# Classification of Cancer Cachexia

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# *Appendix*

# SEARCH STRATEGIES

| Search Date | Search Statement | Results |
|---|---|---|
| **MEDLINE**<br><br>**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**<br><br>**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**<br><br>**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**<br><br>**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.* |
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[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*, **<br><br>*specification of "in the absence of simple starvation" in some studies<br>**some studies did not specify time frame of WL |
| Sarcopenia or Skeletal Muscle index | • ASMI < 7.0 kg/m$^2$ measured by DXA;<br>• 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;<br>• ASMI= <7.26 kg/m$^2$;<br>• Mid-upper-arm muscle area by anthropometry (men <32 cm, women <18 cm);<br>• SMI= the area of skeletal muscle (cm$^2$) of L3/height squared (m$^2$);<br>• SMI= <7 kg/m$^2$ for men and <5.7 kg/m$^2$ for women measured by BIA;<br>• L3-SMI= <45.1 cm$^2$/m$^2$ in males and <36.9 cm$^2$/m$^2$ in females by CT;<br>• SMI= males < 7.26 kg/m$^2$ ; females < 5.45 kg/m$^2$ by BIA<br>• L3 SMI= <40.8 cm$^2$/m$^2$ for men and <34.9 cm$^2$/m$^2$ for women determined using CT data;<br>• 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;<br>• MUAMA: men <32 cm$^2$, women <18cm$^2$<br>• CT: SMI < reference (L3: <55 cm$^2$/m$^2$ for males, <39 cm$^2$/m$^2$ for females;<br>• T4: <66.0 cm$^2$/m$^2$ for males, <51.9 cm$^2$ /m$^2$ for females;<br>• BIA: FFMI without bone: men <14.6 kg/m$^2$, women <11.4 kg/m$^2$;<br>• TPA index <385 mm$^2$/m$^2$ for female, TPA index <545 mm$^2$/m$^2$ for male;<br>• FFMI by BIA (men < 14.6 kg/m$^2$, women < 11.4 kg/m$^2$);<br>• SMI= males <41.6 kg/m$^2$, females <32.0 kg/m$^2$;<br>• L3 SMI= <55 cm$^2$/m$^2$ in men and < 39 cm$^2$/m$^2$ in women;<br>• Upper-middle arm muscle area (men <32 cm$^2$ , women <18 cm$^2$);<br>• DSM-BIA= (men: <7.0 kg/m$^2$, women: <5.7 kg/m$^2$);<br>• SARC-F score ≥ 4/10;<br>• 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).<br>• L3 SMI were 52.4 cm$^2$/m$^2$ for men and 38.5 cm$^2$/m$^2$ for women;<br>• ASMI <7.0 kg/m$^2$ for males and <5.4 kg/m$^2$ for females;<br>• Using the Prado et al. cut-points for Sarcopenia on CT analysis<br>• ASMI consistent with sarcopenia;<br>• 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;<br>• ASMI<7.26 kg/$m^2$ for males and <5.45 kg/$m^2$ by DEXA;<br>• Muscle index= males < 55.4 $cm^2$ /$m^2$ females < 38.9 $cm^2$ /$m^2$ by CT;<br>• 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<br>● WL >=2%, >2% and ≤ 5%, >=5%, >10% (With or without specifiers of: within 6 months, ongoing, unintentional, or in the absence of simple starvation);<br>● >5% over the past 6 mo in the absence of simple starvation (<72 hours without food intake, or difficulty swallowing solid food)<br><br>Precachexia:<br>● Minimal or no weight loss;<br>● >2% and ≤ 5%;<br>● ≤5% during last 6m (involuntary);<br>● Substantial involuntary WL (*ie*,2–5% WL in the 6 mo)<br><br>No Cachexia or Normal Status<br>● WL < 2%<br><br>Refractory<br>● WL ≥ 6% to ≥ 15% |
| Sarcopenia or Skeletal Muscle index | ● Low muscle mass (determined by computed tomography [CT]–imaging;<br>● 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;<br>● MUAMA as a proxy (men <32 $cm^2$, women <18 $cm^2$ );<br>● 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 $kg/m^2$;<br>● 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;<br>● L3 skeletal muscle index: ≦38.5 $cm^2/m^2$ for women and ≦52.4 $cm^2$ /$m^2$ for men);<br>● SMI cutoffs for LSMI were based on a CT-based study of cancer patients by Martin et al;<br>● 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;<br>● 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;<br>● Appendicular skeletal muscle index consistent with sarcopenia (not defined);<br>● Sarcopenia= Males <7.27 Kg $m^{-2}$ ; females <5.45 Kg $m^{-2}$ determined by dual energy X-ray absorptiometry;<br>● FFMI measured by BIA lower than 14.6 $kg/m^2$ in men, and 11.4 $kg/m^2$ in women;<br>● FFM index <5$^{th}$ percentile of age- and sex-specific reference values |
| Body mass index | ● Cachexia: BMI: < 20 $kg/m^2$; |

| | |
|---|---|
| | • Precachexia: BMI≥20 kg/m$^2$;<br>• 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;<br>• Reported energy intake ≤20 kcal/kg;<br>• 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<br>• Karnofsky Performance Score <50 |
| White blood cell count | |
| Hemoglobin | |
| Dysphagia | |
| Stomatitis | |
| Edema | |
| Ascites | |
| Creatinine | |
| Quality of life | |
| Fatigue | |
| Other | • Impaired glucose tolerance (precachexia)<br>• <3 months expected survival (Refractory cachexia)<br>• 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 ($cm^2/m^2$);<br>• 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);<br>• Iliopsoas minor axis (cm) × major axis (cm) × / height squared ($cm^2$ / $m^2$);<br>• 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:<br>● Weight stable or weight gain=0;<br>● Weight loss ≤5%=1;<br>● Weight loss >5% and ≤15%=2;<br>● Weight loss >15%=3 |
| Sarcopenia or Skeletal Muscle index | SARC-F:<br>0= 0;<br>1–3=1;<br>4–6=2;<br>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:<br>● 0–3=0<br>● 4–6=1<br>● 7–10=2 |
| Performance/ Function/ Muscle strength | ECOG:<br>● 0=0;<br>● 1–2=1;<br>● 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:<br>● Weight stable or weight gain=0;<br>● Weight loss ≤5%=1;<br>● Weight loss >5% and ≤15%=2;<br>● Weight loss >15%=3 |
| Sarcopenia or Skeletal Muscle index | SARC-F:<br>● 0= 0;<br>● 1–3=1;<br>● 4–6=2;<br>● 7–10=3 |
| Body mass index | ● ≥20=0;<br>● 18.5-20=1;<br>● < 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:<br>● 0–3=0;<br>● 4–6=1;<br>● 7–10=2<br><br>AND<br><br>Reduced food intake: |

| | |
|---|---|
| | • No reduction or more=0;<br>• Reduce =1 |
| Performance/ Function/ Muscle strength | ECOG:<br>• 0=0;<br>• 1–2=1;<br>• 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:<br>• < 70 = 0<br>• ≧ 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:<br>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.<br><br>Nausea: score 0 = none, score 1 = Mild, can eat, score 2= Moderate, eats less, score 3-4 = Severe, inadequate oral intake; needs IV fluids.<br><br>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;<br>• Appendicle skeletal muscle index by DEXA (kg/m$^2$) <5.45 in females and <7.25 in males;<br>• BIA: Male SMI<7.26 kg/m$^2$, Female SMI<5.45 kg/m$^2$;<br>• 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;<br>• EORTC appetite loss: score ≥3;<br>• 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;<br>• EORTC tiredness: score ≥66.7;<br>• Fatigue= >3 on a visual analog scale (1–10);<br>• 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;<br>• IL-6 >4 pg/ml;<br>• 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;<br>• ≥ 20 $kg/m^2$= 0 |
| C-reactive protein | |
| Albumin | |
| Neutrophil lymphocyte ratio | |
| Anorexia or Appetite loss or Nutrition | Prognostic nutritional index:<br>• <40= 1;<br>• ≥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):<br>● ≥57.7= 1;<br>● <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:<br>● ≤0.38= 0;<br>● 0.38-1.7= 1;<br>● ≥1.7= 2 |
| Sarcopenia or Skeletal Muscle index | SMI (based on CT images at the third lumbar vertebra) $cm^2$ /$m^2$:<br>● Male ≥44.4 or Female ≥35.7= 0;<br>● Male ≥37.5 or Female ≥30.9= 2;<br>● 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:<br>● 0= 0;<br>● 1= 2;<br>● 2= 4;<br>● 3= 6;<br>● 4= 8 |
| C-reactive protein | |
| Albumin | Prealbumin level (mg/L):<br>● ≥180= 0;<br>● <180= 4 |
| Neutrophil lymphocyte ratio | |
| Anorexia or Appetite loss or Nutrition | Appetite status (Not defined):<br>● Good= 0;<br>● Fair= 1;<br>● Poor= 2 |
| Performance/ Function/ Muscle strength | Physical status (Not defined):<br>● Good= 0; |

| | |
|---|---|
| | • Fair= 1;<br>• Poor= 2 |
| White blood cell count | |
| Hemoglobin | |
| Dysphagia | |
| Stomatitis | |
| Edema | |
| Ascites | |
| Creatinine | |
| Quality of life | |
| Fatigue | |
| Other | Inflammation (NLR and CRP level, mg/L):<br>• NLR > 3.5= 3;<br>• NLR≤3.5; CRP > 2.9= 2;<br>• NLR≤3.5; CRP > 2.3= 1;<br>• 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;<br>• >5% over 6 months;<br>• >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;<br>• >10 mg/dL |
| Albumin | • < 3.2 g/dL;<br>• < 32 g/L;<br>• <2.5 g/dL |
| Neutrophil lymphocyte ratio | |
| Anorexia or Appetite loss or Nutrition | • ESAS appetite score, ≥4/10;<br>• 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;<br>• PG-SGA SF box 4 score >2;<br>• PG-SGA box 4, >2 or hand-grip percentile, <50 |
| White blood cell count | >11.000 |

| | |
|---|---|
| Hemoglobin | • <120 g/L<br>• <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 <10$^{th}$ 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)];<br>● >98= No risk;<br>● 92 to 98 = Low risk; |

| | |
|---|---|
| | • 82 to < 92 = Moderate risk;<br>• < 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;<br>• >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<br>• Patient-Generated Subjective Global Assessment (PG-SGA) = Range 0-26<br>• 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<br>• Cancer Stage = I/II, III/IV<br>• 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.<br>• Cancer Stage= I, II, II, IV<br>• 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;<br>Platelets= Range of 0-1100;<br>Abdominal pain= Yes; no;<br>Diarrhea= Yes; no;<br>Vomiting= Yes; no;<br>Other gastrointestinal symptoms= Yes; no;<br>Direct bilirubin µmol/L= Range 0-400;<br>Drinking= Yes; no; |

| | |
|---|---|
| | Tumor stage= I, II, III, IV;<br>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;<br>>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;<br>• 21.0-26.4;<br>• >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 ;<br>• Body-weight standardized hand grip strength < 15 percentile;<br>Calf circumference (left) < 15 percentile |
| Body mass index | • <18.5 if<70 years;<br>• <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<br>• Precachexia: clinical + metabolic manifestations but minimal or WL;<br>Cachexia: WL; or BMI + WL; or low muscle mass + WL;<br>Refractory cachexia: catabolic state unresponsive to anticancer treatment + low performance status + <3 months expected survival.<br>• Normal Status: WL < 2%; or Weight gain and no anorexia; or No sarcopenia;<br>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;<br>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;<br>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%<br>• Cachexia: Weight loss>5%, or BMI + Weight Loss, or Sarcopenia + weight loss;<br>Precachexia: Weight loss≤5% + anorexia + metabolic change<br>• Precachexia: Weight loss + other metabolic disturbances;<br>Cachexia: Weight loss; or BMI and Weight loss;<br>Refractory: Unresponsive to treatment and with a life expectancy <3 months<br>• Sarcopenia + weight loss<br>• Cachexia: At least one of the three criteria: Weight loss, Weight loss + BMI, skeletal muscle index + weight loss;<br>Precachexia was defined as substantial involuntary weight loss (i.e., 2–5% weight loss in the 6mo preceding study measurement)<br>• Cachexia: Weight loss >5% or >10% over past 6 months (in absence of simple starvation); or<br>Sarcopenia alone; or Sarcopenia + >2% WL<br>• Precachexia: Defined using the European Society of Clinical Nutrition and Metabolism Special Interest Group;<br>Cachexia: International consensus definition<br>• Precachexia: an early stage in which clinical and metabolic signs such as anorexia and systemic inflammation can precede substantial (ie, >5%) body weight loss;<br>• Cachexia: Weight loss; or Weight loss + BMI; or Sarcopenia alone;<br>Precachexia: CRP≥5 mg $1^{-1}$ but not meeting criteria for cachexia<br>• Cachexia: Weight loss; or low BMI + WL; or Sarcopenia + WL<br>Precachexia: WL> 2% and < 5%<br>• Cancer Precachexia: Unintentional weight loss; Anorexia; Systemic inflammation<br>Cancer cachexia: Weight loss or sarcopenia; Reduced food intake; Systemic inflammation<br>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<br><br>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)<br><br>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)<br><br>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<br>Body weight loss and composition + inflammation/metabolic disturbances/immunosuppression + physical performance + anorexia + quality of life<br><br>Cutoffs for classifications: No cachexia (≤14), mild cachexia (15–28), moderate cachexia (29–46) and finally, severe cachexia (>46)<br><br>or<br><br>CASCO<br>No Cachexia= Not Defined<br><br>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;<br>• Patients with either biochemical abnormalities= precachexia or score of 1;<br>• Patients without these abnormalities= non-cachexia or score of 1<br><br>or<br><br>• No cachexia= ≥3.5 Albumin (g/dL) and CRP < 10 (mg/L);<br>• Undernourished= < 3.5 Albumin (g/dL) and CRP < 10 (mg/L);<br>• Precachexia= ≥ 3.5 Albumin (g/dL) and CRP ≥10 (mg/L);<br>• Refractory cachexia= < 3.5 Albumin (g/dL) and CRP ≥10 (mg/L)<br><br>or<br><br>• No cachexia= CRP≤10 mg/l and albumin ≥35 g/l;<br>• Undernourished= CRP ≤10 mg/l and albumin <35 g/l;<br>• Precachexia= CRP>10 mg/l and albumin ≥35 g/l;<br>• Refractory cachexia= CRP>10 mg/l and albumin <35 g/l<br><br>or<br><br>• Normal= ≥3.5 mg/dL albumin and ≤0.5mg/dL CRP;<br>• Undernourished= <3.5 mg/dL albumin and ≤0.5mg/dL CRP;<br>• Cancer cachexia potential= ≥3.5 mg/dL albumin and >0.5mg/dL CRP;<br>• Cancer cachexia= <3.5 mg/dL albumin and >0.5mg/dL CRP |
| PG-SGA | • PG-SGA cutoff: 6.5;<br>PG-SGA >=4;<br>• 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)<br><br>• 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;<br>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;<br>Refractory cachexia= Lab(Any) +WL+ Function; Anorexia/decreased food intake + WL+ Function; Lab (Any) +Anorexia/decreased food intake + WL+ Function<br><br>• 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;<br>Cachexia= Abnormal biochemistry + significant weight loss; or decreased food intake + significant weight loss; or abnormal biochemistry + significant weight loss + decreased food intake;<br>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<br><br>• No Cachexia= Abnormal biochemistry alone; anorexia or decreased food intake alone; weight loss alone; none of the above;<br>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;<br>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;<br>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<br>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;<br>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;<br>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$4;<br>Well nourished= not HGS<30kg and no FFMI <14.6kg/m$^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;<br><br>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%<br><br>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%<br><br>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<br><br>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<br><br>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.<br>Fearon 2011: 55 % cachectic, 5 % precachectic, 40 % noncachectic<br>(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).<br><br>The PG-SGA demonstrated good sensibility (87.50%) and accuracy (72%) for cachexia. |
| Chen-2020-31655470 | MUST | Fearon 2011 | Sensitivity= 87.3%<br>Specificity= 77.7%<br>Accuracy= 81.3%<br>AUC 0.825 |
| Chen-2020-31655470 | NRS-2022 | Fearon 2011 | Sensitivity= 76.6%<br>Specificity= 84.3%<br>Accuracy= 91.6%<br>AUC 0.805 |
| Chen-2020-31655470 | MST | Fearon 2011 | Sensitivity= 84.3%<br>Specificity= 98.6%<br>Accuracy= 93.5%<br>AUC 0.914 |
| Chen-2020-31655470 | SNAQ | Fearon 2011 | Sensitivity= 54.3%<br>Specificity= 95.9% |

| Study | Tool Used | Compared to | Psychometric Properties or Other Comparison Outcomes |
|---|---|---|---|
| | | | Accuracy= 80.9%<br>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.<br><br>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:<br><br>Undernourished on mGPS= 1.84 (1.23; 2.75), p= 0.003<br>Precachexia on mGPS= 1.51 (0.69; 3.32), p= 0.303<br>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%;<br>Specificity= 91.8%;<br>Accuracy= 91.3%;<br>AUC= 0.910 |
| Song-2022-36476477 | PG-SGA | Fearon 2011 | Sensitivity= 86.2%;<br>Specificity= 58.3%;<br>Accuracy= 63.1%;<br>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%<br>Cachexia 2 of 3 components (Fearon 2006)= 45%<br>Cachexia (Evans 2008)= 33%<br>Cachexia (Fearon 2011)= 85%<br>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<br>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%).<br><br>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;<br>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<br>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<br>Poor 31 (15) | Previous treatment:<br>Hepatic resection 213 (100)<br>Anatomical resection 135 (63)<br>Treatment for recurrence:<br>Surgical resection 39 (32)<br>RFA 16 (13)<br>Chemoradiotherapy 8 (6.6)<br>TACE/TAI 40 (33)<br>BSC 10 (8.2) | HBsAg positive 45 (21)<br>HCV-Ab positive 63 (30) |
| **Aslan, 2022, 36137881** | 52 | NR | <65: 30 (58)<br>≥65: 22 (42) | 38 (73) | Renal cell carcinoma 52 (100) | Advanced 52 (100) | Metastatic 52 (100) | Nivolumab 52 (100)<br>Nephrectomy 37 (71)<br>1 prior systemic therapy 32 (62)<br>2 prior systemic therapies 20 (38) | Chronic liver[a] disease 0 (0)<br>Nephrotic syndrome[a] 0 (0)<br>Autoimmune diseases[a] 0 (0)<br>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)<br>Lung 86 (36)<br>Breast 36 (15)<br>Prostate 43 (18) | III–IV:<br>lung cancer 87 (36)<br>IV:<br>colon/rectal cancer 76 (31)<br>prostate cancer 43 (18)<br>breast cancer 36 (15) | - | Treatment line<br>First 190 (79)<br>Second 31 (13)<br>Higher than second 20 (8)<br>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)<br>Second line 49 (65.3)<br>Third Line 31 (41.3)<br>>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)<br>II: 124 (21.6)<br>III: 266 (46.2) | Differentiated 422 (73.4%) | Subtotal gastrectomy 575 (100) | Charlson score<br>0: 293 (51.0)<br>1–3: 260 (45.2)<br>4–6: 22 (3.8) |
| **De Oliveira, 2023, 37224572** | 180 | 62 (34.4), white skin color | <60: 76 (42.2)<br>≥60: 104 (57.8) | 73 (40.6) | GIT 49 (27.2)<br>Gynecologic 45 (25.0)<br>Head and neck 26 (14.4)<br>Breast 21 (11.7)<br>Lung 9 (5.0)<br>Skin, bones, and soft tissues 9 (5.0)<br>Others 21 (11.7) | NR | Distant metastasis<br>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)<br>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)<br>Colorectal 47 (48) | Clinical stage<br>0-2: 78 (79.6)<br>3-4: 20 (20.4) | | Surgical approach:<br>Endoscopic 88 (89.8)<br>Open 10 (10.2) | CCI<br>0: 42 (42.9)<br>1: 19 (19.4)<br>≥2: 37 (37.8) |
| **Go, 2020, 32423395** | 228 | | 64.5 (21, 88)<br>≤ 60: 96 (42.1)<br>> 60: 132 (57.9) | 130 (57.0) | Diffuse large B-cell lymphoma 228 (100) | Ann Arbor stage<br>I – II: 100 (43.9)<br>III – IV: 28 (56.1) | - | NR | Active infections 0 (0)[a]<br>Double primary malignancy[a] 0 (0)<br>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)<br>Extensive stage 160 (59.9) | - | Etoposide and platinum 252 (94.4)<br>Irinotecan and cisplatin 15 (5.6)<br>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<br>I-II 112 (42.1)<br>III-IV 154 (57.9) | - | Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) immunochemotherapy 266 (100) | Active infection 0 (0)[a]<br>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)<br>>65: 93 (40.1) | 149 (64.2) | Advanced pancreatic cancer 232 (100) | III 60 (25.9)<br>IV 172 (74.1) | Grade<br>Well diff 15 (6.5)<br>Moderately diff 85 (36.6)<br>Poorly diff 43 (18.5)<br>Unknown 89 (38.4) | CS + adj 24 (10.3)<br>C/T 172 (74.1)<br>C/T + local RT 36 (15.5) | NR |
| **Jafri, 2015, 26604850** | 112 | White 54 (48)<br>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<br>I-II: 40 (15.9)<br>III: 51 (20.2)<br>IV: 161 (63.9) | - | Head and neck free flap reconstruction 252 (100) | Hypothyroidism 53 (21.0)<br>ECOG score 1.0 [0–1]<br>mCCI 1.0 [0–2] |
| **Kamada, 2023, 36725756** | 306 | NR | Median 71.5 [39–96] | 192 (63) | Colorectal cancer 306 (100) | I= 92 (30)<br>II= 97 (32)<br>III= 117 (38) | - | Laparoscopic R0 colorectal resection) 306 (100)<br>Adjuvant chemotherapy 126 (41) | NR |
| **Karmali, 2017, 28417157** | 86 | NR | Median 64<br><60:37 (43)<br>≥60: 49 (57) | 40 (46.5) | Lymphomas 86 (100) | I/II: 31 (36)<br>III/IV: 54 (63)<br>Unknown: 1 (1) | - | DLBCL treatment n = 76<br>Chemotherapy[d] 76 (88.4)<br>MCL treatment N = 10<br>Chemotherapy[e] 9 (10.5)<br>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)<br>IV: 277 (76.7) | | No chemotherapy 177 (49)<br>Surgery only 42 (11.6)<br>Surgery + postoperative RT 122 (33.8)<br>RT only 13 (3.6)<br>With chemotherapy 184 (51)<br>Surgery + postoperative CRT 25 (6.9)<br>CRT 43 (11.9)<br>Induction chemotherapy + surgery +/- postoperative RT/CRT 32 (8.9)<br>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)<br>Pembrolizumab 21 (56.8)<br>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)<br>Carboplatin + paclitaxel /nab-paclitaxel + pembrolizumab 66 (33.7)<br>Carboplatin + paclitaxel + bevacizumab + atezolizumab 29 (14.8)<br>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<br>I: 99 (57)<br>II: 38 (22)<br>III: 38 (2) | - | Laparoscopic or robotic gastrectomy 175 (100)<br>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)<br>Gastric 170 (22.80)<br>Colorectal 199 (26.70)<br>Esophageal 90 (12.10)<br>Hepatobiliary 32 (4.30)<br>Pancreatic 19 (2.50)<br>Breast 22 (2.90)<br>Utero ovarian 21 (2.80)<br>Nasopharyngeal 13 (1.70)<br>Urological 11 (1.50)<br>Other cancer subtypes<br>5 (0.70) | TNM stage<br>I 50 (6.70)<br>II 159 (21.30)<br>III 200 (26.80)<br>IV 337 (45.20 | | Radical resection<br>215 (28.8)<br>Postoperative chemoradiotherapy<br>325 (43.6) | Diabetes 98 (13.1)<br>Hypertension, yes 192 (25.7)<br>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)<br>II+III 302 (49.2) | - | Radical surgery<br>614 (100)<br>Postoperative chemotherapy 376 (61.7) | Diabetes 110 (17.9)<br>Hypertension<br>133 (21.7) |
| **Shimagaki, 2023, 2022782042** | 144 | NR | 69.3 (0.8) | 84 (58.3) | Pancreatic ductal adenocarcinoma 144 (100) | pStage<br>1: 16 (11.1)<br>2: 91 (63.2)<br>3: 25 (17.36)<br>4: 12 (8.3) | - | Curative-intent pancreatectomy 144 (100)<br>Adjuvant Chemotherapy 118 (81.9)<br>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)<br>Gynecology 196 (16.8)<br>Head and Neck 155 (13.3)<br>Lung 125 (10.7)<br>Breast 118 (10.2)<br>Skin 57 (4.9)<br>Bones and soft tissues 39 (3.3)<br>Others 117 (10.0) | Local Advanced 174 (14.9)<br>Metastatic 992 (85.1) | - | Surgery 463 (39.7)<br>Chemotherapy 701 (60.1)<br>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)<br>cStageIII-IV: 100 (41.8) | - | Esophagectomy followed by gastric tube reconstruction 239 (100)<br>None/ESD 107 (44.8)<br>Preoperative treatment, Chemotherapy or chemoradiation 132 (55.2) | CVD 19 (7.9)<br>Pulmonary disease 48 (20.1)<br>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%)<br>Gallbladder 74 (4.4%)<br>Pancreas 78 (4.6%)<br>Stomach 566 (33.4%)<br>Colorectum 759 (44.8%) | I- 494 (29.2%)<br>II- 551 (32.5%)<br>III- 464 (27.4%)<br>IV- 184 (10.9%) | Cancer grade<br>Differentiated 836 (49.4%)<br>Undifferentia-ted 857 (50.6%) | Abdominal surgery 1693 (100) | Co-morbidity 513 (30.3)<br>Respiratory co-morbidity 23 (1.4%)<br>Cardiovascular co-morbidity 446 (26.3%)<br>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<br>T1: 2 (1.7)<br>T2: 5 (4.2)<br>T3: 72 (61.0)<br>T4: 39 (33.1) | - | Initial hepatic resection for CRLM 118 (100)<br>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)<br>Surgery 65 (84.4)<br>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)<br>Lung 29 (14.8)<br>Liver/Biliary/Pancreas 27 (13.8)<br>Breast 21 (10.7)<br>Gastroesophageal 18 (9.2)<br>Colorectal 16 (8.2)<br>Others 52 (26.5) | Cancer stage<br>Local advanced 44 (22.4)<br>Metastatic 152 (77.6) | - | Chemotherapy 66 (33.7)<br>Radiotherapy 12 (6.1)<br>Chemoradiotherapy 21 (10.7)<br>Surgery 8 (4.1)<br>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)<br>IIIb= 24 (60) | - | Patients were included at the start of chemoradiotherapypay 40 (100)<br>Treatment during the previous month[a]<br>Surgery 0 (0)<br>Chemotherapy 0 (0)<br>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)<br>Capecitabine (-B) 8 (12)<br>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)<br>GI tract 109 (65.3)<br>Lung 32 (19.2)<br>Head/neck 19 (11.4) | Cancer stage<br>I: 21 (12.6)<br>II: 23 (7.2)<br>III: 21 (12.6)<br>IV: 111 (66.5)<br>V: 2 (1.2) | - | NR | NR |
| **Wan, 2022, 36212479** | 379 | NR | 60.42 (11.06) | 234 (61.7) | Colorectal cancer 379 (100) | TNM stage<br>I 94 (24.8)<br>II 142 (37.47)<br>III 143 (37.73) | - | Radical surgery 379 (100)<br>Postoperative adjuvant chemotherapy 255 (67.28) | Hypertension 75 (24.67)<br>CHD 15 (4.12)<br>Diabetes 38 (11.14) |
| **Wang, 2023, 37454609** | 10568 | NR | 64.0 (56.0, 70.0) | 6791 (64.3) | HPB 2048 (19.4)<br>Gastroesophageal 3618 (34.2)<br>Colorectal 4092 (46.4) | III-IV: 4353 (41.2) | - | Surgery 10 390 (98.3) | NR |
| **Wiegert, 2020, 32927241** | 1384 | White 595 (43.0)<br>Black 229 (16.5)<br>Other 560 (40.5) | 61.7 (13.4) | 604 (43.6) | Gastrointestinal tract 445 (32.2)<br>Gynecology 229 (16.6)<br>Head/neck 241(14.5)<br>Lung 141 (10.2)<br>Breast 144(10.4)<br>Skin 60 (4.3)<br>Bones and soft tissues 47 (3.4)<br>Leukemia, lymphomas, myeloma 17 (1.2)<br>Others 100 (7.2) | Locally advanced 204 (14.7)<br>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)<br><65:<br>274 (61.8)<br>≥65:<br>169 (38.2) | 180 (40.5) | Digestive system 159 (35.9)<br>Gynecological 91 (20.5)<br>Head and neck 32 (7.2)<br>Breast 46 (10.4)<br>Lung 46 (10.4)<br>Others 69 (15.5) | Locoregional advanced 90 (20.3)<br>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)<br>II: 9 (13.64)<br>III: 21 (31.82)<br>IVabc: 21 (31.82) | - | Adjuvant CRT (cisplatin with radiotherapy) 6 (9.1)<br>Primary CRT (cisplatin with radiotherapy 49 (74.24)<br>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)<br>Esophagus cancer= 182 (3.5)<br>Gastric cancer= 492 (9.3)<br>Hepatic-biliary cancer= 201 (3.8)<br>Pancreatic cancer= 114 (2.2)<br>Colorectal cancer= 829 (15.7)<br>Breast cancer= 1,208 (22.9)<br>Gynecological cancer= 338 (6.4)<br>Urologic cancer= 64 (1.2)<br>Nasopharynx cancer= 23 ( 0.4)<br>Other cancer= 111 (2.1) | I: 829 (15.7)<br>II: 1,304 (24.7)<br>III: 1,379 (26.2)<br>IV: 1,758 (33.4) | - | Surgery 3,513 (66.7)<br>Radiotherapy 550 (10.4)<br>Chemotherapy 3,460 (65.7) | Hypertension 993 (18.8)<br>Diabetes 509 (9.7) Active infection or severe systemic immunodeficient-cy disease[a]<br>0 (0) |
| **Zhuang, 2022, 34797480** | 1215 | NR | Median 65.0 (14.0) | 886 72.9) | Gastric Cancer<br>1215 (100) | TNM stage<br>I: 452 (37.2)<br>II: 286 (23.5)<br>III: 477 (39.3) | - | Radical gastrectomy<br>1215 (100) | CCI<br>0-1: 1105 (90.9)<br>≥2: 110 (9.1) |
| **Zopf, 2020, 2002952037** | 100 | NR | 75.6 (4.7) | 22 (66.7) | Gastro-intestinal 63.6%<br>Bronchial carcinomas 15.2% | NR | NR | NR | CCI<br>1.6 (2.4)<br>Malnourished<br>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)<br>(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)<br>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)<br>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%)<br>N (%)<br>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 |

| | Reviewer Number | Comment | Author Response |
|---|---|---|---|
| | | | 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 |

| | Reviewer Number | Comment | Author Response |
|---|---|---|---|
| | | | 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.<br>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. |

| | Reviewer Number | Comment | Author Response |
|---|---|---|---|
| | 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”). |

| | Reviewer Number | Comment | Author Response |
|---|---|---|---|
| | 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 |

| | Reviewer Number | Comment | Author Response |
|---|---|---|---|
| | | | 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." |