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.