classify patients into 3 cachexia groups: no cachexia, precachexia, and cachexia without specifying any scoring system.

Cachexia Staging Score and Radiotherapy Cachexia Staging Score

Three studies used either the Cachexia Staging Score (CSS) or the Radiotherapy Cachexia Staging Score (R-CSS), a modification of the CSS.[13, 128, 129] The CSS assigns points to measurements of weight loss, strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) questionnaire score, Eastern Cooperative Oncology Group Performance Status (ECOG-PS) score, appetite loss, and abnormal biochemistry, defined as WBC count >10 × 10^9/L, albumin <35 g/L, and

Hb of <120 g/L for males and 110 g/L for females. Total CSS score ranges from 0-12, which is used to classify patients as noncachectic (0-2), precachexia (3-4), cachexia (5-8), or refractory cachexia (9-12). The R-CSS added 3 additional components for age, BMI, and food intake. The total score for the R-CSS ranges 0-17 with scores of 0-3 indicating no cachexia, 4-6 indicating precachexia, 7-12 indicating cachexia, and 13-17 indicating refractory cachexia.

Cancer Cachexia Staging Index

One study described the Cancer Cachexia Staging Index (CCSI).[130] The CCSI assigns point values to subjective and objective measures. Subjective measures include BMI adjusted weight loss grade with cutoffs of 0, 1, 2, 3, and 4, weight loss rates with cutoffs of 0.38 and 1.7 kg/month, inflammation defined by a combination of NLR (cutoff of 3.5) and CRP levels (cutoffs of 2.9 or 2.3mg/L), prealbumin with a cutoff of 180 mg/L, and skeletal muscle index with cutoffs of 44.4 and 35.7 cm^2/m^2 in males and 37.5 and 30.9 cm^2/m^2 in females. Objective measures include appetite and physical status, both assessed as good, fair, or poor. Total scores range from 0-27 with scores <9 defined as no cachexia, score of 9-18 indicating mild or moderate cachexia, and those ≥19 indicating severe cachexia.

Wallengren 2013 Algorithm

Two studies described the Wallengren 2013 algorithm.[79, 123] This algorithm used weight loss, fatigue, and CRP to categorize patients as cachectic or noncachectic based on cutoff values of >2% for weight loss, >3 for fatigue score on a visual analog scale of 1–10 or the ESAS, and CRP >10 mg/L for CRP.

Nomograms to Identify Cachexia

Four studies described nomograms to classify patients as cachectic.[53, 58, 75, 85] The Liu 2022 nomogram was specific to lung cancer patients and included components for cancer stage, albumin, anemia, advanced lung cancer inflammation index, and surgery. The nomogram developed by Huo 2022 included age, nutritional risk screening (NRS 2002), PG-SGA, quality of life (EORTC QLQ–C30), and cancer category (based on site of primary cancer). The nomogram developed by Tan 2023 included cancer site, cancer stage, time from symptom onset to hospitalization, appetite loss (not defined), BMI, SMI [skeletal muscle area (cm^2)/height (m^2)], and NLR. The nomogram by Yin 2022 included BMI, cancer type, anorexia, platelet count, early satiety, abdominal pain, diarrhea, vomiting, CRP, other gastrointestinal symptoms, Hb, direct bilirubin, drinking status, tumor stage, and total protein. Each nomogram utilized the indicated algorithm to calculate a composite score that was associated with cachexia risk.

Cachexia Assessment Scale

One study described the Cachexia Assessment Scale (CAS).[131] The CAS assigns points to investigator-developed assessment questions about functional status, weight loss, BMI, stomatitis, edema, ascites, albumin, Hb, serum creatinine, dysphagia, loss of appetite, diarrhea, nausea, and vomiting. For each component, a score of 0-4 is assigned, with lower scores indicating better outcomes. If 0-1 components receive a score of 1-2 and no components receive a score of 3-4, patients are classified as not cachectic. A combination of 2 or more components receiving a score of 1-2 and 0 receiving a score of 3-4 corresponds with mild cachexia, a combination of 2 or more components receiving a score of 1-2 and 1-2 receiving a score of 3-4 corresponds with moderate cachexia, and any components receiving a score of 1-2 with 3 or more receiving a score of 3-4 corresponds with severe cachexia.

Nutritional Instruments Adapted to Classify Cachexia

Eleven studies described the application of instruments originally developed to identify other symptoms/disease (*eg,* malnutrition and nutritional status) to identify cachexia. It is important to consider that these instruments were originally developed with the intended purpose of identifying conditions related to cachexia and may therefore present challenges in distinguishing between cachexia and the original condition of interest.

Six studies described the Glasgow Prognostic Score (GPS), which was also referred to as the modified Glasgow Prognostic Score (mGPS).[91, 132-136] GPS uses a combination of albumin and CRP to determine a summary score (0 to 2). The CRP cutoffs were 5 and 10 mg/dL, and all 6 studies used the same cutoff for albumin (35 g/L). Four studies used a 4-stage definition which consisted of no cachexia/normal (CRP<10 mg/L, ≤10 mg/L, or ≤0.5 mg/L and albumin ≥35 g/L; score = 0), undernourished (CRP≤10 mg/L, <10 mg/L, or ≤5mg/L and albumin <35 g/L; score = 0), precachexia (CRP>10 mg/L, ≥10mg/L, or >5 mg/L and albumin ≥35 g/L; score = 1), and cachexia or refractory cachexia (CRP>10 mg/L or ≥10 mg/L and albumin <35 g/L; score = 2. One study classified patients as either cachectic or not (score of 2 equated to cachexia[135]), and another study used a 3-stage definition of cachexia including no cachexia (0 component met), precachexia (1 component met), and cachexia (2 components met).

One study described a nutrition status (NS) algorithm.[137] The NS uses a combination of handgrip strength (cutoff of 30 kg), fat-free mass index (cutoff of 14.6 kg/m^2), fatigue, appetite loss, weight loss (cutoff of 5% over 12 months), BMI (cutoff of 20 kg/m^2), CRP (5 mg/L cutoff), Hb (120 g/L cutoff), albumin (32g/L cutoff), and the PG-SGA (cutoff score of 4). Based on these measures, patients were classified as having cachexia, sarcopenia, nutritional risk without sarcopenia or cachexia, or well nourished. Those with handgrip strength or fat-free mass index below the cutoff and at least 2 of the following were classified as cachectic: fatigue, appetite loss, weight loss or BMI, and abnormal blood chemistry. Those who did not meet handgrip or free-fat mas index criteria but had 3 of these components were also classified as cachectic.

Three studies reported on the PG-SGA to identify cachexia.[69, 92, 118] The PG-SGA was originally developed to assess nutritional status using patient-reported weight, symptoms, food intake, activities and function. Each component is scored. Total scores ranged from 0-52. Scores ≥ 9 indicated need for nutritional intervention.[138, 139]

One study used the Global Leadership Initiative on Malnutrition (GLIM) as a tool to identify cachexia, with and without nutritional risk screening using the nutritional risk screening 2002 (NRS-2002).[69] The GLIM was originally developed to assess malnutrition, using measures of weight loss, low BMI, reduced muscle mass, and disease burden. The GLIM was used with and without nutrition risk screening to assess cachexia.

One study used 4 different malnutrition tools to identify cachexia: the malnutrition universal screening tool (MUST), NRS-2002, malnutrition screening tool (MST), and the short nutritional assessment questionnaire (SNAQ)[16]. Cutoffs tested for cachexia identification were ≥1 for the MUST, ≥3 for the NRS-2002, ≥2 for the MST, and ≥2 for the SNAQ.

Other Investigator-Developed Cachexia Assessments

Seven studies reported other investigator-identified algorithms for assessing cachexia. One study described a 4-stage definition, 3 studies described a 3-stage definition, and 3 studies described a 2-stage definition.

Vigano 2017 used a combination of abnormal biochemistry (CRP >10mg/L, WBC >11,000/L, albumin <32 g/L, or Hb <120 g/L in men and <110 g/L in women), decreased food intake (aPG-SGA), moderate or significant weight loss (5% cutoff), and decreased activities and functioning (aPG-SGA) to classify patients into 4 stages (noncachexia, precachexia, cachexia, and refractory cachexia) depending on the combination of criteria met.

Solheim 2011 used BMI (20 kg/m^{-2} cutoff), Karnofsky score (<80), CRP (≥10 $mg1^{-1}$), and appetite loss (EORTC QLQ-C30) to classify patients into 3 stages: no cachexia (less than 2 components), mild cachexia (2-3 components), or severe cachexia (all 4 components). One study described the Cancer Cachexia Score (CCS). The CCS assigns point values of 0 or 1 to sarcopenia (yes/no), BMI (cutoff $20kg/m^2$), prognostic nutritional index (cutoff of 40), and tumor volume (size by T-stage, with a cutoff of 57.5). Three cachexia stages are defined as mild (score of 0-1), moderate (2), and severe (3-4).[115] Wiegert 2021 used a combination of BMI (cutoffs of 21.0 to 26.4), mid-upper-arm muscle area (cutoffs of 38.0 cm^2 for men and 35.5 cm^2 for women), and weight loss (15.0% cutoff) to classify patients into 3 stages (precachexia, cachexia, or refractory cachexia) depending on the combination of criteria met.

Orell-Kotikangas 2017 used the combined definition of low muscle mass (mid-arm muscle area <10^{th} percentile) and low muscle function (hand grip strength <85% normal median value) to categorize patients into 2 stages (cachectic and noncachectic). Of note, this definition included components more closely related to assessing sarcopenia. Go 2020 used a combination of sarcopenia (measured by L3-SMI or PM-SMI) and the geriatric nutritional risk index (GNRI) into 2 stages (high cachexia risk and low cachexia risk). Patients considered to be at high risk for cachexia were those with major GRNI risk, sarcopenia using both L3-SMI and PM-SMI, or moderate GNRI risk plus sarcopenia using 1 measure; otherwise, patients were flagged as low risk of cachexia. Namikawa 2022 classified patients into 2 stages (cachectic and noncachectic) based on either a) weight loss (5%) or weight loss (2%) and BMI (<20 kg/m^2); b) anorexia (not defined); or c) 2 or more of the following: albumin <32 g/L, CRP >5.0 mg/L, and Hb <12 g/dL.

PERFORMANCE CHARACTERISTICS OF ALGORITHMS

Twenty-two of the 32 identified algorithms were compared to either clinical exam or to another cachexia algorithm. In terms of performance characteristics, the Fearon 2011 algorithm was frequently used as a comparator for other cachexia assessments (see Appendix). No study evaluated the performance characteristics of Cachexia Staging Score or Radiotherapy Cachexia Staging Score, Cancer Cachexia Score, nutritional status algorithm, the algorithms developed by Orell-Kotikangas 2017, Solheim 2011, Go 2020, Namikawa 2022, Wiegert 2021, or the combined use of the Fearon 2011 and Evans 2008 algorithms. Among algorithms that were compared to either clinical exam or to another cachexia algorithm performance, there is no obvious best choice.

Fearon 2011 and Its Modifications

One study found only slight agreement, defined by the study as a Kappa of 0.00–0.20, between the Fearon 2011 algorithm and a clinical assessment of cachexia based on oncologists' opinion (Kappa 0.049, 95% CI [–0.079, 0.176], $p = 0.457$).[77]

Cachexia Index and Its Modifications

Three NRCS compared the CXI or H-CXI to the Fearon 2011 algorithm.[49, 84, 130] One study found that significantly more patients were classified as cachectic (according to Fearon 2011) in the low-CXI compared to the high-CXI group (35% vs 22%, $p = 0.01$).[80] The other NRCS found no significant difference in the proportion of patients classified as cachectic (according to Fearon 2011) in the low-CXI versus high-CXI groups (50.9% vs 41.6%, $p = 0.09$).[49] Finally, 1 study found a greater proportion of patients in the low H-CXI group were classified as cachectic using the Fearon 2011algorithm compared to the high-H-CXI group (31.0% vs 17.6%; *p* NR). The same study found a low H-CXI was independently associated with risk of developing cancer cachexia as defined by the Fearon 2011 algorithm in the multivariable analysis. [84]

Evans 2008

Three NRCS compared the Evans 2008 to the Fearon 2011 algorithm.[78, 88, 102] Two studies found more patients were classified as cachectic using the Evans compared to the Fearon (27.5% vs 17.5%, *p* NR). In this study, 31.0% of patients classified as noncachectic by the Evans 2008 algorithm were classified as precachexia by the Fearon algorithm.[102] Another study found that 45.5% of patients with cancer were classified as cachectic using the Evans 2008 algorithm compared to 39.4% using the Fearon 2011 algorithm (*p* NR).[88] One other NRCS reported fewer patients were classified as cachectic according to the Evans 2008 algorithm compared to Fearon 2011 (40% vs 70%, *p* NR).[78]

Modified Glasgow Prognostic Score

Two studies compared the mGPS to the Fearon 2011 algorithm. One study found that fewer patients were classified as cachectic using the mGPS compared to Fearon 2011 criteria (60% no cachexia, 5% undernourished, 25% precachectic, and 10% refractory cachexia vs 40% noncachectic, 5% precachectic, and 55% cachectic), but these differences were not significant (McNemar's test $p = 0.43$).[91] Another study found that patients identified as cachectic using the Fearon 2011 criteria had greater odds of being classified as having refractory cachexia (OR = 2.83, [1.73, 4.60]) or undernourished (OR = 1.84, [1.23, 2.75]) in the mGPS.[136]

PG-SGA

Three studies compared the PG-SGA to Evans 2008. One NRCS compared the PG-SGA with a cutoff of 6.5 to the Evans 2008 algorithm (sensitivity = 79.8%, specificity = 72.3%, and AUC of 0.846).[118] Another NRCS compared the PG-SGA to the Fearon 2011 algorithm (sensitivity = 86.2%, specificity = 58.3%, and AUC = 0.778).[69] A third NRCS reported a positive correlation between PG-SGA score and the categories of cachexia proposed by Fearon ($r = 0.54$; $p < 0.0001$).[92]

Wallengren 2013

Two studies compared the Wallengren 2013 algorithm to a reference algorithm. One NRCS found that more patients were classified as cachectic according to the Wallengren algorithm (37%) compared to the Fearon 2006 algorithm (12% based on all 3 components of the Fearon 2006 algorithm and 45%

based on 2 of 3 of these components) and the Evans 2008 algorithm (33%). The same study found that fewer patients were classified as cachectic according to the Wallengren algorithm compared to the Fearon 2011 algorithm (37% vs 85%, *p* NR).[79] Another NRCS found fewer patients were classified as cachectic according to Wallengren algorithm (13.8%) compared to the Vigano 2017 algorithm (8.2% not cachectic, 20.8% were precachectic, 17.3% cachectic, and 53.3% refractory cachexia).[123]

Nomograms

All 4 identified nomograms were compared against the Fearon 2011 algorithm. Liu 2022 reported AUCs of 0.702 for the training set and 0.688 for the validation set.[58] Huo 2022 reported a sensitivity of 0.826, specificity of 0.862, and AUC of 0.925 in the development cohort and 0.854, 0.829, and 0.923 (*p* NR) in the validation cohort.[53] Tan 2023 reported an AUC of 0.751 (95% CI [0.725, 0.777], $p < 0.001$) in the application cohort, indicating that this tool can identify those with and without cachexia.[75] Yin 2022 reported an accuracy of 0.714, kappa of 0.396, sensitivity of 0.580, specificity of 0.808, positive predictive value of 0.679, and negative predictive value of 0.733 for on the final model used to create the nomogram.[85]

Other Algorithms

One NRCS compared the CCSG/Fearon 2006 algorithm to the Fearon 2011, and found both algorithms classified a similar proportion of patients as cachectic (64% vs 60%, McNamar's test $p = 0.75$).[81]

One NRCS reported a moderate correlation between CASCO and subjective cachexia diagnoses from specialized oncologists ($\rho = 0.412$, $p < 0.001$). The same study reported a strong correlation between the CASCO and miniCASCO ($r = 0.964$, $p < 0.001$.)[125]

Using the Fearon 2011 algorithm as the reference determination of cachexia, the CCSI had an area under the receiver operating characteristics curve (AUC) to evaluate test accuracy of 0.911.[130]

One NRCS compared the GLIM to the Fearon 2011 algorithm. The GLIM had a sensitivity of 100%, specificity of 60.7%, accuracy of 67.4%, and AUC of 0.835. When nutritional risk screening (NRS-2002) was added, the GLIM had a sensitivity of 88.8%, specificity of 91.8%, accuracy of 91.3%, and AUC of 0.910.[69]

One study compared the MUST, NRS-2002, MST, and SNAQ to the Fearon 2011 definition of cachexia.[16] For 3 instruments, sensitivity was between 76.6% and 87.3% and in 1 instrument (SNAQ) sensitivity was 54.3%. For all 4 instruments, specificity was between 77.7% and 98.6%, accuracy was between 80.9% and 93.5%, and AUC was between 0.751 and 0.914.

One NRCS found a significant correlation between the CAS and PG-SGA ($r = 0.58$, $p = 0.04$). However, it was not clear if the PG-SGA was used by the authors to define cachexia or malnutrition.[131]

OUTCOMES FOR PATIENTS FOLLOWING CACHEXIA CLASSIFICATION

Forty-nine studies reported the adjusted association between cachexia as determined with a described algorithm and a prioritized outcome. The majority of studies were from Japan ($N = 13$), China ($N = 9$), and Korea ($N = 5$), with 3 conducted in the US. The studies were conducted between 1991 and 2002 and with a wide range of follow-up durations (10 days to 12 years). A total of 31,317 patients were included. The mean age of patients in 24 studies ranged from 57.8 to 75.6 years; the median age in 22 studies was between 57 and 83 years. In 2 studies, the majority of patients were ≤65 years old, and 1

study reported that the majority of patients were ≥60 years old. Males made up 40.5% to 100% of patients. Only 3 studies reported information on patient race/ethnicity, with White patients making up less than half of all participants in these studies (34.4-48%), Black patients making up 52% and 16.5% of samples in 2 of these studies, and 1 study reporting 40.5% of patients of "other" race. The studies included patients with a variety of cancers, including cancers of the head and neck; gastrointestinal tract; lung; breast; prostate; pancreas; skin, bones, and soft tissue; gynecological; genitourinary; and others, with patients with more advanced stages making up the majority of patients included. See the Appendix for further details on cancer treatments and patient comorbidities in each study. Overall survival was the most commonly reported outcome (reported on 50 times in 44 studies) followed by progression-free survival ($N = 11$), disease-free survival ($N = 8$), and relapse-free survival ($N = 2$). Other outcomes included function ($N = 2$), hospitalization ($N = 2$), or cachexia relevant burden or severity ($N = 2$). No study evaluated cachexia progression or feeding tube placement.

Two studies used propensity score matching to adjust for confounding and had no other concerns (therefore both low risk of bias). The remaining 47 studies used multivariable regression to adjust for confounding. Forty studies had moderate risk of bias due to concerns over attrition bias due to large loss to follow-up, lack of clear reporting or clear eligibility criteria, or because of analysis used for adjustment. Seven studies had high risk of bias. Six of these either adjusted for multiple cachexia algorithms in the same model, or adjusted for variables that were also included components of the cachexia algorithm. The seventh study had concerns surrounding high loss to follow-up, unclear reporting or eligibility criteria, and adjustment method used.

Overall, regardless of classification algorithm, overall survival, cancer progression-free survival, and disease-free survival were worse for patients with cancer cachexia. Those with cancer cachexia also had worse relapse-free survival, worse symptom burden, and longer hospital length of stay. Results in functional outcomes were inconsistent. No study reported feeding tube placement or cachexia progression outcomes.

Fearon 2011 Algorithm

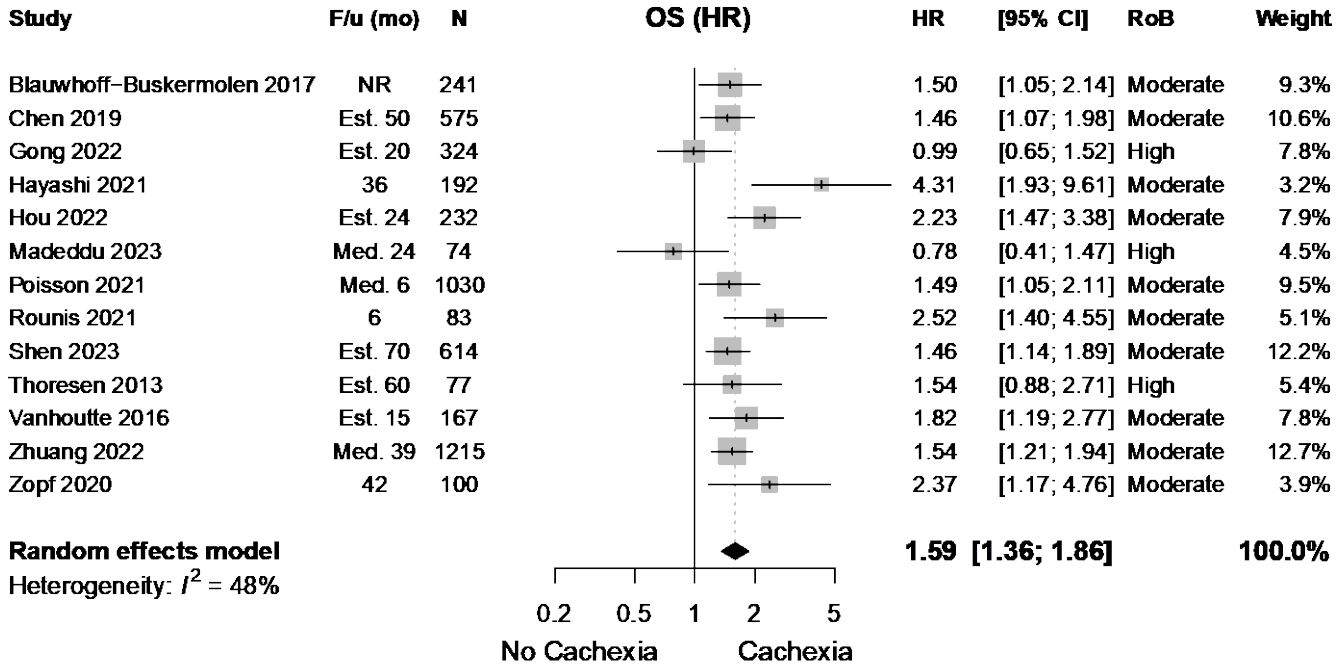
In summary (Table 3), patients identified as cachectic using the Fearon 2011 algorithm had worse overall mortality (moderate confidence), progression-free survival (moderate confidence), and disease-free survival (low confidence) when compared to noncachectic patients. Cachectic patients also had greater hospital and ICU length of stay (low confidence) and greater perception of dysphagia (low confidence). No studies used the Fearon 2011 algorithm to assess function outcomes, cachexia progression, or feeding tube placement.

Overall Survival

Fifteen studies reported overall survival for patients with and without cachexia based on the Fearon 2011 algorithm or some modification of this algorithm. Two studies were excluded from meta-analysis. One NRCS classified patients by the number of Fearon 2011 algorithm criteria met (see Appendix).[65] The NRCS found worse mortality for patients who met all 3 Fearon 2011 criteria compared to those who only met 1 or 2 of the criteria (HR = 1.40, 95% CI [1.078, 1.819]). Another NRCS used a modified version of the Fearon 2011, and thus was excluded from the meta-analysis, but found a similar association (HR = 2.93, 95 % CI [1.03, 8.34]). They also found an imprecise estimate of survival difference between precachectic and noncachectic patients (HR = 0.78, 95 % CI [0.30, 2.03]).[102]

Thirteen NRCSs found a significantly worse mortality among people with cachexia (pooled HR= 1.59, 95% CI [1.36, 1.86]; Figure 1). Only 1 study found a lower hazard of dying among those with cachexia, but the estimate was non-significant with a wide confidence interval.[61] Notably, this study controlled for multiple definitions of cachexia within the same models, raising concerns of collinearity.[49]

Figure 1. Overall Survival for Fearon 2011

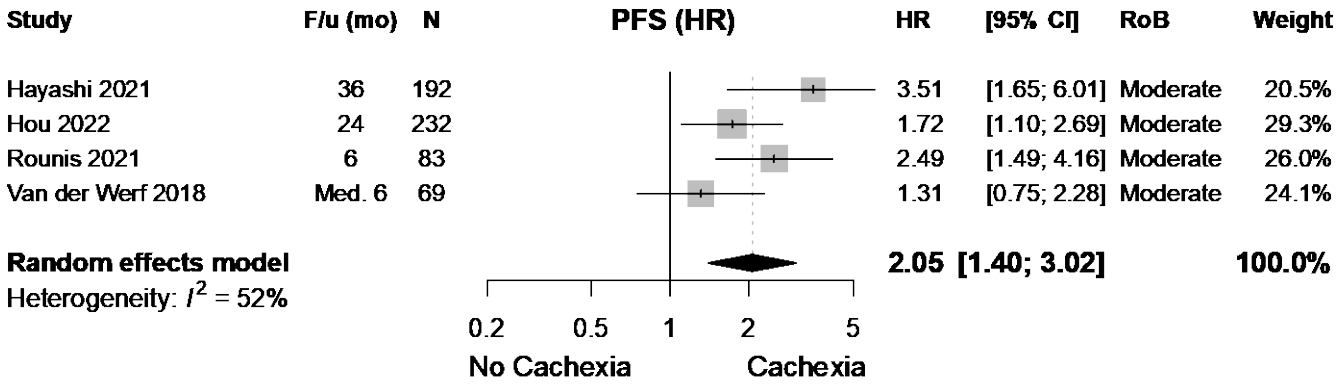


Abbreviations. Est=estimated based on KM curve; F/u=follow-up; HR=hazard ratio; Med=Median; mo=month; N=sample size; NR=not reported; OS=overall survival; RoB=risk of bias.

Cancer Progression-Free Survival

Four NRCSs reported cancer progression-free survival for people classified with and without cachexia following the Fearon 2011 algorithm. Pooled data from 4 studies found significantly worse cancer progression-free survival for people with versus without cachexia (pooled HR = 2.05, 95% CI [1.40, 3.02]; Figure 2).

Figure 2. Progression-Free Survival for Fearon 2011



Abbreviations. F/u=follow-up; HR=hazard ratio; Med=median; mo=month; N=sample size; PFS=progression-free survival; RoB=risk of bias.

Disease-Free Survival

One NRCS found worse disease-free survival among people classified as cachectic using the Fearon 2011 algorithm (HR= 1.53, 95% CI [1.21, 1.94]).[87]

Hospital Length-of-Stay-Related Outcomes

Two NRCSs reported hospital length of stay for people with and without cachexia using the Fearon 2011 algorithm. One NRCS found a significantly longer postoperative length of stay for patients with cachexia compared to their noncachectic counterparts (β = 2.41 days, 95% CI [0.28, 4.55]).[48] Another NRCS found a significantly longer median hospital stay for patients classified as cachectic than their noncachectic counterparts matched on propensity score (10.0 vs 7.0 days, $p < 0.001$).[54] The same study also reported cachectic patients had significantly longer intensive care unit (ICU) stays (median [IQR] 2.0 [2–3] vs 2.0 [2–2], $p < 0.001$), and cachectic patients had a greater risk for having an ICU stay >48 hours compared to patients without cachexia (RR [95% CI] = 2.06 [1.40, 3.04]). A prospective study found a greater risk of a score of 3 or more on the EAT-10 among those with cachexia (HR = 9.00, 95% CI [2.48, 32.62]), which indicated a greater perception of oropharyngeal dysphagia.[83]

Table 3. Summary of Findings for Fearon 2011[a]

Outcome	Studies (Patients); Design	Methodological Limitations	Indirectness	Imprecision	Inconsistency	Other Issues	Summary[a]	Overall Confidence
Overall Survival	15 (4,924); NRCS, Validation[43, 44, 51, 52, 61, 63-65, 68, 76, 78, 87, 88, 102, 118]	Moderate[b]	Direct	Precise	Consistent	None	Fearon: sumHR 1.59 (1.36, 1.86) Mod Fearon: HR 2.93 (1.03, 8.34)[c] 3 vs 1-2 criteria: HR 1.40 (1.08, 1.82)[c]	Moderate
Progression-Free Survival	4 (576); NRCS[51, 52, 64, 77]	Moderate[d]	Direct	Precise	Consistent	None	SumHR 2.05 (1.40, 3.02)	Moderate
Disease-Free survival	1 (1215); NRCS[87]	Moderate[d]	Direct	Precise	Consistent	Single Study	HR 1.53 (1.21, 1.94)	Low
Hospitalizations	2 (350); NRCS[48, 54]	Moderate[e]	Direct	Imprecise[f]	Consistent	N/A	Overall LOS and ICU day significantly longer in those with cachexia compared to no cachexia. Greater risk of prolonged IUC stay (RR = 2.06 [1.40, 3.04])	Low
Cachexia Symptom Burden	1 (66); NRCS[83, 140]	Moderate[d]	Direct	Precise	Consistent	Single Study	EAT-10 ≥3 HR = 9.00 (2.48, 32.62)	Low
Cachexia Progression	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Function	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Feeding Tube Placement	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence

Notes. [a] HR estimates >1 indicate worse outcome (*eg,* higher likelihood of death); [b] Three studies were rated as high risk of bias and 12 were rated as moderate risk of bias; [c] One study; [d] All included studies were rated as having moderate risk of bias; [e] One study was rated as low risk of bias and 1 was rated as moderate risk of bias; [f] Imprecise estimate for postoperative length of stay.

Abbreviations. EAT-10=eating assessment tool; HR=hazard ratio; ICU=intensive care unit; IQR=interquartile range; LOS=length of stay; N/A=not applicable; NRCS=nonrandomized comparative study; RR=relative risk; sumHR=summary (or pooled) hazard ratio.

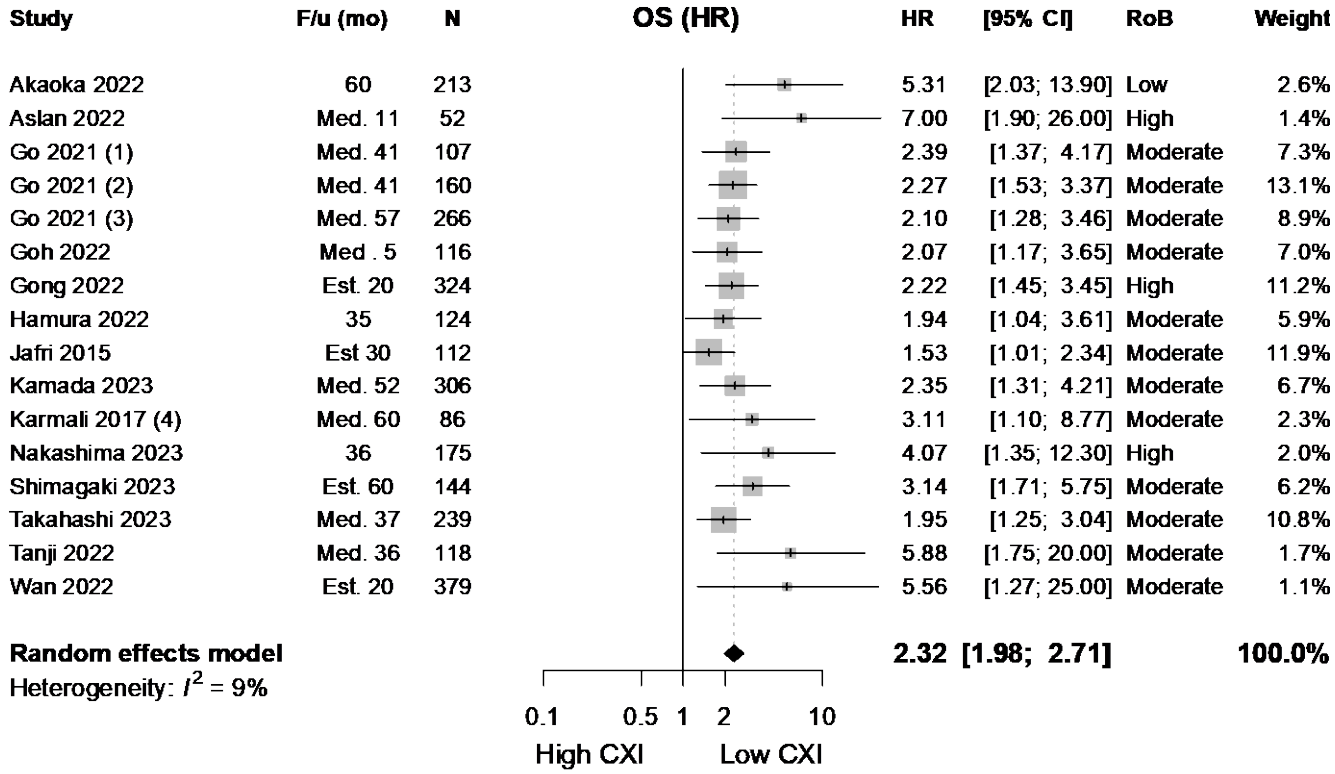
Cachexia Index

In summary (Table 4), using the CXI, people identified as cachectic, having low CXI, or stage II cachexia had worse overall mortality (low confidence), progression-free survival (moderate confidence), disease-free survival (moderate confidence), or relapse-free survival (low confidence) compared to those who were not. No studies used the CXI to assess cachexia symptom burden, functional levels, hospitalization outcomes, cachexia progression, or feeding tube placement.

Overall Survival

Sixteen studies evaluated overall survival based on the Cachexia Index (CXI) or a modification of this algorithm. Studies applied unique cutoffs (*eg,* based on population specific Youden's index values or based on median values) to classify patients as low CXI or high CXI. One study used median CXI values to classify patients as stage I cachexia and stage II cachexia, with those in stage II having a lower CXI.[110] The majority of these studies used the CXI as a biomarker for cachexia and its prognosis, but only 2 studies explicitly labeled the low-CXI group as "cachectic" and the high-CXI group as "noncachectic." One study used a modified version of the CXI that included hand grip strength and, thus, was excluded from the pooled analysis. This study reported greater mortality in patients with low H-CXI group versus high H-CXI (HR = 1.61, 95% CI[1.45, 1.79]).[84] The pooled data from 15 studies found a significantly worse overall mortality for patients with low CXI compared to high CXI (pooled HR = 2.32, 95% CI [1.98, 2.71]; Figure 3).

Figure 3. Overall Survival



Notes. CXI indicates cachexia or cachexia risk. (1) Estimate from Go 2021 (PMID 34001060) for patients with limited-stage disease; (2) Estimate from Go 2021 (PMID 34001060) for patients with extensive-stage disease; (3) Estimate from PMID 34676685; (4) 95% CI calculated from reported *p*-value.

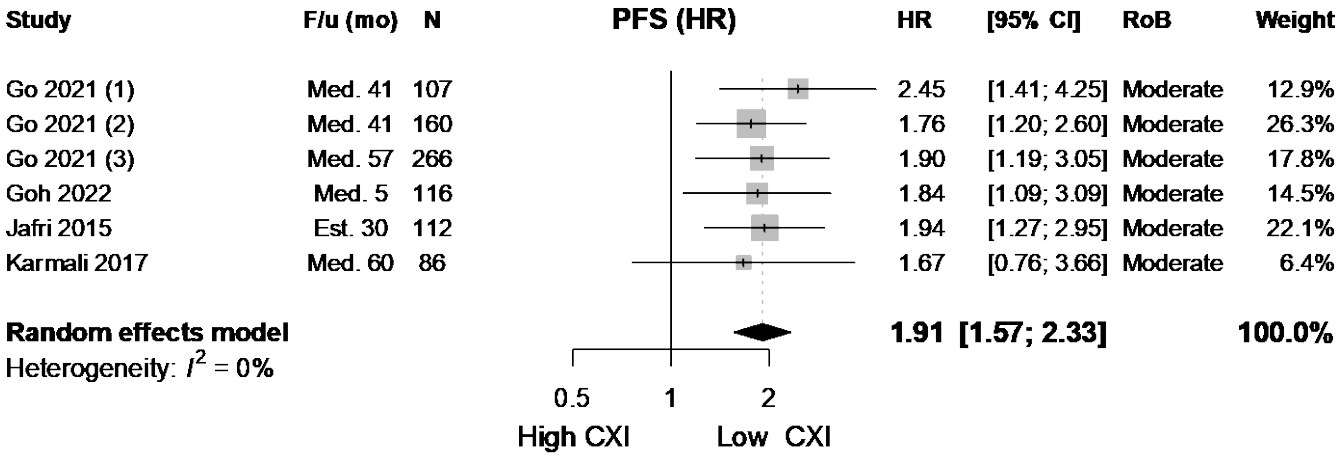
Abbreviations. Est=estimated based on KM curve; F/u=follow-up; H=high CXI; HR=hazard ratio; L=low CXI; Med=median; mo=month; N=sample size; OS=overall survival; RoB=risk of bias.

One NRCS found no significant difference in overall survival between patients classified as intermediate-CXI compared to high CXI (HR =1.72, 95% CI [0.99, 2.97]).[107] This was the only study to use the intermediate-CXI classification. While the results of the intermediate versus high-CXI groups were excluded from the meta-analysis, this study also compared low-CXI versus high-CXI groups, the results of which were included in the meta-analysis. Importantly, 1 NRCS conducted a propensity score match analysis and multivariable regression. The propensity score match analysis but not multivariable regression analysis found a significantly worse mortality for those in the low-CXI group ($p = 0.041$ and $p = 0.940$, respectively).[103]

Cancer Progression-Free Survival

Five NRCSs found a significantly worse progression-free survival for patients classified as low CXI (pooled HR = 1.91, 95% CI [1.57, 2.33]; Figure 4).

Figure 4. Progression-Free Survival



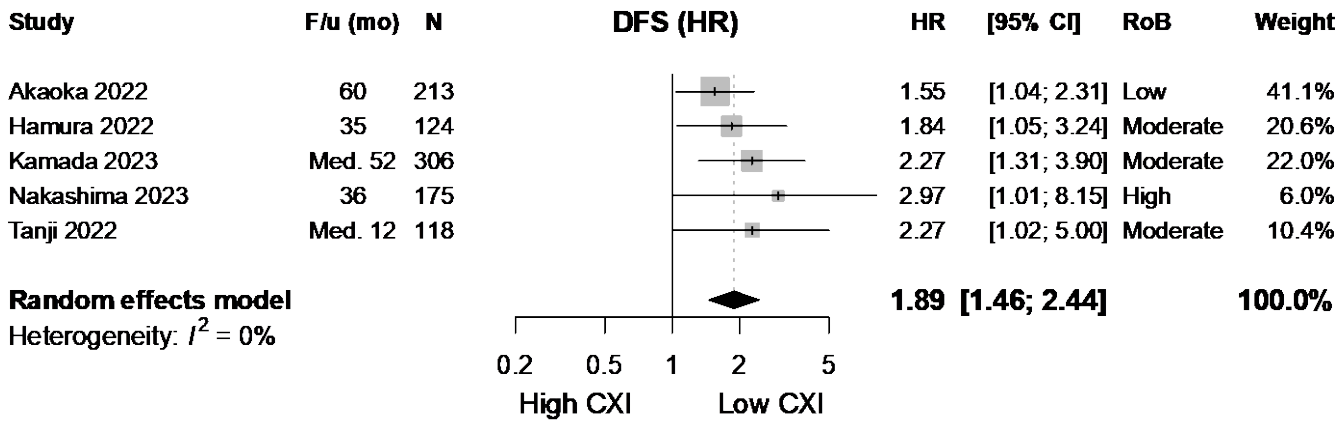
Notes. Go 2021 (1) = Patients with limited-stage small cell lung cancer from PMID 34001060; Go 2021 (2) = Patients with extensive-stage small cell lung cancer from PMID 34001060; Go 2021 (3) = patients with diffuse large B-cell lymphoma from PMID 34676685.

Abbreviations. Est=estimated based on KM curve; F/u=follow-up; HR=hazard ratio; Med=median; mo=month; N=sample size; PFS=progression-free survival; RoB=risk of bias.

Disease-Free Survival

Pooled data from 5 studies showed significantly worse disease-free survival for patients classified low CXI (pooled HR = 1.89, 95% CI [1.46, 2.44]; Figure 5).

Figure 5. Disease-Free Survival



Abbreviations. CXI=cancer cachexia index; DFS=disease-free survival; F/u=follow-up; HR=hazard ratio; Med=median; mo=month; N=sample size; RoB=risk of bias.

Relapse-Free Survival

One study reported significantly worse relapse-free survival for those classified as low CXI compared to high CXI (HR = 1.58, 95% CI [1.06, 2.34]).[141]

Table 4. Summary of Findings for Cachexia Index[a]

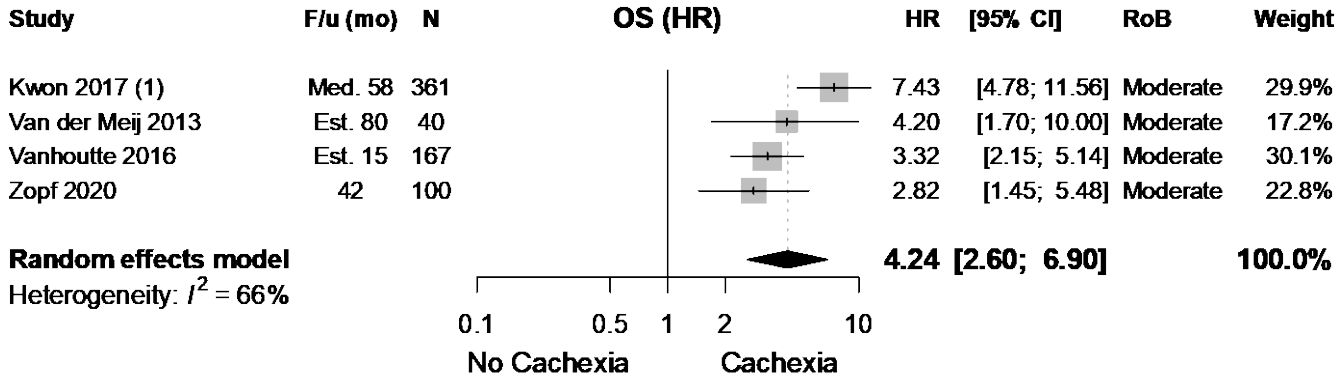
Outcome	Studies (Patients); Design	Methodological Limitations	Indirectness	Imprecision	Inconsistency	Other Issues	Summary	Overall Confidence
Overall Survival	16 (8,191); NRCS; Validation[49, 80, 84, 103, 104, 106-114, 116, 141]	Moderate[b]	Indirect[c]	Precise	Consistent		Pooled HR = 2.32 (1.98, 2.71) Modified CXI[a] HR = 1.61 (1.45, 1.79)	Low
Progression-Free Survival	5 (847); NRCS[106-108, 110, 112]	Moderate[d]	Direct	Precise	Consistent		Pooled HR = 1.91 (1.57, 2.33)	Moderate
Disease-Free Survival	5 (936); NRCS [103, 109, 111, 113, 116]	Moderate[e]	Direct	Precise	Consistent		Pooled HR = 1.89 (1.46, 2.44)	Moderate
Relapse-Free Survival	1 (239); NRCS[141]	Moderate[f]	Direct	Precise	Consistent	Single study	HR = 1.58 (1.06, 2.34)	Low
Function	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Hospitalizations	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Cachexia Progression	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Cachexia Symptom Burden	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Feeding Tube Placement	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence

Notes. [a] One study used a modified version of the CXI; [b] Three studies were rated as high risk of bias, 1 was rated as low risk, and 12 were rated as moderate risk;[c] Studies used different cutoff values to distinguish low versus high groups; [d] All studies were rated as moderate; [e] One study was rated as high risk of bias, 1 study was rated as low, and 3 were rated as moderate risk of bias; [f] Study was rated as moderate risk due to use of multivariable regression for adjustment.

Evans 2008 Algorithm

In summary (Table 5), 4 studies compared overall survival by cachexia based on the Evans 2008 algorithm. Pooled data showed significantly worse overall survival among those classified as cachectic (pooled HR = 4.24, 95% CI [2.60, 6.90]; Figure 6). No studies used the Evans 2008 algorithm to assess cachexia symptom burden, functional levels, hospitalization outcomes, cachexia progression, and feeding tube placement.

Figure 6. Overall Survival for Evans 2008



Notes. (1) = Comparison in this study was between patients with sustained cachexia both before and after treatment versus patients without cachexia at all time periods.

Abbreviations. Est=Estimated based on KM curve; F/u=follow-up; HR=hazard ratio; Med=median; mo=month; N=sample size; OS=overall survival; RoB=risk of bias.

Table 5. Summary of Findings for Evans 2008

Outcome	Studies (Patients); Design	Methodological Limitations	Indirectness	Imprecision	Inconsistency	Other Issues	HR (95% CI)	Quality
Overall Survival	4 (668); NRCS[78, 88, 102, 119]	Moderate[a]	Direct	Precise	Consistent		Pooled HR = 4.24 (2.60, 6.90)	Moderate
Function	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Hospitalizations	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Cachexia Progression	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Cachexia Symptom Burden	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence
Feeding Tube Placement	0	N/A	N/A	N/A	N/A	N/A	N/A	No evidence

Notes. [a] All studies rated as moderate risk of bias.

Fearon 2006

Two studies used the Fearon 2006 algorithm (see Appendix), which included weight loss, CRP, and energy intake components and found worse mortality for people classified with cachexia. One study reported significantly worse overall survival among those classified as cachectic compared to their counterparts without cachexia (HR = 2.26, 95% CI [1.18, 4.32]).[76] Another study found significantly worse 6 month mortality rates among patients who met 2 of 3 of the Fearon 2006 criteria or all 3 criteria compared to people who did not meet any criteria (HR = 2.23, $p < 0.001$ and HR = 2.96, $p < 0.001$). The same study found worse mortality rates among patients with stage II or III cancer who met 2 of 3 and all 3 Fearon 2006 compared to people not meeting any criteria (HR = 2.40, $p < 0.001$ and 4.94, $p < 0.001$). However, there were no significant differences in mortality in patients with stage IV cancer who met 2 of 3 or all 3 Fearon 2006 compared to people not meeting any criteria (HR = not reported).[124] No studies used the Fearon 2006 algorithm to assess cachexia symptom burden, functional levels, hospitalization outcomes, cachexia progression, or feeding tube placement.

Glasgow Prognostic Score

Two studies used the GPS to classify patients as cachectic (see Appendix). One study found significantly worse overall survival among patients classified as precachectic or with refractory cachexia compared to no cachexia (HR = 2.00, 95% CI [1.34, 2.98] and HR = 2.45, 95% CI [1.34, 2.98]).[136] The same study also reported no significant difference in hyporexia between those with precachexia and no cachexia, but people with refractory cachexia had greater odds of hyporexia (OR = 3.20, 95% CI [2.25, 4.55]), nausea (OR = 2.13, 95% CI [1.52, 2.99]), intestinal constipation (OR = 1.75, 95% CI [1.26, 2.44]), xerostomia (OR = 2.00, 95% CI [1.43, 2.80]), dysgeusia (OR = 1.89, 95% CI [(1.36, 2.63]), and fatigue (OR = 1.06, 95% CI [0.53, 1.59]). Another study found those classified as noncachectic (GPS) had greater odds of stable or improved Karnofsky performance status outcomes compared to those classified as having refractory cachexia (OR = 1.95 [1.01, 3.47]). In the same study, quality of life measured by improved or stable (vs not) Karnofsky performance status appeared to differ between patients classified as cachectic and those with refractory cachexia (OR = 0.45, 95% CI [0.29, 1.03]), but this difference was not significant.[132] No studies used the GPS to assess hospitalization outcomes, cachexia progression, or feeding tube placement.

Other Assessments

Eleven other studies applying 12 different algorithms to classify patients as cachectic reported on overall ($N = 11$),[75, 115, 120, 123, 128, 130, 137, 142-145] progression-free ($N = 2$),[120, 142] disease-free ($N = 2$),[115, 144] relapse-free survival ($N = 1$),[75] or function ($N = 1$)[137](see Appendix).

Nine of 11 studies found significantly worse overall survival (range in HR = 1.34 to 11.0) for people classified as cachectic compared to those without cachexia, or to those with more severe cachexia. One study reported worse overall survival for people classified to the severe cachexia group compared to those with moderate or mild cachexia by the Cancer Cachexia Score (HR = 2.94, 95% CI [1.81, 4.75]).[115] In a sample of people with cancer who were receiving support from a palliative care team, 1 study used the Cachexia Staging Score and reported worse overall survival in patients with precachexia (HR = 2.78, 95% CI [0.62, 12.46]), cachexia (HR = 4.77, 95% CI [1.09, 20.80]), and refractory cachexia (HR = 11.00, 95% CI [2.37, 51.07]) compared to those without cachexia.[128] Another study used the Cachexia Staging System in palliative care patients and reported worse overall survival among those with cachexia (HR = 1.35, 95% CI [1.12, 1.99]) and refractory cachexia (HR = 1.84, 95% CI [1.21, 2.79]) compared to those with precachexia.[145] A study of patients with cancers of various

sites used the Cancer Cachexia Staging Index to identify patients with mild, moderate, or severe cachexia. The study reported worse overall survival for people with mild or moderate cachexia (HR = 2.17, 95% CI [1.64, 2.88]) or severe cachexia (HR = 3.99 (2.45, 6.49) compared to people without cachexia.[130] One study of palliative care patients with cancer reported worse overall survival in people identified as cachectic using the algorithm developed by Wallengren (HR = 2.21, 95% CI [1.86, 2.62]) compared to those who did not.[123] The same study also used an algorithm developed by Vigano and found worse survival in patients with precachexia (HR = 1.87, 95% CI [1.28, 2.73]), cachexia (HR = 2.39, 95% CI [1.64, 3.49]), and refractory cachexia (HR = 2.87, 95% CI [2.01, 4.10]) compared to people without cachexia.[123]

An NRCS found worse overall survival among those in the high compared to low cachexia risk group using an algorithm that combined the GNRI and sarcopenia (HR = 3.35, 95% CI [2.17, 5.17]).[142] One study reported worse overall survival for patients with cachexia (a combination of mid-arm muscle area and hand grip strength to identify cachexia) compared to those without (HR = 2.8, 95% CI [1.30, 6.13]).[144] One study used an investigator-developed algorithm based on a combination of several published definitions of cachexia and found worse overall survival for patients with advance gastric cancer who developed cachexia within 6 months of chemotherapy compared to those who did not (HR = 1.34, 95% CI [1.16, 2.09]).[143] Another study reported worse overall survival (HR = 7.80, 95% CI [1.43, 42.48]) in the high cancer cachexia risk group (investigator-developed nomogram) compared to the low cachexia risk group.[75] An NRCS found no significant difference in overall survival between people with non-small lung cancer classified as cachectic (combined Evans 2008 and Fearon 2011 algorithms) and those who were noncachectic (HR = 1.27, CI % [0.71, 2.27]).[120] Another NRCS found no significant difference in overall survival (*p* NR) between patients with metastatic castrate-resistant prostate cancer classified with cachexia (nutritional status algorithm) compared to those classified as well nourished.[137]

Two studies reported significantly worse progression-free survival among people with cachexia. One NRCS found worse progression-free survival among those in the high compared to low cachexia risk group using a combination of the GNRI and sarcopenia (HR = 2.77, 95% CI [1.83, 4.12]) [142] An NRCS of people with non-small lung cancer found significantly worse progression-free survival in cachectic patients (combined Evans 2008 and Fearon 2011 algorithms) compared to noncachectic patients (HR = 1.64, 95% CI [1.06, 2.55]).[120]

Two studies reported worse disease-free survival among people with cachexia. One study reported worse disease-free survival for people classified to the severe cachexia group compared to those with moderate or mild cachexia by the Cancer Cachexia Score (HR = 2.33, 95% CI [1.55, 3.51]).[115] A study of patients with cancers of the head and neck reported worse disease-free survival (2.8, 95% CI [1.38, 5.82]) for patients with cachexia (a combination of mid-arm muscle area and hand grip strength to identify cachexia) compared to those without.[144]

One study reported worse relapse-free survival (HR = 4.79, 95% CI [1.80, 12.78]) in the high cancer cachexia risk group (investigator-developed nomogram) compared to the low cachexia risk group. [75] One study reported worse health-related quality of life between patients with metastatic castrate-resistant prostate cancer classified with cachexia (nutritional status algorithm) compared to those classified as well nourished (OR = 1.75, 95% CI [0.37, 8.33]).[137]

COMPARISONS BETWEEN ALGORITHMS

Three studies found worse overall mortality for patients identified as cachectic using the Evans 2008 criteria compared to the Fearon 2011 algorithm or a modified form of this (HR = 3.32, 95% CI [2.15, 5.14] vs 1.82 [1.19, 2.77]; 2.82 [1.45, 5.48] vs 2.37 [1.174, 4.764]; and 4.2 [1.7, 10.0] vs 2.93 [1.03, 8.34], *p* NR for all).[78, 88, 102] One study found greater mortality in patients identified as cachectic using the CXI algorithm compared to Fearon 2011 (HR = 2.22, 95% CI [1.45, 3.45] vs 0.99 [0.65, 1.52], *p* NR).[46] One study found worse mortality in patients identified as cachectic using the Fearon 2006 algorithm compared to Fearon 2011 (HR = 2.26, 95% CI [1.18, 4.32] vs 1.54 [0.88, 2.71], *p* NR).[49, 76] Another study reported similar overall mortality for patients identified as cachectic using the Vigano and Wallengren algorithms (HR = 2.39, 95% CI [1.64, 3.49] vs 2.21, 95% CI [1.86, 2.62], *p* NR).[123] No study compared algorithms for outcomes related to function, hospitalization, symptom burden, cachexia progression, or feeding tube placement.

DISCUSSION

We identified 114 studies that described 32 unique algorithms to diagnose or stage cachexia. Of the 32 algorithms, 22 were compared to a clinical exam or against the Fearon 2011 algorithm, 5 compared results to another cachexia algorithm, and 1 compared the developed algorithm to several existing algorithms (including Fearon 2011). Forty-nine studies evaluated the adjusted association between cachexia and a prioritized outcome in analyses. Across the 32 algorithms, anorexia, appetite, or nutrition; sarcopenia; and weight loss, BMI, and albumin were the most commonly used components, but there were more than 20 different components used across all algorithms. The most frequently evaluated outcomes were related to survival. Few studies reported on function, hospitalization, or cachexia symptom burden. Key findings include the following:

Key Findings

- The most frequently evaluated algorithms included the Fearon 2011, the Cachexia Index, and Evans 2008 algorithms.
- Twenty-two algorithms were compared against a clinical exam or another cachexia algorithm in 23 studies. Fearon 2011 was used as a comparison algorithm in 17 of these studies.
- Fearon 2011, Cachexia Index, and Evans 2008 algorithms found worse survival outcomes for people with cachexia compared to those without cachexia. Among other algorithms, the majority found worse survival in cachectic compared to noncachectic patients.
- The cachexia algorithms that categorized patients by severity, including the Glasgow Prognostic Score, Cancer Cachexia Score, Cancer Cachexia Staging Index, Vigano 2017 algorithm, Cachexia Staging System, and Cachexia Staging Score, found worse survival outcomes in those with more severe cachexia compared to less severe cachexia.
- Patients with cachexia based on the Fearon 2011 criteria had longer hospital and ICU stays.
- There may not be a difference in survival outcomes between precachectic and noncachectic populations.
- There was sparse reporting of outcomes relating to function, hospitalization, and cachexia symptom burden. No studies reported outcomes of cachexia progression or feeding tube placement.
- Worse overall mortality is predicted by the Evans 2008 algorithm, Fearon 2006 algorithm, or CXI compared to the Fearon 2011 algorithm.

A recent systematic review estimated that as many as half of cancer patients in the US develop cachexia,[5] but in practice diagnosing cachexia is difficult. There is great clinical interest in being able to prospectively identify people at high risk of developing cachexia or in the early stages of the disorder. Complicating practice are the wide variety of cachexia definitions and algorithms described in medical literature. To improve measurement of cachexia requires consensus definitions with algorithms that are easy to implement in routine practice. Recent guidelines from the European Society for Medical Oncology state that a comprehensive cachexia assessment should include information about nutritional, metabolic, and functional status; nutritional barriers; gastrointestinal dysfunction;

distress and quality of life; and cancer-related factors.[140] However, we found the algorithms of cachexia described in the literature included only some of these criteria. For example, Fearon 2011, which was the most commonly reported algorithm, includes only information on weight loss, BMI, and sarcopenia, leaving out many of these assessment criteria. Further, while there have been recent efforts to distinguish cachexia from malnutrition or sarcopenia alone,[146, 147] the nuanced relationship between these syndromes was not always clear in the identified algorithms. Some algorithms assessing cachexia used only components to identify malnutrition or sarcopenia, while other algorithms included components to help distinguish cachexia from these conditions.

Five studies reported worse overall mortality when using the Evans 2008 algorithm, CXI, or Fearon 2006 compared to the Fearon 2011 algorithm. The Evans 2008, CXI, and Fearon 2006 algorithms each include components beyond weight to assess cachexia, such as markers of inflammation. The differences in the strength of these associations and the algorithms used underscore the need for careful consideration, not only of availability of components but also of the outcomes being targeted when selecting an algorithm to use to identify cachexia. Although survival is important, patients may value other outcomes (*eg*, quality of life). Studies did not systematically evaluate the association between other patient-centered outcomes and the algorithms. Understanding the ability of different algorithms to assess these patient-centered outcomes is important when selecting which may be best to use.

While 69% of the algorithms were empirically compared to a clinical exam or another cachexia algorithm, validating cachexia algorithms is challenging given the lack of a well-established gold standard or reference case. Cachexia prevalence varied widely based on algorithms used. For instance, 1 study found that 52% of patients were identified as cachectic using the Fearon algorithm, but only 9% of those same patients were cachectic when identified by clinical assessment.[77] Another study comparing Fearon 2006, Fearon 2011, and Evans 2008 algorithms reported prevalence rates of 12% to 85% depending on the algorithm.[79] Variation in measures or tools to assess individual components also made it challenging to evaluate algorithms. For example, across studies that used the Fearon 2011 algorithm, sarcopenia was measured by CT, BIA, MUAMA, DEXA, SARC-F, and other tools. Further, cutoffs for what was considered "sarcopenia" varied widely by study. For instance, a study comparing 3 different methods of measuring sarcopenia reported that in 241 patients, 13% of patients were identified as sarcopenic by MUAMA, but 59% of these same patients were identified as sarcopenic using CT, and 93% using BIA.[43] While cost, burden, and availability of tools for measuring components are important considerations,[148] the lack of consistency adds further complication to the identification of cachexia. Additionally, few of the included studies (that were not conducted in East Asia) provided detailed information about the racial makeup of study samples, but racial differences in body composition should also be considered when establishing component cutoffs, such as BMI.[149]

An important limitation of the evidence base is the sparse reporting of outcomes of interest to the operational partners. Most studies reported survival-related outcomes. No study reported feeding tube placement or cachexia progression outcomes, and few studies reported on function, hospitalizations, or cachexia symptom burden. Additionally, a large number of studies were excluded because they did not report adjusted associations between cachexia and outcomes (see Appendix). Some included studies adjusted for individual components of the cachexia algorithm which raised concerns of collinearity, and some studies adjusted for multiple definitions of cachexia in the same model.

Strengths and Limitations of the Systematic Review Process

A strength of our review was the detailed coding of algorithm components, scoring functions, and definitions. Our approach to evaluating algorithms provides a foundation to understand nuanced scoring criteria beyond face level labels of the individual algorithm components (*eg,* BMI or weight loss). For example, sarcopenia was commonly included in the algorithms and our coding conveys how this measure was collected and incorporated within and across algorithms.

One limitation of this review relates to the terminology surrounding cachexia. In the literature, the term cachexia was sometimes used interchangeably with related syndromes, such as malnutrition or anorexia. We included only studies that explicitly used the term "cachexia" to avoid incorrectly including studies that were not specific to cachexia. Because of this approach, it is possible that we excluded studies that may have assessed cachexia but used a different term. Conversely, this approach may also have led to the inclusion of studies that did not explicitly distinguish between cachexia and other related conditions such as malnutrition or sarcopenia, since these terms may be used interchangeably in the literature. This review was intended to focus on classification algorithms that used >1 component, such as weight, to identify cachexia. However, for the Fearon 2011 algorithm, cachexia could be defined by either weight measures alone, or weight loss in combination with sarcopenia. It is possible that patients included in these studies were identified as cachectic based solely on weight measures. As mentioned, the assessment of many components, such as sarcopenia or SMI, was not uniform across studies, even across studies using the same algorithm. The variation in the measurement of these criteria made comparing outcomes across studies challenging. Further, for some assessment tools, such as the CXI, we had to use study-specific cutoffs for cachexia classifications, which may make these definitions less applicable to other external samples. Additionally, while necessary in order to reduce any potential confounding between groups, our choice to only include studies that adjusted for confounding limited the number of studies and type of outcomes included in our analyses of the association between algorithms and outcomes, but by doing so, we excluded studies with clear confounder bias.

IMPLICATIONS FOR VA POLICY AND PRACTICE

VA diagnoses over 50,000 Veterans with cancer annually[18] and has made significant investments to deliver the most effective treatments to Veterans regardless of their location through cancer genomics, tele-oncology, and clinical trials. More broadly, the advent of immunotherapies and other targeted therapies has led to rapid advances in treating cancers that, until relatively recently, were considered untreatable. For people with cachexia, the accompanying weight loss, functional decline, and malnutrition hamper their ability to tolerate treatments and associated adverse effects.[150, 151] As VA continues to invest in oncology programs, collecting patient-reported outcomes (and cachexia factors) such as anorexia, fatigue, and quality of life could inform both oncologic and cachexia end points. Among the studies we identified, only 2 were conducted within the VA and both reported on the Fearon 2011 algorithm. The components of other well-performing cachexia algorithms (*eg*, weight loss, sarcopenia, anorexia) can by readily measured among VA patients with cancer. However, it is important to note that nearly 40% of available studies were conducted in China or Japan, which may limit the generalizability of evidence on the contribution of each component to algorithm performance.

Systematic collection of cachexia-related data is a necessary but complex task in a busy clinical environment, with implications for both front-line health care staff and VA's data infrastructure. For example, weight loss can be obtained from the VA medical record. In contrast, anorexia and functional decline are neither systematically measured in Veterans nor stored in a common location in the VA

electronic medical record. Thus, implementation of a standardized cachexia measure would require VA leadership support, development of the collection infrastructure, education of the oncology field, and the monitoring/re-enforcement of the importance of collection. Alongside these steps, it will likely be valuable to implement predictive analytics to identify those Veterans most at risk for cachexia and focus assessments on them.

Effective management of cachexia requires timely identification. The importance of identifying cachexia early and by severity is also highlighted by the role of emerging therapeutics. Few studies reported on patient quality of life or function, which are measures that may be sensitive to health system features. Again, this represents an opportunity for VA, which has the capability of collecting patient-reported outcomes and other measures.[152] Being able to uniformly collect these data points could help improve understanding and identification of cachexia.

FUTURE RESEARCH

While a variety of cachexia algorithms have been reported, few studies directly compared cachexia algorithms. Direct comparisons are needed to understand which algorithm may be best for early identification of cachexia patient outcomes. Future studies should be explicitly designed to compare algorithms and evaluate outcomes using propensity score or regression adjustment methods that control for known and potential sources of confounding. There is also a need to validate algorithms against, at minimum, an agreed upon reference standard (*eg,* Fearon 2011), and to validate these within specific populations, such as Veterans. This includes validation of biomarkers and other surrogate end points. Most cachexia classification algorithms included only 2 stages (presence or absence of cachexia), and there is a need to expand research on algorithms that more finely characterize cachexia severity and outcomes associated with cachexia severity. Few studies reported prioritized outcomes of interest. While survival outcomes based on cachexia status are of interest, other more modifiable outcomes such as patient quality of life or functional status should be included in future studies to clarify the impact of cachexia and cachexia interventions on these outcomes. Further, clinically meaningful outcomes should be considered when developing future algorithms. Finally, if new algorithms are developed, these should take a comprehensive approach to assessing potential components of cachexia beyond those of weight and sarcopenia.

CONCLUSIONS

Standardizing the identification of cancer cachexia can improve practice and support targeted interventions. Health systems aiming to implement an algorithm in routine practice should focus on feasibility and ease of use. The Fearon 2011, Cachexia Index, and Evans 2008 algorithms were the most frequently described. While many of the identified algorithms incorporate components for anorexia, appetite, or nutrition; albumin; sarcopenia; and/or weight loss to assess cachexia, the overall literature base included more than 20 different components in a variety of combinations. Patients classified as cachectic had worse survival outcomes. Studies are needed to identify optimal cachexia algorithms and to better understand the relationship between cachexia severity and outcomes such as cachexia progression, function, or quality of life.

REFERENCES

1. Bruggeman AR, Kamal AH, LeBlanc TW, Ma JD, Baracos VE, Roeland EJ. Cancer Cachexia: Beyond Weight Loss. *J Oncol Pract*. Nov 2016;12(11):1163-1171. doi:10.1200/jop.2016.016832
2. Baker Rogers J, Syed K, Minteer JF. Cachexia. *StatPearls*. StatPearls Publishing Copyright © 2024, StatPearls Publishing LLC.; 2024.
3. Nutrition in Cancer Care (PDQ®)–Health Professional Version. Updated November 2023. https://www.cancer.gov/about-cancer/treatment/side-effects/appetite-loss/nutrition-hp-pdq#_23_toc
4. Dev R. Measuring cachexia-diagnostic criteria. *Ann Palliat Med*. Jan 2019;8(1):24-32. doi:10.21037/apm.2018.08.07
5. Anker MS, Holcomb R, Muscaritoli M, et al. Orphan disease status of cancer cachexia in the USA and in the European Union: a systematic review. *J Cachexia Sarcopenia Muscle*. Feb 2019;10(1):22-34. doi:10.1002/jcsm.12402
6. Vaughan VC, Martin P, Lewandowski PA. Cancer cachexia: impact, mechanisms and emerging treatments. *J Cachexia Sarcopenia Muscle*. Jun 2013;4(2):95-109. doi:10.1007/s13539-012-0087-1
7. Song M, Zhang Q, Tang M, et al. Associations of low hand grip strength with 1 year mortality of cancer cachexia: a multicentre observational study. *J Cachexia Sarcopenia Muscle*. Dec 2021;12(6):1489-1500. doi:10.1002/jcsm.12778
8. Naito T, Okayama T, Aoyama T, et al. Unfavorable impact of cancer cachexia on activity of daily living and need for inpatient care in elderly patients with advanced non-small-cell lung cancer in Japan: a prospective longitudinal observational study. *BMC Cancer*. Nov 28 2017;17(1):800. doi:10.1186/s12885-017-3795-2
9. Arthur ST, Van Doren BA, Roy D, Noone JM, Zacherle E, Blanchette CM. Cachexia among US cancer patients. *J Med Econ*. Sep 2016;19(9):874-80. doi:10.1080/13696998.2016.1181640
10. Li X, Hu C, Zhang Q, et al. Cancer cachexia statistics in China. *Precision Nutrition*. 2022;1(1)
11. Gannavarapu BS, Lau SKM, Carter K, et al. Prevalence and Survival Impact of Pretreatment Cancer-Associated Weight Loss: A Tool for Guiding Early Palliative Care. *J Oncol Pract*. Apr 2018;14(4):e238-e250. doi:10.1200/jop.2017.025221
12. Ozorio GA, Barão K, Forones NM. Cachexia Stage, Patient-Generated Subjective Global Assessment, Phase Angle, and Handgrip Strength in Patients with Gastrointestinal Cancer. *Nutr Cancer*. Jul 2017;69(5):772-779. doi:10.1080/01635581.2017.1321130
13. Zhou T, Wang B, Liu H, et al. Development and validation of a clinically applicable score to classify cachexia stages in advanced cancer patients. *J Cachexia Sarcopenia Muscle*. Apr 2018;9(2):306-314. doi:10.1002/jcsm.12275
10.1002/jcsm.12275. Epub 2018 Jan 25.
14. Evans WJ, Morley JE, Argilés J, et al. Cachexia: a new definition. *Clin Nutr*. Dec 2008;27(6):793-9. doi:10.1016/j.clnu.2008.06.013
15. Martin L. Diagnostic criteria for cancer cachexia: data versus dogma. *Curr Opin Clin Nutr Metab Care*. May 2016;19(3):188-98. doi:10.1097/mco.0000000000000272
16. Chen XY, Zhang XZ, Ma BW, et al. A comparison of four common malnutrition risk screening tools for detecting cachexia in patients with curable gastric cancer. *Nutrition*. Feb 2020;70:110498. doi:10.1016/j.nut.2019.04.009
10.1016/j.nut.2019.04.009. Epub 2019 Apr 26.
17. Cao Z, Zhao K, Jose I, Hoogenraad NJ, Osellame LD. Biomarkers for Cancer Cachexia: A Mini Review. *Int J Mol Sci*. Apr 26 2021;22(9)doi:10.3390/ijms22094501

18. Zullig LL, Sims KJ, McNeil R, et al. Cancer Incidence Among Patients of the U.S. Veterans Affairs Health Care System: 2010 Update. *Mil Med*. Jul 2017;182(7):e1883-e1891. doi:10.7205/milmed-d-16-00371
19. Affairs UDoV. Veterans Health Administration. https://www.va.gov/health/aboutvha.asp
20. Affairs UDoV. National Oncology Program. https://www.cancer.va.gov/index.html
21. Roeland EJ, Bohlke K, Baracos VE, et al. Management of Cancer Cachexia: ASCO Guideline. *J Clin Oncol*. Jul 20 2020;38(21):2438-2453. doi:10.1200/jco.20.00611
22. Cosci F, Fava GA. Staging of mental disorders: systematic review. *Psychother Psychosom*. 2013;82(1):20-34. doi:10.1159/000342243
23. Grande AJ, Silva V, Sawaris Neto L, Teixeira Basmage JP, Peccin MS, Maddocks M. Exercise for cancer cachexia in adults. *Cochrane Database Syst Rev*. Mar 18 2021;3(3):Cd010804. doi:10.1002/14651858.CD010804.pub3
24. Hammond S, Erridge S, Mangal N, Pacchetti B, Sodergren MH. The Effect of Cannabis-Based Medicine in the Treatment of Cachexia: A Systematic Review and Meta-Analysis. *Cannabis Cannabinoid Res*. Dec 2021;6(6):474-487. doi:10.1089/can.2021.0048
25. Jin X, Xu XT, Tian MX, Dai Z. Omega-3 polyunsaterated fatty acids improve quality of life and survival, but not body weight in cancer cachexia: A systematic review and meta-analysis of controlled trials. *Nutr Res*. Nov 2022;107:165-178. doi:10.1016/j.nutres.2022.09.009
26. Mbeutcha A, Rouprêt M, Kamat AM, et al. Prognostic factors and predictive tools for upper tract urothelial carcinoma: a systematic review. *World J Urol*. Mar 2017;35(3):337-353. doi:10.1007/s00345-016-1826-2
27. Millar SC, Arnold JB, Thewlis D, Fraysse F, Solomon LB. A systematic literature review of tibial plateau fractures: What classifications are used and how reliable and useful are they? *Injury*. Mar 2018;49(3):473-490. doi:10.1016/j.injury.2018.01.025
28. Moore ZE, Patton D. Risk assessment tools for the prevention of pressure ulcers. *Cochrane Database Syst Rev*. Jan 31 2019;1(1):Cd006471. doi:10.1002/14651858.CD006471.pub4
29. Niels T, Tomanek A, Freitag N, Schumann M. Can Exercise Counteract Cancer Cachexia? A Systematic Literature Review and Meta-Analysis. *Integr Cancer Ther*. Jan-Dec 2020;19:1534735420940414. doi:10.1177/1534735420940414
30. Potter R, Probyn K, Bernstein C, Pincus T, Underwood M, Matharu M. Diagnostic and classification tools for chronic headache disorders: A systematic review. *Cephalalgia*. May 2019;39(6):761-784. doi:10.1177/0333102418806864
31. Rahman A, O'Connor DB, Gather F, et al. Clinical Classification and Severity Scoring Systems in Chronic Pancreatitis: A Systematic Review. *Dig Surg*. 2020;37(3):181-191. doi:10.1159/000501429
32. Schiavo G, Forgerini M, Lucchetta RC, Mastroianni PC. A comprehensive look at explicit screening tools for potentially inappropriate medication: A systematic scoping review. *Australas J Ageing*. Sep 2022;41(3):357-382. doi:10.1111/ajag.13046
33. Simon L, Baldwin C, Kalea AZ, Slee A. Cannabinoid interventions for improving cachexia outcomes in cancer: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. Feb 2022;13(1):23-41. doi:10.1002/jcsm.12861
34. Stevenson JM, Williams JL, Burnham TG, et al. Predicting adverse drug reactions in older adults; a systematic review of the risk prediction models. *Clin Interv Aging*. 2014;9:1581-93. doi:10.2147/cia.S65475
35. Stynes S, Konstantinou K, Dunn KM. Classification of patients with low back-related leg pain: a systematic review. *BMC Musculoskelet Disord*. May 23 2016;17:226. doi:10.1186/s12891-016-1074-z

36. Wang J, Wang Y, Tong M, Pan H, Li D. Medical Cannabinoids for Cancer Cachexia: A Systematic Review and Meta-Analysis. *Biomed Res Int*. 2019;2019:2864384. doi:10.1155/2019/2864384
37. Balduzzi S RG, Schwarzer G "How to perform a meta-analysis with R: a practical tutorial. *Evidence-Based Mental Health*. 2019:153–160.
38. Anderson LJ, Chong N, Migula D, et al. Muscle mass, not radiodensity, predicts physical function in cancer patients with or without cachexia. *Oncotarget*. 2020;11(20):1911-1921. doi:https://dx.doi.org/10.18632/oncotarget.27594
39. Du C, Wang C, Guan X, et al. Asprosin is associated with anorexia and body fat mass in cancer patients. *Support Care Cancer*. Mar 2021;29(3):1369-1375. doi:10.1007/s00520-020-05621-8 10.1007/s00520-020-05621-8. Epub 2020 Jul 13.
40. Álvaro Sanz E, Abilés J, Garrido Siles M, Pérez Ruíz E, Alcaide García J, Rueda Domínguez A. Impact of weight loss on cancer patients' quality of life at the beginning of the chemotherapy. *Support Care Cancer*. Feb 2021;29(2):627-634. doi:10.1007/s00520-020-05496-9 10.1007/s00520-020-05496-9. Epub 2020 May 18.
41. Anderson LJ, Lee J, Mallen MC, et al. Evaluation of physical function and its association with body composition, quality of life and biomarkers in cancer cachexia patients. *Clin Nutr*. Mar 2021;40(3):978-986. doi:10.1016/j.clnu.2020.07.001 10.1016/j.clnu.2020.07.001. Epub 2020 Jul 15.
42. Blauwhoff-Buskermolen S, Langius JA, Heijboer AC, Becker A, de van der Schueren MA, Verheul HM. Plasma Ghrelin Levels Are Associated with Anorexia but Not Cachexia in Patients with NSCLC. *Front Physiol*. 2017;8:119. doi:10.3389/fphys.2017.00119 10.3389/fphys.2017.00119. eCollection 2017.
43. Blauwhoff-Buskermolen S, Langius JAE, Becker A, Verheul HMW, de van der Schueren MAE. The influence of different muscle mass measurements on the diagnosis of cancer cachexia. *J Cachexia Sarcopenia Muscle*. Aug 2017;8(4):615-622. doi:10.1002/jcsm.12200 10.1002/jcsm.12200. Epub 2017 Apr 26.
44. Chen X, Zeng Y, Huang Y, et al. Preoperative Cachexia predicts poor outcomes in young rather than elderly gastric cancer patients: a prospective study. *Cancer Manag Res*. 2019;11:8101-8110. doi:10.2147/cmar.S213237 10.2147/CMAR.S213237. eCollection 2019.
45. da Rocha IMG, Marcadenti A, de Medeiros GOC, et al. Is cachexia associated with chemotherapy toxicities in gastrointestinal cancer patients? A prospective study. *J Cachexia Sarcopenia Muscle*. Apr 2019;10(2):445-454. doi:10.1002/jcsm.12391 10.1002/jcsm.12391. Epub 2019 Mar 28.
46. De Waele E, Demol J, Caccialanza R, et al. Unidentified cachexia patients in the oncologic setting: Cachexia UFOs do exist. *Nutrition*. Jul-Aug 2019;63-64:200-204. doi:10.1016/j.nut.2019.02.015 10.1016/j.nut.2019.02.015. Epub 2019 Feb 27.
47. Deng M, Aberle MR, van Bijnen AAJHM, et al. Lipocalin-2 and neutrophil activation in pancreatic cancer cachexia. *Frontiers in Immunology*. 2023;14:1159411. doi:https://dx.doi.org/10.3389/fimmu.2023.1159411
48. Fukuta A, Saito T, Murata S, et al. Impact of preoperative cachexia on postoperative length of stay in elderly patients with gastrointestinal cancer. *Nutrition*. Feb 2019;58:65-68. doi:10.1016/j.nut.2018.06.022 10.1016/j.nut.2018.06.022. Epub 2018 Oct 11.

49. Gong C, Wan Q, Zhao R, Zuo X, Chen Y, Li T. Cachexia Index as a Prognostic Indicator in Patients with Gastric Cancer: A Retrospective Study. *Cancers (Basel)*. Sep 10 2022;14(18)doi:10.3390/cancers14184400 10.3390/cancers14184400.
50. Hadzibegovic S, Porthun J, Lena A, et al. Hand grip strength in patients with advanced cancer: A prospective study. *J Cachexia Sarcopenia Muscle*. Jun 15 2023;doi:10.1002/jcsm.13248 10.1002/jcsm.13248.
51. Hayashi N, Sato Y, Fujiwara Y, et al. Clinical Impact of Cachexia in Head and Neck Cancer Patients Who Received Chemoradiotherapy. *Cancer Manag Res*. 2021;13:8377-8385. doi:10.2147/cmar.S329581 10.2147/CMAR.S329581. eCollection 2021.
52. Hou YC, Chen CY, Huang CJ, et al. The Differential Clinical Impacts of Cachexia and Sarcopenia on the Prognosis of Advanced Pancreatic Cancer. *Cancers (Basel)*. Jun 26 2022;14(13)doi:10.3390/cancers14133137 10.3390/cancers14133137.
53. Huo Z, Chong F, Yin L, et al. Development and validation of an online dynamic nomogram system for predicting cancer cachexia among inpatients: a real-world cohort study in China. *Support Care Cancer*. Dec 22 2022;31(1):72. doi:10.1007/s00520-022-07540-2 10.1007/s00520-022-07540-2.
54. Jones AJ, Davis KP, Novinger LJ, et al. Postoperative consequences of cancer cachexia after head and neck free flap reconstruction. *Head Neck*. Jul 2022;44(7):1665-1677. doi:10.1002/hed.27072 10.1002/hed.27072. Epub 2022 Apr 29.
55. LeBlanc TW, Nickolich M, Rushing CN, Samsa GP, Locke SC, Abernethy AP. What bothers lung cancer patients the most? A prospective, longitudinal electronic patient-reported outcomes study in advanced non-small cell lung cancer. *Support Care Cancer*. Dec 2015;23(12):3455-63. doi:10.1007/s00520-015-2699-4 10.1007/s00520-015-2699-4. Epub 2015 Mar 21.
56. LeBlanc TW, Nipp RD, Rushing CN, et al. Correlation between the international consensus definition of the Cancer Anorexia-Cachexia Syndrome (CACS) and patient-centered outcomes in advanced non-small cell lung cancer. *J Pain Symptom Manage*. Apr 2015;49(4):680-9. doi:10.1016/j.jpainsymman.2014.09.008 10.1016/j.jpainsymman.2014.09.008. Epub 2014 Nov 4.
57. Liao WC, Chen PR, Huang CC, et al. Relationship between pancreatic cancer-associated diabetes and cachexia. *J Cachexia Sarcopenia Muscle*. Aug 2020;11(4):899-908. doi:10.1002/jcsm.12553 10.1002/jcsm.12553. Epub 2020 Feb 25.
58. Liu CA, Zhang Q, Ruan GT, et al. Novel Diagnostic and Prognostic Tools for Lung Cancer Cachexia: Based on Nutritional and Inflammatory Status. *Front Oncol*. 2022;12:890745. doi:10.3389/fonc.2022.890745 10.3389/fonc.2022.890745. eCollection 2022.
59. Loumaye A, De Barsy M, Nachit M, et al. Role of activin A and myostatin in human cancer cachexia. *Journal of Clinical Endocrinology and Metabolism*. 2015;100(5):2030-2038. doi:https://dx.doi.org/10.1210/jc.2014-4318
60. Luvián-Morales J, Castillo-Aguilar J, Delgadillo-González M, et al. Validation of the QLQ-CAX24 instrument in cervical cancer and its association with cachexia classifications. *Jpn J Clin Oncol*. Mar 30 2023;53(4):304-312. doi:10.1093/jjco/hyac199 10.1093/jjco/hyac199.

61. Madeddu C, Busquets S, Donisi C, et al. Effect of Cancer-Related Cachexia and Associated Changes in Nutritional Status, Inflammatory Status, and Muscle Mass on Immunotherapy Efficacy and Survival in Patients with Advanced Non-Small Cell Lung Cancer. *Cancers*. 2023;15(4):1076. doi:https://dx.doi.org/10.3390/cancers15041076
62. Ohmae N, Yasui-Yamada S, Furumoto T, et al. Muscle mass, quality, and strength; physical function and activity; and metabolic status in cachectic patients with head and neck cancer. *Clin Nutr ESPEN*. Feb 2023;53:113-119. doi:10.1016/j.clnesp.2022.12.006
10.1016/j.clnesp.2022.12.006. Epub 2022 Dec 9.
63. Poisson J, Martinez-Tapia C, Heitz D, et al. Prevalence and prognostic impact of cachexia among older patients with cancer: a nationwide cross-sectional survey (NutriAgeCancer). *J Cachexia Sarcopenia Muscle*. Dec 2021;12(6):1477-1488. doi:10.1002/jcsm.12776
10.1002/jcsm.12776. Epub 2021 Sep 14.
64. Rounis K, Makrakis D, Tsigkas AP, et al. Cancer cachexia syndrome and clinical outcome in patients with metastatic non-small cell lung cancer treated with PD-1/PD-L1 inhibitors: results from a prospective, observational study. *Transl Lung Cancer Res*. Aug 2021;10(8):3538-3549. doi:10.21037/tlcr-21-460
10.21037/tlcr-21-460.
65. Ruan GT, Yang M, Zhang XW, et al. Association of Systemic Inflammation and Overall Survival in Elderly Patients with Cancer Cachexia - Results from a Multicenter Study. *J Inflamm Res*. 2021;14:5527-5540. doi:10.2147/jir.S332408
10.2147/JIR.S332408. eCollection 2021.
66. Ruan GT, Zhang Q, Zhang X, et al. Geriatric Nutrition Risk Index: Prognostic factor related to inflammation in elderly patients with cancer cachexia. *J Cachexia Sarcopenia Muscle*. Dec 2021;12(6):1969-1982. doi:10.1002/jcsm.12800
10.1002/jcsm.12800. Epub 2021 Sep 29.
67. Schwarz S, Prokopchuk O, Esefeld K, et al. The clinical picture of cachexia: a mosaic of different parameters (experience of 503 patients). *BMC Cancer*. Feb 14 2017;17(1):130. doi:10.1186/s12885-017-3116-9
10.1186/s12885-017-3116-9.
68. Shen XD, Wang X, Zheng ZJ, et al. The differential effects of sarcopenia and cachexia on overall survival for pancreatic ductal adenocarcinoma patients following pancreatectomy: A retrospective study based on a large population. *Cancer Med*. May 2023;12(9):10438-10448. doi:10.1002/cam4.5779
10.1002/cam4.5779. Epub 2023 Mar 20.
69. Song M, Zhang Q, Liu T, et al. Efficacy of Global Leadership Initiative on Malnutrition as potential cachexia screening tool for patients with solid cancer. *Nutr J*. Dec 7 2022;21(1):73. doi:10.1186/s12937-022-00829-2
10.1186/s12937-022-00829-2.
70. Srdic D, Plestina S, Sverko-Peternac A, Nikolac N, Simundic AM, Samarzija M. Cancer cachexia, sarcopenia and biochemical markers in patients with advanced non-small cell lung cancer-chemotherapy toxicity and prognostic value. *Support Care Cancer*. Nov 2016;24(11):4495-502. doi:10.1007/s00520-016-3287-y
10.1007/s00520-016-3287-y. Epub 2016 May 28.
71. Stene GB, Balstad TR, Leer ASM, et al. Deterioration in Muscle Mass and Physical Function Differs According to Weight Loss History in Cancer Cachexia. *Cancers (Basel)*. Dec 3 2019;11(12)doi:10.3390/cancers11121925
10.3390/cancers11121925.

72. Sullivan ES, Daly LE, Scannell C, et al. A large, multi-centre prospective study demonstrating high prevalence of malnutrition associated with reduced survival in ambulatory systemic anti-cancer therapy patients. *Clin Nutr ESPEN*. Dec 2022;52:208-217. doi:10.1016/j.clnesp.2022.10.009 10.1016/j.clnesp.2022.10.009. Epub 2022 Oct 25.
73. Sun L, Quan XQ, Yu S. An Epidemiological Survey of Cachexia in Advanced Cancer Patients and Analysis on Its Diagnostic and Treatment Status. *Nutr Cancer*. 2015;67(7):1056-62. doi:10.1080/01635581.2015.1073753 10.1080/01635581.2015.1073753. Epub 2015 Aug 28.
74. Suno M, Endo Y, Nishie H, Kajizono M, Sendo T, Matsuoka J. Refractory cachexia is associated with increased plasma concentrations of fentanyl in cancer patients. *Ther Clin Risk Manag*. 2015;11:751-7. doi:10.2147/tcrm.S79374 10.2147/TCRM.S79374. eCollection 2015.
75. Tan S, Xu J, Wang J, et al. Development and validation of a cancer cachexia risk score for digestive tract cancer patients before abdominal surgery. *J Cachexia Sarcopenia Muscle*. Apr 2023;14(2):891-902. doi:10.1002/jcsm.13207 10.1002/jcsm.13207. Epub 2023 Mar 7.
76. Thoresen L, Frykholm G, Lydersen S, et al. Nutritional status, cachexia and survival in patients with advanced colorectal carcinoma. Different assessment criteria for nutritional status provide unequal results. *Clin Nutr*. Feb 2013;32(1):65-72. doi:10.1016/j.clnu.2012.05.009 10.1016/j.clnu.2012.05.009. Epub 2012 Jun 12.
77. van der Werf A, van Bokhorst QNE, de van der Schueren MAE, Verheul HMW, Langius JAE. Cancer Cachexia: Identification by Clinical Assessment versus International Consensus Criteria in Patients with Metastatic Colorectal Cancer. *Nutr Cancer*. Nov-Dec 2018;70(8):1322-1329. doi:10.1080/01635581.2018.1504092 10.1080/01635581.2018.1504092. Epub 2018 Sep 20.
78. Vanhoutte G, van de Wiel M, Wouters K, et al. Cachexia in cancer: what is in the definition? *BMJ Open Gastroenterol*. 2016;3(1):e000097. doi:10.1136/bmjgast-2016-000097 10.1136/bmjgast-2016-000097. eCollection 2016.
79. Wallengren O, Lundholm K, Bosaeus I. Diagnostic criteria of cancer cachexia: relation to quality of life, exercise capacity and survival in unselected palliative care patients. *Support Care Cancer*. Jun 2013;21(6):1569-77. doi:10.1007/s00520-012-1697-z 10.1007/s00520-012-1697-z. Epub 2013 Jan 13.
80. Wan Q, Yuan Q, Zhao R, et al. Prognostic value of cachexia index in patients with colorectal cancer: A retrospective study. *Front Oncol*. 2022;12:984459. doi:10.3389/fonc.2022.984459
81. Wesseltoft-Rao N, Hjermstad MJ, Ikdahl T, et al. Comparing two classifications of cancer cachexia and their association with survival in patients with unresected pancreatic cancer. *Nutr Cancer*. 2015;67(3):472-80. doi:10.1080/01635581.2015.1004728
82. Willemsen ACH, De Moor N, Van Dessel J, et al. The predictive and prognostic value of weight loss and body composition prior to and during immune checkpoint inhibition in recurrent or metastatic head and neck cancer patients. *Cancer Med*. Apr 2023;12(7):7699-7712. doi:10.1002/cam4.5522 10.1002/cam4.5522. Epub 2022 Dec 9.
83. Willemsen ACH, Pilz W, Hoeben A, Hoebers FJP, Schols A, Baijens LWJ. Oropharyngeal dysphagia and cachexia: Intertwined in head and neck cancer. *Head Neck*. Apr 2023;45(4):783-797. doi:10.1002/hed.27288 10.1002/hed.27288. Epub 2022 Dec 30.

84. Xie H, Ruan G, Wei L, et al. Hand grip strength-based cachexia index as a predictor of cancer cachexia and prognosis in patients with cancer. *J Cachexia Sarcopenia Muscle*. Feb 2023;14(1):382-390. doi:10.1002/jcsm.13139
10.1002/jcsm.13139. Epub 2022 Nov 29.
85. Yin L, Cui J, Lin X, et al. Identifying cancer cachexia in patients without weight loss information: machine learning approaches to address a real-world challenge. *Am J Clin Nutr*. Nov 2022;116(5):1229-1239. doi:10.1093/ajcn/nqac251
10.1093/ajcn/nqac251. Epub 2023 Feb 10.
86. Zhou D, Zhang Y, Mamtawla G, et al. Iron overload is related to muscle wasting in patients with cachexia of gastric cancer: using quantitative proteome analysis. *Medical Oncology*. 2020;37(12):113. doi:https://dx.doi.org/10.1007/s12032-020-01439-w
87. Zhuang CL, Dong QT, Shi HP, et al. Cachexia Versus Sarcopenia in Clinical Characteristics and Prognostic Value After Radical Gastrectomy for Gastric Cancer: A Large-Scale Prospective Study. *Ann Surg Oncol*. Apr 2022;29(4):2348-2358. doi:10.1245/s10434-021-11084-w
10.1245/s10434-021-11084-w. Epub 2021 Nov 19.
88. Zopf Y, Schink K, Reljic D, et al. Assessing cachexia in older patients: Different definitions - But which one is the most practical for clinical routine? *Archives of Gerontology and Geriatrics*. 2020;86:103943. doi:https://dx.doi.org/10.1016/j.archger.2019.103943
89. Aktas A, Lorton CM, Griffin O, et al. Application of the 2011 international consensus cancer cachexia classification in routine oncology dietetic practice: An observational study. *Nutr Clin Pract*. Aug 2023;38(4):790-797. doi:10.1002/ncp.10915
10.1002/ncp.10915. Epub 2022 Nov 9.
90. Antoun S, Morel H, Souquet PJ, et al. Staging of nutrition disorders in non-small-cell lung cancer patients: utility of skeletal muscle mass assessment. *J Cachexia Sarcopenia Muscle*. Aug 2019;10(4):782-793. doi:10.1002/jcsm.12418
10.1002/jcsm.12418. Epub 2019 Apr 1.
91. Bye A, Wesseltoft-Rao N, Iversen PO, et al. Alterations in inflammatory biomarkers and energy intake in cancer cachexia: a prospective study in patients with inoperable pancreatic cancer. *Med Oncol*. Jun 2016;33(6):54. doi:10.1007/s12032-016-0768-2
10.1007/s12032-016-0768-2. Epub 2016 Apr 27.
92. Cavalcante Martins FF, de Pinho NB, de Carvalho Padilha P, et al. Patient-generated subjective global assessment predicts cachexia and death in patients with head, neck and abdominal cancer: A retrospective longitudinal study. *Clin Nutr ESPEN*. Jun 2019;31:17-22. doi:10.1016/j.clnesp.2019.03.013
10.1016/j.clnesp.2019.03.013. Epub 2019 Apr 5.
93. ÉB NB, Daly LE, Power DG, Cushen SJ, MacEneaney P, Ryan AM. Computed tomography diagnosed cachexia and sarcopenia in 725 oncology patients: is nutritional screening capturing hidden malnutrition? *J Cachexia Sarcopenia Muscle*. Apr 2018;9(2):295-305. doi:10.1002/jcsm.12258
10.1002/jcsm.12258. Epub 2017 Dec 21.
94. Gumpper-Fedus K, Hart PA, Belury MA, et al. Altered Plasma Fatty Acid Abundance Is Associated with Cachexia in Treatment-Naive Pancreatic Cancer. *Cells*. 2022;11(5):910. doi:https://dx.doi.org/10.3390/cells11050910
95. Jager-Wittenaar H, Dijkstra PU, Dijkstra G, et al. High prevalence of cachexia in newly diagnosed head and neck cancer patients: An exploratory study. *Nutrition*. Mar 2017;35:114-118. doi:10.1016/j.nut.2016.11.008
10.1016/j.nut.2016.11.008. Epub 2016 Dec 14.

96. Johns N, Hatakeyama S, Stephens NA, et al. Clinical classification of cancer cachexia: phenotypic correlates in human skeletal muscle. *PLoS One*. 2014;9(1):e83618. doi:10.1371/journal.pone.0083618
10.1371/journal.pone.0083618. eCollection 2014.
97. Johns N, Stretch C, Tan BH, et al. New genetic signatures associated with cancer cachexia as defined by low skeletal muscle index and weight loss. *J Cachexia Sarcopenia Muscle*. Feb 2017;8(1):122-130. doi:10.1002/jcsm.12138
10.1002/jcsm.12138. Epub 2016 Aug 5.
98. Morikawa A, Naito T, Sugiyama M, et al. Impact of Cancer Cachexia on Hospitalization-associated Physical Inactivity in Elderly Patients with Advanced Non-small-cell Lung Cancer. *Asia Pac J Oncol Nurs*. Oct-Dec 2018;5(4):377-382. doi:10.4103/apjon.apjon_20_18
10.4103/apjon.apjon_20_18.
99. Op den Kamp CM, Langen RC, Snepvangers FJ, et al. Nuclear transcription factor κ B activation and protein turnover adaptations in skeletal muscle of patients with progressive stages of lung cancer cachexia. *Am J Clin Nutr*. Sep 2013;98(3):738-48. doi:10.3945/ajcn.113.058388
10.3945/ajcn.113.058388. Epub 2013 Jul 31.
100. Penafuerte CA, Gagnon B, Sirois J, Murphy J, MacDonald N, Tremblay ML. Identification of neutrophil-derived proteases and angiotensin II as biomarkers of cancer cachexia. *Br J Cancer*. Mar 15 2016;114(6):680-7. doi:10.1038/bjc.2016.3
10.1038/bjc.2016.3. Epub 2016 Mar 8.
101. Solís-Martínez O, Álvarez-Altamirano K, Cardenas D, Trujillo-Cabrera Y, Fuchs-Tarlovsky V. Cancer Cachexia Affects Patients with Head and Neck Cancer in All Stages of Disease: A Prospective Cross-Sectional Study. *Nutr Cancer*. 2022;74(1):82-89. doi:10.1080/01635581.2020.1869792
10.1080/01635581.2020.1869792. Epub 2021 Jan 16.
102. van der Meij BS, Schoonbeek CP, Smit EF, Muscaritoli M, van Leeuwen PA, Langius JA. Pre-cachexia and cachexia at diagnosis of stage III non-small-cell lung carcinoma: an exploratory study comparing two consensus-based frameworks. *Br J Nutr*. Jun 28 2013;109(12):2231-9. doi:10.1017/s0007114512004527
10.1017/S0007114512004527. Epub 2012 Nov 16.
103. Akaoka M, Haruki K, Taniai T, et al. Clinical significance of cachexia index in patients with hepatocellular carcinoma after hepatic resection. *Surg Oncol*. Dec 2022;45:101881. doi:10.1016/j.suronc.2022.101881
10.1016/j.suronc.2022.101881. Epub 2022 Nov 3.
104. Aslan V, Kılıç ACK, Sütcüoğlu O, et al. Cachexia index in predicting outcomes among patients receiving immune checkpoint inhibitor treatment for metastatic renal cell carcinoma. *Urol Oncol*. Nov 2022;40(11):494.e1-494.e10. doi:10.1016/j.urolonc.2022.07.018
10.1016/j.urolonc.2022.07.018. Epub 2022 Sep 20.
105. Demirelli B, Babacan NA, Ercelep Ö, et al. Modified Glasgow Prognostic Score, Prognostic Nutritional Index and ECOG Performance Score Predicts Survival Better than Sarcopenia, Cachexia and Some Inflammatory Indices in Metastatic Gastric Cancer. *Nutr Cancer*. 2021;73(2):230-238. doi:10.1080/01635581.2020.1749290
10.1080/01635581.2020.1749290. Epub 2020 Apr 9.
106. Go SI, Park MJ, Lee GW. Clinical significance of the cachexia index in patients with small cell lung cancer. *BMC Cancer*. May 17 2021;21(1):563. doi:10.1186/s12885-021-08300-x
10.1186/s12885-021-08300-x.
107. Go SI, Park MJ, Park S, et al. Cachexia index as a potential biomarker for cancer cachexia and a prognostic indicator in diffuse large B-cell lymphoma. *J Cachexia Sarcopenia Muscle*. Dec 2021;12(6):2211-2219. doi:10.1002/jcsm.12837

10.1002/jcsm.12837. Epub 2021 Oct 21.
108. Goh MJ, Kang W, Jeong WK, et al. Prognostic significance of cachexia index in patients with advanced hepatocellular carcinoma treated with systemic chemotherapy. *Sci Rep*. May 10 2022;12(1):7647. doi:10.1038/s41598-022-11736-1
10.1038/s41598-022-11736-1.
109. Hamura R, Haruki K, Shirai Y, et al. Preoperative cachexia index can predict the prognosis of extrahepatic biliary tract cancer after resection. *Surg Oncol*. Sep 2022;44:101825. doi:10.1016/j.suronc.2022.101825
10.1016/j.suronc.2022.101825. Epub 2022 Jul 31.
110. Jafri SH, Previgliano C, Khandelwal K, Shi R. Cachexia Index in Advanced Non-Small-Cell Lung Cancer Patients. *Clin Med Insights Oncol*. 2015;9:87-93. doi:10.4137/cmo.S30891
111. Kamada T, Haruki K, Nakashima K, et al. Prognostic significance of the cachexia index in patients with stage I-III colorectal cancer who underwent laparoscopic surgery. *Surg Today*. Feb 1 2023;doi:10.1007/s00595-023-02646-4
10.1007/s00595-023-02646-4.
112. Karmali R, Alrifai T, Fughhi IAM, et al. Impact of cachexia on outcomes in aggressive lymphomas. *Ann Hematol*. Jun 2017;96(6):951-956. doi:10.1007/s00277-017-2958-1
10.1007/s00277-017-2958-1. Epub 2017 Apr 17.
113. Nakashima K, Haruki K, Kamada T, et al. Usefulness of the cachexia index as a prognostic indicator for patients with gastric cancer. *Annals of Gastroenterological Surgery*. 2023;doi:https://dx.doi.org/10.1002/ags3.12669
114. Shimagaki T, Sugimachi K, Mano Y, et al. Cachexia index as a prognostic predictor after resection of pancreatic ductal adenocarcinoma. *Annals of Gastroenterological Surgery*. 2023;doi:https://dx.doi.org/10.1002/ags3.12686
115. Takano Y, Kodera K, Tsukihara S, et al. Association of a newly developed Cancer Cachexia Score with survival in Stage I-III colorectal cancer. *Langenbecks Arch Surg*. Apr 12 2023;408(1):145. doi:10.1007/s00423-023-02883-8
10.1007/s00423-023-02883-8.
116. Tanji Y, Furukawa K, Haruki K, et al. Significant impact of cachexia index on the outcomes after hepatic resection for colorectal liver metastases. *Annals of Gastroenterological Surgery*. 2022;6(6):804-812. doi:https://dx.doi.org/10.1002/ags3.12578
117. Chen HW, Chen YC, Yang LH, et al. Impact of cachexia on oncologic outcomes of sarcopenic patients with upper tract urothelial carcinoma after radical nephroureterectomy. *PLoS One*. 2021;16(4):e0250033. doi:10.1371/journal.pone.0250033
10.1371/journal.pone.0250033. eCollection 2021.
118. Cong M, Song C, Xu H, et al. The patient-generated subjective global assessment is a promising screening tool for cancer cachexia. *BMJ Support Palliat Care*. May 2022;12(e1):e39-e46. doi:10.1136/bmjspcare-2020-002296
10.1136/bmjspcare-2020-002296. Epub 2020 Aug 21.
119. Kwon M, Kim RB, Roh JL, et al. Prevalence and clinical significance of cancer cachexia based on time from treatment in advanced-stage head and neck squamous cell carcinoma. *Head Neck*. Apr 2017;39(4):716-723. doi:10.1002/hed.24672
10.1002/hed.24672. Epub 2016 Dec 21.
120. Morimoto K, Uchino J, Yokoi T, et al. Impact of cancer cachexia on the therapeutic outcome of combined chemoimmunotherapy in patients with non-small cell lung cancer: a retrospective study. *Oncoimmunology*. 2021;10(1):1950411. doi:10.1080/2162402x.2021.1950411
10.1080/2162402X.2021.1950411. eCollection 2021.

121. Vigano AAL, Del Fabbro E, Bruera E, Borod M. The cachexia clinic: From staging to managing nutritional and functional problems in advanced cancer patients. *Critical Reviews in Oncogenesis*. 2012;17(3):293-304. doi:https://dx.doi.org/10.1615/CritRevOncog.v17.i3.70
122. White R, Weekes CE, Grant R, Baldwin C, Ahmed H. Determining the prevalence and severity of cancer cachexia in advanced non-small cell lung cancer and its relationship with chemotherapy outcomes. *Support Care Cancer*. Sep 2020;28(9):4373-4380. doi:10.1007/s00520-019-05259-1 10.1007/s00520-019-05259-1. Epub 2020 Jan 8.
123. Wiegert EVM, de Oliveira LC, Calixto-Lima L, Mota ESLMSD, Peres WAF. Cancer cachexia: Comparing diagnostic criteria in patients with incurable cancer. *Nutrition*. Nov-Dec 2020;79-80:110945. doi:10.1016/j.nut.2020.110945
124. Fearon KC, Voss AC, Hustead DS. Definition of cancer cachexia: effect of weight loss, reduced food intake, and systemic inflammation on functional status and prognosis. *Am J Clin Nutr*. Jun 2006;83(6):1345-50. doi:10.1093/ajcn/83.6.1345 10.1093/ajcn/83.6.1345.
125. Argilés JM, Betancourt A, Guàrdia-Olmos J, et al. Validation of the CAchexia SCOre (CASCO). Staging Cancer Patients: The Use of miniCASCO as a Simplified Tool. *Front Physiol*. 2017;8:92. doi:10.3389/fphys.2017.00092
126. Ballyuzek MF, Mashkova MV, Arutjunyan AV, Duke VA. [Melatonin as a marker of the grade of cardiac disorders during cachexia development in oncological patients of different ages]. *Adv Gerontol*. 2017;30(1):70-77.
127. Argilés JM, López-Soriano FJ, Toledo M, Betancourt A, Serpe R, Busquets S. The cachexia score (CASCO): a new tool for staging cachectic cancer patients. *J Cachexia Sarcopenia Muscle*. Jun 2011;2(2):87-93. doi:10.1007/s13539-011-0027-5
128. Ueshima J, Maeda K, Shimizu A, et al. Cachexia staging score predicts survival in patients with cancer who receive palliative care. *Nutrition*. Feb 2023;106:111880. doi:10.1016/j.nut.2022.111880
129. Yi H, Wang Y, Liang Q, Li X, Chen C, Mao X. R-CSS: A clinically applicable score to classify cachexia stages in patients with cancer undergoing intensity-modulated radiation therapy. *Asia Pac J Oncol Nurs*. Jan 2023;10(1):100164. doi:10.1016/j.apjon.2022.100164 10.1016/j.apjon.2022.100164. eCollection 2023 Jan.
130. Wang J, Tan S, Xu J, et al. Development and application of the Cancer Cachexia Staging Index for the diagnosis and staging of cancer cachexia. *Nutrition*. Jun 4 2023;114:112114. doi:10.1016/j.nut.2023.112114 10.1016/j.nut.2023.112114.
131. Gabison R, Gibbs M, Uziely B, Ganz FD. The cachexia assessment scale: Development and psychometric properties. *Oncology Nursing Forum*. 2010;37(5):635-640. doi:https://dx.doi.org/10.1188/10.ONF.635-640
132. de Oliveira LC, Rosa K, Gaspar T, Paiva BSR, Paiva CE, Peres WAF. Clinical usefulness of the Patient-Generated Subjective Global Assessment and modified Glasgow Prognostic Score in decision making concerning the indication of enteral nutritional therapy in patients with incurable cancer receiving palliative care. *Nutrition*. Aug 2023;112:112057. doi:10.1016/j.nut.2023.112057 10.1016/j.nut.2023.112057. Epub 2023 Apr 24.
133. Fukushima T, Nakano J, Ishii S, et al. Characteristics of muscle function and the effect of cachexia in patients with haematological malignancy. *Eur J Cancer Care (Engl)*. Mar 2019;28(2):e12956. doi:10.1111/ecc.12956 10.1111/ecc.12956. Epub 2018 Oct 25.

134. Matsuzuka T, Suzuki M, Saijoh S, et al. [Assessment of Cachexia in Head and Neck Cancer Patients Based on a Modified Glasgow Prognostic Score]. *Nihon Jibiinkoka Gakkai Kaiho*. Feb 2016;119(2):125-8. doi:10.3950/jibiinkoka.119.125
10.3950/jibiinkoka.119.125.
135. Naito T, Tashiro M, Ishida T, Ohnishi K, Kawakami J. Cancer cachexia raises the plasma concentration of oxymorphone through the reduction of CYP3A but not CYP2D6 in oxycodone-treated patients. *J Clin Pharmacol*. Aug 2013;53(8):812-8. doi:10.1002/jcph.112
10.1002/jcph.112. Epub 2013 Jun 3.
136. Silva GAD, Wiegert EVM, Calixto-Lima L, Oliveira LC. Clinical utility of the modified Glasgow Prognostic Score to classify cachexia in patients with advanced cancer in palliative care. *Clin Nutr*. May 2020;39(5):1587-1592. doi:10.1016/j.clnu.2019.07.002
10.1016/j.clnu.2019.07.002. Epub 2019 Jul 20.
137. Cavka L, Pohar Perme M, Rotovnik Kozjek N, Seruga B. Prognostic Impact of Nutritional Status on Overall Survival and Health-Related Quality of Life in Men with Advanced Prostate Cancer. *Nutrients*. Feb 20 2023;15(4)doi:10.3390/nu15041044
10.3390/nu15041044.
138. V IJ-H, Heerschop S, Wanten G, van den Berg M. Evaluation of the Validity and Feasibility of the GLIM Criteria Compared with PG-SGA to Diagnose Malnutrition in Relation to One-Year Mortality in Hospitalized Patients. *J Acad Nutr Diet*. Mar 2022;122(3):595-601. doi:10.1016/j.jand.2021.07.011
139. Jager-Wittenaar H, Ottery FD. Assessing nutritional status in cancer: role of the Patient-Generated Subjective Global Assessment. *Curr Opin Clin Nutr Metab Care*. Sep 2017;20(5):322-329. doi:10.1097/mco.0000000000000389
140. Arends J, Strasser F, Gonella S, et al. Cancer cachexia in adult patients: ESMO Clinical Practice Guidelines(☆). *ESMO Open*. Jun 2021;6(3):100092. doi:10.1016/j.esmoop.2021.100092
141. Takahashi K, Masuda T, Ishikawa Y, et al. A Novel Frailty Grade Combined with Cachexia Index and Osteopenia in Esophagectomy. *World J Surg*. Jun 2023;47(6):1503-1511. doi:10.1007/s00268-023-06942-5
10.1007/s00268-023-06942-5. Epub 2023 Feb 21.
142. Go SI, Kim HG, Kang MH, Park S, Lee GW. Prognostic model based on the geriatric nutritional risk index and sarcopenia in patients with diffuse large B-cell lymphoma. *BMC Cancer*. May 18 2020;20(1):439. doi:10.1186/s12885-020-06921-2
10.1186/s12885-020-06921-2.
143. Namikawa T, Marui A, Yokota K, et al. Frequency and prognostic impact of cachexia during drug treatment for unresectable advanced gastric cancer patients. *Surg Today*. Nov 2022;52(11):1560-1567. doi:10.1007/s00595-022-02493-9
10.1007/s00595-022-02493-9. Epub 2022 Mar 24.
144. Orell-Kotikangas H, Österlund P, Mäkitie O, et al. Cachexia at diagnosis is associated with poor survival in head and neck cancer patients. *Acta Otolaryngol*. Jul 2017;137(7):778-785. doi:10.1080/00016489.2016.1277263
10.1080/00016489.2016.1277263. Epub 2017 Jan 26.
145. Wiegert EVM, de Oliveira LC, Calixto-Lima L, Chaves GV, Silva Lopes MS, Peres WAF. New cancer cachexia staging system for use in clinical practice. *Nutrition*. Oct 2021;90:111271. doi:10.1016/j.nut.2021.111271
146. Muscaritoli M, Imbimbo G, Jager-Wittenaar H, et al. Disease-related malnutrition with inflammation and cachexia. *Clin Nutr*. Aug 2023;42(8):1475-1479. doi:10.1016/j.clnu.2023.05.013

147. Meza-Valderrama D, Marco E, Dávalos-Yerovi V, et al. Sarcopenia, Malnutrition, and Cachexia: Adapting Definitions and Terminology of Nutritional Disorders in Older People with Cancer. *Nutrients*. Feb 26 2021;13(3)doi:10.3390/nu13030761
148. Dunne RF, Loh KP, Williams GR, Jatoi A, Mustian KM, Mohile SG. Cachexia and Sarcopenia in Older Adults with Cancer: A Comprehensive Review. *Cancers (Basel)*. Nov 25 2019;11(12)doi:10.3390/cancers11121861
149. Ueshima J, Inoue T, Saino Y, et al. Diagnosis and prevalence of cachexia in Asians: A scoping review. *Nutrition*. Mar 2024;119:112301. doi:10.1016/j.nut.2023.112301
150. Chowdhry SM, Chowdhry VK. Cancer cachexia and treatment toxicity. *Curr Opin Support Palliat Care*. Dec 2019;13(4):292-297. doi:10.1097/spc.0000000000000450
151. Andreyev HJ, Norman AR, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer*. Mar 1998;34(4):503-9. doi:10.1016/s0959-8049(97)10090-9
152. Coles TM, Wilson SM, Kim B, Beckham JC, Kinghorn WA. From obligation to opportunity: future of patient-reported outcome measures at the Veterans Health Administration. *Transl Behav Med*. Nov 25 2019;9(6):1157-1162. doi:10.1093/tbm/ibz121

Appendix

SEARCH STRATEGIES

Search Date	Search Statement	Results
MEDLINE **Through August 1, 2023**	"Cachexia"[Mesh] OR Cachexi*[tiab] OR "Emaciation"[Mesh] OR emaciation[tiab] OR "wasting syndrome"[tiab] OR "wasting disease"[tiab] OR "Wasting Syndrome"[Mesh]	18,089
	"Neoplasms"[Mesh] OR cancer*[tiab] OR malignan*[tiab] OR neoplasm*[tiab] OR carcinoma*[tiab] OR tumor*[tiab] OR tumour*[tiab]	5,066,418
	diagnos*[tiab] OR "Diagnosis"[Mesh] OR (classific*[tiab] AND (rule[tiab] OR model[tiab])) OR "clinical predict*"[tiab] OR "clinical rule*"[tiab] OR "decision rule*"[tiab] OR "decision support system"[tiab] OR "Clinical Decision Rules"[Mesh] OR "severity assessment"[tiab] OR grading[tiab] OR "predict* model"[tiab] OR "predict* rule"[tiab] OR "predict* tool"[tiab] OR "prognostic factor"[tiab] OR scor* system[tiab] OR staging[tiab] OR stage[tiab]	11,519,238
	"address"[pt] OR "autobiography"[pt] OR "bibliography"[pt] OR "biography"[pt] OR "case reports"[pt] OR "comment"[pt] OR "congress"[pt] OR "dictionary"[pt] OR "directory"[pt] OR "festschrift"[pt] OR "government publication"[pt] OR "historical article"[pt] OR "interview"[pt] OR "lecture"[pt] OR "legal case"[pt] OR "legislation"[pt] OR "news"[pt] OR "newspaper article"[pt] OR "patient education handout"[pt] OR "periodical index"[pt] OR "comment"[ti] OR "Editorial"[Publication Type] OR "ephemera"[pt] OR "in vitro techniques"[mh] OR "introductory journal article"[pt] OR ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] OR rat[tw] OR cow[tw] OR cows[tw] OR chicken*[tw] OR horse[tw] OR horses[tw] OR mice[tw] OR mouse[tw] OR bovine[tw] OR sheep[tw] OR ovine[tw] OR murinae[tw] OR cats[tw] OR cat[tw] OR dog[tw] OR dogs[tw] OR rodent[tw]	11,686,889
	(((#1) AND (#2)) AND (#3)) NOT (#4)	2,232
EMBASE **Through August 1, 2023**	exp cachexia/	17650
	emaciation/	954
	wasting syndrome/	4926
	wasting disease/	4926
	(cachexia or emaciation or wasting syndrome or wasting disease).mp.	31300
	1 or 2 or 3 or 4 or 5	31300
	neoplasm/	443739
	malignant neoplasm/	100561
	cancer/	154050
	tumor/	311947
	tumour/	443739
	carcinoma/	50739
	(neoplasm or malignan* or cancer or tumor* or tumour* or carcinoma*).mp.	6448572

Search Date	Search Statement	Results
	7 or 8 or 9 or 10 or 11 or 12 or 13	6448572
	diagnosis/	1404200
	decision support system/	27119
	clinical decision rule/	679
	staging/	37738
	grading/	69838
	prediction/	502381
	(diagnos* or diagnosis or (classific* and (rule or model)) or clinical predict* or clinical rule* or decision rule* or decision support system or clinical decision rules or severity assessment or grading or predict* model or predict* rule or predict* tool or prognostic factor or scor* system or staging or stage).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	9182202
	15 or 16 or 17 or 18 or 19 or 20 or 21	9474448
	6 and 14 and 22	5655
	limit 23 to (human and (article or article in press))	2693
Cochrane Library **Through August 1, 2023**	MeSH descriptor: [Cachexia] explode all trees	454
	MeSH descriptor: [Emaciation] explode all trees	7
	MeSH descriptor: [Wasting Syndrome] explode all trees	260
	(Cachexia OR Cachexi* OR Emaciation OR emaciation OR wasting syndrome OR wasting disease):ti,ab,kw (Word variations have been searched)	2205
	#1 OR #2 OR #3 OR #4	2205
	MeSH descriptor: [Neoplasms] explode all trees	112129
	(Neoplasms OR cancer*OR malignan* OR neoplasm* OR carcinoma* OR tumor* OR tumour*):ti,ab,kw (Word variations have been searched)	177000
	#6 OR #7	192895
	MeSH descriptor: [Diagnosis] explode all trees	445641
	MeSH descriptor: [Clinical Decision Rules] explode all trees	43
	(diagnos* OR Diagnosis OR classific* AND rule OR model OR clinical predict* OR clinical rule* OR decision rule* OR decision support system OR Clinical Decision Rules OR severity assessment OR grading OR predict* model OR predict* rule OR predict* tool OR prognostic factor OR scor* system OR staging OR stage):ti,ab,kw (Word variations have been searched)	705440
	#9 OR #10 OR #11	934863
	#5 AND #8 AND #12	398

Search Date	Search Statement	Results
ClinicalTrials.gov **Through August 1, 2023**	(Cachexia OR Cachexi* OR Emaciation OR wasting syndrome OR wasting disease) AND (Neoplasms OR cancer* OR malignan* OR neoplasm* OR carcinoma* OR tumor* OR tumour*) AND (diagnos* OR Diagnosis OR (classific* AND (rule OR model)) OR clinical predict* OR clinical rule* OR decision rule* OR decision support system OR Clinical Decision Rules OR severity assessment OR grading OR predict* model OR predict* rule OR predict* tool OR prognostic factor OR scor* system OR staging OR stage)	176
Total after deduplication		4,546

STUDIES EXCLUDED DURING FULL-TEXT SCREENING

Citation and *Reason for Exclusion*
Abraham M, Kordatou Z, Barriuso J, et al. Early recognition of anorexia through patient-generated assessment predicts survival in patients with oesophagogastric cancer. *PLoS One*. 2019;14(11):e0224540. doi:10.1371/journal.pone.0224540. *Not specific to cachexia.*
Alberici Pastore C, Paiva Orlandi S, González MC. Association between an inflammatory-nutritional index and nutritional status in cancer patients. *Nutr Hosp*. Jan-Feb 2013;28(1):188-93. doi:10.3305/nh.2013.28.1.6167. *Not specific to cachexia.*
Anandavadivelan P, Johar A, Lagergren P. The weight loss grading system as a predictor of cancer cachexia in oesophageal cancer survivors. *Eur J Clin Nutr*. Dec 2022;76(12):1755-1761. doi:10.1038/s41430-022-01183-6. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Andrew IM, Waterfield K, Hildreth AJ, Kirkpatrick G, Hawkins C. Quantifying the impact of standardized assessment and symptom management tools on symptoms associated with cancer-induced anorexia cachexia syndrome. *Palliat Med*. Dec 2009;23(8):680-8. doi:10.1177/0269216309106980. *Not specific to cachexia.*
Argilés JM, López-Soriano FJ, Toledo M, Betancourt A, Serpe R, Busquets S. The cachexia score (CASCO): a new tool for staging cachectic cancer patients. J Cachexia Sarcopenia Muscle. Jun 2011;2(2):87-93. doi:10.1007/s13539-011-0027-5.
Arrieta O, Luvián-Morales J, Turcott JG, Oñate-Ocaña LF. Quality of life and anorexia/cachexia in lung cancer: validation of the Spanish version of the FAACT instrument. *Qual Life Res*. Oct 2018;27(10):2709-2718. doi:10.1007/s11136-018-1930-4. *Not specific to cachexia.*
Arthur ST, Van Doren BA, Roy D, Noone JM, Zacherle E, Blanchette CM. Cachexia among US cancer patients. *Journal of medical economics*. 2016;19(9):874-880. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Aust S, Knogler T, Pils D, et al. Skeletal muscle depletion and markers for cancer cachexia are strong prognostic factors in epithelial ovarian cancer. *PLoS One*. 2015;10(10):e0140403. doi:10.1371/journal.pone.0140403. *Not specific to cachexia.*
Avan A, Avan A, Le Large TY, et al. AKT1 and SELP polymorphisms predict the risk of developing cachexia in pancreatic cancer patients. *Plos one*. 2014;9(9):e108057. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Bachmann J, Heiligensetzer M, Krakowski-Roosen H, Büchler MW, Friess H, Martignoni ME. Cachexia worsens prognosis in patients with resectable pancreatic cancer. *J Gastrointest Surg*. Jul 2008;12(7):1193-201. doi:10.1007/s11605-008-0505-z. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Bachmann J, Ketterer K, Marsch C, et al. Pancreatic cancer related cachexia:Influence on metabolism and correlation to weight loss and pulmonary function. *BMC Cancer*. Jul 28 2009;9:255. doi:10.1186/1471-2407-9-255. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Barreiro E, Salazar-Degracia A, Sancho-Muñoz A, Gea J. Endoplasmic reticulum stress and unfolded protein response profile in quadriceps of sarcopenic patients with respiratory diseases. *J Cell Physiol*. Jul 2019;234(7):11315-11329. doi:10.1002/jcp.27789. *Examines cachexia but provides no description of cachexia definition.*
Bilir C, Engin H, Can M, Temi YB, Demirtas D. The prognostic role of inflammation and hormones in patients with metastatic cancer with cachexia. *Med Oncol*. Mar 2015;32(3):56. doi:10.1007/s12032-015-0497-y. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*

Citation and *Reason for Exclusion*
Blauwhoff-Buskermolen S, Langius JA, Heijboer AC, Becker A, de van der Schueren MA, Verheul HM. Plasma ghrelin levels are associated with anorexia but not cachexia in patients with NSCLC. *Front Physiol*. 2017;8:119. doi:10.3389/fphys.2017.00119. *Duplicate.*
Blum D, Stene GB, Solheim TS, et al. Validation of the consensus-definition for cancer cachexia and evaluation of a classification model--a study based on data from an international multicentre project (EPCRC-CSA). *Ann Oncol*. Aug 2014;25(8):1635-42. doi:10.1093/annonc/mdu086. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Bourdel-Marchasson I, Diallo A, Bellera C, et al. One-year mortality in older patients with cancer: Development and external validation of an MNA-based prognostic score. *PLoS One*. 2016;11(2):e0148523. doi:10.1371/journal.pone.0148523. *Not specific to cachexia.*
Bozzetti F, Mariani L. Defining and classifying cancer cachexia: A proposal by the SCRINIO Working Group. *JPEN J Parenter Enteral Nutr*. Jul-Aug 2009;33(4):361-7. doi:10.1177/0148607108325076. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Buentzel J, Schulz M, Aperdannier L, Bleckmann A, Binder C. Metabolic changes in blood-derived extracellular vesicles of malnourished breast cancer patients. *Anticancer Res*. Jun 2023;43(6):2593-2599. doi:10.21873/anticanres.16426. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Burkart M, Schieber M, Basu S, et al. Evaluation of the impact of cachexia on clinical outcomes in aggressive lymphoma. *Br J Haematol*. Jul 2019;186(1):45-53. doi:10.1111/bjh.15889. *Not specific to cachexia.*
Burney BO, Hayes TG, Smiechowska J, et al. Low testosterone levels and increased inflammatory markers in patients with cancer and relationship with cachexia. *J Clin Endocrinol Metab*. May 2012;97(5):E700-9. doi:10.1210/jc.2011-2387. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Caillet P, Liuu E, Raynaud Simon A, et al. Association between cachexia, chemotherapy and outcomes in older cancer patients: A systematic review. Clin Nutr. Dec 2017;36(6):1473-1482. doi:10.1016/j.clnu.2016.12.003. *Unrelated SR.*
Camus V, Lanic H, Kraut J, et al. Prognostic impact of fat tissue loss and cachexia assessed by computed tomography scan in elderly patients with diffuse large B-cell lymphoma treated with immunochemotherapy. *Eur J Haematol*. Jul 2014;93(1):9-18. doi:10.1111/ejh.12285.
Cong M, Song C, Xu H, et al. The patient-generated subjective global assessment is a promising screening tool for cancer cachexia. *BMJ Support Palliat Care*. May 2022;12(e1):e39-e46. doi:10.1136/bmjspcare-2020-002296. *Duplicate.*
Constantin GB, Firescu D, Voicu D, et al. Analysis of prognostic factors in complicated colorectal cancer operated in emergency. *Chirurgia (Bucur)*. Jan-Feb 2020;115(1):23-38. doi:10.21614/chirurgia.115.1.23. *Examines cachexia but provides no description of cachexia definition.*
Cui J, Zhou L, Wee B, Shen F, Ma X, Zhao J. Predicting survival time in noncurative patients with advanced cancer: a prospective study in China. *J Palliat Med*. May 2014;17(5):545-52. doi:10.1089/jpm.2013.0368. *Examines cachexia but provides no description of cachexia definition.*
Cury SS, de Moraes D, Oliveira JS, et al. Low muscle mass in lung cancer is associated with an inflammatory and immunosuppressive tumor microenvironment. *J Transl Med*. Feb 11 2023;21(1):116. doi:10.1186/s12967-023-03901-5. *Not specific to cachexia.*[a]
Dai L, Fang Q, Li P, Liu F, Zhang X. Oncologic outcomes of patients with sarcomatoid carcinoma of the hypopharynx. *Front Oncol*. 2019;9:950. doi:10.3389/fonc.2019.00950. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Daniele A, Ferrero A, Fuso L, et al. Palliative care in patients with ovarian cancer and bowel obstruction. *Support Care Cancer*. Nov 2015;23(11):3157-63. doi:10.1007/s00520-015-2694-9. *<10 cachexia patients.*

Citation and *Reason for Exclusion*
Davis MP, Yavuzsen T, Kirkova J, et al. Validation of a simplified anorexia questionnaire. *Journal of pain and symptom management*. 2009;38(5):691-697. *Not specific to cachexia.*
de Oliveira LC, da Costa Rosa KS, Gaspar T, Paiva BSR, Paiva CE, Peres WAF. Clinical usefulness of the Patient-Generated Subjective Global Assessment and modified Glasgow Prognostic Score in decision making concerning the indication of enteral nutritional therapy in patients with incurable cancer receiving palliative care. *Nutrition*. 2023;112:112057. *Duplicate.*
De Waele E, Demol J, Caccialanza R, et al. Unidentified cachexia patients in the oncologic setting: Cachexia UFOs do exist. *Nutrition*. Jul-Aug 2019;63-64:200-204. doi:10.1016/j.nut.2019.02.015. *Not peer reviewed.*
Del Fabbro E, Dev R, Hui D, Palmer L, Bruera E. Effects of melatonin on appetite and other symptoms in patients with advanced cancer and cachexia: a double-blind placebo-controlled trial. *J Clin Oncol*. Apr 1 2013;31(10):1271-6. doi:10.1200/jco.2012.43.6766. *Not specific to cachexia.*
Demiray G, Değirmencioğlu S, Uğurlu E, Yaren A. Effects of serum leptin and resistin levels on cancer cachexia in patients with advanced-stage non-small cell lung cancer. *Clin Med Insights Oncol*. 2017;11:1179554917690144. doi:10.1177/1179554917690144. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Di Sebastiano KM, Yang L, Zbuk K, et al. Accelerated muscle and adipose tissue loss may predict survival in pancreatic cancer patients: the relationship with diabetes and anaemia. *Br J Nutr*. Jan 28 2013;109(2):302-12. doi:10.1017/s0007114512001067. *Not specific to cachexia.*
Dijksterhuis WPM, Latenstein AEJ, van Kleef JJ, et al. Cachexia and dietetic interventions in patients with esophagogastric cancer: A multicenter cohort study. *J Natl Compr Canc Netw*. Jan 8 2021;19(2):144-152. doi:10.6004/jnccn.2020.7615. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Dodson S, Dobs A, Hancock M, Johnston M, Steiner M. The impact of less than 8% weight loss on overall survival in subjects with non-small cell lung cancer (NSCLC) treated in a phase IIb trial of GTx-024. *Journal of Clinical Oncology*. 2011;29(15_suppl):9117-9117. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Douglas E, McMillan DC. Towards a simple objective framework for the investigation and treatment of cancer cachexia: the Glasgow Prognostic Score. Cancer Treat Rev. Jul 2014;40(6):685-91. doi:10.1016/j.ctrv.2013.11.007. *Review article.*
Famil-Dardashti A, Hajigholami A, Badri S, Yekdaneh A, Moghaddas A. The role of Trigonella, Cichorium, and Foeniculum herbal combination in the treatment of cancer-induced Anorexia/Cachexia: a quasi-experimental study. *International Journal of Cancer Management*. 2020;13(8). *Examines cachexia but provides no description of cachexia definition.*
Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol*. May 2011;12(5):489-95. doi:10.1016/s1470-2045(10)70218-7. *Not design of interest.*
Gannavarapu BS, Lau SKM, Carter K, et al. Prevalence and survival impact of pretreatment cancer-associated weight loss: A tool for guiding early palliative care. *J Oncol Pract*. Apr 2018;14(4):e238-e250. doi:10.1200/jop.2017.025221. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Ge Y-Z, Ruan G-T, Zhang K-P, et al. Which anthropometric measurement is better for predicting survival of patients with cancer cachexia? *British Journal of Nutrition*. 2022;127(12):1849-1857. *Not design of interest.*
Gelhorn HL, Gries KS, Speck RM, et al. Comprehensive validation of the functional assessment of anorexia/cachexia therapy (FAACT) anorexia/cachexia subscale (A/CS) in lung cancer patients with involuntary weight loss. *Qual Life Res*. Jun 2019;28(6):1641-1653. doi:10.1007/s11136-019-02135-7. *Not specific to cachexia.*

Citation and *Reason for Exclusion*
Gilmore LA, Olaechea S, Gilmore BW, et al. A preponderance of gastrointestinal cancer patients transition into cachexia syndrome. *J Cachexia Sarcopenia Muscle*. Dec 2022;13(6):2920-2931. doi:10.1002/jcsm.13086. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Gouma DJ, von Meyenfeldt MF. [Prognostic factors for the survival time in gallbladder carcinoma]. *Ned Tijdschr Geneeskd*. Feb 1 1992;136(5):225-9. Prognostische factoren voor de overlevingsduur bij het galblaascarcinoom. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Han J, Lu C, Meng Q, Halim A, Yean TJ, Wu G. Plasma concentration of interleukin-6 was upregulated in cancer cachexia patients and was positively correlated with plasma free fatty acid in female patients. *Nutr Metab (Lond)*. 2019;16:80. doi:10.1186/s12986-019-0409-9. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Han J, Tang M, Lu C, Shen L, She J, Wu G. Subcutaneous, but not visceral, adipose tissue as a marker for prognosis in gastric cancer patients with cachexia. *Clin Nutr*. Sep 2021;40(9):5156-5161. doi:10.1016/j.clnu.2021.08.003. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Hayashi N, Sato Y, Fujiwara Y, et al. Clinical impact of cachexia in head and neck cancer patients who received chemoradiotherapy. *Cancer management and research*. 2021:8377-8385. *Duplicate.*
Hilal Z, Rezniczek GA, Klenke R, Dogan A, Tempfer CB. Nutritional status, cachexia, and anorexia in women with peritoneal metastasis and intraperitoneal chemotherapy: a longitudinal analysis. *J Gynecol Oncol*. Nov 2017;28(6):e80. doi:10.3802/jgo.2017.28.e80. *Examines cachexia but provides no description of cachexia definition.*
Huo Z, Chong F, Yin L, et al. Development and validation of an online dynamic nomogram system for predicting cancer cachexia among inpatients: a real-world cohort study in China. *Support Care Cancer*. Dec 22 2022;31(1):72. doi:10.1007/s00520-022-07540-2. *Duplicate.*[a]
Ishihara H, Kondo T, Omae K, et al. Sarcopenia and the modified Glasgow Prognostic Score are significant predictors of survival among patients with metastatic renal cell carcinoma who are receiving first-line sunitinib treatment. *Target Oncol*. Oct 2016;11(5):605-617. doi:10.1007/s11523-016-0430-0. *Not specific to cachexia.*
Jafri SH, Previgliano C, Khandelwal K, Shi R. Cachexia index in advanced non-small-cell lung cancer patients. *Clin Med Insights Oncol*. 2015;9:87-93. doi:10.4137/cmo.S30891. *Duplicate.*
Jager-Wittenaar H, Dijkstra PU, Dijkstra G, et al. High prevalence of cachexia in newly diagnosed head and neck cancer patients: An exploratory study. *Nutrition*. 2017;35:114-118. *Duplicate.*
Jankowska R, Kosacka M. [Cancer cachexia syndrome in patients with lung cancer]. *Wiad Lek*. 2003;56(7-8):308-12. Wyniszczenie nowotworowe u pacjentów z rakiem płuca. *Examines cachexia but provides no description of cachexia definition.*
Jatoi A, Daly BD, Hughes VA, Dallal GE, Kehayias J, Roubenoff R. Do patients with nonmetastatic non-small cell lung cancer demonstrate altered resting energy expenditure? *Ann Thorac Surg*. Aug 2001;72(2):348-51. doi:10.1016/s0003-4975(01)02847-8. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Johns N, Hatakeyama S, Stephens NA, et al. Clinical classification of cancer cachexia: phenotypic correlates in human skeletal muscle. *PloS one*. 2014;9(1):e83618. *Duplicate.*
Junjun H, Jian C, Lin G, Yong G, Hong W, Lijin R. A retrospective study on the pain situation and safety of oxycodone in cachectic cancer pain patients. 2020. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*

Citation and *Reason for Exclusion*
Kaduka LU, Bukania ZN, Opanga Y, et al. Malnutrition and cachexia among cancer out-patients in Nairobi, Kenya. *J Nutr Sci*. 2017;6:e63. doi:10.1017/jns.2017.61. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Kays JK, Shahda S, Stanley M, et al. Three cachexia phenotypes and the impact of fat-only loss on survival in FOLFIRINOX therapy for pancreatic cancer. *J Cachexia Sarcopenia Muscle*. Aug 2018;9(4):673-684. doi:10.1002/jcsm.12307. *Examines cachexia but provides no description of cachexia definition.*
Kazemi-Bajestani SMR, Becher H, Butts C, et al. Undiagnosed cardiac deficits in non-small cell carcinoma patients in the candidate population for anti-cachexia clinical trials. *Support Care Cancer*. Apr 2019;27(4):1551-1561. doi:10.1007/s00520-018-4561-y. *Not specific to cachexia.*
Keane N, Fragkos KC, Patel PS, et al. Performance status, prognostic scoring, and parenteral nutrition requirements predict survival in patients with advanced cancer receiving home parenteral nutrition. *Nutr Cancer*. Jan 2018;70(1):73-82. doi:10.1080/01635581.2018.1380206. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Kim HL, Belldegrun AS, Freitas DG, et al. Paraneoplastic signs and symptoms of renal cell carcinoma: implications for prognosis. *J Urol*. Nov 2003;170(5):1742-6. doi:10.1097/01.ju.0000092764.81308.6a. *Not clear if the definition of cachexia was multi-component.*
Kim HL, Han KR, Zisman A, Figlin RA, Belldegrun AS. Cachexia-like symptoms predict a worse prognosis in localized t1 renal cell carcinoma. *J Urol*. May 2004;171(5):1810-3. doi:10.1097/01.ju.0000121440.82581.d3. *Not clear if the definition of cachexia was multi-component.*
Kim HL, Belldegrun AS, Freitas DG, et al. Paraneoplastic signs and symptoms of renal cell carcinoma: implications for prognosis. *The Journal of urology*. 2003;170(5):1742-1746. *Duplicate.*
Krzystek-Korpacka M, Matusiewicz M, Diakowska D, et al. Acute-phase response proteins are related to cachexia and accelerated angiogenesis in gastroesophageal cancers. *Clin Chem Lab Med*. 2008;46(3):359-64. doi:10.1515/cclm.2008.089. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Lasheen W, Walsh D. The cancer anorexia-cachexia syndrome: myth or reality? *Support Care Cancer*. Feb 2010;18(2):265-72. doi:10.1007/s00520-009-0772-6. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Latenstein AEJ, Dijksterhuis WPM, Mackay TM, et al. Cachexia, dietetic consultation, and survival in patients with pancreatic and periampullary cancer: A multicenter cohort study. *Cancer Med*. Dec 2020;9(24):9385-9395. doi:10.1002/cam4.3556. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Laviano A, Calder PC, Schols AM, Lonnqvist F, Bech M, Muscaritoli M. Safety and tolerability of targeted medical nutrition for cachexia in non-small-cell lung cancer: a randomized, double-blind, controlled pilot trial. *Nutrition and cancer*. 2020;72(3):439-450. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Law S, Fok M, Cheng S, Wong J. A comparison of outcome after resection for squamous cell carcinomas and adenocarcinomas of the esophagus and cardia. *Surgery, gynecology & obstetrics*. 1992;175(2):107-112. *Not specific to cachexia.*
Lena A, Wilkenshoff U, Hadzibegovic S, et al. Clinical and prognostic relevance of cardiac wasting in patients with advanced cancer. *Journal of the American College of Cardiology*. 2023;81(16):1569-1586. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Letilovic T, Vrhovac R. Influence of additional criteria from a definition of cachexia on its prevalence--good or bad thing? *Eur J Clin Nutr*. Aug 2013;67(8):797-801. doi:10.1038/ejcn.2013.121. *Not specific to cachexia.*

Citation and *Reason for Exclusion*
Letilovic T, Vrhovac R. Influence of additional criteria from a definition of cachexia on its prevalence—good or bad thing? *European journal of clinical nutrition*. 2013;67(8):797-801. *Duplicate.*
Li Y, Chen Y, Zeng Y, et al. Enteral nutrition combined with improved-sijunzi decoction shows positive effect in precachexia cancer patients: A retrospective analysis. *Evid Based Complement Alternat Med*. 2021;2021:7357521. doi:10.1155/2021/7357521. *Not specific to cachexia.*
Lortie J, Rush B, Osterbauer K, et al. Myosteatosis as a shared biomarker for sarcopenia and cachexia using MRI and Ultrasound. *Front Rehabil Sci*. 2022;3:896114. doi:10.3389/fresc.2022.896114. *Not specific to cachexia.*
Luvián-Morales J, Castillo-Aguilar J, Delgadillo-González M, et al. Validation of the QLQ-CAX24 instrument in cervical cancer and its association with cachexia classifications. *Japanese Journal of Clinical Oncology*. 2023;53(4):304-312. *Duplicate.*
Martin L, Birdsell L, Macdonald N, 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*. Apr 20 2013;31(12):1539-47. doi:10.1200/jco.2012.45.2722. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Martin L, Muscaritoli M, Bourdel-Marchasson I, et al. Diagnostic criteria for cancer cachexia: reduced food intake and inflammation predict weight loss and survival in an international, multi-cohort analysis. *J Cachexia Sarcopenia Muscle*. Oct 2021;12(5):1189-1202. doi:10.1002/jcsm.12756. *Not specific to cachexia.*
Meregaglia M, Borsoi L, Cairns J, Tarricone R. Mapping health-related quality of life scores from FACT-G, FAACT, and FACIT-F onto preference-based EQ-5D-5L utilities in non-small cell lung cancer cachexia. *The European Journal of Health Economics*. 2019;20:181-193. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Miyawaki T, Naito T, Doshita K, et al. Predicting the efficacy of first-line immunotherapy by combining cancer cachexia and tumor burden in advanced non-small cell lung cancer. *Thorac Cancer*. Jul 2022;13(14):2064-2074. doi:10.1111/1759-7714.14529. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Molfino A, Emerenziani S, Tonini G, et al. Early impairment of food intake in patients newly diagnosed with cancer. *Front Nutr*. 2022;9:997813. doi:10.3389/fnut.2022.997813. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Mondello P, Lacquaniti A, Mondello S, et al. Emerging markers of cachexia predict survival in cancer patients. *BMC Cancer*. Nov 16 2014;14:828. doi:10.1186/1471-2407-14-828. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Morimoto K, Uchino J, Yokoi T, et al. Impact of cancer cachexia on the therapeutic outcome of combined chemoimmunotherapy in patients with non-small cell lung cancer: a retrospective study. *Oncoimmunology*. 2021;10(1):1950411. *Duplicate.*
Moses AG, Maingay J, Sangster K, Fearon KC, Ross JA. Pro-inflammatory cytokine release by peripheral blood mononuclear cells from patients with advanced pancreatic cancer: relationship to acute phase response and survival. *Oncol Rep*. Apr 2009;21(4):1091-5. doi:10.3892/or_00000328. *Examines cachexia but provides no description of cachexia definition.*
Mu W, Katsoulakis E, Whelan CJ, Gage KL, Schabath MB, Gillies RJ. Radiomics predicts risk of cachexia in advanced NSCLC patients treated with immune checkpoint inhibitors. *Br J Cancer*. Jul 2021;125(2):229-239. doi:10.1038/s41416-021-01375-0. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Nakajima N. Differential diagnosis of cachexia and refractory cachexia and the impact of appropriate nutritional intervention for cachexia on survival in terminal cancer patients. *Nutrients*. Mar 12 2021;13(3)doi:10.3390/nu13030915. *Not design of interest.*

Citation and *Reason for Exclusion*
Nakayama H, Suzuki M, Kato T, Echizen H. Vancomycin pharmacokinetics in patients with advanced cancer near end of life. *Eur J Drug Metab Pharmacokinet*. Dec 2019;44(6):837-843. doi:10.1007/s13318-019-00564-w. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Nelson KA, Walsh D. The cancer anorexia-cachexia syndrome: a survey of the Prognostic Inflammatory and Nutritional Index (PINI) in advanced disease. *J Pain Symptom Manage*. Oct 2002;24(4):424-8. doi:10.1016/s0885-3924(02)00508-0. *Not specific to cachexia.*
Nemer L, Krishna SG, Shah ZK, et al. Predictors of pancreatic cancer-associated weight loss and nutritional interventions. *Pancreas*. Oct 2017;46(9):1152-1157. doi:10.1097/mpa.0000000000000898. *Not specific to cachexia.*
Ogiwara H, Takahashi S, Kato Y, et al. Diminished visceral adipose tissue in cancer cachexia. *J Surg Oncol*. Oct 1994;57(2):129-33. doi:10.1002/jso.2930570211. *Examines cachexia but provides no description of cachexia definition.*
Olaechea S, Gannavarapu BS, Alvarez C, et al. Primary Tumor Fluorine-18 Fluorodeoxydglucose ((18)F-FDG) is associated with cancer-associated weight loss in non-small cell lung cancer (NSCLC) and portends worse survival. *Front Oncol*. 2022;12:900712. doi:10.3389/fonc.2022.900712. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Olaechea S, Gilmore A, Alvarez C, Gannavarapu BS, Infante R, Iyengar P. Associations of prior chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids with cachexia incidence and survival. *Front Oncol*. 2022;12:922418. doi:10.3389/fonc.2022.922418. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Olaechea S, Sarver B, Liu A, et al. Race, ethnicity, and socioeconomic factors as determinants of cachexia incidence and outcomes in a retrospective cohort of patients with gastrointestinal tract cancer. *JCO Oncol Pract*. Jul 2023;19(7):493-500. doi:10.1200/op.22.00674. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Op den Kamp CM, Langen RC, Snepvangers FJ, et al. Nuclear transcription factor κ B activation and protein turnover adaptations in skeletal muscle of patients with progressive stages of lung cancer cachexia. *The American journal of clinical nutrition*. 2013;98(3):738-748. *Duplicate.*
Ose J, Gigic B, Lin T, et al. Multiplatform urinary metabolomics profiling to discriminate cachectic from non-cachectic colorectal cancer patients: Pilot results from the ColoCare Study. *Metabolites*. Sep 6 2019;9(9)doi:10.3390/metabo9090178. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Ozorio GA, Barão K, Forones NM. Cachexia stage, patient-generated subjective global assessment, phase angle, and handgrip strength in patients with gastrointestinal cancer. *Nutr Cancer*. Jul 2017;69(5):772-779. doi:10.1080/01635581.2017.1321130. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Pausch T, Hartwig W, Hinz U, et al. Cachexia but not obesity worsens the postoperative outcome after pancreatoduodenectomy in pancreatic cancer. *Surgery*. Sep 2012;152(3 Suppl 1):S81-8. doi:10.1016/j.surg.2012.05.028. *Not specific to cachexia.*
Permuth JB, Clark Daly A, Jeong D, et al. Racial and ethnic disparities in a state-wide registry of patients with pancreatic cancer and an exploratory investigation of cancer cachexia as a contributor to observed inequities. *Cancer Med*. Jun 2019;8(6):3314-3324. doi:10.1002/cam4.2180. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Petrusel L, Rusu I, Leucuta DC, et al. Relationship between cachexia and perineural invasion in pancreatic adenocarcinoma. *World J Gastrointest Oncol*. Dec 15 2019;11(12):1126-1140. doi:10.4251/wjgo.v11.i12.1126. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*

Citation and *Reason for Exclusion*
Prokopchuk O, Hermann CD, Schoeps B, et al. A novel tissue inhibitor of metalloproteinases-1/liver/cachexia score predicts prognosis of gastrointestinal cancer patients. *J Cachexia Sarcopenia Muscle*. Apr 2021;12(2):378-392. doi:10.1002/jcsm.12680y. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Reid J, Mills M, Cantwell MM, Cardwell CR, Murray LJ, Donnelly M. Thalidomide for managing cancer cachexia. *Cochrane database of systematic reviews*. 2012;(4). *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Rich NE, Phen S, Desai N, et al. Cachexia is prevalent in patients with hepatocellular carcinoma and associated with worse prognosis. *Clin Gastroenterol Hepatol*. May 2022;20(5):e1157-e1169. doi:10.1016/j.cgh.2021.09.022. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Roy I, Huang K, Bhakta A, Marquez E, Spangenberg J, Jayabalan P. Relationship between cachexia and the functional progress of patients with cancer in inpatient rehabilitation. *Am J Phys Med Rehabil*. Feb 1 2023;102(2):99-104. doi:10.1097/phm.0000000000002024. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Rydén M, Agustsson T, Laurencikiene J, et al. Lipolysis--not inflammation, cell death, or lipogenesis--is involved in adipose tissue loss in cancer cachexia. *Cancer*. Oct 1 2008;113(7):1695-704. doi:10.1002/cncr.23802. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Rydzek J, Gąsior ZT, Dąbek J, Wojnar J, Skrzypek M. Assessment of risk factors for mortality in patients with cardiovascular disease and a history of treatment for malignancy. *Kardiol Pol*. 2015;73(9):730-9. doi:10.5603/KP.a2015.0071. *Examines cachexia but provides no description of cachexia definition.*
Salsman JM, Beaumont JL, Wortman K, Yan Y, Friend J, Cella D. Brief versions of the FACIT-fatigue and FAACT subscales for patients with non-small cell lung cancer cachexia. *Support Care Cancer*. May 2015;23(5):1355-64. doi:10.1007/s00520-014-2484-9. *Not specific to cachexia.*
Sato H, Naito T, Ishida T, Kawakami J. Relationships between oxycodone pharmacokinetics, central symptoms, and serum interleukin-6 in cachectic cancer patients. *Eur J Clin Pharmacol*. Dec 2016;72(12):1463-1470. doi:10.1007/s00228-016-2116-z. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Schiessel DL, Vicente Cavagnari MA, Mazur CE, et al. The relationship between unintentional weight loss, grading system and overall survival in gastric cancer patients. *Nutr Cancer*. 2022;74(5):1745-1753. doi:10.1080/01635581.2021.1964545. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Shen S, Araujo JL, Altorki NK, et al. Variation by stage in the effects of prediagnosis weight loss on mortality in a prospective cohort of esophageal cancer patients. *Dis Esophagus*. Sep 1 2017;30(9):1-7. doi:10.1093/dote/dox073. *Examines cachexia but provides no description of cachexia definition.*
Shibata M, Takekawa M. Increased serum concentration of circulating soluble receptor for interleukin-2 and its effect as a prognostic indicator in cachectic patients with gastric and colorectal cancer. *Oncology*. 1999;56(1):54-8. doi:10.1159/000011930. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Shiono M, Huang K, Downey RJ, et al. An analysis of the relationship between metastases and cachexia in lung cancer patients. *Cancer Med*. Sep 2016;5(9):2641-8. doi:10.1002/cam4.841. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Shukuya T, Takahashi K, Shintani Y, et al. Epidemiology, risk factors and impact of cachexia on patient outcome: Results from the Japanese Lung Cancer Registry Study. *J Cachexia Sarcopenia Muscle*. Jun 2023;14(3):1274-1285. doi:10.1002/jcsm.13216. *Not specific to cachexia.*

Citation and *Reason for Exclusion*
Siregar A, Chandra DN, Rinaldi I. Correlation of Patient Generated-subjective Global Assessment with Serum C-reactive Protein Level in Stage I–IV Head-and-neck Cancer. *Open Access Macedonian Journal of Medical Sciences*. 2022;10(B):389-394. *Not specific to cachexia.*
Sirvent-Ochando M, Murcia-Lopez A, Sangrador-Pelluz C, Espla S, Garrido-Siles M, Abiles J. NUTRI-ONCOCARE: New integral nutrition care model to prevent and treat malnutrition in cancer patients. *Farm Hosp*. Apr 15 2021;45(3):109-114. NUTRI-ONCOCARE: Nuevo modelo integral de atención nutricional para prevenir y tratar la desnutrición en pacientes con cáncer. doi:10.7399/fh.11299. *Not specific to cachexia.*
Song M, Zhang Q, Liu T, et al. Efficacy of global leadership initiative on malnutrition as potential cachexia screening tool for patients with solid cancer. *Nutrition Journal*. 2022;21(1):73. *Duplicate.*
Song M, Zhang Q, Tang M, et al. Associations of low hand grip strength with 1 year mortality of cancer cachexia: a multicentre observational study. *Journal of cachexia, sarcopenia and muscle*. 2021;12(6):1489-1500. *Duplicate.*
Stene GB, Balstad TR, Leer ASM, et al. Deterioration in muscle mass and physical function differs according to weight loss history in cancer cachexia. *Cancers*. 2019;11(12):1925. *Duplicate.*
Stephens NA, Gray C, MacDonald AJ, et al. Sexual dimorphism modulates the impact of cancer cachexia on lower limb muscle mass and function. *Clin Nutr*. Aug 2012;31(4):499-505. doi:10.1016/j.clnu.2011.12.008. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Stuart SP, Tiley EH, 3rd, Boland JP. Feeding gastrostomy: A critical review of its indications and mortality rate. *South Med J*. Feb 1993;86(2):169-72. *Examines cachexia but provides no description of cachexia definition.*
Sutandyo N, Cintakaweni DMW, Setiawan L, Hariani R, Utami N. Association of body composition and handgrip strength with Interleukin-6 (IL-6) and Vitamin D level in cancer patients. *Int J Gen Med*. 2023;16:1995-2001. doi:10.2147/ijgm.S388457. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Szefel J, Kruszewski WJ, Szajewski M, Ciesielski M, Danielak A. bioelectrical impedance analysis to increase the sensitivity of screening methods for diagnosing cancer cachexia in patients with colorectal cancer. *J Nutr Metab*. 2020;2020:3874956. doi:10.1155/2020/3874956. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Takayama K, Atagi S, Imamura F, et al. Quality of life and survival survey of cancer cachexia in advanced non-small cell lung cancer patients-Japan nutrition and QOL survey in patients with advanced non-small cell lung cancer study. *Support Care Cancer*. Aug 2016;24(8):3473-80. doi:10.1007/s00520-016-3156-8. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Temel JS, Bondarde SA, Jain MM, et al. Evaluation of quality of life from a phase II study of anamorelin HCl in NSCLC patients. American Society of Clinical Oncology; 2013. *Not specific to cachexia.*
Tewes, M. (n.d.). Analysis of cachexia-associated parameters in patients with metastatic disease pancreatobiliary carcinomas with and without exercise therapy. German Clinical Trials Register. https://drks.de/search/en/trial/DRKS00021179#studyResults. *Not design of interest.*
Thoresen L, Frykholm G, Lydersen S, et al. Nutritional status, cachexia and survival in patients with advanced colorectal carcinoma. Different assessment criteria for nutritional status provide unequal results. *Clinical Nutrition*. 2013;32(1):65-72. *Duplicate.*
Vagnildhaug OM, Brunelli C, Hjermstad MJ, et al. A prospective study examining cachexia predictors in patients with incurable cancer. *BMC Palliat Care*. Jun 4 2019;18(1):46. doi:10.1186/s12904-019-0429-2. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*

Citation and *Reason for Exclusion*
Vagnildhaug OM, Blum D, Wilcock A, et al. The applicability of a weight loss grading system in cancer cachexia: a longitudinal analysis. *J Cachexia Sarcopenia Muscle*. Oct 2017;8(5):789-797. doi:10.1002/jcsm.12220. *Not specific to cachexia.*
van der Meij BS, Schoonbeek CP, Smit EF, Muscaritoli M, van Leeuwen PA, Langius JA. Pre-cachexia and cachexia at diagnosis of stage III non-small-cell lung carcinoma: an exploratory study comparing two consensus-based frameworks. *British journal of nutrition*. 2013;109(12):2231-2239. *Duplicate.*
Vasconcelos de Matos L, Coelho A, Cunha R, et al. Association of weight change, inflammation markers and disease staging with survival of patients undergoing chemotherapy for Pancreatic Adenocarcinoma. *Nutr Cancer*. 2022;74(2):546-554. doi:10.1080/01635581.2021.1903049. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Vigano AL, di Tomasso J, Kilgour RD, et al. The abridged patient-generated subjective global assessment is a useful tool for early detection and characterization of cancer cachexia. *J Acad Nutr Diet*. Jul 2014;114(7):1088-1098. doi:10.1016/j.jand.2013.09.027. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Vigano A, Del Fabbro E, Bruera E, Borod M. The cachexia clinic: from staging to managing nutritional and functional problems in advanced cancer patients. *Critical Reviews™ in Oncogenesis*. 2012;17(3). *Duplicate.*
Vigneron C, Laousy O, Chassagnon G, et al. Assessment of functional and nutritional status and skeletal muscle mass for the prognosis of critically Ill solid cancer patients. *Cancers*. 2022;14(23):5870. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Wan Q, Wang Z, Zhao R, et al. CT-determined low skeletal muscle mass predicts worse overall survival of gastric cancer in patients with cachexia. *Cancer Med*. Jan 2023;12(2):1492-1500. doi:10.1002/cam4.5040. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Watanabe D, Horiguchi A, Tasaki S, et al. Impact of body mass index on clinicopathological outcomes in patients with renal cell carcinoma without anorexia-cachexia syndrome. *Molecular and Clinical Oncology*. 2018;8(1):47-53. *Not specific to cachexia.*
Wiegert EVM, de Oliveira LC, Calixto-Lima L, e Silva MSdM, Peres WAF. Cancer cachexia: Comparing diagnostic criteria in patients with incurable cancer. *Nutrition*. 2020;79:110945. *Duplicate.*
Willemsen AC, Pilz W, Hoeben A, Hoebers FJ, Schols AM, Baijens LW. Oropharyngeal dysphagia and cachexia: Intertwined in head and neck cancer. *Head & Neck*. 2023;45(4):783-797. *Duplicate.*
Xie H, Ruan G, Wei L, et al. Comprehensive comparison of the prognostic value of systemic inflammation biomarkers for cancer cachexia: a multicenter prospective study. *Inflamm Res*. Nov 2022;71(10-11):1305-1313. doi:10.1007/s00011-022-01626-7. *Not design of interest.*
Xie H, Ruan G, Zhang Q, et al. Combination of nutritional risk index and handgrip strength on the survival of patients with cancer cachexia: A multi-center cohort study. *J Inflamm Res*. 2022;15:1005-1015. doi:10.2147/jir.S352250. *Not design of interest.*
Xie H, Ruan G, Zhang Q, et al. Combination of nutritional risk index and handgrip strength on the survival of patients with cancer cachexia: A multi-center cohort study. *Journal of Inflammation Research*. 2022:1005-1015. *Duplicate.*
Yang QJ, Zhao JR, Hao J, et al. Serum and urine metabolomics study reveals a distinct diagnostic model for cancer cachexia. *J Cachexia Sarcopenia Muscle*. Feb 2018;9(1):71-85. doi:10.1002/jcsm.12246. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*

Citation and *Reason for Exclusion*
Yin L, Cui J, Lin X, et al. Triceps skinfold-albumin index significantly predicts the prognosis of cancer cachexia: A multicentre cohort study. *J Cachexia Sarcopenia Muscle*. Feb 2023;14(1):517-533. doi:10.1002/jcsm.13156. *Not design of interest.*
Zhou T, Yang K, Thapa S, Liu H, Wang B, Yu S. Differences in symptom burden among cancer patients with different stages of cachexia. *J Pain Symptom Manage*. May 2017;53(5):919-926. doi:10.1016/j.jpainsymman.2016.12.325. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Ziętarska M, Krawczyk-Lipiec J, Kraj L, Zaucha R, Małgorzewicz S. Nutritional status assessment in colorectal cancer patients qualified to systemic treatment. *Contemporary Oncology/Współczesna Onkologia*. 2017;21(2):157-161. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*
Zwickl H, Hackner K, Köfeler H, et al. Reduced LDL-cholesterol and reduced total cholesterol as potential indicators of early cancer in male treatment-naïve cancer patients with pre-cachexia and cachexia. *Front Oncol*. 2020;10:1262. doi:10.3389/fonc.2020.01262. *Only includes weight measurements to define cachexia/does not use a multicriteria classification diagnosis.*

[a]Duplicate

RISK OF BIAS ASSESSMENTS

Author, Year, PMID, Design	Outcomes assessors bias	Attrition bias	Clear reporting	Clear eligibility criteria	Algorithms adequately described	Outcomes fully defined	Representativeness of the cohort	Comparator representativeness	Adjustment for confounders	Other bias	Overall RoB
Akaoka, 2022, 36371905, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (High concern)[a]	Low
Aslan, 2022, 36137881, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (High concern)[b]	No (Low concern)	High
Blauwhoff-Buskermolen, 2017, 28447434, NRCS	No (Low concern)	No (Low concern)	No (High concern)[c]	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Cavka, 2023, 36839402, NRCS	No (Low concern)	Yes (High concern)[d]	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Chen, 2019, 31564970, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
de Oliveira, 2023, 37224572, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Fearon, 2006, 16762946, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Fukuta, 2019, 30316109, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Go Se, 2020, 32423395, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Go Se, 2021, 34676685, NRCS	No (Low concern	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Go SI, 2021, 34001060, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Goh, 2022, 35538112, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Gong, 2022, 36139560, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (High concern)[b]	No (Low concern)	High

Author, Year, PMID, Design	Outcomes assessors bias	Attrition bias	Clear reporting	Clear eligibility criteria	Algorithms adequately described	Outcomes fully defined	Representativeness of the cohort	Comparator representativeness	Adjustment for confounders	Other bias	Overall RoB
Hamura, 2022, 35947886, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Hayashi, 2021, 34795523, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Hou, 2022, 35804906, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Jafri, 2015, 26604850, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	Yes (High concern)[e]	Moderate
Jones, 2022, 35488469, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	No (Low concern)	Low
Kamada, 2023, 36725756, NRCS	No (Low concern)	Unclear	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Karmali, 2017, 28417157, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Kwon, 2017, 28000343, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Madeddu, 2023, 36831431, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (High concern)[b]	No (Low concern)	High
Morimoto, 2021, 34290909, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	No (High conern)[f]	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Nakashima, 2023, 37663966, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (High concern)[g]	No (Low concern)	High
Namikawa, 2022, 3532229, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	No (High concern)[g]	Unclear	Yes (Moderate concern)	No (Low concern)	Moderate
Orell-Kotikangas, 2017,	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate

Author, Year, PMID, Design	Outcomes assessors bias	Attrition bias	Clear reporting	Clear eligibility criteria	Algorithms adequately described	Outcomes fully defined	Representativeness of the cohort	Comparator representativeness	Adjustment for confounders	Other bias	Overall RoB
28125312, NRCS											
Poisson, 2021, 34519440, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Rounis, 2021, 34584855, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Ruan, 2021, 34737602, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Shen, 2023, 36938648, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Shimagaki, 2023, 2022782042, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Silva, 2020, 31377013, Single group	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Takahashi, 2023, 36802232, Single group	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Takano, 2023, 37043018, Single gorup	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Tan, 2023, 36880286, Validation	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (High concern)[g]	No (Low concern)	High
Tanji, 2022, 36338593,Single group	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Thoresen, 2013, 22695408, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (High concern)[b]	No (Low concern)	High
Ueshima, 2023, 36436335, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate

Author, Year, PMID, Design	Outcomes assessors bias	Attrition bias	Clear reporting	Clear eligibility criteria	Algorithms adequately described	Outcomes fully defined	Representativeness of the cohort	Comparator representativeness	Adjustment for confounders	Other bias	Overall RoB
Van der Meij, 2013, 23153477, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Van der Werf, 2018, 30235002, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Vanhoutte, 2016, 27843571, NRCS	No (Low concern)	Unclear	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Wan, 2022, 36212479, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Wang, 2023, 37454609, Validation	No (Low concern)	Yes (High concern)[d]	No (High concern)[h]	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	High
Wiegert, 2021, 34004417, Single group	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Wiegert, 2020, 32927241, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Willemsen, 2023, 36583567, NRCS	Yes (High concern)[i]	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Xie, 2023, 36447437, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Zhuang, 2022, 34797480, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate
Zopf, 2020, 2002952037, NRCS	No (Low concern)	No (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Low concern)	Yes (Moderate concern)	No (Low concern)	Moderate

Notes. [a] Controlled for variables in the model that were included in the propensity score; [b] Multivariable models controlled for multiple assessments of cachexia; [c] Unclear if the final survival analysis was 3 separate models or 1 model with 3 definitions of cachexia; [d] High lost to follow-up; [e] High number of eligible participants were not included due to missing information; [f] Not reported; [g] Multivariable model controlled for a variable that was also included as part of the cachexia assessment variable; [h] Unclear how the development and application samples were used, or which model controlled for potential confounding; [i] Outcomes were self-reported.

COMPONENT DETAILS

Algorithm/Instrument	Fearon 2011 (Without Modification)
Number of classifications	2
Weight loss	Weight loss ≥2%, 2-5%, ≥5% over the prior six months OR ≥10% over the prior ten months*, ** *specification of "in the absence of simple starvation" in some studies **some studies did not specify time frame of WL
Sarcopenia or Skeletal Muscle index	• ASMI < 7.0 kg/m^2 measured by DXA; • Lumbar SMI < 43 cm^2 / m^2 (males with BMI less than 25 kg/m^2) or < 53 cm^2 /m^2 (males with BMI ≥ 25 kg/m^2) measured by CT; • ASMI= <7.26 kg/m^2; • Mid-upper-arm muscle area by anthropometry (men <32 cm, women <18 cm); • SMI= the area of skeletal muscle (cm^2) of L3/height squared (m^2); • SMI= <7 kg/m^2 for men and <5.7 kg/m^2 for women measured by BIA; • L3-SMI= <45.1 cm^2/m^2 in males and <36.9 cm^2/m^2 in females by CT; • SMI= males < 7.26 kg/m^2 ; females < 5.45 kg/m^2 by BIA • L3 SMI= <40.8 cm^2/m^2 for men and <34.9 cm^2/m^2 for women determined using CT data; • L3: <55 cm^2/m^2 for males, <39 cm^2/m^2 for females, T4: <66.0 cm^2/m^2 for males, <51.9 cm^2/m^2 for females; • MUAMA: men <32 cm^2, women <18cm^2 • CT: SMI < reference (L3: <55 cm^2/m^2 for males, <39 cm^2/m^2 for females; • T4: <66.0 cm^2/m^2 for males, <51.9 cm^2 /m^2 for females; • BIA: FFMI without bone: men <14.6 kg/m^2, women <11.4 kg/m^2; • TPA index <385 mm^2/m^2 for female, TPA index <545 mm^2/m^2 for male; • FFMI by BIA (men < 14.6 kg/m^2, women < 11.4 kg/m^2); • SMI= males <41.6 kg/m^2, females <32.0 kg/m^2; • L3 SMI= <55 cm^2/m^2 in men and < 39 cm^2/m^2 in women; • Upper-middle arm muscle area (men <32 cm^2 , women <18 cm^2); • DSM-BIA= (men: <7.0 kg/m^2, women: <5.7 kg/m^2); • SARC-F score ≥ 4/10; • European working group on sarcopenia in older people (EWGSOP) using first criterion (low muscle mass) plus either second criterion (low muscle strength) or third criterion (low muscle performance). • L3 SMI were 52.4 cm^2/m^2 for men and 38.5 cm^2/m^2 for women; • ASMI <7.0 kg/m^2 for males and <5.4 kg/m^2 for females; • Using the Prado et al. cut-points for Sarcopenia on CT analysis • ASMI consistent with sarcopenia; • SMI=37.81 cm^2/m^2 for women and 43.13 cm^2/m^2 for men based on CT;

	• Lumbar skeletal muscle index of <38.5 cm^2 /m^2 for women and <52.5 cm^2 / m^2 for men; • ASMI<7.26 kg/m^2 for males and <5.45 kg/m^2 by DEXA; • Muscle index= males < 55.4 cm^2 /m^2 females < 38.9 cm^2 /m^2 by CT; • Low SMI was defined using the cut-off values for SMI described in 2013 by Martin et al
Body mass index	BMI: < 20 kg/m^2 or <18.5 kg/m^2
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. ASMI=appendicular skeletal muscle index; BIA=bioelectrical impedance; BMI=body mass index; cm=centimeter; CT=computed tomography; DSM=direct segmental multi-frequency; DXA/DEXA=dual energy X-ray absorptiometry; FFMI=fat-free mass index; kg=kilograms; L3=third lumbar spin vertebrae; m=meter; MUAMA=mid-upper-arm muscle area; SARC-F=strength, assistance walking, rising from a chair, climbing stairs, and falls screening tool; SMI=skeletal muscle index; TPA=total psoas area; WL=weight loss.

Algorithm/Instrument	Fearon 2011 (With Modification or Staging)
Number of classifications	2-4
Weight loss	Cachexia ● WL >=2%, >2% and ≤ 5%, >=5%, >10% (With or without specifiers of: within 6 months, ongoing, unintentional, or in the absence of simple starvation); ● >5% over the past 6 mo in the absence of simple starvation (<72 hours without food intake, or difficulty swallowing solid food) Precachexia: ● Minimal or no weight loss; ● >2% and ≤ 5%; ● ≤5% during last 6m (involuntary); ● Substantial involuntary WL (*ie*,2–5% WL in the 6 mo) No Cachexia or Normal Status ● WL < 2% Refractory ● WL ≥ 6% to ≥ 15%
Sarcopenia or Skeletal Muscle index	● Low muscle mass (determined by computed tomography [CT]–imaging; ● Sarcopenia= <43 cm^2/m^2 if BMI < 25 kg/m^2 and SMM index <53 cm^2/m^2 if BMI ≥ 25 kg/m^2 for men; and SMM index <41 cm^2/m^2 in woman, based on by L3 CT imaging, anthropometric, dual energy X-ray absorptiometry, or bioelectrical impedance; ● MUAMA as a proxy (men <32 cm^2, women <18 cm^2); ● Using CT at L3: SMI < 41 cm^2/m^2 for females with any BMI, < 43 cm^2/m^2 for males with a BMI < 24.9 kg/m^2, and <53 cm^2/m^2 for males with a BMI > 25 kg/m^2; ● Appendicular skeletal muscle index: <7.26 kg/m^2 kg/m^2 in men or <5.45 kg/m^2 in women based on dual energy x-ray absorptiometry; ● L3 skeletal muscle index: ≦38.5 cm^2/m^2 for women and ≦52.4 cm^2 /m^2 for men); ● SMI cutoffs for LSMI were based on a CT-based study of cancer patients by Martin et al; ● Defined based on the lumbar skeletal muscle index cutoffs of <43.0 cm^2/m^2 for men with a BMI <25.0 kg/m^2, <53.0 cm^2/m^2 for men with a BMI ≥25.0 kg/m^2, and <41.0 cm^2/m^2 for women; ● Defined as lumbar skeletal muscle mass index of <43.0 cm^2 /m^2 for men with a BMI <25.0 kg/m^2, <53.0 cm^2/m^2 for men with a BMI ≥25.0, and <41.0 cm^2/m^2 in women; ● Appendicular skeletal muscle index consistent with sarcopenia (not defined); ● Sarcopenia= Males <7.27 Kg m^{-2} ; females <5.45 Kg m^{-2} determined by dual energy X-ray absorptiometry; ● FFMI measured by BIA lower than 14.6 kg/m^2 in men, and 11.4 kg/m^2 in women; ● FFM index <5th percentile of age- and sex-specific reference values
Body mass index	● Cachexia: BMI: < 20 kg/m^2;

	• Precachexia: BMI≥20 kg/m^2; • Refractory: BMI ≤ 20 kg/m^2 to ≤22 kg/m^2 ≤ BMI
C-reactive protein	≥8 mg/L or ≥5 mg 1^{-1}
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	• EORTC questionnaire, answering question 13: a little, quite a bit, or very much; • Reported energy intake ≤20 kcal/kg; • Appetite <5 cm (VAS), energy intake <84 kJ/kg body weight per d (84 kJ (20 kcal)/kg/d) or energy intake <70 % of TEE
Performance/ Function/ Muscle strength	• ECOG 0-4 or 3-4 • Karnofsky Performance Score <50
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	• Impaired glucose tolerance (precachexia) • <3 months expected survival (Refractory cachexia) • Unresponsive to treatment

Notes. BIA=bioelectrical impedance analysis; BMI=body mass index; cm=centimeter; CRP=C reactive protein; CT=computed tomography; ECOG=Eastern Cooperative Oncology Group; EORTC=European Organization for Research and Treatment of Cancer; FFM=fat-free mass; FFMI=fat-free mass index; kcal=kilocalorie; kg=kilograms; kJ=kilojoule; L3=third lumbar vertebra; m=meter; mo=months; PS=performance status; SMI=skeletal muscle index; SMM=skeletal muscle mass; TEE=total energy expenditure; VAS=visual analog scale; WL=weight loss.

Algorithm/Instrument	Cachexia Index (CXI)
Number of classifications	Continuous score, 2
Weight loss	
Sarcopenia or Skeletal Muscle index	• Calculated using both L3-SMI and PM-SMI based on cross-sectional area of the psoas, paraspinal, and abdominal wall muscles at the L3 vertebral level and the pectoralis major and minor muscles at the T4 vertebral level; The SMI was calculated as the area of the L3 region muscle/the height squared (cm^2/m^2); • Area of psoas muscle/height2 (The psoas muscle area was calculated as: length of the long axis of the psoas muscle × length of the short axis × π, at the third lumbar vertebral level using axial imaging of preoperative computed tomography); • Iliopsoas minor axis (cm) × major axis (cm) × / height squared (cm^2 / m^2); • Iliopsoas major axis (mm) × iliopsoas minor axis (mm) ×π/100
Body mass index	
C-reactive protein	
Albumin	Albumin, Serum Albumin
Neutrophil lymphocyte ratio	Calculated by dividing the absolute neutrophil count by the absolute lymphocyte count[a]
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Notes. [a] One study included a cutoff of 3.41 for NLR but it was not clear if this was used for the CXI.
Abbreviations. SMI=skeletal muscle index.

Algorithm/Instrument	Cachexia Staging Score (CSS)
Number of classifications	3
Weight loss	Weight loss over 6 months: ● Weight stable or weight gain=0; ● Weight loss ≤5%=1; ● Weight loss >5% and ≤15%=2; ● Weight loss >15%=3
Sarcopenia or Skeletal Muscle index	SARC-F: 0= 0; 1–3=1; 4–6=2; 7–10=3
Body mass index	
C-reactive protein	
Albumin	<35 g/L
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Appetite loss based on patient-reported numerical rating scale with a range of 0–10: ● 0–3=0 ● 4–6=1 ● 7–10=2
Performance/ Function/ Muscle strength	ECOG: ● 0=0; ● 1–2=1; ● 3–4=2
White blood cell count	> 10* 10^9 /L
Hemoglobin	<120/110g/L for male/female
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	

Quality of life	
Fatigue	
Other	

Abbreviations. ECOG=Eastern Cooperative Oncology Group; g=grams; L=liter; SARC-F=strength, assistance with walking, rising from a chair, climbing stairs, and falls; WBC=white blood cell.

Algorithm/Instrument	**Radiotherapy Cachexia Staging Score (R-CSS)**
Number of classifications	3
Weight loss	Weight loss over 6 months: ● Weight stable or weight gain=0; ● Weight loss ≤5%=1; ● Weight loss >5% and ≤15%=2; ● Weight loss >15%=3
Sarcopenia or Skeletal Muscle index	SARC-F: ● 0= 0; ● 1–3=1; ● 4–6=2; ● 7–10=3
Body mass index	● ≥20=0; ● 18.5-20=1; ● < 18.5=2
C-reactive protein	
Albumin[a]	<35g/L
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Appetite loss based on patient-reported numerical rating scale with a range of 0–10: ● 0–3=0; ● 4–6=1; ● 7–10=2 AND Reduced food intake:

	• No reduction or more=0; • Reduce =1
Performance/ Function/ Muscle strength	ECOG: • 0=0; • 1–2=1; • 3–4=2
White blood cell count[a]	> 10 * 10^9 /L
Hemoglobin[a]	<120/110g/L for male/female
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	Age: • < 70 = 0 • ≧ 70 =1

Notes. [a] Abnormal biochemistry including WBC, albumin and Hb will be scored as the following: all normal score = 0, 1 of the 3 abnormal score = 1, more than 1 abnormal score = 2, so abnormal biochemistry score range 0-2.

Abbreviations. BMI=body mass index; ECOG=Eastern Cooperative Oncology Group; g=grams; L=liter; SARC-F=strength, assistance with walking, rising from a chair, climbing stairs, and falls; WBC=white blood cell.

Algorithm/Instrument	**Cachexia Assessment Scale (CAS)**
Number of classifications	4
Weight loss	Weight loss in the 6 past months: Score 0 = <5%, score 1= 5%–10%, score 2= 10%–20%, score 3-4 = > 20%
Sarcopenia or Skeletal Muscle index	
Body mass index	Score 0 = <19 (normal), score 1-2= 17-19 (moderate), score 3-4 = < 17 (severe weight loss)
C-reactive protein	

Albumin	Score 0 = 30-50 g/L, score 1-2 = 20-30 g/L, score 3-4 = <20 g/L
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Loss of appetite: Score 0 = normal, score 1= mild loss, score 2 = moderate loss, score 3-4 = severe loss, IV fluid needed
Performance/ Function/ Muscle strength	Score 0 = fully active, score 1= can perform light activity, score 2 = limited activity, 50% of the time, score 3= 50% of time is spent in bed; needs help with activities of daily living, score 4 = Totally dependent on help for activities of daily living
White blood cell count	
Hemoglobin	Score 0 = normal, score 1= 10 g/L (normal), score 2 = 8-9.9 g/L, score 3= 6.5–7.9 g/L, score 4 = < 6.5 g/L
Dysphagia	Score 0 = None, score 1= Symptomatic, able to eat a regular diet, score 2 =Symptomatic, altered eating, uses oral supplements, score 3= Symptomatic, severely altered eating or swallowing; IV fluids needed, score 4 = Needs IV or total parenteral nutrition
Stomatitis	Score 0 = None, score 1= Pain, sores, and erythema of mucosa, score 2 = Pain, patchy ulcerations, but still able to eat, score 3= Pain, confluent ulceration; needs IV fluids, score 4 = Same as 3; also needs total parenteral nutrition
Edema	Edema (pretibial or sacral): score 0 = None, score 1= +1, score 2 = +2, score 3-4 = +3
Ascites	Score 0 = None, score 1= Asymptomatic, score 2 = Symptomatic; needs diuretic, score 3 = Symptomatic; needs centesis, score 4 = Danger to life
Creatinine	Score 0 = normal, score 1-4 =< 10% less than low end of normal range
Quality of life	
Fatigue	
Other	Diarrhea, Nausea, vomiting: “Diarrhea: score 0 = none, score 1 = Baseline to 4 stools above baseline, score 2 = 4–6 stools over baseline, score 3-4 = > 7 stools per day; IV fluids needed for possible electrolyte imbalance. Nausea: score 0 = none, score 1 = Mild, can eat, score 2= Moderate, eats less, score 3-4 = Severe, inadequate oral intake; needs IV fluids. Vomiting; score 0 = none, score 1 = Once a day, score 2= 2–5 times per day, score 3-4 = >= 6 times per day, continuous; needs IV fluids

Abbreviations. IV=intravenous.

Algorithm/Instrument	**Evans 2008**
Number of classifications	2
Weight loss	≥5% in the past 6 or 12 months

Sarcopenia or Skeletal Muscle index	• FFM index below the 10th percentile by age- and sex-specific reference values; • Appendicle skeletal muscle index by DEXA (kg/m^2) <5.45 in females and <7.25 in males; • BIA: Male SMI<7.26 kg/m^2, Female SMI<5.45 kg/m^2; • Low ASMI: <7.26 kg/m^2 for males and <5.45 kg/m^2 for females or mid-arm muscle circumference (AMC): cut-off below the 10th percentile of a Swedish reference population, with low muscle mass: ASMI or AMC below cut-off; FFMI: female/male < 15.0/ 17.0 kg/m²
Body mass index	Ranging from 18.5 to 22 kg/m^2
C-reactive protein	>5 mg/L
Albumin	<3.2g/dL; S-albumin<32 g/L or S-albumin<35 g/L
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	• Appetite <5 cm (VAS), energy intake <84 kJ/kg body weight per d (84 kJ (20 kcal)/kg/g) or energy intake <70 % of TEE; • EORTC appetite loss: score ≥3; • Total caloric intake <20 kcal/kg body weight; <70% of usual food intake; Mean energy intake adjusted for age, sex, and weight
Performance/ Function/ Muscle strength	Decreased muscle strength or low handgrip strength; HGS below the lowest tertile extracted from age- and sex-specific reference values
White blood cell count	
Hemoglobin	< 12 g/dL or 117 g/l
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	• EORTC-QLQC30 score of 3 or 4; • EORTC tiredness: score ≥66.7; • Fatigue= >3 on a visual analog scale (1–10); • Physical of mental weariness resulting from exertion; an inability to continue exercise at the same intensity with a resultant deterioration in performance
Other	• Inflammatory markers; • IL-6 >4 pg/ml; • Underlying chronic disease

Abbreviations. ASMI=appendicular skeletal muscle index; BIA=bioelectrical impedance analysis; BMI=body mass index; DEXA=dual-energy X-ray absorptiometry; dL=deciliter; EORTC=European Organization for Research and Treatment of Cancer; EORTC-QLQC30=European Organization for Research and Treatment of Cancer quality of life questionnaire; FFM=fat-free mass; FFMI=fat-free mass index; g=grams; HGS=hand grip strength; kcal=kilocalorie; kg=kilograms; kJ=kilojoule; L=liters; m=meters; mg=milligrams; ml=milliliters; pg=picogram; S-albumin=serum albumin; SMI=skeletal muscle index; TEE=total energy expenditure; VAS=visual analog scale.

Algorithm/Instrument	**Cancer Cachexia Score (CCS)**
Number of classifications	3
Weight loss	
Sarcopenia or Skeletal Muscle index	Sarcopenia= SMI (based on skeletal muscle in the L3 region) below the cut-of value (≤43.75 cm^2/m^2 for men and ≤41.10 cm^2/m^2 for women); Sarcopenia “Yes”=1, Sarcopenia “No”=0)
Body mass index	• < 20 kg/m^2=1; • ≥ 20 kg/m^2= 0
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Prognostic nutritional index: • <40= 1; • ≥40= 0
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	

Other	Tumor volume (size × T stage): ● ≥57.7= 1; ● <57.7= 0

Abbreviations. cm=centimeter; kg=kilograms; L3=third lumbar vertebra; m=meter; SMI=skeletal muscle index.

Algorithm/Instrument	**Cancer Cachexia staging Index (CCSI)**
Number of classifications	3
Weight loss	Weight loss rate, kg/month: ● ≤0.38= 0; ● 0.38-1.7= 1; ● ≥1.7= 2
Sarcopenia or Skeletal Muscle index	SMI (based on CT images at the third lumbar vertebra) cm^2 /m^2: ● Male ≥44.4 or Female ≥35.7= 0; ● Male ≥37.5 or Female ≥30.9= 2; ● Male <37.5 or Female <30.9=4
Body mass index	BMI-adjusted weight loss grade (WLGS) assessed according to protocol described by Martin et al., where a cutoff of: ● 0= 0; ● 1= 2; ● 2= 4; ● 3= 6; ● 4= 8
C-reactive protein	
Albumin	Prealbumin level (mg/L): ● ≥180= 0; ● <180= 4
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Appetite status (Not defined): ● Good= 0; ● Fair= 1; ● Poor= 2
Performance/ Function/ Muscle strength	Physical status (Not defined): ● Good= 0;

	• Fair= 1; • Poor= 2
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	Inflammation (NLR and CRP level, mg/L): • NLR > 3.5= 3; • NLR≤3.5; CRP > 2.9= 2; • NLR≤3.5; CRP > 2.3= 1; • NLR≤3.5; CRP≤2.3= 0

Abbreviations. cm=centimeter; CRP=C reactive protein; kg=kilograms; L=liters; m=meter; mg=milligrams; NLR=neutrophil-to-lymphocyte ratio.

Algorithm/Instrument	**Cancer Cachexia Study Group (CCSG)/Fearon 2006**
Number of classifications	2
Weight loss	Weight loss ≥10%
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	CRP ≥10 mg/L
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Energy intake ≤1500 kcal/day

Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. CRP=C reactive protein; kcal=kilocalorie; L=liters; mg=milligrams.

Algorithm/Instrument	**CASCO and miniCASCO**
Number of classifications	3-4
Weight loss	Weight loss of 5% or more
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	CRP
Albumin	Plasma Albumin, Plasma Pre-Albumin
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Anorexia as measured by the SNAQ[a]
Performance/ Function/ Muscle strength	Physical performance using a questionnaire of 5 questions related to physical activity or reduction in muscle strength to four scores by the Harrison scale
White blood cell count	

Hemoglobin	Hemoglobin or anemia
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	Quality of life based on a questionnaire of 25 questions from QLQ-C30 (EORTC QLQ-C30)
Fatigue	Fatigue based on the answers given in the Quality of Life (SF-36) and Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) questionnaires
Other	Other inflammatory markers including Plasma IL-6, Plasma lactate, Plasma triglycerides, Plasma urea, ROS plasma levels, Glucose tolerance, test/HOMA index altered, Absolute lymphocyte number; Lean body mass assessed through: Conventional BIA, DXA, CT scan analysis at L2-L3.

Notes. [a]Questionnaire of 4 questions extracted from SNAQ of St. Louis VA Medical Centre.

Abbreviations. BIA=bioelectrical impedance analysis; CRP=C reactive protein; CT=computed tomography; DXA=dual-energy X-ray absorptiometry; EORTC-QLQC30= European Organization for Research and Treatment of Cancer quality of life questionnaire; g=grams; Hb=memoglobin L=liters; L2/L3=second/third lumbar vertebra; mg=milligrams; ROS=reactive oxygen species; SNAQ=Simplified Nutritional Appetite Questionnaire.

Algorithm/Instrument	**Glasgow Prognostic Score or modified Glasgow Prognostic Score**
Number of classifications	3 or 4
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	1.0 mg/dL; 0.5 mg/dL
Albumin	3.5 g/dL
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	

White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. CRP=C reactive protein; dL=deciliter; g=grams; L=liters; mg=milligrams.

Algorithm/Instrument	**Patient-Generated Subjective Global Assessment (PG-SGA)**
Number of classifications	2 or 3
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	

Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	PG-SGA

Algorithm/Instrument	**Fearon 2011 and Evans 2008 combined**
Number of classifications	2 - 4
Weight loss	• ≤5% over 6 months; • >5% over 6 months; • >2%
Sarcopenia or Skeletal Muscle index	ASMI: <7.26 kg/m^2 for males, <5.45 kg/m^2 for females
Body mass index	<20 kg/m^2;
C-reactive protein	• > 0.5 mg/dL; • >10 mg/dL
Albumin	• < 3.2 g/dL; • < 32 g/L; • <2.5 g/dL
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	• ESAS appetite score, ≥4/10; • PG-SGA box 2, >1 or ≥1
Performance/ Function/ Muscle strength	• PG-SGA or hand grip strength Cachexia= PG-SGA box 4, ≤2 or hand-grip percentile, ≥50; • PG-SGA SF box 4 score >2; • PG-SGA box 4, >2 or hand-grip percentile, <50
White blood cell count	>11.000

Hemoglobin	• <120 g/L • <120 g/L (men), 110 g/L (women)
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. BMI=body mass index; CRP=C reactive protein; dL=deciliter; ESAS=Edmonton Symptom Assessment System; g=grams; kg=kilograms; L=liters; m=meter; mg=milligrams; PG-SGA=Patient-Generated Subjective Global Assessment; SF=short form; WBC=white blood cell; WL=weight loss.

Algorithm/Instrument	**Hand Grip Strength-Based Cachexia Index (HGS CXI)**
Number of classifications	2
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	
Albumin	Albumin
Neutrophil lymphocyte ratio	Calculated by dividing the absolute neutrophil count by the absolute lymphocyte count
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	Hand grip strength based on dynamometer with maximum strength in their dominant hand
White blood cell count	
Hemoglobin	

Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. g=grams; kg=kilograms; L=liters; m=meter; NLR=neutrophil-to-lymphocyte ratio.

Algorithm/Instrument	**Wallengren 2013**
Number of classifications	2
Weight loss	>2%
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	>10 mg/L
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	

Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	>3 on VAS or ESAS
Other	

Abbreviations. CRP=C reactive protein; ESAS=Edmonton Symptom Assessment System; VAS=visual analog scale.

Algorithm/Instrument	**Nutritional Screening Assessment**
Number of classifications	4
Weight loss	>5 % in the last year
Sarcopenia or Skeletal Muscle index	FFMI< 14.6 kg/m^2
Body mass index	< 20 kg/m^2
C-reactive protein	> 5 mg/L
Albumin	< 32 g/L
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Appetite loss (Not defined)
Performance/ Function/ Muscle strength	Hand grip strength < 30kg
White blood cell count	
Hemoglobin	< 120 g/L
Dysphagia	
Stomatitis	
Edema	
Ascites	

Creatinine	
Quality of life	
Fatigue	Fatigue (not defined)
Other	PG-SGA ≥ 4

Abbreviations. BMI=body mass index; FFMI=fat-free mass index; g=grams; HGS=hand grip strength; kg=kilograms; L=liters; m=meter; mg=milligrams; PG-SGA=Patient-Generated Subjective Global Assessment.

Algorithm/Instrument	**Orell-Kotikangas 2017**
Number of classifications	2
Weight loss	
Sarcopenia or Skeletal Muscle index	Low MAMA <10th percentile; MAMA calculated according to the following equation: MAMA (cm^2) = [MAC (cm) – (0.3142 x TSF (mm)]^2/(4 x 3.142)
Body mass index	
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	Low HGS (<85% of normal median value) measured by Jamar handgrip dynamometer
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	

Fatigue
Other

Abbreviations. cm=centimeter; HGS=hand grip strength; MAC=mid-arm circumference; MAMA=mid-arm muscle area; mm=millimeter; TSF=triceps skinfold.

Algorithm/Instrument	**Solheim 2011**
Number of classifications	3
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	< 20kg/m^2
C-reactive protein	≥10 mg /L
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Appetite loss (a response of little or greater on EORTC QLQ-C30 item ‘have you lacked appetite?’)
Performance/ Function/ Muscle strength	Karnofsky score < 80
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. EORTC-QLQC30=European Organization for Research and Treatment of Cancer quality of life questionnaire; kg=kilograms; L=liters; m=meter; mg=milligrams.

Algorithm/Instrument	**Go 2020**
Number of classifications	2
Weight loss	
Sarcopenia or Skeletal Muscle index	Sarcopenia: (L3-SMI, 52.4 cm^2/m^2 in males and 38.5 cm^2/m^2 in females; PM-SMI, 4.4 cm^2/m^2 in males and 3.1 cm^2/m^2 in females) non-sarcopenia-both, neither L3-nor PM-SMI at sarcopenic level; sarcopenia-L3/PM alone, only one of SMIs at sarcopenic level; and sarcopenia-both, both L3- and PM-SMIs at sarcopenic level
Body mass index	
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	GNRI formula = 1.489 × serum albumin level (g/L) + 41.7 × [actual body weight/ideal body weight (kg)]; ● >98= No risk; ● 92 to 98 = Low risk;

	• 82 to < 92 = Moderate risk; • < 82 = Major risk

Abbreviations. cm=centimeter; g=grams; GNRI=Geriatric Nutritional Risk Index; kg=kilograms; L3=third lumbar vertebra; L=liters; m=meter; PM=pectoralis muscle; SMI=skeletal muscle index.

Algorithm/Instrument	**Namikawa 2022**
Number of classifications	2
Weight loss	• >5% within the last 6 months; • >2% within the last 6 months;
Sarcopenia or Skeletal Muscle index	
Body mass index	<20 kg/m^2
C-reactive protein	>5.0 mg/L
Albumin	<3.2 g/dL
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Anorexia (not defined)
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	<12 g/dL
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. dL=deciliter; g=grams; kg=kilograms; L=liters; m=meter; mg=milligrams.

Algorithm/Instrument	Huo 2022
Number of classifications	Continuous
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Nutritional Risk Screening 2002
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	European Organization for Research and Treatment of Cancer QLQ-C30 score
Fatigue	
Other	• Age= Range 0-120 • Patient-Generated Subjective Global Assessment (PG-SGA) = Range 0-26 • Cancer category = Range 0-9

Algorithm/Instrument	**Liu 2022**
Number of classifications	Continuous
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	
Albumin	35 g/L
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	<120 g/L in men or <110 g/L in women
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	• Advanced lung cancer inflammation index(ALI): BMI × albumin (g/dL)/NLR= High, low • Cancer Stage = I/II, III/IV • Surgery= Yes, no

Abbreviations. BMI=body mass index; dL=deciliter; g=grams; L=liters; NLR=neutrophil-to-lymphocyte ratio.

Algorithm/Instrument	Tan 2023
Number of classifications	Continuous
Weight loss	
Sarcopenia or Skeletal Muscle index	SMI: 37.81 cm^2/m^2 for women and 43.13 cm^2/m^2 for men based on CT at L3
Body mass index	BMI kg/m^2
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	NLR
Anorexia or Appetite loss or Nutrition	Appetite loss= Yes, no
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	• Cancer Site= Liver, colorectum, gallbladder, stomach, pancreas. • Cancer Stage= I, II, II, IV • Time from symptom onset to hospitalization (month)

Abbreviations. BMI=body mass index; cm=centimeter; CT=computed tomography; L3=third lumbar vertebra; m=meter; NLR=neutrophil-to-lymphocyte ratio; SMI=skeletal muscle index.

Algorithm/Instrument	Yin 2022
Number of classifications	
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	Range 5-40 kg/m^2
C-reactive protein	Range=0-1800 mg/L
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Early satiety (not defined) = No, yes; Anorexia (not defined) = No, yes
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	Max of 280 g/L
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	Cancer type= Breast, other, respiratory, gastrointestinal; Platelets= Range of 0-1100; Abdominal pain= Yes; no; Diarrhea= Yes; no; Vomiting= Yes; no; Other gastrointestinal symptoms= Yes; no; Direct bilirubin µmol/L= Range 0-400; Drinking= Yes; no;

	Tumor stage= I, II, III, IV; Total protein, g/L= Range 0-110

Abbreviations. g=grams; L=liters; µmol=micromole.

Algorithm/Instrument	**Vigano 2017**
Number of classifications	4
Weight loss	≤5% over past 6 months; >5% over past 6 months
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	>10 mg/L
Albumin	<32 g/L
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	aPG-SGA box 2 score >=1
Performance/ Function/ Muscle strength	aPG-SGA box 4 score >2
White blood cell count	> 11,000/L
Hemoglobin	<120g/L in men; <110g/L in women
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. aPG-SGA=abridged Patient-Generated Subjective Global Assessment; BMI=body mass index; CRP=C reactive protein; g=grams; L=liters; mg=milligrams; WBC=white blood cell; WL=weight loss.

Algorithm/Instrument	**Wiegert 2021**
Number of classifications	3
Weight loss	<15%, >=15% in the past 6 mo
Sarcopenia or Skeletal Muscle index	Mid upper-arm muscle area (cm^2) (MUAMA): ≥38.0/ ≥35.5 for men/women; <38.0/<35.5 cm^2 for men/women
Body mass index	• <21.0; • 21.0-26.4; • >26.4 kg/m^2
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	

Abbreviations. BMI=body mass index; cm=centimeter; kg=kilograms; m=meter; MUAMA=mid-upper-arm muscle area; WL=weight loss.

Algorithm/Instrument	**Global Leadership Initiative on Malnutrition (GLIM)**
Number of classifications	2
Weight loss	>5% within past 6 months
Sarcopenia or Skeletal Muscle index	• Mid arm muscle circumference < 15 percentile ; • Body-weight standardized hand grip strength < 15 percentile; Calf circumference (left) < 15 percentile
Body mass index	• <18.5 if<70 years; • <20 if >70 years
C-reactive protein	•
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	Nutritional Risk Screening 2002
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	Disease burden (not specified)

Abbreviations. BMI=body mass index; NRS-2002=Nutritional Risk Screening 2002.

Algorithm/Instrument	**Malnutrition Universal Screening Tool (MUST)**
Number of classifications	2
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	MUST

Algorithm/Instrument	**Nutritional Risk Screening (NRS)-2002**
Number of classifications	2
Weight loss	

Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	NRS-2002

Algorithm/Instrument	**Malnutrition Screening Tool (MST)**
Number of classifications	**2**
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	

Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	
Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	MST

Algorithm/Instrument	**Short Nutritional Assessment Questionnaire (SNAQ)**
Number of classifications	2
Weight loss	
Sarcopenia or Skeletal Muscle index	
Body mass index	
C-reactive protein	
Albumin	
Neutrophil lymphocyte ratio	
Anorexia or Appetite loss or Nutrition	

Performance/ Function/ Muscle strength	
White blood cell count	
Hemoglobin	
Dysphagia	
Stomatitis	
Edema	
Ascites	
Creatinine	
Quality of life	
Fatigue	
Other	SNAQ

DEFINITIONS BY ALGORITHM

Algorithm/Instrument	Cachexia Definition
Fearon 2011 (without modification)	Cachexia= Weight loss; or low BMI + Weight Loss; or Sarcopenia+ weight loss
Fearon 2011 (with modification or staging)	• Cachexia: Weight loss; or Weight loss + BMI; or Sarcopenia alone • Precachexia: clinical + metabolic manifestations but minimal or WL; Cachexia: WL; or BMI + WL; or low muscle mass + WL; Refractory cachexia: catabolic state unresponsive to anticancer treatment + low performance status + <3 months expected survival. • Normal Status: WL < 2%; or Weight gain and no anorexia; or No sarcopenia; Precachexia: 2% ≤ WL ≤ 5% and BMI ≥ 20 and no features of cachexia; or Anorexia and no cachexia; or WL < 2% and sarcopenia and no anorexia; Cachexia: WL > 5% and no features of refractory cachexia; or 2% ≤ WL ≤ 5% and BMI < 20 and no refractory cachexia; or WL > 2% and sarcopenia and no features of refractory cachexia; Refractory cachexia: ECOG PS 3–4 and BMI < 20 and WL ≥ 6%; or ECOG PS 3–4 and 20 ≤ BMI < 22 and WL ≥ 11%; or ECOG PS 3–4 and 22 ≤ BMI and WL ≥ 15% • Cachexia: Weight loss>5%, or BMI + Weight Loss, or Sarcopenia + weight loss; Precachexia: Weight loss≤5% + anorexia + metabolic change • Precachexia: Weight loss + other metabolic disturbances; Cachexia: Weight loss; or BMI and Weight loss; Refractory: Unresponsive to treatment and with a life expectancy <3 months • Sarcopenia + weight loss • Cachexia: At least one of the three criteria: Weight loss, Weight loss + BMI, skeletal muscle index + weight loss; Precachexia was defined as substantial involuntary weight loss (i.e., 2–5% weight loss in the 6mo preceding study measurement) • Cachexia: Weight loss >5% or >10% over past 6 months (in absence of simple starvation); or Sarcopenia alone; or Sarcopenia + >2% WL • Precachexia: Defined using the European Society of Clinical Nutrition and Metabolism Special Interest Group; Cachexia: International consensus definition • Precachexia: an early stage in which clinical and metabolic signs such as anorexia and systemic inflammation can precede substantial (ie, >5%) body weight loss; • Cachexia: Weight loss; or Weight loss + BMI; or Sarcopenia alone; Precachexia: CRP≥5 mg 1^{-1} but not meeting criteria for cachexia • Cachexia: Weight loss; or low BMI + WL; or Sarcopenia + WL Precachexia: WL> 2% and < 5% • Cancer Precachexia: Unintentional weight loss; Anorexia; Systemic inflammation Cancer cachexia: Weight loss or sarcopenia; Reduced food intake; Systemic inflammation Refractory cancer cachexia: Variable degree of 'cancer cachexia'; Cancer disease both pro-catabolic and not responsive to anticancer treatment; Low performance score;<3 months expected survival.

Cachexia Index (CXI)	(SMI x Albumin)/NLR For Dichotomous classification based on Youden's index or median CXI
Cachexia Staging Score (CSS)	Total CSS= Weight loss score+ SARC-F Value score + ECOG PS value score + Appetite loss score + Abnormal biochemistry score (based on WBC, Albumin, Hemoglobin, where All normal=0, One of the three abnormal=1, and More than one abnormal= 2) CSS classifications by total score: noncachexia (score: 0–2), precachexia (score: 3–4), cachexia (score: 5–8), and refractory cachexia (score: 9–12).
Radiotherapy Cachexia Staging Score (R- CSS)	Total R-CSS= Weight loss score+ SARC-F Value score + ECOG PS value score + Appetite loss score + Age + BMI + Reduced food intake + Abnormal biochemistry score (based on WBC, albumin, hemoglobin, where All normal=0, One of the three abnormal=1, and More than one abnormal= 2) R- CSS classifications by total score: noncachexia (score:0–3), precachexia (score: 4-6), cachexia (score: 7-12), and refractory cachexia (score: 13-17).
Cachexia Assessment Scale (CAS)	0-1 items scored level 1-2 AND 0 items scored level 3-4= No Cachexia; 2+ items scored level 1-2 AND 0 items scored level 3-4= Mild Cachexia; 2+ items scored level 1-2 AND 1-2 items scored level 3-4= Moderate Cachexia; Any items scored level 1-2 AND 3+ items scored level 3-4= Severe Cachexia
Evans 2008	Weight loss or low BMI + any 3 of the following: fatigue, anorexia, sarcopenia, muscle strength, anemia, hypoalbuminemia, or abnormal serum biochemistry components
Cancer Cachexia Score (CCS)	0–1= mild; 2= moderate; 3–4= severe
Cancer Cachexia staging Index (CCSI)	<9= no cachexia; 9-18= mild or moderate cachexia; >=19= severe cachexia
Cancer Cachexia Study Group (CCSG)/Fearon 2006	Fulfillment of 2 criteria or all 3 criteria
CASCO and miniCASCO	CASCO and miniCASCO Body weight loss and composition + inflammation/metabolic disturbances/immunosuppression + physical performance + anorexia + quality of life Cutoffs for classifications: No cachexia (≤14), mild cachexia (15–28), moderate cachexia (29–46) and finally, severe cachexia (>46) or CASCO No Cachexia= Not Defined Precachexia= a 5% weight loss to the initial value over one year, the presence of fatigue grade I–II (mild or moderate), anorexia, grade 0–I (absent or mild); according to the Short Nutritional Assessment Questionnaire (SNAQ), a reduction in muscle strength to four scores by the Harrison scale, changes in biochemical indices, such as CRP > 10 mg/L, albumin <35 g/L, and Hb < 120 g/L.

	Cachexia= over 5% weight loss against the initial value over 1 year, the presence of fatigue grade II–III (moderate or severe), anorexia grade I–III (mild or severe) by SNAQ, a reduction in muscle strength to 2–3 scores, changes in blood analysis, such as CRP > 10 mg/L, albumin < 35 g/L, Hb < 120 g/L
Glasgow Prognostic Score or modified Glasgow Prognostic Score	• Patients with both elevated CRP (>10 mg/L) and hypoalbuminemia (<3.5 g/L) =cachexia or a score of 2; • Patients with either biochemical abnormalities= precachexia or score of 1; • Patients without these abnormalities= non-cachexia or score of 1 or • No cachexia= ≥3.5 Albumin (g/dL) and CRP < 10 (mg/L); • Undernourished= < 3.5 Albumin (g/dL) and CRP < 10 (mg/L); • Precachexia= ≥ 3.5 Albumin (g/dL) and CRP ≥10 (mg/L); • Refractory cachexia= < 3.5 Albumin (g/dL) and CRP ≥10 (mg/L) or • No cachexia= CRP≤10 mg/l and albumin ≥35 g/l; • Undernourished= CRP ≤10 mg/l and albumin <35 g/l; • Precachexia= CRP>10 mg/l and albumin ≥35 g/l; • Refractory cachexia= CRP>10 mg/l and albumin <35 g/l or • Normal= ≥3.5 mg/dL albumin and ≤0.5mg/dL CRP; • Undernourished= <3.5 mg/dL albumin and ≤0.5mg/dL CRP; • Cancer cachexia potential= ≥3.5 mg/dL albumin and >0.5mg/dL CRP; • Cancer cachexia= <3.5 mg/dL albumin and >0.5mg/dL CRP
PG-SGA	• PG-SGA cutoff: 6.5; PG-SGA >=4; • Based on PG-SGA nutritional status of well nourished, moderately well malnourished, and severely malnourished (scores not provided)
Fearon 2011 and Evans 2008 combined	• Weight loss of more than 5% of the body weight within the 6 months before chemoimmunotherapy initiation, or weight loss of more than 2% + BMI, along with laboratory values above the expected reference values (C-reactive protein, serum albumin or hemoglobin) • Precachexia= Lab measure(Any)+Anorexia/decreased food intake; Lab measure (Any)+WL; Anorexia/decreased food intake + WL; Lab measure(Any)+Anorexia/decreased food intake + WL;

	Cachexia= Lab measure (Any)+WL + Function; Anorexia/decreased food intake +WL + Function; Lab measure (Any)+Anorexia/decreased food intake +WL + Function; Cachexia caused by low BMI and sarcopenia= Lab measure (Any)+ Function + BMI and WL; or Sarcopenia + WL; Lab measure (Any)+Anorexia/decreased food intake + Function + BMI and WL; or Sarcopenia + WL; Refractory cachexia= Lab(Any) +WL+ Function; Anorexia/decreased food intake + WL+ Function; Lab (Any) +Anorexia/decreased food intake + WL+ Function • Precachexia= Abnormal Biochemistry + decreased food intake; or abnormal biochemistry + moderate weight loss; or decreased food intake + moderate weight loss; or Abnormal biochemistry + decreased food intake + moderate weight loss; Cachexia= Abnormal biochemistry + significant weight loss; or decreased food intake + significant weight loss; or abnormal biochemistry + significant weight loss + decreased food intake; Refractory cachexia= Abnormal biochemistry + significant weight loss + decreased activities and functioning; or decreased food intake + significant weight loss + decreased activities and functioning; or abnormal biochemistry + decreased food intake + significant weight loss + decreased activities and functioning; or patients presenting with serum albumin <25 g/L+ decreased performance • No Cachexia= Abnormal biochemistry alone; anorexia or decreased food intake alone; weight loss alone; none of the above; Precachexia= Abnormal Biochemistry + anorexia or decreased food intake; or abnormal biochemistry + moderate weight loss; or anorexia or decreased food intake + moderate weight loss; or Abnormal biochemistry+ anorexia or decreased food intake + moderate weight loss; Cachexia= Abnormal Biochemistry + anorexia or decreased food intake + decrease in function; or anorexia or decreased food intake + weight loss + decrease in function; or Abnormal biochemistry+ anorexia or decreased food intake + weight loss + decrease in function; Cachexia cause by low BMI or sarcopenia= Abnormal Biochemistry + decrease in function + low BMI and WL or sarcopenia and WL; or anorexia or decreased food intake + decrease in function+ low BMI and WL or sarcopenia and WL; or anorexia or decreased food intake + decrease in function+ low BMI and WL or sarcopenia and WL; or abnormal biochemistry + anorexia or decreased food intake + decrease in function+ low BMI and WL or sarcopenia and WL Refractory cachexia= Abnormal biochemistry + significant weight loss + decreased activities and functioning; or anorexia or decreased food intake + significant weight loss + decreased activities and functioning; or abnormal biochemistry+ anorexia or decreased food intake + significant weight loss + decreased activities and functioning
HGS CXI	[HGS (kg)/height (m)^2 × serum albumin (g/L)]/NLR
Wallengren 2013	Weight loss + fatigue + CRP
Nutritional Screening Assessment	Cachexia= HGS or FFMI and 2 of the following: fatigue; appetite loss; >5% weight loss in the last year or BMI<20 kg/m^2; abnormal blood test; or Three of the following: fatigue; appetite loss; >5% weight loss in the last year or BMI<20 kg/m^2; abnormal blood test; Sarcopenia= HGS or FFMI without 2 of the following: fatigue; appetite loss; >5% weight loss in the last year or BMI<20 kg/m^2; abnormal blood test; Nutritional risk without criteria for sarcopenia or cachexia= not HGS and no FFMI; No 3 out of 4 of fatigue; appetite loss; >5% weight loss in the last year or BMI<20 kg/m^2; abnormal blood test, but yes on PG-SGA $\geq$4; Well nourished= not HGS<30kg and no FFMI <14.6kg/m^2, No 3 out of 4 of fatigue; appetite loss; >5% weight loss in the last year or BMI<20 kg/m^2; abnormal blood test and no PG=SGA $\geq$4

Orell-Kotikangas 2017	Low MAMA + Low HGS
Solheim 2011	Low body mass index + low performance + increased inflammatory biomarker + appetite loss; Patients were divided into three groups dependent on whether they had all four cachexia components (severe cachexia), two or three cachexia components (mild cachexia) or less than two cachexia components (no cachexia).
Go 2020	High cachexia risk group= major GNRI risk, sarcopenia-both, or moderate GNRI risk with sarcopenia-L3/PM alone; Else low cachexia risk group
Namikawa 2022	Cachexia= Body weight loss of 5% or a loss of 2% with a BMI of<20 kg/m^2 within the last 6 months; Anorexia; ≥2 of the following: Albumin, C-reactive protein, Hemoglobin
Huo 2022	Continuous score based on nomogram
Liu 2022	Continuous score based on nomogram
Tan 2023	Continuous score based on nomogram
Yin 2022	Continuous score based on nomogram
Vigano 2017	Precachexia= Abnormal biochemistry (CRP, or WBC, or lbumin, or Hemoglobin) + Decreased food intake; or Abnormal biochemistry (CRP, or WBC, or Albumin, or Hemoglobin) + WL≤ 5%; or Decreased food intake + WL≤ 5%; or Abnormal biochemistry (CRP, WBC, Albumin, Hemoglobin) + Decreased food intake + WL ≤5% Cachexia= Abnormal biochemistry (CRP, or WBC, or Albumin, or Hemoglobin)+ WL>5%; or Decreased food intake + WL>5%; or Abnormal biochemistry (CRP, or WBC, or Albumin, or Hemoglobin) + decreased food intake + WL>5% Refractory Cachexia= Abnormal biochemistry (CRP, or WBC, or Albumin, or Hemoglobin)+ WL>5% + Decreased activities and functioning; or Decreased food intake + WL>5% + Decreased activities and functioning; or Abnormal biochemistry (CRP, or WBC, or Albumin, or Hemoglobin) + Decreased food intake + WL>5% + Decreased activities and functioning
Wiegert 2021	Precachexia= BMI>26.4 + (MUAMA= ≥38.0 males; ≥35.5 females)+ %WL<15.0 Cachexia= BMI>26.4 + (MUAMA= ≥38.0 males; ≥35.5 females) + %WL≥15.0; or BMI>26.4 + (MUAMA= <38.0 males; <35.5 females) + (%WL= <15.0 or ≥15); or BMI= 21.0 to 26.4 + (MUAMA= ≥38.0 males; ≥35.5 females) + (%WL= <15.0 or ≥15); or BMI= 21.0 to 26.4 + (MUAMA= <38.0 males; <35.5 females) + %WL<15.0; or BMI<21.0 + %WL<15.0 Refractory Cachexia= BMI= 21.0 to 26.4 + (MUAMA= <38.0 males; <35.5 females) + %WL≥15.0; or BMI<21.0 + %WL≥15.0
Global Leadership Initiative on Malnutrition (GLIM)	(Weight loss OR BMI OR Reduced Muscle Mass) + Disease Burden (without NRS-2002)
Malnutrition Universal Screening Tool (MUST)	MUST ≥1
Nutritional Risk Screening (NRS)-2002	NRS-2002 ≥3

Malnutrition Screening Tool (MST)	MST ≥2
Short Nutritional Assessment Questionnaire (SNAQ)	SNAQ ≥2

Abbreviations: BMI=body mass index; CASCO/miniCASCO=cachexia score; CRP=C-reactive protein; CSS=Cachexia Staging Score; CXI=Cachexia index; ECOG/ECOG-PS=Eastern Cooperative Oncology Group; FFMI= Fat-Free Mass Index; g=grams; GLIM=Global Leadership Initiative on Malnutrition; GNRI=Geriatric Nutritional Risk Index; Hb=hemoglobin; HGS=hand grip strength; kg=kilograms; L=liters; L3=third lumbar vertebra; m=meters; MAMA/MUAMA=mid-upper arm muscle area; mg=milligrams; mo=months; MST=Malnutrition Screening Tool; MUST=Malnutrition Universal Screening Tool; NLR=neutrophil lymphocyte ratio; NRS-2002=Nutritional Risk Screening; PG-SGA=Patient-Generated Subjective Global Assessment; PM=pectoralis muscle; R-CSS=Radiotherapy Cachexia Staging Score; SARC-F=Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falls questionnaire; SNAQ=Short Nutritional Assessment Questionnaire; WBC=white blood cell; WL=weight loss.

PERFORMANCE CHARACTERISTICS

Study	Tool Used	Compared to	Psychometric Properties or Other Comparison Outcomes
Argilés-2017-28261113	CASCO	Subjective diagnosis of specialized oncologists (concurrent validity) based on the following question: "Before applying CASCO, what is your perception of severity of patient's cachexia according to the following scale 0 (normal, absence of cachexia), 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 (terminal, evident cachexia)."	Pearson correlation coefficient (rs = 0.412, p < 0.001).
Argilés-2017-28261113	miniCASCO	CASCO	Coefficient (r = 0.964; df = 19.50; p < 0.001)
Bye-2016-27119533	mGPS	Fearon 2011	mGPS: 65 % noncachectic, 5 % undernourished, 25 % precachectic, 10 % refractory cachexia. Fearon 2011: 55 % cachectic, 5 % precachectic, 40 % noncachectic (McNemar's test p = 0.43)
Cavalcante-Martins-2019-31060829	PG-SGA	Fearon 2011	80.6% of patients classified as well nourished by PG-SGA showed no evidence of cachexia; 60% of patients with severe malnourishment were classified with refractory cachexia. A positive correlation between PG-SGA score and Fearon's categories of cachexia was also observed (r= 0.54; p < 0.0001). The PG-SGA demonstrated good sensibility (87.50%) and accuracy (72%) for cachexia.
Chen-2020-31655470	MUST	Fearon 2011	Sensitivity= 87.3% Specificity= 77.7% Accuracy= 81.3% AUC 0.825
Chen-2020-31655470	NRS-2022	Fearon 2011	Sensitivity= 76.6% Specificity= 84.3% Accuracy= 91.6% AUC 0.805
Chen-2020-31655470	MST	Fearon 2011	Sensitivity= 84.3% Specificity= 98.6% Accuracy= 93.5% AUC 0.914
Chen-2020-31655470	SNAQ	Fearon 2011	Sensitivity= 54.3% Specificity= 95.9%

Study	Tool Used	Compared to	Psychometric Properties or Other Comparison Outcomes
			Accuracy= 80.9% AUC 0.751
Cong-2022-32826265	PG-SGA	Evans	PG-SGA of 6.5 had a sensitivity of 79.8% and a specificity of 72.3% for cachexia, and the area under the ROC curve was 0.846 (95% CI 0.826 to 0.866, p<0.001). The PPV and NPV were 20.68% and 97.53%, respectively.
Gabison-2010-20797955	CAS	PG-SGA (and other measures, though PG-SGA was referred to as the gold standard)	r = 0.58, p = 0.04
Gong-2022-36139560	CXI	Fearon 2011	Patients in the high CXI group had a lower rate of cancer cachexia (41.6% vs 50.9%,) but this difference was not significant (p = 0.09)
Huo-2022-36543973	Huo 2022 nomogram	Fearon 2011	The C-index of the diagnostic nomogram predicting the existence of cancer cachexia was 0.925 (95%CI, 0.916–0.934, p < 0.001) in the development cohort, and was 0.923 (95%CI=0.909–0.937, p < 0.001) in the validation cohort. AUC of 0.925, sensitivity of 0.826, and specificity of 0.862 in the development cohort; and an AUC of 0.923, sensitivity of 0.854, and specificity of 0.829 in the validation cohort.
Liu-2022-35898878	Liu 2022 nomogram	Fearon 2011	AUCs of diagnostic nomogram in the training and validation sets were 0.702 and 0.688, respectively
Silva-2020-31377013	mGPS	Fearon 2011	Odds ratio of being diagnosed was cachectic using Fearon criteria based on mGPS score: Undernourished on mGPS= 1.84 (1.23; 2.75), p= 0.003 Precachexia on mGPS= 1.51 (0.69; 3.32), p= 0.303 Refractor cachexia on mGPS= 2.83 (1.73; 4.60), p= <0.001
Song-2022-36476477	Global Leadership Initiative on Malnutrition	Fearon 2011	Sensitivity= 100%; Specificity= 60.7%; Accuracy= 67.4%; AUC= 0.835
Song-2022-36476477	Global Leadership Initiative on Malnutrition + Nutritional Risk Screening 2002	Fearon 2011	Sensitivity= 88.8%; Specificity= 91.8%; Accuracy= 91.3%; AUC= 0.910
Song-2022-36476477	PG-SGA	Fearon 2011	Sensitivity= 86.2%; Specificity= 58.3%; Accuracy= 63.1%; AUC= 0.778

Study	Tool Used	Compared to	Psychometric Properties or Other Comparison Outcomes
Tan-2023-36880286	Tan 2023 nomogram	Fearon 2011	AUC value of 0.760 (95% CI 0.747–0.774, p < 0.001), 0.743 (95% CI 0.726–0.761, p < 0.001), and 0.751 (95% CI 0.725–0.777, p < 0.001) in development, validation, and application cohorts, respectively
van-der-Meij-2013-23153477	Cancer-Specific Framework for Cachexia (Modified Fearon)	Evans (General framework for cachexia)	27.5% of patients were identified as cachectic using the general framework, compared to 17.5% using the cancer-specific framework 31.0% of patients who were identified as not cachectic by the general framework were identified as precachectic using the cancer-specific framework
van-der-Werf-2018-30235002	Fearon 2011	Clinical assessment comprised of the oncologists' opinion based on the patient's clinical presentation.	Kappa 0.049, 95% CI –0.079–0.176, p =0.457
Vanhoutte-2016-27843571	Evans, Fearon 2011	N/A	70% developed cachexia according to the Fearon 2011 definition and 40% according to the Evans 2008 definition, but neither were compared to any specific "gold standard"; examined prognostic differences as well (not reported here)
Wallengren-2013-23314651	Self Developed	Multiple	Cachexia all 3 components (Fearon 2006)= 12% Cachexia 2 of 3 components (Fearon 2006)= 45% Cachexia (Evans 2008)= 33% Cachexia (Fearon 2011)= 85% Cachexia (WL>2 %, fatigue>3, CRP>10)= 37%
Wan-2022-36212479	CXI	Fearon 2011	35% Low CXI group patients were classified as cachectic by Fearon criteria; 22% of High CXI group patients were classified as cachexia by Fearon criteria (p= 0.01)
Wang-2023-37454609	Cancer Cachexia Staging Index	Fearon 2011	Discrimination of CCSI in assessing cancer cachexia: AUC=0.911
Wesseltoft-Rao-2015-25710201	Fearon 2006, Fearon 2011	N/A	There was a high agreement (35/45; 78%) with respect to the classification of patients as cachectic or noncachectic (McNamar's test p= 0.75); neither were compared to any specific "gold standard"
Wiegert-2020-32927241	Wallengren, Vigano	N/A	Wallengren: 13.8% of patients were cachectic and 86.2% of patients were not cachectic Vigano: 17.3% of patients were cachectic, 20.8% as Precachexia, 53.3% as refractory cachexia, and 8.2% as Not cachectic
Xie-2023-36447437	H-CXI	Fearon 2011	The low H-CXI group had a higher risk of developing cancer cachexia than the high H-CXI group (discovery cohort: 39.3% vs 23.6%; internal validation cohort: 40.2% vs 24.8; external validation cohort: 31.0% vs 17.6%). In the multivariate logistic regression models, a low H-CXI was independently associated with a high risk of cancer cachexia
Yin-2022-36095136	Machine learning model	Fearon 2011	AUC = 0.763; 95% CI: 0.747, 0.780; Accuracy = 0.714; κ = 0.396; sensitivity = 0.580; specificity = 0.808; positive predictive value = 0.679, negative predictive value = 0.733
Zopf-2020-31561063	Evans, Fearon 2011	N/A	Evans: 45.5% of patients with cancer were identified as cachectic Fearon 2011: 39.4% of patients were identified as cachectic

Abbreviations: AUC=area under the curve; CAS=Cachexia assessment scale; CASCO=cachexia score; CI=confidence interval; CRP=C-reactive protein; CXI/H-CXI=Cachexia index/Hand grip strength-based cachexia index; df=degrees of freedom; mGPS=Modified Glasgow Prognostic Score; MUST=Malnutrition Universal Screening Tool; MST=Malnutrition Screening Tool; N/A=not applicable; NPV=Negative predictive value; NRS-2002=Nutritional Risk Screening; PG-SGA=Patient-Generated Subjective Global Assessment; PPV=Positive predictive value; SNAQ=Short Nutritional Assessment Questionnaire; ROC=Receiver operator curve; WL=weight loss.

DESIGN DETAILS

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria
Akaoka, 2022, 36371905, Japan	NRCS	2008-2018	All patients had to undergo hepatic resection for primary HCC after hepatic resection and have available data regarding their CXI.	NR
Aslan, 2022, 36137881, Turkey	NRCS	2020-2021	Patients treated with nivolumab as a second-line or later therapy, 18 or older, with a histologically confirmed renal cell carcinoma diagnosis and had undergone an abdominal computed tomography examination within one month before starting nivolumab treatment.	Patients with comorbidities that could impact CXI laboratory components.
Blauwhoff-Buskermolen, 2017, 28447434, Netherlands	NRCS	NR	Patients aged 18 years or older with advanced prostate, lung, breast, or colorectal cancer who were scheduled for palliative chemotherapy treatment	Systemic treatment in the past month, clinically overt ascites or serious pitting edema, and missing values for one of the muscle measurements were exclusion criteria.
Cavka, 2023, 36839402, Slovenia	NRCS	2016-2018	Patients with early metastatic castrate-resistant prostate cancer.	Cognitive impairment, ECOG performance status ≥ 3, previous nutritional counseling within the last six months, inserted heart device (at the time of recruitment, it was the contraindication for bioimpedance analysis), and unwillingness to participate.
Chen, 2019, 31564970, China	NRCS	2014-2016	Gastric cancer who underwent subtotal gastrectomy.	Patients lacking imaging data.
de Oliveira, 2023, 37224572, Brazil	NRCS	2019-2021	Patients aged 18 or older, with confirmed histopathologic diagnosis of advanced-stage malignant neoplasm, regardless of tumor location; KPS >= 30%; initiating enteral nutrition; no confirmed diagnosis of infectious diseases (including, as of the COVID-19 pandemic, no confirmed diagnosis of severe acute respiratory syndrome coronavirus 2); ability to provide the necessary information to complete the PG-SGA SF; and informed consent (by reading and signing the informed consent form).	Withdrawal of consent to participate in the research (for any reason) and absence of a KPS in the medical records within ~30 days of baseline.

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria
Fearon, 2006, 16762946, UK	NRCS	NR	Lost ≥ 5% of their pre-illness stable weight during the previous 6 months, had a ≤60, and had a life expectancy > 2 months.	Undergone surgery, endoscopic stenting, radiotherapy, or chemotherapy during the previous 4 weeks; had other active medical conditions (major gastrointestinal disease, chronic renal failure, uncontrolled diabetes, and HIV); a body mass index > 30; or received medication that could profoundly modulate metabolism or weight.
Fukuta, 2019, 30316109, Japan	NRCS	2015-2017	Patients with gastric or colorectal cancer ≥60 years of age who were scheduled to undergo curative surgery were eligible.	Experiencing simultaneous cancers or missing data.
Go, 2020, 32423395, Korea	NRCS	2004-2017	DLBCL patients treated with R-CHOP as first-line treatment, ≥18 years, with baseline CT scans for chest and abdomen, and the records for height, body weight, and serum albumin level measured within a week before the beginning of R-CHOP.	Active infections, double primary malignancy, histologic transformation from low-grade lymphoma, and lack of information for the NCCN-IPI at the time of measurement of Geriatric Nutritional Risk Index and sarcopenia.
Go, 2021, 34676685, Korea	NRCS	2004-2020	Patients diagnosed with DLBCL, age ≥18 years and availability of the data required to calculate CXI measured within one (laboratory test) or 2 (CT scans) weeks before the initiation of R-CHOP.	Patients with double primary cancers and active infection and in whom the enhanced International Prognostic Index designed using the NCCN-IPI could not be calculated.
Go, 2021, 34001060, Korea	NRCS	2006-2020	Consecutive male small-cell lung cancer patients receiving etoposide or irinotecan plus platinum combination chemotherapy as first-line treatment (with or without radiotherapy).	Female patients, with another type of cancer and/or a serious active infection.
Goh, 2022, 35538112, Korea	NRCS	2018-2020	Patients with advanced HCC who were treated with lenvatinib as a first-line systemic therapy.	
Gong, 2022, 36139560, China	NRCS[a]	2016-2021	Pathology confirmed gastric cancer ; adult patients; no history of neoadjuvant therapy; the abdominal CT scan was performed in our hospital.	Inability to tolerate radical or palliative surgery; a history of other malignancies.
Hamura, 2022, 35947886, Japan	NRCS	2008-2020	NR	NR
Hayashi, 2021, 34795523, Japan	NRCS	2015-2018	NR	NR

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria
Hou, 2022, 35804906, Taiwan	NRCS	2011-2021	Advanced pancreatic cancer patients.	NR
Jafri, 2015, 26604850, USA	NRCS	2000-2011	Patients diagnosed with stage IV NSCLC.	Patients were excluded if they had prior history of NSCLC presenting with relapse, prior history of another cancer in the preceding 5 years, and those with incomplete medical information or follow-up.
Jones, 2022, 35488469, USA	NRCS	2014-2019	Patients who underwent head and neck cancer ablation and free tissue reconstruction.	Presence of distant metastatic disease, presence of secondary primary malignancy, no malignancy on final histopathology, non-squamous cell carcinoma, HPV/p16-positive disease, presence of autoimmune deficiency (e.g., AIDS) or immunosuppression, and no 30-day preoperative abdominal CT scan to determine sarcopenia.
Kamada, 2023, 36725756, Japan	NRCS	2010-2020	Patients who underwent laparoscopic R0 colorectal resection for colorectal cancer.	Patients who had stage 0 or IV colorectal cancer, multiple cancers, perioperative death, who underwent emergency surgery, and who had missing data on clinicopathological factors and follow-up were excluded
Karmali, 2017, 28417157, USA	NRCS	1991-2015	Patients diagnosed with DLBCL and mantle cell lymphoma .	Patients who did not have baseline imaging of high quality available in our electronic imaging database for measures of muscle indices (as described below).
Kwon, 2017, 28000343, Korea	NRCS	2006-2012	Patients with advanced stage head and neck squamous cell carcinoma treated with curative intent.	Age under 18 years at diagnosis, tumors of nasopharyngeal or paranasal sinus origin, distant metastases, a previous cancer within 5 years, synchronous SPCs, and a loss of survivor follow-up within 1 year.

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria
Madeddu, 2023, 36831431, Italy	NRCS	2017-2021	Patients that met the following criteria: Stage IV histologically proven NSCLC eligible for nivolumab or pembrolizumab monotherapy, age ≥18 years, measurable disease according to RECIST 1.1 assessed by CT before starting the immunotherapy (no more than one month earlier), ECOG PS 0–2, and laboratory liver and renal function values in accordance with standardized approved criteria for ICI treatment (bilirubin, alkaline phosphatase and transaminase levels < 1.5 × normal upper limits; sodium > 125 mmol/L; normal calcium; creatinine clearance > 40 mL/min).	Active malignancy other than NSCLC, EGFR/ALK/ROS1 oncogene-addicted NSCLC, diagnosis of concomitant autoimmune disease in an active phase, previous or concomitant episode of thyroiditis or hypophysitis, acute cardiac failure and unstable coronary angina, presence of symptomatic brain metastases or metastases requiring high-dose steroid therapy, serological positivity for hepatitis B or C viruses and HIV, baseline aspartate amino transferase levels >2.5 times the normal levels and baseline total bilirubin levels ≥3 times the normal levels, pregnant women or lactating mothers, and inability to provide verbal or written informed consent.
Morimoto, 2021, 34290909, Japan	NRCS	2019-2020	Patients with non-small cell lung cancer.	Patients had been treated with steroids, patients had incomplete body weight assessment findings during the study period, missing laboratory results, the EGFR and ALK mutation status was not assessed in 5 patients, and 2 patients received chemoimmunotherapy before tyrosine kinase inhibitors administration
Nakashima, 2023, 37663966, Japan	NRCS	2011-2019	Patients who underwent laparoscopic or robotic gastrectomy.	Patients with remnant gastric cancer and locally advanced unresectable tumors.
Namikawa, 2022, 35322296, Japan	NRCS	2007-2019	Patients with unresectable advanced or recurrent gastric cancer who were treated with systemic drugs, including cytotoxic or molecular targeted agents.	NR
Orell-Kotikangas, 2017, 28125312, Finland	NRCS	NR	Patients with histologically verified diagnosis of head and neck squamous cell carcinoma.	Renal failure (creatinine >1.5-times upper limit of normal), hepatic failure (serum bilirubin >1.5-times upper limit of normal), heart failure, and palliative intent of treatment.
Poisson, 2021, 34519440, France	NRCS	NR	Cancer patients >70 years old. Referred for geriatric assessment prior to treatment choice and initiation. Patients with complete weight loss and SARC-F data.	Missing weight loss complete data. Missing SARC-F Score.
Rounis, 2021, 34584855, Greece	NRCS	2017-2020	Be candidates for receiving treatment with programmed cell death protein 1 (PD1) /programmed death ligand 1 (PD-L1) inhibitors for metastatic NSCLC	Individuals with EGFR mutations or ALK translocations were excluded before the initial screening.

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria
Ruan, 2021, 34737602, China	NRCS	2012-2019	Age of 18 years and older, hospitalization time of 2 days or longer, diagnosis of cancer, and existence of signed consent form.	Age of less than 18 years, hospitalization of less than 2 days, refusal to sign the consent form, and admitted to ICU at the beginning of recruitment.
Shen, 2023, 36938648, China	NRCS	2015-2022	Age ≥18; radical surgery for pancreatic ductal adenocarcinoma; available abdominal CT scans within 1 week before the operation	Patients undergoing palliative surgery; with liver or other sites metastasis; cases with a history of severe metabolic disease or other cancers within 5 years; patients without any follow-up information.
Shimagaki, 2023, 2022782042, Japan	NRCS	2014-2021	NR	The cases that resulted in non-resection were excluded from the analysis.
Silva, 2020, 31377013, Brazil	NRCS	2016-2018	Age ≥20 years old, KPS >= 30%, and ability to answer the necessary information and/or accompanied by someone capable of it.	NR
Takahashi, 2023, 36802232, Japan	NRCS	2008-2020	NR	Patients undergoing 2-stage operation (n = 5) and those without perioperative CT (n = 2) were excluded.
Takano, 2023, 37043018, Japan	NRCS	2014-2020	NR	33 patients were excluded (1 patient for postoperative mortality, 22 patients for additional resection after endoscopic mucosal resection, 5 for T stage 4b, and 5 for insufficient data).
Tan, 2023, 36880286, Tan	Validation[a]	2020[a]	Individuals aged ≥18 years who underwent abdominal surgery for digestive tract cancer (liver, gallbladder, pancreatic, gastric, or colorectal cancer)	No complete clinical data for the diagnosis of cachexia, underwent emergency, or had a previous cancer history.
Tanji, 2022, 36338593, Japan	NRCS	2007-2017	NR	NR
Thoresen, 2013, 22695408, Norway and Canada	NRCS	2004-2006	Histopathologically or cytodiagnostically confirmed adenocarcenoma of the colon and rectum at stage IV, 18 and older, and able to communicate freely in English (for Canada recruitment).	Too confused to fill in the questionnaires; individuals who were pregnant, had a pacemaker, or were HIV+ (Canada recruitment).
Ueshima, 2023, 36436335, Japan	NRCS	2019-2020	Patients with cancer who were supported by a palliative care team	Patients whose data were missing information about SARC-F, percentage of weight loss in the previous 6 months, anorexia, calf circumference, and the presence of edema.
Van der Meij, 2013, 23153477, Netherlands	NRCS[a]	2005-2008	Histologically or cytologically proven stage III NSCLC; life expectancy of at least 3 months	Surgery, chemotherapy, or radiation during the previous month; edema, ascites, or severe co-morbidities; those who used high-dose corticosteroids or fish oil

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria
van der Werf, 2018, 30235002, Netherlands	NRCS	NR	Patients diagnosed with metastasized colorectal cancer, were scheduled for first-line palliative chemotherapy with capecitabine monotherapy, capecitabine and oxaliplatin (CAPOX), or infusional 5-fluorouracil and oxaliplatin (FOLFOX) and had a World Health Organization performance score of 0–2.	NR
Vanhoutte, 2016 27843571, Belgium	NRCS	2012-2013	Ambulatory patients with cancer of 18 years or more, with digestive, lung, breast, or head/neck tumors, with WHO performance status of 0–2, without a pacemaker and who received previous therapy admitted to a standard care facility and provided signed informed consent were eligible for the study.	NR
Wan, 2022, 36212479, China	NRCS[a]	2020-2021	Patients with colorectal cancer undergoing radical surgery, between 18 and 80 years, with the preoperative CT scan being performed in the corresponding hospital of this study.	Patients undergoing emergency or non-radical surgery; having a history of other malignancies.
Wang, 2023, 37454609, China	Validation[a]	2019-2021	Patients with esophageal, gastric, colorectal, hepatic, pancreatic, or biliary cancer, over 18 years, ability to give informed consent, being conscious and cooperative, ability to tolerate a physical performance evaluation, and no history of prior gastrointestinal surgery.	Patients with a final pathology of benign disease were excluded during data analysis.
Wiegert, 2021, 34004417, Brazil	Validation	2016-2020	Incurable cancer (locoregional advanced or metastatic cancer proven by histologic, cytologic, or radiologic evidence); not receiving any antineoplastic treatment with curative intent; age ≥20; both sexes; and KPS ≥ 30%. KPS scores (ranging from 0 [death] to 100 [full function]) were assigned according to patient-reported daily physical function.	NR
Wiegert, 2020, 32927241, Brazil	Validation[a]	2016-2020	Generalized malignant disease or advanced local tumor growth and were not receiving any antineoplastic treatment with curative intent. Incurable cancer, both sexes, age ≥20 y, and KPS ≥30%.	NR
Willemsen, 2023, 36583567, Netherlands	NRCS	2018-2021	Patients with head and neck squamous cell carcinoma, were treated with primary or adjuvant CRT/BRT with curative intent between October 2018 and July 2021.	Histopathology other than squamous cell carcinoma, reirradiation of the head and neck, a second primary cancer, a history of stroke and/or a neurodegenerative disorder (*eg*, myotonic dystrophy, Parkinson's disease), and a history of total laryngectomy or total glossectomy.

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Inclusion Criteria	Exclusion Criteria
Xie, 2023, 36447437, China	Validation	2012-2020	Patients with histopathologically confirmed malignancy, with complete serological and anthropometric data and patients over 18 years of age who voluntarily agreed to participate in this study.	Patients with clinical evidence of active infection or severe systemic immunodeficiency disease; patients admitted to the intensive care unit at the beginning of recruitment; and patients with a hospital stay of <48 hours.
Zhuang, 2022, 34797480, China	NRCS	2014-2019	Gastric cancer patients who underwent curative gastrectomy with histological evidence of gastric adenocarcinoma, available abdominal CT, and no severe cognitive impairment.	Patients who eventually suffered from motor system diseases and were unable to complete the measurement of handgrip strength and gait speed, patients who received neoadjuvant chemotherapy, and patients with multiple tumors.
Zopf, 2020, 2002952037, Germany	NRCS[a]	2014-2014	70 years old, only when no severe cognitive disorders were present, a measurement BIA in a standing position was possible, there was no end-of-life situation and the patients were able to communicate and answer to questions.	NR

Notes. [a] Validation study comparing cachexia instruments; [b] Application cohort only.

Abbreviations. BIA=bioelectrical impedance analysis; BRT=bioradiotherapy; CRT=chemoradiotherapy; CT=computed tomography; CXI=cachexia index; DLBCL=diffuse large B-cell lymphoma; ECOG=Eastern Cooperative Oncology Group; EGFR=estimated glomerular filtration rate; HCC=hepatocellular carcinoma; ICU=intensive care unit; KPS=Karnofsky performance status; NCCN-IPI=International Prognostic Index designed using the National Comprehensive Cancer Network database; NR=not reported; NRCS=nonrandomized comparative study; NSCLC=non-small cell lung cancer; PGS-GA=Patient-Generated Subjective Global Assessment; R-CHOP=rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone; RECIST=Response Evaluation Criteria in Solid Tumors version 1.1; SARC-F=strength, assistance walking, rising from a chair, climbing stairs, and falls; WHO=World Health Organization.

BASELINE CHARACTERISTICS

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Akaoka, 2022, 36371905	213	NR	Median 68 (61-74)	171 (80.3)	Hepatocellular carcinoma 213 (100)	NR	Tumor differentiation Poor 31 (15)	Previous treatment: Hepatic resection 213 (100) Anatomical resection 135 (63) Treatment for recurrence: Surgical resection 39 (32) RFA 16 (13) Chemoradiotherapy 8 (6.6) TACE/TAI 40 (33) BSC 10 (8.2)	HBsAg positive 45 (21) HCV-Ab positive 63 (30)
Aslan, 2022, 36137881	52	NR	<65: 30 (58) ≥65: 22 (42)	38 (73)	Renal cell carcinoma 52 (100)	Advanced 52 (100)	Metastatic 52 (100)	Nivolumab 52 (100) Nephrectomy 37 (71) 1 prior systemic therapy 32 (62) 2 prior systemic therapies 20 (38)	Chronic liver[a] disease 0 (0) Nephrotic syndrome[a] 0 (0) Autoimmune diseases[a] 0 (0) Systemic infection (that could affect the CXIs laboratory components)[a] 0 (0)

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Blauwhoff-Buskermolen, 2017, 28447434	241	NR	64 (10)	130 (54)	Colorectal 76 (31) Lung 86 (36) Breast 36 (15) Prostate 43 (18)	III–IV: lung cancer 87 (36) IV: colon/rectal cancer 76 (31) prostate cancer 43 (18) breast cancer 36 (15)	-	Treatment line First 190 (79) Second 31 (13) Higher than second 20 (8) Surgery in past 6 months 37 (15)	NR
Cavka, 2023, 36839402	75	NR	Median 74.1 (68.6-79.4)	75 (100)	Prostate cancer 75 (100)	Advanced 75 (100)	-	First line 73 (97.3) Second line 49 (65.3) Third Line 31 (41.3) >3 lines 26 (34.7)	NR
Chen, 2019, 31564970	575	NR	64.41 (10.6)	433 (75.3)	Gastric cancer 575 (100)	I: 185 (32.2) II: 124 (21.6) III: 266 (46.2)	Differentiated 422 (73.4%)	Subtotal gastrectomy 575 (100)	Charlson score 0: 293 (51.0) 1–3: 260 (45.2) 4–6: 22 (3.8)
De Oliveira, 2023, 37224572	180	62 (34.4), white skin color	<60: 76 (42.2) ≥60: 104 (57.8)	73 (40.6)	GIT 49 (27.2) Gynecologic 45 (25.0) Head and neck 26 (14.4) Breast 21 (11.7) Lung 9 (5.0) Skin, bones, and soft tissues 9 (5.0) Others 21 (11.7)	NR	Distant metastasis No 157 (87.2)	NR	NR

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Fearon, 2006, 16762946	170	NR	67.9 (9.3)	90 (52.9)	Pancreatic cancer 170 (100)	II 89 (53) III/IV 79 (47)	Unresectable 170 (100)	No systemic treatment, Radiotherapy, resection, endoscopic stenting[a] (during the previous 4 wks) 170 (100)	Active medical conditions 0 (0)[a,b]
Fukuta, 2019, 30316109	98	NR	73.4[c]	70 (71.4)	Gastric 51 (52) Colorectal 47 (48)	Clinical stage 0-2: 78 (79.6) 3-4: 20 (20.4)		Surgical approach: Endoscopic 88 (89.8) Open 10 (10.2)	CCI 0: 42 (42.9) 1: 19 (19.4) ≥2: 37 (37.8)
Go, 2020, 32423395	228		64.5 (21, 88) ≤ 60: 96 (42.1) > 60: 132 (57.9)	130 (57.0)	Diffuse large B-cell lymphoma 228 (100)	Ann Arbor stage I – II: 100 (43.9) III – IV: 28 (56.1)	-	NR	Active infections 0 (0)[a] Double primary malignancy[a] 0 (0) Histologic transformation from low-grade lymphoma 0 (0)[a]
Go, 2021, 34001060	267	NR	68.1 (63, 73.8)	267 (100)	Small cell lung cancer 267 (100)	Limited stage 107 (40.1) Extensive stage 160 (59.9)	-	Etoposide and platinum 252 (94.4) Irinotecan and cisplatin 15 (5.6) Prophylactic cranial irradiation 115 (43.1)	NR
Go, 2021, 34676685	266	NR	Median 67.3 (57, 73.5)	150 (56.4)	Diffuse large B-cell lymphoma 266 (100)	Ann Arbor stage I-II 112 (42.1) III-IV 154 (57.9)	-	Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) immunochemotherapy 266 (100)	Active infection 0 (0)[a] Double primary Cancers[a] 0 (0)

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Goh, 2022, 35538112	116	NR	Median 60 (52, 67)	98 (82.4)	Hepatocellular carcinoma 116 (100)	BCLC stage C 105 (90.5)	-	Lenvatinib: 116 (100) Previous treatment a 84 (72.4)	Hypertension 38 (29.3) Diabetes 22 (19.0) Viral hepatitis 91 (78.4)
Gong, 2022, 36139560	324	NR	57.88 (11.96)	217 (67)	Gastric cancer 324 (100)	TNM stage: I: 90 (27.78) II: 77 (23.77) III: 124 (38.27) IV: 33 (10.19)	-	Postoperative adjuvant chemotherapy 275 (84.88) Surgery 324 (100)	Hypertension 51 (15.74) CHD 8 (2.47) Diabetes 23 (7.1) COPD 19 (5.86) Pulmonary infection 22 (6.79) Abdominal infection 10 (3.09)
Hamura, 2022, 35947886	124	NR	Median 70 (61–74)	94 (76)	Extrahepatic biliary tract cancer 124 (100)	TNM Stage I: 34 (27) II: 62 (50) III: 28 (23)	Tumor grade Well to moderate 103 (83) Poor 21 (17)	Resection 124 (100) Adjuvant-chemotherapy 63 (51)	NR
Hayashi, 2021, 34795523	192	NR	Median 60.2 [20, 78]	159 (82.8)	Head and neck cancer 192 (100)	I–III 115 (59.9) IV 77 (40.1)	-	Concurrent chemoradiotherapy (with cisplatin) 192 (100)	NR

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Hou, 2022, 35804906	232	NR	≤65: 139 (59.9) >65: 93 (40.1)	149 (64.2)	Advanced pancreatic cancer 232 (100)	III 60 (25.9) IV 172 (74.1)	Grade Well diff 15 (6.5) Moderately diff 85 (36.6) Poorly diff 43 (18.5) Unknown 89 (38.4)	CS + adj 24 (10.3) C/T 172 (74.1) C/T + local RT 36 (15.5)	NR
Jafri, 2015, 26604850	112	White 54 (48) Black 58 (52)	Median 57 [34–88]	78 (70)	Non-small cell lung cancer 112 (100)	Stage IV 112 (100)	-	Any chemotherapy 73 (65.2)	NR
Jones, 2022, 35488469	252	NR	61.5 (11.5)	164 (65.1)	Head and neck cancer 252 (100)	AJCC stage I-II: 40 (15.9) III: 51 (20.2) IV: 161 (63.9)	-	Head and neck free flap reconstruction 252 (100)	Hypothyroidism 53 (21.0) ECOG score 1.0 [0–1] mCCI 1.0 [0–2]
Kamada, 2023, 36725756	306	NR	Median 71.5 [39–96]	192 (63)	Colorectal cancer 306 (100)	I= 92 (30) II= 97 (32) III= 117 (38)	-	Laparoscopic R0 colorectal resection) 306 (100) Adjuvant chemotherapy 126 (41)	NR
Karmali, 2017, 28417157	86	NR	Median 64 <60:37 (43) ≥60: 49 (57)	40 (46.5)	Lymphomas 86 (100)	I/II: 31 (36) III/IV: 54 (63) Unknown: 1 (1)	-	DLBCL treatment n = 76 Chemotherapy[d] 76 (88.4) MCL treatment N = 10 Chemotherapy[e] 9 (10.5) Observed 1 (1.2)	NR

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Kwon, 2017, 28000343	361	NR	Median 60 [26–82]	302 (83.7)	Head and neck squamous cell carcinoma	III: 84 (23.3) IV: 277 (76.7)		No chemotherapy 177 (49) Surgery only 42 (11.6) Surgery + postoperative RT 122 (33.8) RT only 13 (3.6) With chemotherapy 184 (51) Surgery + postoperative CRT 25 (6.9) CRT 43 (11.9) Induction chemotherapy + surgery +/- postoperative RT/CRT 32 (8.9) Induction chemotherapy + RT/CRT 84 (23.3)	NR
Madeddu, 2023, 36831431	74		69.3 (11.3) [47–88]	54 (73)	Non-small cell lung cancer 74 (100)	IV 74 (100)	-	Nivolumab16 (43.2) Pembrolizumab 21 (56.8) Previous line 32 (43)	NR
Morimoto, 2021, 34290909	196		Median 69 [37–85]	142 (72.4)	Non-small cell lung cancer 196 (100)	III/IV: 159 (81.1)	-	Platinum + pemetrexed + pembrolizumab 96 (49.0) Carboplatin + paclitaxel /nab-paclitaxel + pembrolizumab 66 (33.7) Carboplatin + paclitaxel + bevacizumab + atezolizumab 29 (14.8) Carboplatin + pemetrexed + atezolizumab 5 (2.5)	NR
Nakashima, 2023, 37663966	175	NR	Median 70 [38–92]	119 (68)	Gastric cancer (adenocarcinoma) 175 (100)	TNM stage I: 99 (57) II: 38 (22) III: 38 (2)	-	Laparoscopic or robotic gastrectomy 175 (100) Adjuvant chemotherapy 60 (35)	NR

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Namikawa, 2022, 35322296	134	NR	Median 69 (63–76)	90 (67.2)	Advanced gastric cancer 134 (100)	NR	Disease status Initially metastatic 88 (65.7) Unresectable, recurrent 134 (100)	Number of chemotherapy regimens 1: 65 (48.5) 2 or more: 69 (51.5) Recession 0 (0) Note:	COPD 9 (6.72) Chronic kidney disease 12 (8.96) CHF 11 (8.21) Liver cirrhosis 9 (6.72) Diabetes mellitus 20 (14.93)
Orell-Kotikangas,	65	NR	Median 61 (61–64)	50 (76.9)	Head and neck cancer 65 (100)	I–II: 11 (17.0) III–IV: 53 (81.5)	-	Definitive (chemo) radiotherapy or combined treatment of surgery and post-operative (chemo)-radiotherapy 65 (100)	Comorbidities[a] Renal failure (creatinine >1.5-times upper limit of normal) 0 (0) Hepatic failure (serum bilirubin >1.5-times upper limit of normal) 0 (0) Heart failure 0 (0)

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Poisson, 2021, 34519440	1030	NR	Median 83 (79–87)	493 (47.9)	Breast 167 (16.2) Colerectal 157 (15.2) Upper gastrointestinal tract 144 (14.0) Lung 105 (10.2) Gynaecological 97 (9.4) Urinary tract 91 (8.8) Prostate 81 (7.9) Haematological 55 (5.3) Skin 44 (4.3) Head and neck 39 (3.8) Other 50 (4.9)	NR	Metastasis (missing n = 8) 40.7 (42.1)	**Current therapy:** (missing data n = 18) Surgery 302 (29.8) Radiotherapy 245 (24.2) Targeted therapy 75 (7.4) Hormone therapy 128 (12.6) Immunotherapy 38 (3.8) Supportive care 98 (9.7) **Prior therapy:** (missing data n = 1) in previous 12 months. Surgery 173 (54.4) Chemotherapy 89 (27.9) Radiotherapy 48 (15.1) Targeted therapy 15 (4.7) Hormone therapy 64 (20.1) Immunotherapy 7 (2.2)	CCI, Median (IQR) (missing data n = 37) 5 (3–7) Most frequent comorbidities: Rheumatologic disease 20.2% Renal disease 18.2% Chronic lung disease 14.4% Diabetes 13.1% CHF 12.9%
Rounis, 2021, 34584855	83	NR	Median 66 [39–81]	70 (84.3)	Non-small cell lung cancer 83 (100)	NR	-	Immunotherapy agent Nivolumab 54 (65.1) Pembrolizumab 26 (31.3) Atezolizumab 3 (3.6)	NR

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Ruan, 2021, 34737602	746	NR	72.00 (5.24)	489 (65.5)	Lung 164 (22.00) Gastric 170 (22.80) Colorectal 199 (26.70) Esophageal 90 (12.10) Hepatobiliary 32 (4.30) Pancreatic 19 (2.50) Breast 22 (2.90) Utero ovarian 21 (2.80) Nasopharyngeal 13 (1.70) Urological 11 (1.50) Other cancer subtypes 5 (0.70)	TNM stage I 50 (6.70) II 159 (21.30) III 200 (26.80) IV 337 (45.20		Radical resection 215 (28.8) Postoperative chemoradiotherapy 325 (43.6)	Diabetes 98 (13.1) Hypertension, yes 192 (25.7) CHD 70 (9.4)
Shen, 2023, 36938648	614	NR	59.9 (10.3)	368 (59.9)	Pancreatic ductal adenocarcinoma 614 (100)	0+I 312 (50.8) II+III 302 (49.2)	-	Radical surgery 614 (100) Postoperative chemotherapy 376 (61.7)	Diabetes 110 (17.9) Hypertension 133 (21.7)
Shimagaki, 2023, 2022782042	144	NR	69.3 (0.8)	84 (58.3)	Pancreatic ductal adenocarcinoma 144 (100)	pStage 1: 16 (11.1) 2: 91 (63.2) 3: 25 (17.36) 4: 12 (8.3)	-	Curative-intent pancreatectomy 144 (100) Adjuvant Chemotherapy 118 (81.9) Preoperative Chemotherapy 49 (34.0)	NR

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Silva, 2020, 31377013	1166	NR	62 (13.4)	500 (42.9)	GI tract 359 (30.8) Gynecology 196 (16.8) Head and Neck 155 (13.3) Lung 125 (10.7) Breast 118 (10.2) Skin 57 (4.9) Bones and soft tissues 39 (3.3) Others 117 (10.0)	Local Advanced 174 (14.9) Metastatic 992 (85.1)	-	Surgery 463 (39.7) Chemotherapy 701 (60.1) Radiotherapy 508 (43.6)	NR
Takahashi, 2023, 36802232	239	NR	Median 68.8 (62.1-72.7)	201 (84.1)	Esophageal cancer 239 (100)	cStageI-II: 139 (58.2) cStageIII-IV: 100 (41.8)	-	Esophagectomy followed by gastric tube reconstruction 239 (100) None/ESD 107 (44.8) Preoperative treatment, Chemotherapy or chemoradiation 132 (55.2)	CVD 19 (7.9) Pulmonary disease 48 (20.1) Diabetes 22 (9.2)
Takano, 2023, 37043018	396	NR	74.7[c] [23-98]	232 (58.6)	Colorectal cancer 396 (100)	Stage I–III 396 (100)	-	Radical resection 396 (100)	NR
Tan[f], 2023, 36880286	1693	NR	Median 64 (14) (Application cohort only)	1081 (63.9)	Liver 216 (12.8%) Gallbladder 74 (4.4%) Pancreas 78 (4.6%) Stomach 566 (33.4%) Colorectum 759 (44.8%)	I- 494 (29.2%) II- 551 (32.5%) III- 464 (27.4%) IV- 184 (10.9%)	Cancer grade Differentiated 836 (49.4%) Undifferentia-ted 857 (50.6%)	Abdominal surgery 1693 (100)	Co-morbidity 513 (30.3) Respiratory co-morbidity 23 (1.4%) Cardiovascular co-morbidity 446 (26.3%) Diabetes 156 (9.2%)

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Tanji, 2022, 36338593	118	NR	Median 66 [60–75]	81 (68.6)	Colorectal cancer 118 (100)	T factor T1: 2 (1.7) T2: 5 (4.2) T3: 72 (61.0) T4: 39 (33.1)	-	Initial hepatic resection for CRLM 118 (100) Neoadjuvant chemotherapy 41 (34.7)	NR
Thoresen, 2013, 22695408	77	NR	Median 63 (22-85)	41 (53)	Colorectal carcinoma (adenocarcinoma) 77 (100)	Stage IV 77 (100)	-	Radiation pre-surgery 12 (15.6) Surgery 65 (84.4) Intended to be treated with chemotherapy 66 (85.7)	NR
Ueshima, 2023, 36436335	196	NR	65.8 (14)	83 (42.3)	Head and neck 33 (16.8) Lung 29 (14.8) Liver/Biliary/Pancreas 27 (13.8) Breast 21 (10.7) Gastroesophageal 18 (9.2) Colorectal 16 (8.2) Others 52 (26.5)	Cancer stage Local advanced 44 (22.4) Metastatic 152 (77.6)	-	Chemotherapy 66 (33.7) Radiotherapy 12 (6.1) Chemoradiotherapy 21 (10.7) Surgery 8 (4.1) Palliative care alone 89 (45.4)	NR
van-der-Meij-2013-23153477	40	NR	57.8 (10.1)	21 (52.5)	NSCLC 40 (100)	IIIa= 16 (40) IIIb= 24 (60)	-	Patients were included at the start of chemoradiotherapypay 40 (100) Treatment during the previous month[a] Surgery 0 (0) Chemotherapy 0 (0) Radiotherapy 0 (0)	Edema, ascites or severe co-morbidities[a] 0 (0)
Van der Werf, 2018, 30235002	69	NR	65 (11)	46 (67)	Colorectal cancer 69 (100)	NR	-	CAPOX (-B) 53 (77) Capecitabine (-B) 8 (12) FOLFOX (-B) 8 (12)	NR

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Vanhoutte, 2016, 27843571	167		63.96 (11.04)	112 (67.1)	Breast 7 (4.2) GI tract 109 (65.3) Lung 32 (19.2) Head/neck 19 (11.4)	Cancer stage I: 21 (12.6) II: 23 (7.2) III: 21 (12.6) IV: 111 (66.5) V: 2 (1.2)	-	NR	NR
Wan, 2022, 36212479	379	NR	60.42 (11.06)	234 (61.7)	Colorectal cancer 379 (100)	TNM stage I 94 (24.8) II 142 (37.47) III 143 (37.73)	-	Radical surgery 379 (100) Postoperative adjuvant chemotherapy 255 (67.28)	Hypertension 75 (24.67) CHD 15 (4.12) Diabetes 38 (11.14)
Wang, 2023, 37454609	10568	NR	64.0 (56.0, 70.0)	6791 (64.3)	HPB 2048 (19.4) Gastroesophageal 3618 (34.2) Colorectal 4092 (46.4)	III-IV: 4353 (41.2)	-	Surgery 10 390 (98.3)	NR
Wiegert, 2020, 32927241	1384	White 595 (43.0) Black 229 (16.5) Other 560 (40.5)	61.7 (13.4)	604 (43.6)	Gastrointestinal tract 445 (32.2) Gynecology 229 (16.6) Head/neck 241(14.5) Lung 141 (10.2) Breast 144(10.4) Skin 60 (4.3) Bones and soft tissues 47 (3.4) Leukemia, lymphomas, myeloma 17 (1.2) Others 100 (7.2)	Locally advanced 204 (14.7) Metastatic 1180 (85.3)	-		

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Wiegert[f], 2021, 34004417	443	NR	61.7 (13.3) <65: 274 (61.8) ≥65: 169 (38.2)	180 (40.5)	Digestive system 159 (35.9) Gynecological 91 (20.5) Head and neck 32 (7.2) Breast 46 (10.4) Lung 46 (10.4) Others 69 (15.5)	Locoregional advanced 90 (20.3) Distant metastasis 353 (79.7)	-	Antineoplastic treatment with curative intent[a] 0 (0)	NR
Willemsen, 2023, 36583567	66	NR	Median 61 (13)	50 (75.75)	Head and neck squamous cell carcinoma 66 (100)	I: 15 (22.73) II: 9 (13.64) III: 21 (31.82) IVabc: 21 (31.82)	-	Adjuvant CRT (cisplatin with radiotherapy) 6 (9.1) Primary CRT (cisplatin with radiotherapy 49 (74.24) Primary BRT (cetuximab wit radiotherapy) 11 (16.7)	Second primary cancer[a] 0 (0)

Author, Year, PMID	N Analyzed	Race /Ethnicity, N (%)	Age (Years), Mean, (SD) Median (IQR) [Range]	Male, %	Type of Cancer, N (%)	Stage of Cancer, N (%)	Other Cancer Details	Cancer Treatments Received, N (%)	Comorbidities, N (%)
Xie[g], 2023, 36447437	5270	NR	58.09 (10.57)	2389 (45.3)	Lung cancer= 1,708 (32.4) Esophagus cancer= 182 (3.5) Gastric cancer= 492 (9.3) Hepatic-biliary cancer= 201 (3.8) Pancreatic cancer= 114 (2.2) Colorectal cancer= 829 (15.7) Breast cancer= 1,208 (22.9) Gynecological cancer= 338 (6.4) Urologic cancer= 64 (1.2) Nasopharynx cancer= 23 (0.4) Other cancer= 111 (2.1)	I: 829 (15.7) II: 1,304 (24.7) III: 1,379 (26.2) IV: 1,758 (33.4)	-	Surgery 3,513 (66.7) Radiotherapy 550 (10.4) Chemotherapy 3,460 (65.7)	Hypertension 993 (18.8) Diabetes 509 (9.7) Active infection or severe systemic immunodeficient-cy disease[a] 0 (0)
Zhuang, 2022, 34797480	1215	NR	Median 65.0 (14.0)	886 72.9)	Gastric Cancer 1215 (100)	TNM stage I: 452 (37.2) II: 286 (23.5) III: 477 (39.3)	-	Radical gastrectomy 1215 (100)	CCI 0-1: 1105 (90.9) ≥2: 110 (9.1)
Zopf, 2020, 2002952037	100	NR	75.6 (4.7)	22 (66.7)	Gastro-intestinal 63.6% Bronchial carcinomas 15.2%	NR	NR	NR	CCI 1.6 (2.4) Malnourished 7 (21.2)

Notes. [a] Extracted from exclusion criteria, [b] Active medical conditions = major gastrointestinal disease, chronic renal failure, uncontrolled diabetes, and HIV; [c] Calculated by research team; [d] Number of patients received chemotherapy as following: R-CHOP = 67, DA-EPOCH = 7, R-CHOP + bortozemib = 1, HyperCVAD = 1; [e] Number of

patients received chemotherapy as following: R-CHOP ± botezomib = 3; Rituximab ± bortezomib = 2; hyperCVAD ± bortezomib = 3; bendamustine, rituximab = 1; [f] These data are related to validation cohort only; [g] The data are related to external validation cohort only.

Abbreviations. BCLC=Barcelona Clinic Liver Cancer, BR=bendamustine, rituximab; BRT=bioradiotherapy; BSC=best supportive care; CCI=Charlson Comorbidity Index; CHD=coronary heart disease, CHF=congestive heart failure; CKD=chronic kidney disease, COPD=chronic obstructive pulmonary disease; CRLM=colorectal liver metastases; CRT=chemoradiotherapy; CS=conversion surgery; C/T=chemotherapy; DA-EPOCH=dose adjusted-etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin; DLBCL=diffuse large b-cell lymphoma, DM=diabetes mellitus, ED=extensive disease; HPB=hepatopancreatobiliary; hyperCVAD=cyclophosphamide, doxorubicin, vincristine, and prednisone alternating with high-dose methotrexate, and cytarabine; IQR=interquartile range; LD=limited disease, MCL=mantle cell lymphoma; N=sample size; PMID=PubMed ID; R-CHOP=rituximab-cyclophosphamide; RFA=radiofrequency ablation; RT=radiotherapy; SD=standard deviation; TACE=transcatheter arterial chemoembolization; TAI=transcatheter arterial infusion chemotherapy; wks=weeks.

KQ2 OUTCOMES

Overall Survival

Author, Year, PMID	Assessment/Tool Cachexia	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
International Consensus/Fearon 2011					
Blauwhoff-Buskermolen, 2017, 28447434	International consensus/Fearon 2011	NR	Cachexia vs No cachexia (using MUAMA for muscle)	2.00 (1.42, 2.83)	<0.001
	International consensus/Fearon 2011	NR	Cachexia vs No cachexia (using CT for muscle)	1.64 (1.15, 2.34)	0.006
	International consensus/Fearon 2011	NR	Cachexia vs No cachexia (using BIA for muscle)	1.50 (1.05, 2.14)	0.025
Chen, 2019, 31564970	International consensus/Fearon 2011	Estimated 50(mo)[a]	Cachexia vs No cachexia	1.46 (1.07, 1.98)	0.017
Gong, 2022, 36139560	International consensus/Fearon 2011	Estimated 20 (mo)	Cachexia vs No cachexia	0.99 (0.65, 1.52)	0.99
Hayashi, 2021, 34795523	International consensus/Fearon 2011	3 (y)	Cachexia vs No cachexia	4.31 (1.93, 9.61)	<0.01
Hou, 2022, 35804906	International consensus/Fearon 2011	Estimated 24 (mo)[a]	Cachexia vs No cachexia	2.23 (1.47, 3.38)	0.000
Madeddu, 2023, 36831431	International consensus/Fearon 2011	Median 24 (mo) (range: 5-63)	Cachexia vs No cachexia	0.78 (0.41, 1.47)	0.4392
Poisson, 2021, 34519440	International consensus/Fearon 2011	Median 6.1 (mo) (range: 0.03-30.3)	Cachexia vs No cachexia	1.49 (1.05, 2.11)	0.024
Rounis, 2021, 34584855	International consensus/Fearon 2011	6 (mo)	Cachexia vs No cachexia	2.52 (1.4, 4.55)	0.002
Ruan, 2021, 34737602	International consensus/Fearon 2011	1-5 (y)	High-risk group (satisfying 3 diagnostic criteria) vs low-risk group (satisfying only 1 or 2 diagnostic criteria)	1.40 (1.078, 1.819)	0.012

Author, Year, PMID	Assessment/Tool Cachexia	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
Shen, 2023, 36938648	International consensus/Fearon 2011	Estimated 70 (mo)[a]	Cachexia vs No cachexia	1.46 (1.14, 1.89)	< 0.01
Thoresen, 2013, 22695408	European Palliative Care Research Collaborative (*ie*, Fearon 2011)	Estimated 5 (y)[a] or until death	Cachexia vs No cachexia	1.54 (0.88, 2.71)	0.13
Vanhoutte, 2016, 27843571	International consensus/Fearon 2011	Estimated 15 (mo)[a]	Cachexia vs No cachexia	1.82 (1.19, 2.77)	0.006
Zhuang, 2022, 34797480	International consensus/Fearon 2011	Median 39 (mo)	Cachexia vs No cachexia	1.54 (1.21, 1.94)	0.001
Zopf, 2020, 31561063	International consensus/Fearon 2011	3.5 (y)	Cachexia vs No cachexia	2.37 (1.174, 4.764)	0.016
Cancer Cachexia Index (CXI)					
Akaoka, 2022, 36371905	Cachexia index (CXI)	5 (y)	Low CXI vs High CXI	5.31 (2.03, 13.9) *According to the status of CXI by propensity score-matched analysis, Low CXI was not associated with disease-free survival (p = 0.940), but it was significantly associated with worse overall survival (p = 0.041)*	<0.01
Aslan, 2022, 36137881	Cachexia index (CXI)	Median 11.4 (mo) (range: 0.7-63) (48 mo for High CXI group, 7 mo for low CXI group)	Low CXI vs High CXI (CXI cutoff: median 39.32)	7 (1.9, 26)	0.003
Go, 2021, 34676685	Cachexia index (CXI)	Median 56.6 (mo)	Intermediate CXI vs High CXI[c]	1.72 (0.99, 2.97)	0.054
	Cachexia index (CXI)	Median 56.6 (mo)	Low CXI vs High CXI[c]	2.10 (1.28, 3.46)	0.003
	Cachexia index (CXI)	Median 41 (mo)	Low CXI vs High CXI	2.39 (1.37, 4.17)	0.002

Author, Year, PMID	Assessment/Tool Cachexia	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
Go, 2021, 34001060			(Limited-stage disease) (CXI cutoff: 5.82)		
	Cachexia index (CXI)	Median 41 (mo)	Low CXI vs High CXI (Extensive-stage disease) (CXI cutoff: 3.83)	2.27 (1.53, 3.37)	<0.001
Goh, 2022, 35538112	Cachexia index (CXI)	Median 5.3 (mo) (range 3.4-8.2)	Low CXI vs High CXI (CXI cutoff: 53)	2.07 (1.17, 3.65)	0.01
Gong, 2022, 36139560	Cachexia index (CXI)	Estimated 20 (mo)	Low-CXI vs High-CXI (mean CXI: 146.20 (54.24) in high CXI group and 64.35 (20.97) in low CXI group)	2.22 (1.45, 3.45)[d]	<0.001
Hamura, 2022, 35947886	Cachexia index (CXI)	2.9 (y) (IQR:1.6 to 5.6)	Low CXI vs High CXI (CXI cutoffs: 0.21 for male and 0.07 for female)	1.94 (1.04, 3.61)	0.04
Jafri, 2015, 26604850	Cachexia index (CXI)	Estimated 30 (mo)[a]	Stage II cachexia vs Stage I cachexia (CXI Cutoff: 35)	1.53 (1.01, 2.34)	0.0459
Kamada, 2023, 36725756	Cachexia index (CXI)	Median 51.9 (mo) (range: 3.6-115.2)	Low CXI vs High CXI (Cutoffs: 8.4 for males and 5.6 for females)	2.35 (1.31, 4.21)	0.004
Karmali, 2017, 28417157	Cachexia index (CXI)	Median 59.5 (mo)	Cachexia vs No cachexia (CXI Cutoff: 49.8)	3.11 (1.10, 8.77)	0.032
Nakashima, 2023, 37663966	Cachexia index (CXI)	3 (y)	Cachexia low vs Cachexia high	4.07 (1.35, 12.3)	0.01
Shimagaki, 2023, 37927935	Cancer Cachexia Index (CXI)	Estimated 5 (y)[a]	Low CXI vs High CXI (Cutoffs: 22.9 for Men, 16.58 for Women based on Tanji et al 2022)	3.14 (1.71, 5.75)	0.0002
Takahashi, 2023,	Cancer Cachexia Index (CXI)	Median 37 (mo) (range: 2-143)	Low CXI vs High CXI[b]	1.95 (1.25, 3.04)	< 0.01

Author, Year, PMID	Assessment/Tool Cachexia	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
36802232			(Cutoffs: 75 based on ROC curve)		
Tanji, 2022, 36338593	Cancer Cachexia Index (CXI)	Median 3.03 (y)	Low CXI vs High CXI (Cutoffs: 22.9 for men, 16.58 for women)	5.88 (1.75, 20)[d]	< 0.01
Wan, 2022, 36212479	Cachexia Index (CXI)	Estimated 20 (mo)[a]	High CXI vs Low CXI (Cutoffs: <1087 for male, <1164 for female based on ROC curve and Youden index)	5.56 (1.27, 25)[d]	0.02
Evans					
Kwon, 2017, 28000343	Evans	Median 57.6 (mo) (range: 12.3-103.9)	Patients with cachexia at pretreatment or immediately after treatment but not there after vs patients without cachexia at all time periods	1.12 (0.66, 1.91)	0.676
	Evans	Median 57.6 (mo) (range: 12.3-103.9)	Patients with no cachexia at pretreatment or immediately after treatment but newly developed cachexia at 6- or 12-months post-treatment vs patients without cachexia at all time periods	5.84 (3.42, 9.97)	<0.001
	Evans	Median 57.6 (mo) (range: 12.3-103.9)	Patients with sustained cachexia both before and after treatment vs patients without cachexia at all time periods	7.43 (4.78, 11.56)	<0.001
Vanhoutte, 2016, 27843571	Evans	Estimated 15 (mo)[a]	Cachexia vs No cachexia	3.32 (2.15, 5.14)	<0.0001
Van-der-Meij, 2013, 23153477	Evans	80 (mo)	Cachexia vs No cachexia	4.2 (1.7, 10.0)	0.001

Author, Year, PMID	Assessment/Tool Cachexia	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
Zopf, 2020, 31561063	Evans	3.5 (y)	Cachexia vs No cachexia	2.82 (1.45, 5.48)	0.002
Studies Using Other Cachexia Assessment Tools or Combinations of Assessment Tools					
Cavka, 2023, 36839402	Nutritional status algorithm	Estimated 50-60 (mo)[a]	Cachexia vs Well-nourished	*We could not prove the significance of the Nutrition Status category for OS when accounting for potential confounding factors.*	-
Fearon, 2006, 16762946	Fearon 2006/Cancer Cachexia Study Group Criteria	6 (mo)	Met all 3 components of cachexia profile vs No	2.96 (NR)	<0.001
	Fearon 2006/Cancer Cachexia Study Group Criteria	6 (mo)	Met all ≥ 2 of 3 components of cachexia profile vs No	2.23 (NR)	<0.001
	Fearon 2006/Cancer Cachexia Study Group Criteria	6 (mo)	Met all 3 components of cachexia profile vs No (In patients with localized disease; stage II and II)	4.94 (NR)	<0.001
	Fearon 2006/Cancer Cachexia Study Group Criteria	6 (mo)	Met all ≥ 2 of 3 components of cachexia profile vs No (In patients with localized disease; stage II and II)	2.40 (NR)	<0.001
	Fearon 2006/Cancer Cachexia Study Group Criteria	6 (mo)	Met all 3 components of cachexia profile vs No (In patients with metastatic disease; stage IV)	NS	NS
	Fearon 2006/Cancer Cachexia Study Group Criteria	6 (mo)	Met all ≥ 2 of 3 components of cachexia profile vs No (In patients with metastatic disease; stage IV)	NS	NS
Go,2020, 32423395	Combination of GNRI and sarcopenia	Median 71.1 (mo)	High cachexia risk vs Low cachexia risk	3.35 (2.17, 5.17)	<0.001
Morimoto, 2021, 34290909	Evans 2008 and Fearon 2011	Median 13.8 (mo)	Cachexia vs No cachexia	1.27 (0.71, 2.27)	0.42

Author, Year, PMID	Assessment/Tool Cachexia	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
Namikawa, 2022, 35322296	Combined Evans, Fearon, and Hamauchi	Estimated 80 (mo)[a]	Cachexia within 6 mo of treatment vs No cachexia within 6 mo of treatment	1.34 (1.16, 2.09)	0.019
Orell-Kotikangas, 2017, 28125312	Combined MAMA and HGS	Median 68 (mo) (IQR: 20-77)	Cachexia vs No cachexia	2.8 (1.30, 6.13)	0.009
Silva, 2020, 31377013	Glasgow Prognostic score	2 (y)	Precachexia vs No cachexia (mGPS score: 1 vs 0)	2.00 (1.34, 2.98)	0.001
			Refractory cachexia vs No cachexia (mGPS: 2 vs 0)	2.45 (1.34, 2.98)	<0.001
Takano, 2023, 37043018	Cancer Cachexia Score (CCS)	NR	Severe cachexia vs Moderate or Mild cachexia (CCS score: 3-4 vs 2 or 0-1)	2.94 (1.81, 4.75)	<0.001
Tan, 2023, 36880286	Self-Developed Nomogram	Estimated 2 (y)	High vs Low Cancer Cachexia Risk (Cutoff of predictive probability of nomogram = 0.18)	7.80 (1.43, 42.48)	0.018
Thoresen, 2013, 22695408	Fearon 2006/Cancer Cachexia Study Group Criteria	Estimated 5 (y)[a] or until death	Cachexia vs No cachexia	2.26 (1.18, 4.32)	0.014
Wang, 2023, 37454609	Cancer Cachexia Staging Index (CCSI)	Median 76 (wk)	Mild or Moderate cachexia vs No cachexia (CCSI score: 9-18 vs <9)	2.17 (1.64, 2.88)	< 0.001
			Severe cachexia vs No cachexia (CCSI score: ≥ 19 vs <9)	3.99 (2.45, 6.49)	< 0.001
Wiegert, 2020, 32927241	Vigano 2017	90 (d) or Date of Death	Precachexia vs No cachexia	1.87 (1.28, 2.73)	0.001
			Cachexia vs No cachexia	2.39 (1.64, 3.49)	< 0.001

Author, Year, PMID	Assessment/Tool Cachexia	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
			Refractory cachexia vs No cachexia	2.87 (2.01, 4.10)	< 0.001
	Wallengren 2013	90 (d) or Date of Death	Cachexia vs No cachexia	2.21 (1.86, 2.62)	< 0.001
Wiegert, 2021, 34004417	Cachexia Staging System	180 (d)	Cachexia vs Precachexia	1.35 (1.12, 1.99)	0.002
			Refractory cachexia vs Precachexia	1.84 (1.21, 2.79)	0.004
Ueshima, 2023, 36436335	Cachexia Staging Score (CSS)	NR	Precachexia vs No cachexia (CSS score: 3-4 vs 0-2)	2.78 (0.62, 12.46)	0.182
			Cachexia vs No cachexia (CSS score: 5-8 vs 0-2)	4.77 (1.09, 20.80)	0.038
			Refractory cachexia vs No cachexia (CSS score: 9-12 vs 0-2)	11.00 (2.37, 51.07)	0.002
Van-der-Meij, 2013, 23153477	Modified Fearon 2011	80 (mo)	Precachexia vs No cachexia	0.78 (0.30, 2.03)	0.62
	Modified Fearon 2011	80 (mo)	Cachexia vs No cachexia	2.93 (1.03, 8.34)	0.04
Xie, 2023, 36447437	HGS-based Cancer Cachexia Index (CXI)	20.07 (12.17, 44.67) Median (IQR)	Low H-CXI vs High H-CXI (cutoffs: 175 for male, 113 for female based on standardized log-rank statistics of survival)	Continuous: 1.19 (1.12, 1.27)[d,e] Categorial: 1.61 (1.45, 1.79)[d,e]	Continuous <0.001 Categorial <0.001

Notes. [a] Estimated based on the figure of KM curve; [b] Including patients with and without osteopenia in both groups; [c] High-CXI group (high L3-CXI and high PM-CXI), intermediate-CXI group (high L3-CXI and low PM-CXI), and low-CXI group (low L3-CXI and low PM-CXI), cutoff values for L3-CXI and PM-CXI cut offs were 40.43 and 5.60, respectively; [d] The data were inverted by research team to reflect the Low vs High CXI; [e] External cohort only.

Abbreviations. d=day; EPCC=elderly patients with cancer cachexia (High risk = satisfying three diagnostic criteria at the same time, Low risk = satisfying only 1 or 2 diagnostic criteria); GNRI=Geriatric Nutritional Risk Index; HGS=hand grip strength; MAMA=mid-arm muscle area; mo=month; OS=overall survival; wk=week; y=year.

Disease-Free Survival

Author, Year, PMID	Assessment/Tool	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
Cachexia Index (CXI)					
Akaoka, 2022, 36371905	Cachexia index (CXI)	5 (y)	Low CXI vs High CXI	1.55 (1.04, 2.31)	0.03
Hamura, 2022, 35947886	Cachexia index (CXI)	2.9 (y) (IQR 1.6–5.6)	Low CXI vs High CXI (CXI cutoffs: 0.21 for male and 0.07 for female)	1.84 (1.05, 3.24)	0.03
Kamada, 2023, 36725756	Cachexia index (CXI)	Median 51.9 (mo) (range: 3.6-115.2)	Low CXI vs High CXI (Cutoffs: 8.4 for males and 5.6 for females)	2.27 (1.31, 3.90)	0.003
Nakashima, 2023, 37663966	Cachexia index (CXI)	3 (y)	Cachexia low vs Cachexia high	2.97 (1.01, 8.15)	0.03
Tanji, 2022, 36338593	Cachexia index (CXI)	Median 1.01 (y)	Low CXI vs High CXI (Cutoffs: 22.9 for men, 16.58 for women)	2.27 (1.02, 5.0)[1]	0.04
Studies Using Other Assessment Tools					
Orell-Kotikangas, 2017, 28125312	Combined MAMA and HGS	Median 68 (mo) (IQR: 20-77)	Cachexia vs No cachexia	2.8 (1.38, 5.82)	0.004
Takano, 2023, 37043018	Cancer Cachexia Score (CCS)	Unclear	Severe cancer cachexia vs mild or moderate	2.33 (1.55, 3.51)	<0.001
Zhuang, 2022, 34797480	International consensus/Fearon 2011	Median 39 (mo) (after surgery)	Cachexia vs No cachexia	1.53 (1.21, 1.94)	<0.001

Notes. [1] Data were flipped to reflect Low vs High CXI.

Relapse-Free Survival

Author, Year, PMID	Assessment/Tool	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
Takahashi, 2023, 36802232	Cachexia index (CXI)	Median 37 (mo) (range: 2-143)	Low CXI vs High CXI[b] (Cutoffs: 75 based on ROC curve)	1.58 (1.06, 2.34)	0.02
Tan, 2023, 36880286	Self-Developed Nomogram	Estimated 2 (y)	High vs Low cancer cachexia risk (Cutoff of predictive probability of nomogram = 0.18)	4.79 (1.80–12.78)	0.002

Progression-Free Survival

Author, Year, PMID	Assessment/Tool	Follow-Up	Comparator	Results HR (95% CI)	Reported p Value (HR)
International Consensus/Fearon 2011					
Hayashi, 2021, 34795523	International consensus/Fearon 2011	3 (y)	Cachexia vs No cachexia	3.51 (1.65, 6.01)	<0.001
Hou, 2022, 35804906	International consensus/Fearon 2011	Estimated 24 (mo)	Cachexia vs No cachexia	1.72 (1.10, 2.69)	0.017
Rounis, 2021, 34584855	International consensus/Fearon 2011	6 (mo)	Cachexia vs No cachexia	2.49 (1.49, 4.16)	<0.001
Van der Werf, 2018, 30235002	International consensus/Fearon 2011	Median 198 (d) (IQR:137–298)	Cachexia vs No cachexia	1.31 (0.75, 2.28)	0.339
Cachexia Index (CXI)					
Go, 2021, 34676685	Cachexia index (CXI)	Median 56.6 (mo)	Intermediate CXI vs High CXI[b]	1.63 (0.96, 2.76)	0.071
	Cachexia index (CXI)	Median 56.6 (mo)	Low CXI vs High CXI[b]	1.90 (1.19, 3.05)	0.007
Go, 2021, 34001060	Cachexia index (CXI)	Median 41 (mo)	Low CXI vs High CXI (Limited-stage disease) (CXI cutoff: 5.82)	2.45 (1.41, 4.25)	0.002
	Cachexia index (CXI)	Median 41 (mo)	Low CXI vs High CXI (Extensive-stage disease) (CXI cutoff: 3.83)	1.76 (1.20, 2.6)	0.004
Goh, 2022, 35538112	Cachexia index (CXI)	Median 5.3 (mo) (range 3.4-8.2)	Low CXI vs High CXI (CXI cutoff: 53)	1.84 (1.09, 3.09)	0.02
Jafri, 2015, 26604850	Cachexia index (CXI)	Estimated 30 (mo)[a]	Stage II cachexia vs Stage I cachexia (CXI cutoff: 35)	1.94 (1.27, 2.95)	0.0022
Karmali, 2017, 28417157	Cachexia index (CXI)	Median 59.5 (mo)	Cachexia vs No cachexia (CXI cutoff: 49.8)	1.67 (0.76, 3.66)[b]	0.2

Studies Using Other Assessment Tools					
Go,2020, 32423395	Combination of GNRI and sarcopenia	Median 71.1 (mo)	High cachexia risk vs Low cachexia risk	2.77 (1.83, 4.12)	<0.001
Morimoto, 2021, 34290909	Evans 2008 and Fearon 2011	Median 13.8 (mo)	Cachexia vs No cachexia	1.64 (1.06, 2.55)	0.03

Notes. [a] Estimated based on the figure of KM curve; [b] High-CXI group (high L3-CXI and high PM-CXI), intermediate-CXI group (high L3-CXI and low PM-CXI), and low-CXI group (low L3-CXI and low PM-CXI), cutoff values for L3-CXI and PM-CXI were 40.43 and 5.60, respectively; [b] 95% CI calculated by research team.

Function (QOL, ECOG, KPS, ADLs, Measures of Mobility, Exercise Tolerance, Fatigue, *etc*)

Author, Year, PMID	Assessment/Tool	Follow-Up	Definition	Comparator	Results OR (95%CI)	Reported p Value
Cavka, 2023, 36839402	Nutritional status algorithm	6 (mo)	Health-related quality of life (HRQoL)	Cachexia vs Well-nourished	1.75 (0.37, 8.33)	0.48
de Oliveira, 2023, 37224572	Modified Glasgow Prognostic Score	30 (d)	Function or QOL measured by Improved or stable Karnofsky Performance Status	Noncachexia vs Refractory cachexia	1.95 (1.01, 3.47)	0.02
	Modified Glasgow Prognostic Score	30 (d)	Function or QOL measured by Improved or stable Karnofsky Performance Status	Malnourished vs Refractory cachexia	1.06 (1.01, 1.42)	0.04
	Modified Glasgow Prognostic Score	30 (d)	Function or QOL measured by Improved or stable Karnofsky Performance Status	Cachexia vs Refractory cachexia	0.45 (0.29, 1.03)	0.082

Hospitalizations (With Reason If Available)

Author, Year, PMID	Assessment/Tool	Follow-Up	Definition	Comparator	Results	Reported p Value
Fukuta, 2019, 30316109	International consensus/Fearon 2011	30 (d)	Postoperative length of stay (d) (Duration between day of surgery and day of discharge from GI ward)	Cachexia vs No cachexia	B=2.41 (0.28, 4.55)	0.027
Jones, 2022, 35488469	International consensus/Fearon 2011	Discharge	Hospital stays (d)	Cachexia vs No cachexia	10.0 (7-15) vs 7.0 (7-13) Median (IQR)	<0.001
	International consensus/Fearon 2011	Discharge	Total ICU stay (d)	Cachexia vs No cachexia	2.0 (2-3) vs 2.0 (2- 2) Median (IQR)	<0.001
	International consensus/Fearon 2011	During hospitalization	ICU stay for prolonged (> 48 h)	Cachexia vs No cachexia	67 (28.6%) vs 30 (13.7%) N (%) RR=2.06(1.40, 3.04)[a]	<0.001

Cachexia-Relevant Symptom Burden/Severity (Anorexia, Nausea, Vomiting) (Only Symptoms Not in the Algorithm Included)

Author, Year, PMID	Assessment/ Tool	Follow-Up	Definition	Comparator	Results n/N (%), Effect Size (95% CI)	P Value
Silva, 2020, 31377013	Glasgow Prognostic score	NR	Symptoms of nutritional impact, hyporexia	Precachexia vs No cachexia	OR (95% CI) 1.50 (0.80, 2.80)	0.21
				Refractory cachexia vs No cachexia	OR (95% CI) 3.20 (2.25, 4.55)	<0.001
			Symptoms of nutritional impact, Nausea	Precachexia vs No cachexia	OR (95% CI) 1.78 (0.93, 3.39)	0.079
				Refractory cachexia vs No cachexia	OR (95% CI) 2.13 (1.52, 2.99)	<0.001
			Symptoms of nutritional impact, Intestinal Constipation	Precachexia vs No cachexia	OR (95% CI) 1.08 (0.58, 2.00)	0.79
				Refractory cachexia vs No cachexia	OR (95% CI) 1.75 (1.26, 2.44)	<0.001
			Symptoms of nutritional impact, Xerostomia	Precachexia vs No cachexia	OR (95% CI) 1.02 (0.55, 1.89)	0.95
				Refractory cachexia vs No cachexia	OR (95% CI) 2.00 (1.43, 2.80)	<0.001
			Symptoms of nutritional impact, Dysgeusia	Precachexia vs No cachexia	OR (95% CI) 1.44 (0.77, 2.72)	0.25
				Refractory cachexia vs No cachexia	OR (95% CI) 1.89 (1.36, 2.63)	<0.001
			Symptoms of nutritional impact, Fatigue	Precachexia vs No cachexia	OR (95% CI) 0.32 (-0.69, 1.33),	0.53
				Refractory cachexia vs No cachexia	OR (95% CI) 1.06 (0.53, 1.59)	<0.001
Willemsen, 2023, 36583567	International consensus/Fearon 2011	6 (mo)	EAT-10 ≥ 3 (self-perception of presence of Oropharyngeal dysphagia)	Cachexia vs No cachexia	HR (95% CI) 9.000 (2.483, 32.619)	NR

Notes. [a] Calculated by the research team.

Abbreviations. EAT=Eating Assessment Tool.

PEER REVIEW COMMENTS AND RESPONSES

Reviewer Number	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?		
1	Yes	Thank you.
2	Yes	Thank you.
3	Yes	Thank you.
Is there any indication of bias in our synthesis of the evidence?		
1	No	Thank you.
2	No	Thank you.
3	No	Thank you.
Are you aware of any published or unpublished studies that we may have overlooked?		
1	No	Thank you.
2	No	Thank you.
3	No	Thank you.
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.		
1	Thank you very much for the opportunity to provide input on this work. I only have minor comments which are included below.	Thank you.
1	Overall, it would be useful to have a sense of any temporal relationships to see how the filed is evolving. Did you notice something was more common in the early years that is now being replaced by something else?	We identified no temporal relationship between data of publication and components included in algorithms. However, several of the more recent algorithms identified developed nomograms as part of their assessment for cachexia. We have commented on this in the results section.
1	What is “hyperoxia” as discussed in the GPS section (page xi, executive summary)?	This is a typo and should be "hyporexia" per the cited study. While not defined in the cited study, this appears to be a decrease in appetite, which was clarified in the report.
1	Consider adding in the discussion of the executive summary that definitions of cachexia should include clinically relevant outcomes (page xii). As defined by the FDA, these capture how patients feel, function, or survive, or some other outcome that is evidently relevant (i.e., hospitalizations).	We have modified the text to include the following, “There is a need to expand research on the use of algorithms that assess severity of cachexia and outcomes associated with cachexia severity, and for cachexia definitions to assess more clinically relevant

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			outcomes, such as those related to patient experiences and functioning."
	1	Purpose (p5): The definition of cachexia is truncated, leaving out the most important part, which is that it leads to functional impairment.	We agree. This section of the report has been removed and incorporated into the background section, which notes cachexia leads to decreased physical and psychological functioning.
	1	Background (p5): Regarding computer tomography, most of them use images obtained for clinical purposes (opportunistic). However, these images are currently not clinically evaluated for sarcopenia.	We have added the following text to the sentence regarding computer tomography, "…or these images may be obtained for other clinical purposes but not evaluated for sarcopenia."
	1	On table 1 (p 8) define "L"	We have fixed the typo.
	1	There's a typo on p15: "The Ghrelin Frontier: Targeting Muscle Atrophy with Precision"	We did not find this typo or this phrase.
	1	The following sentence is confusing: "One study included a 4-stage definition of cachexia defined as no cachexia, precachexia, cachexia, cachexia caused by low BMI or sarcopenia, and refractory cachexia groups."	The sentence was misstated and has been revised in both the text and tables to reflect the accurate description of these algorithms.
	1	P22: incomplete sentence: "longer hospital length of stay and."	Thank you. We have edited this sentence to say "and longer hospital stay."
	1	Table 3 typo: "feeling tube"	We have fixed the typo
	1	P32: Can you explain the concept of hyperoxia? Or is it a typo?	This is a typo and should be "hyporexia" per the cited study. While not defined in the cited study, this appears to be a decrease in appetite, which was clarified in the text.
	1	P35: I'm not sure the term "gold standard" is accurate here since there isn't one for cachexia. I know the "" mean that but you could be more explicit.	We agree and have removed this terminology throughout and instead listed these as comparators.
	1	Consider adding to the conclusions (p36) the fact that clinically meaningful outcomes should be taken into account when developing algorithms. Also, it is worth mentioning that all the biomarkers and other surrogate endpoints (CRP, albumin, muscle mass) will need to be validated in the specific population tested and this is a challenge until effective treatments are developed.	We agree and have added language to the future research section regarding the need for algorithms to account for clinically meaningful outcomes. We have commented on the need to validate biomarker and surrogate endpoints in this section as well. We have also added to the executive summary: "Newly developed algorithms should focus on comprehensive

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			assessments of cachexia and should consider clinically meaningful outcomes beyond survival."
	1	P37: consider adding that when new algorithms are developed they will need to be specifically tested in VA populations to ascertain their validity in veterans.	We agree. We have updated the text to include the following, "There is also a need to validate algorithms against, at minimum, an agreed upon reference standard (eg, Fearon 2011), and to validate these within specific populations, such as Veterans."
	1	Appendix D. Is the 10% weight loss over the previous 10 or 12 months? Please check the source. Also, please correct those m2 to m2 when needed.	We have clarified that time period was 10 months. We have corrected the m2 superscripts as needed.
	2	Page 10 (6) line 20/21 in methods, suggest adding "years of age" to >/= 18	We have added your suggestion
	2	Page 11, algorithm: "were classified as cachexic" or cachectic? Same issue on page 15 under Glasgow prognostic score. Cachectic appears to be used most often throughout the paper. This appears again on page 33 in cachexia index section and on several other pages throughout the document. Consider choosing 1 spelling variation for consistency.	We have updated all to "cachectic."
	2	Page 13 (9), typo in notes "Notes. Based on number of times this outcomes was reported", " Met all 3 factors of cachexia profile vs no" "Met all ≥ 2 of 3 factors of cachexia profile vs no" (assuming this is either none or no cachexia)	Thank you for your careful reading of the text. We have corrected the typo and clarified the text as needed.
	2	Page 14 (x - changes to page numbering?), Fearon 2011 - clarify higher or lower progression free-survival (reading this it's saying higher survival but I'm assuming based on the table this should be lower progression free survival, or worse progression free survival) and disease-free survival similar clarification required. Same issue with Cachexia Index section. Page 15 (xi), other assessments phrases these differently "significantly worse" vs higher.	We have changed "higher" to "worse" for clarification and added this distinction for progression-free and disease-free survival. Changes were made to both the Fearon 2011 and Cachexia Index sections on this page.
	2	Page 15 (line 10/11) - even though it's assumed GPS stands for Glasgow Prognostic Score, consider defining within the paragraph or earlier in the document.	We have added the full name of the instrument before the abbreviation in this section.
	2	Page 26 (8, line 44), outcomes, KQ3 functional levels (quality of life, L, Eastern...) - not sure what "L" is/if this is a typo	We have fixed the typo.

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	2	Page 30 (12, line 38/39), "other gastrointestinal symptoms (unspecified)plasma IL-6" needs a comma and space between unspecified and plasma	We have fixed the typos.
	2	Page 33, Fearon 2011 - typos: SARC-F instead of SCAR-F (line 16), "or nutritional assessments assessment" (line 21), "normal statusy" (line 26)	We have fixed the typos.
	2	Page 34 - typo: "and anorexia was assessment by visual analog score" (line 5/6); consider having the acronym VAS in the earlier mention (line 5/6) of visual analog score instead of the 2nd mention (line 8).	We have fixed the typos and have updated the location of the VAS abbreviation.
	2	Page 35 - typo: "of weight loss, the strength, assistance with walking," (line 9, delete "the"); delete period "by Tan 2023." (line 51); consider replacing ; with , here: "abdominal pain, diarrhea; vomiting," (line 55)	We have fixed the typos.
	2	Page 36 - typo: " fatigue, appetite loss, weigh loss (cutoff of 5% over 12 months)" (line 42/43)	We have fixed the typo.
	2	Page 37 - typo: "Wiegert 2021 used a combination of BMI (cutoff s of 21.0 and 26.4)" (extra space on cutoffs)	We have fixed the typo.
	2	Page 38 - typos: " had greater odds of being classifies as having refractory cachexia" and "Three studies compares the PGS-SGA to Evans 2008. One NRCS compared the PGS-SGA to Evans 2008. algorithm (sensitivity = 79.8%, specificity = 72.3%, and AUC of 0.846) cachexia.131" (change to: compared, PG-SGA x2, consider removal of period after Evans, and question placement of the word cachexia at end of sentence)	We have fixed the typos.
	2	Page 39 - typo: "Another NRCS compared the PGS-SGA" (PG-SGA); " to the Wallengren. algorithm compared to Fearon 2011" (consider removal of period); "predictive value of 0.7 33" (remove space)	We have fixed the typos.
	2	Page 40 (22) - typo: " longer hospital length of stay and. Results in functional" (line 57-58)	We have fixed the typo.
	2	Page 41, first paragraph, same issue as Page 14 regarding phrasing of higher vs worse outcomes	Thank you; we updated all terminology on this page to indicate “worse” mortality (instead of “higher”).

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	2	Page 41 (23) - typo: "Notably, this study controlled for multiple definitions of cachexia within in the same models raising concerns of collinearity." (within in) (line 30/31)	We have fixed the typos.
	2	Page 44, first paragraph, same issues as Page 14 regarding phrasing of higher vs worse outcomes	Thank you; we updated all terminology on this page to indicate “worse” mortality (instead of “higher”). We have also updated this terminology throughout the report for consistency.
	2	Page 50 (32), (line 54) "in patients with precachexia (HR= 2.78, 95% CI [0.62, 12.46]); cachexia (HR= 4.77, 95% CI [1.09, 20.80]), and refractory cachexia" consider changing ; to ,	We have made the suggested punctuation change.
	2	Page 54 (line 10/11) " The Evans 2008,CXI, and Fearon 2006 algorithms each" (space needed after 2008)	We have fixed the typo.
	3	Page 3: Abbreviations Table Line 46 – NRL --> NLR	We have fixed the typo.
	3	Missing abbreviations: HGS, WL, GC, HCC, PC, NSCLC, CRC, DLBCL, MCL, CRT, BRT, HPB (many of these were found only in tables and while in the context, oncology professionals may know or guess the abbreviations, non-oncology based clinicians might not)	Per ESP style formatting, the abbreviations table only include those terms that are abbreviated in the text of the paper. All other tables provide an individual list of included abbreviations. However, we realized there was no abbreviations section for Appendix G, so we have added this. We added the full text of HGS in text in one instance of the paper.
	3	Page 15, Line 16: SCAR-F - SARC-F	We have fixed the typo.
	3	Page 15, line 26: statusy --> status	We have fixed the typo.
	3	Page 16, line 16: “visual analog score” --> visual analog scale?	We have made this correction.
	3	Page 16, 2nd paragraph: The descriptions of the different stages of cachexia or unclear. Where it says “3-stage definition…”, it lists 4 categories.	Thank you, this was an error. This has been updated in both the text and tables to reflect the accurate description of these algorithms.
	3	Page 16, line 38: is CRP ≤ 10 mg/L supposed to be CRP ≥ 10 mg/L?	We have made this correction.
	3	Page 17, lines 49 & 51. Remove “.” After Huo 2022 and Tan 2023	We have fixed the typo.
	3	Page 18, line 30: cut-offs for CRP unclear or missing	We have added the missing cutoff to the text.
	3	Page 18, line 41: is the “fat free mass index” a common measurement tool that should be familiar to all reading? I have not clear on what the measurement is, how it is done, etc.	This measure was mentioned in several studies but the details of this were not described. We have added the

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			clarification of “measuring low muscle” per several of the cited articles.
	3	Page 18, line 53: Suggest rephrase to: “Each parameter is scored. Total scores ranged from 0-52. Scores ≥ 9 indicated need for nutritional intervention.	We agree and have included the suggested rephrasing of this sentence.
	3	Page 20-21, lines 59-12: These (PG-SGA, GLIM, MST, MUST, SNAQ, NRS-2002) are all malnutrition screening or assessment tools. You acknowledge that in the report in passing, but I would point it out more clearly in this section. It seems to me that our inability to distinguish between and treat malnutrition and cachexia stems from the continued use of imprecise tools in the research. Are malnutrition and cachexia really the same thing, maybe to different degrees? Or do they have different etiologies and treatments?	To clarify this issue, at the beginning of this section, we added the following, “It is important to consider that these instruments were originally developed with the intended purpose of identifying conditions related to cachexia, and may therefore present challenges in distinguishing between cachexia and the original condition of interest.”
	3	Same thing on line 42 with the Orell-Kotikangas definition. This description sounds more like sarcopenia. (I understand that all of these met the inclusion criteria and should therefore be included; I would just suggest pointing this out a little more clearly throughout.	Thank you; we have added the following to this section, “Of note, this definition included parameters more closely related to assessing sarcopenia.”
	3	Page 21, line 50-52: the criteria as it’s written here isn’t entirely clear. Is it any of these alone, or do they need 2+?	We have updated the criterion to clarify that it includes any of these alone.
	3	Page 24, line 46-47: “(median [IQR] 2.0 [2-3] vs 2.0 [2-2], p<0.001)” – is this a typo?	These were the results published in the original article. We agree they are poorly reported.
	3	Page 27, Figure 5: Referencing appendix I, it looks like the results listed in the table might be backwards? If not, need some discussion about why low CXI had worse progression-free survival than high CXI?	Lower CXI scores are associated with poorer health. We have updated the titles for figures 4-6 to help clarify. These now state: (Low CXI [cachectic] vs High CXI [Noncachectic]). While not all studies that used the CXI explicitly indicated these categories, we have added this for clarification to the figures.
	3	Page 32, line 60: “Caner” --> “Cancer	We have fixed the typo.
	3	In your limitations (page 37), you discuss that the use of terminology around cachexia may have caused the elimination of some studies that may have assessed cachexia but used another term. I would argue that it also led to the inclusion of some studies that were assessing malnutrition or sarcopenia rather than cachexia.	Thank you for this comment. We agree and have added the following sentence to reflect this viewpoint, “Conversely, this approach may also have led to the inclusion of studies that did not explicitly distinguish between cachexia and other related conditions such as malnutrition or sarcopenia, since these terms may be

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			used interchangeably in the literature." We have also commented on this in the executive summary.
	3	Appendix E, page 57: How was sarcopenia defined?	Appendix E provides overall definitions of cachexia based on the parameters included in each algorithm. The specific details for how each of these parameters are defined, including the various definitions of sarcopenia across studies, can be found in Appendix D.
	3	*Discussion: On page 5, paragraph beginning on line 24 provides a robust definition of cachexia. Do you think that all of the ways researchers are defining cachexia in research is faithful to that definition? I would argue that many – including Fearon 2011 – are not.	As mentioned in the discussion, while current guidelines suggest the inclusion of nutritional, metabolic, and functional status; nutritional barriers; gastrointestinal dysfunction; distress and quality of life; and cancer related factors when assessing cachexia, the algorithms identified in this review only include some of these components. We have added the following sentence to the section on future research: "Finally, if new algorithms are developed, these should take a comprehensive approach to assessing potential components of cachexia beyond those of weight and sarcopenia. We have also added to the executive summary: Newly developed algorithms should focus on comprehensive assessments of cachexia and should consider clinically meaningful outcomes beyond survival."