Objectives: Muscle mass is one of the key components in defining sarcopenia and is known to be important for locomotion and body homeostasis. Lean mass is commonly used as a surrogate of muscle mass and has been shown to be associated with increased mortality. However, the relationship of lean mass with mortality may be affected by different clinical conditions, modalities used, cut-off point to define low or normal lean mass, and even types of cancer among cancer patients. Thus, we aim to perform a comprehensive meta-analysis of lean mass with mortality by considering all these factors.

Methods: Systematic search was done in PubMed, Cochrane Library and Embase for articles related to lean mass and mortality. Lean mass measured by dual X-ray absorptiometry, bioelectrical impedance analysis, and computerized tomography were included.

Results: The number of relevant studies has increased continuously since 2002. A total of 188 studies with 98,468 people were included in the meta-analysis. The association of lean mass with mortality was most studied in cancer patients, followed by people with renal diseases, liver diseases, elderly, people with cardiovascular disease, lung diseases, and other diseases. The meta-analysis can be further conducted in subgroups based on measurement modalities, site of measurements, definition of low lean mass adopted, and types of cancer for studies conducted in cancer patients.

Conclusions: This series of meta-analysis provided insight and evidence on the relationship between lean mass and mortality in all directions, which may be useful for further study and guideline development.

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Given the importance of sarcopenia, it has been endorsed as an independent condition by the International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM) Code in 2016. Nevertheless, there is no consensus on the definition of sarcopenia, although several definitions have been proposed for sarcopenia in elderly and cancer patients [4–7]. The Asian Working Group for Sarcopenia (AWGS) recommended using dual X-ray absorptiometry (DXA) as one of the diagnostic tools for sarcopenia [4]. However, a recent study suggested that lean mass measured by DXA should not be used in defining sarcopenia, since inconsistent associations were observed for DXA-derived lean mass with various clinical outcomes, such as fall, mobility limitation, and hip fractures [8]. Notably, the authors [8] and others [9] acknowledged the limitation of measurement method (measurement of lean mass instead of muscle mass) and studied population (relatively healthy elderly) may affect the validity of the conclusion.

Indeed, it is commonly observed in the literature that muscle mass was measured using different methods, and different cut-offs of muscle mass were adopted in defining people as having normal or low muscle mass, making the comparison and interpretation difficult. Although a few meta-analyses were conducted to evaluate the relationship between lean mass and mortality, the analyses were either small-scale, conducted in a subgroup with a particular health condition only, or combined the data based on dichotomized lean mass phenotype [10–13]. We are thus lacking a comprehensive overview of how lean mass contributes to mortality. The performance of lean mass in predicting mortality in different health conditions and measurement modalities are also unknown. To evaluate the relationship of lean mass with mortality comprehensively, we conducted a large-scale meta-analysis of the association between lean mass and mortality.

2. Methods

2.1. Search strategy and selection criteria

In this systematic review and meta-analysis, we searched PubMed, Cochrane Library and Embase for articles published up to December 20, 2017. The following algorithms were used for the literature search:

("lean mass" OR "ALM" OR "muscle mass") AND ("death" OR "mortality" OR "outcome");
("lean mass" OR "Body composition" OR "muscle mass" OR "sarcopenia" OR "bio-impedance" OR "frailty") AND ("death" OR "mortality" OR "cause of death" OR "fatal outcome" OR "mortality, premature" OR "survival rate" OR "mortal" OR "fatal") AND ("cohort studies" OR "follow-up studies" OR "longitudinal studies" OR "prospective studies" OR "retrospective studies" OR "cohort" OR "longitudinal" OR "prospective" OR "follow-up" OR "retrospective") AND ("association" OR "associated");
("lean mass" OR "Body composition" OR "muscle mass" OR "sarcopenia" OR "bio-impedance" OR "bioimpedance") AND ("death" OR "mortality" OR "cause of death" OR "fatal outcome" OR "mortality, premature" OR "survival rate" OR "mortal" OR "fatal" OR "survival") OR "prognosis" OR "prognostic").

The inclusion criteria were original studies investigating the relationship between lean mass and all-cause mortality or overall survival. The reference lists of systematic reviews and meta-analyses were also checked for inclusion of additional literatures. We only included studies reporting the association between all-cause mortality and muscle mass measured by computerized tomography (CT), dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA) reported as "reduced lean mass" (ie, lean mass was treated as continuous variable) or "low lean mass" (ie, lean mass was treated as a binary variable, low vs normal lean mass). The pre-specified exclusion criteria were as follows: non-human studies; studies using the following exposures: other surrogates of muscle mass (estimated glomerular filtration rate [eGFR], creatinine level, or lean mass ratio), anthropometric measurement of muscle mass (such as skinfold measurement, mid-arm circumference, etc), rate of change in muscle mass, sarcopenia defined using composite criteria (low lean mass in combination with muscle strength and physical performance); and studies with insufficient data for meta-analysis (studies reporting lean mass as continuous variable without providing standard deviation [SD] for standardized hazard ratio [HR] calculation and studies providing P-values only). Notably, although mid-arm muscle area was considered an acceptable assessment of muscle mass in cancer cachexia [6], the European Working Group on Sarcopenia in Older People (EWGSOP) commented that this method is prone to error and it is not recommended for routine use in the diagnosis of sarcopenia [5].

The PRISMA guideline was followed when evaluating search results. Each paper was screened by title and abstract for eligibility independently by 3 investigators (G.K.L, M.C, C.L.C). Any discrepancy was resolved by consensus. Data extraction was performed by 2 investigators (G.K.L and M.C) and cross-checked by a third investigator (G.H.L). The following information was recorded for each study: first author’s name, year of publication, study design, population, sex, ethnicity, health status, median or mean age, follow-up duration, source of lean mass, types of lean mass, lean mass unit, cut-off definition of sarcopenia, HR with associated 95% confidence intervals (95% CI) and P-values for overall survival. HR and 95% CI were obtained from the fully-adjusted model if available. Otherwise, the crude model would be used. We contacted the corresponding authors if any of the required information was unclear in the article, and the paper was included when the relevant information was provided. Additionally, quality appraisal was done using a modified Newcastle Ottawa Scale (NOS) by J.M and cross-checked by G.K.L (Supplementary Table 1). A modified NOS was applied because some questions were not applicable in the current study, such as selection of non-exposed cohort, demonstration that outcome of interest (ie, mortality in the current study) was not present at start of the study. In the current meta-analysis, studies of good quality were defined as 2 stars in selection domain AND 1/2 stars in comparability domain AND 1/2 stars in outcome/exposure domain; studies of fair quality were defined as 1 star in selection domain AND 1/2 stars in comparability domain AND 1/2 stars in outcome/exposure domain, and poor quality was defined as studies not meeting the criteria of good or fair quality. Any discrepancy in the data extraction and quality appraisal was addressed by discussion and consensus, with involvement of another author if necessary.

We attempted to identify and exclude duplicate data from research studies presented in separate publications. For cases in which we identified multiple studies with duplicated or overlapping data (by population, time and place), we selected the study with the longest follow-up time. When these studies had the same follow-up time, the study with the largest sample size was selected. If lean mass was measured at different sites in the same cohort, we selected the lean mass data based on the following order: whole body lean mass > appendicular lean mass > skeletal muscle > psoas muscle. If various muscle mass indices were used, the index was selected according to the following order: lean mass/height² > lean mass/BMI > lean mass only. For various low lean mass cut-offs in cancer, the result was selected according to the following order: Martin > Prado > Optimal stratification > cut-off based on median of study population.
2.2. Data analysis

For studies with lean mass as a continuous variable, data could not be directly combined because different units of lean mass were used in different studies. Therefore, in order to combine the estimates across different studies, HR and 95% CI were expressed in standardized units [14] (per SD decrease in lean mass). For studies using lean mass as a binary cut-off, high lean mass was used as reference. The HR and 95% CI of each study were entered into Review Manager 5.3 (RevMan, Cochrane, United Kingdom) by G.K.L and cross-checked by P.C.A. If there was mismatch in 95% CI between the calculated values in Revman and those reported in the study publication, either upper or lower 95% CI was chosen as reference according to the calculated P-value in Revman, with the one with a P-value closest to the P-value reported in the study chosen. If numeric HR and/or 95% CI were not available in the literature, these were calculated based on beta, SE, and/or P-value provided in the literature.

All statistical analyses were performed using RevMan. The pooled HR and corresponding 95% CI were estimated using a random-effect model. Publication bias was appraised using funnel plots to test for asymmetry. We used the I² statistic to evaluate the proportion of total variation in the study estimates which was due to heterogeneity.

3. Results

We identified 9,602 articles, of which 977 met the inclusion criteria. After excluding 431 duplicate studies, 546 full-text articles were retrieved. We excluded another 358 articles due to the irrelevant data, population overlap, poor/unclear data, or the articles were conference abstracts without available details. A total of 188 studies were included in the current meta-analysis (Fig. 1). Detailed characteristics of included studies are provided in Supplementary Tables 2–5. The number of studies by publication year (including those first published online) is shown in Fig. 2, and the number of studies increased continuously over time. Among the 188 included articles, 104, 81, and 3 of them were respectively classified as good-, fair-, and poor-quality studies (Supplementary Table 6).

Data from a total of 98,468 people were included in the meta-analysis (Table 1, Supplementary Table 2). The association of sarcopenia with mortality was most studied in cancer patients (n = 100) [15–114], followed by people with renal diseases (n = 21) [115–135], liver diseases (n = 18) [136–153], elderly (n = 16) [154–169], people with cardiovascular diseases (n = 11) [170–180], lung diseases (n = 11) [181–191], and other diseases (n = 11) [192–202]. For the method used to measure lean mass (Table 1, Supplementary Table 3), computed tomography (CT) was the most used modality (n = 138) [20–114,133–135,138–153,171–180,188–191,194–202], followed by BIA (n = 29) [15–18,115–126,136,137,154–157,181–187], and DXA (n = 21) [19,127–132,158–168,170,192,193]. After excluding cancer-related studies in the calculation, CT remained the most commonly used method in assessing lean mass (n = 43), followed by BIA (n = 25) and DXA (n = 20). Majority (n = 120) of the studies used low lean mass as the exposure (Table 1, Supplementary Table 4). Fifty studies used reduced lean mass, while 18 studies investigated both low lean mass and reduced lean mass. After excluding cancer-related studies in the calculation, majority of the studies (n = 40) used reduced lean mass as exposure, 37 studies used low lean mass as exposure, while 11 studies examined both.

Among studies conducted in cancer populations, 95 of them studied CT-measured lean mass with mortality (Table 2). The most frequently studied cancer type was gastrointestinal cancer (n = 21), followed by liver and intrahepatic bile duct (n = 20), urinary tract (n = 13), pancreatic (n = 10), lung (n = 8), ovarian and endometrial (n = 7), multiple (n = 5), hematopoietic (n = 4), breast (n = 3), bile duct (n = 2), head and neck (n = 1), and prostate (n = 1) cancer. The most frequently studied lean mass index was L3 skeletal muscle index (n = 70), followed by L3 psoas index (n = 11) (Table 2).

In defining low lean mass in cancer studies (Table 3,

![Fig. 1. Study attrition diagram.](image-url)
Supplementary Table 4), threshold suggested by Martin et al was the most often used (n = 20), followed by Prado et al (n = 15), and international consensus of cancer cachexia (n = 8). Other definitions were mostly derived from different statistical methods based on the study cohort, such as optimal stratification, ROC, median, etc.

4. Discussion

In this study involving 188 studies and 98,468 participants from 34 countries, we examined the associations of lean mass with all-cause mortality across a wide range of healthy people and patients, across different measurement modalities, and various definition of sarcopenia. As we can see the number of studies in relation to lean mass and mortality has increased continuously since 2002, this is therefore a timely comprehensive systematic review and meta-analysis of the relationship between lean mass and mortality, especially when efforts are being put in the definition of sarcopenia.

Although sarcopenia is a well-recognized issue in the elderly population, this systematic review and meta-analysis found that only 16 out of 188 studies were conducted in the elderly population. On the other hand, more than half (n = 100; 53.2%) of the studies were conducted in patients with cancer. This could be explained by the clinical management of cancer as CT is routinely used to monitor disease progression in cancer patients. Thus, lean mass measurement can be retrieved from existing CT data in many studies, which facilitated the research of sarcopenia in cancer patients. This also explained why CT was the most often used imaging method.
modality in evaluating lean mass (138 out of 188 studies). However, given the high radiation dose of CT, it is not justifiable to use CT purely for sarcopenia research. On the other hand, DXA has a much lower dose of radiation, while BIA is radiation-free. Therefore, these DXA and BIA may be more suitable for lean mass measurement in sarcopenia research in non-cancer patients.

For DXA and BIA, sarcopenia is usually defined using appendicular lean mass, as suggested by consensus. On the other hand, the most common skeletal site in defining sarcopenia in cancer was cross-sectional area (CSA) of muscles at the L3 vertebral level. Two indices can be derived from the muscles at the L3 vertebral level, namely L3 skeletal muscle index and L3 psoas index. L3 skeletal muscle index calculated the CSA of all muscles at the L3 vertebral level, whereas L3 psoas index calculated the CSA of psoas muscle only at the L3 vertebral level. These 2 indices were said to be interchangeable, but whether these indices had similar association with mortality is largely unknown.

Lean mass was commonly analyzed as a binary trait, i.e., low vs normal lean mass. There were several operational definitions of low lean mass, such as the International Working Group on Sarcopenia [203], Society of Sarcopenia, Cachexia and Wasting Disorders [204], FNHI [205], and European Working Group on Sarcopenia in Older People (EWGSOP) [5]. Recently, consensus by EWGSOP was updated (known as EWGSOP2) [7], and such update was found to affect study result slightly [206]. It is therefore important to have a consensus on the definition, so that the findings could be compared across studies. Conversely, since there was no consensus on the cutoff point used for defining low lean mass or sarcopenia in cancer patients, many different methods were used to define sarcopenia. The definition provided by Martin et al [207] and Prado et al [208] were most often used. Optimal stratification [209], which defines sarcopenia based on the most significant cut-off point using log rank test, is the third most commonly used method. This is similar to the ROC method, which defines the optimal cut-off point using Youden’s index. However, these cut-off points are expected to be study-specific, and may over-estimate the effect if there is no validation study. These methods (optimal stratification or ROC) may be useful in deriving a cut-off point in a specific population, while the generalizability of these findings is largely unknown.

Our current study aims to provide insight on these issues, especially to address a recent recommendation by the Sarcopenia Definitions and Outcomes Consortium (SDOC). In the latest analyses by SDOC, they found that lean mass measured by DXA was not a good predictor of multiple adverse outcomes in the elderly [8], thus proposing inclusion of gait speed and grip strength, but not lean mass, in the definition of sarcopenia. In fact, low lean mass (defined as ALM/HT<sup>2</sup> < 5.45 and 7.26 in women and men, respectively) was consistently associated with increased risk of mortality in both women and men in their study [8]. Therefore, whether lean mass should be excluded from use in the definition of sarcopenia remains an open question, while our current study has provided further evidence in this aspect.

Although the current study has evaluated the association of different parameters of lean mass on mortality, we acknowledge that our analyses are insufficient to address these questions directly. For example, the best way to compare the usefulness of different modalities, cut-off points, or site of muscle measurements is to compare these differences directly in the same study. The current analysis was only able to summarize evidences from multiple studies, in which the difference in estimates could be due to the study design and population, instead of the intrinsic difference between the modalities, cut-off points, and site of muscle measurement under investigation. However, only a very limited number of studies were conducted for direct comparison. It is important to have an international collaboration in answering these questions directly, which is essential for developing clinical guidelines of sarcopenia, not only for the elderly, but also for patients with different diseases. In addition, due to tremendous work of the current meta-analysis, we only updated the literature until the end of 2017. We understand there were publications on sarcopenia and mortality published from 2018 to 2020, however the number of studies included in the current study should enable us to come up with a conclusion on whether lean mass is associated with mortality. We hope that the current work will provide a useful resource to the field for future research and guideline development.

In conclusion, this series of meta-analysis of lean mass and mortality could provide insight and evidence on the relationship between lean mass and mortality in all directions, which may be useful for further study and guideline development, especially when there are growing efforts to move from risk assessment to intervention of sarcopenia [9].

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**Table 2**

| Cancer category                        | Total | L3 Skeletal Muscle Index | L3 Psoas Index | Others |
|----------------------------------------|-------|-------------------------|----------------|--------|
| Bile duct (excludes intrahepatic)      | 2     | 1                       | 1              |        |
| Breast                                 | 3     | 3                       | 1              |        |
| Gastrointestinal                       | 21    | 18                      | 2              | 3      |
| Head and neck                          | 1     | 1                       | 3              | 1      |
| Hematopoietic                          | 4     | 3                       | 1              |        |
| Liver and intrahepatic bile duct       | 20    | 15                      | 2              | 3      |
| Lung                                   | 8     | 4                       | 1              | 3      |
| Ovarian and endometria                 | 7     | 4                       | 2              | 1      |
| Pancreatic                             | 10    | 5                       | 3              | 2      |
| Prostate                               | 1     | 1                       | 3              | 1      |
| Urinary tract                          | 13    | 10                      | 2              | 1      |
| Multiple                               | 5     | 5                       | 4              |        |
| Overall                                | 95    | 70                      | 11             | 14     |

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**Table 3**

Cutoff definition of low lean mass in cancer studies.

| Cutoff                                      | n   |
|---------------------------------------------|-----|
| Martin                                      | 20  |
| Prado                                       | 15  |
| International consensus of cancer cachexia  | 8   |
| Other cohort cut-offs                       | 7   |
| Optimal stratification                      | 10  |
| ROC                                         | 8   |
| Quantities/percentiles                      | 7   |
| Median                                      | 8   |
| Others                                      | 7   |
| Total                                       | 90  |
Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ofaos.2021.01.001.

References

[1] Schnyder S, Handschin C. Skeletal muscle as an endocrine organ: PGC-1α, myokines and exercise. Bone 2015;50:115–25.
[2] Cheung CL, Lam KS, Cheung BM. Evaluation of cutpoints for low lean mass and slow gait speed in predicting death in the National Health and Nutrition Examination Survey 1999-2004. J Gerontol A Biol Sci Med Sci 2016;71:90–5.
[3] Lee DH, Keum N, Hu FB, Orav EJ, Rimm EB, Willett WC, et al. Predicted lean body mass, fat mass, and all cause and cause specific mortality in men: prospective US cohort study. BMJ 2018;362.
[4] Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc 2014;15:95–101.
[5] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. Age Ageing 2010;39:412–23.
[6] Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011;12:489–95.
[7] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:601.
[8] Cawthon PM, Manini T, Patel SM, Newman A, Traverso T, Kiel DP, et al. Prolonged survival and low muscle mass in older men and women: the health, aging and body composition study. J Am Geriatr Soc 2004;52:1375–80.
[9] Choi M, Oh S, Lee I, Oh S, Won D. Sarcopenia is negatively associated with total psoas volume on short- and long-term outcomes in patients undergoing curative resection for pancreatic adenocarcinoma: a new tool to assess sarcopenia. J Gastrointest Surg 2015;19:1591–602.
[10] Antonou S, Lanoy E, Iacovelli R, Allibges-Sauvin L, Llorot Y, Merad-Taoufik M, et al. Skeletal muscle density predicts prognosis in patients with metastatic renal cell carcinoma treated with targeted therapies. Cancer 2013;119:3377–84.
[11] Antonou S, Bayar A, Hlela A, Laplanche A, Fizazi K, di Palma M, et al. High subcutaneous adipose tissue density predicts the prognosis in metastatic castration-resistant prostate cancer patients in post chemotherapy setting. Eur J Cancer 2015;51:2570–7.
[12] Begni P, Gigante E, Antonelli G, Carbonetto F, Iannicelli E, Anania G, et al. Sarcopenia predicts reduced survival in patients with hematopoeitic cancer at first diagnosis. Ann Hepatol 2016;15:107–14.
[13] Black D, Mackay C, Ramsay G, Hanoodi Z, Nantahkanuman S, Park K, et al. Prognostic value of computed tomography: measured parameters of body composition in primary operable gastrointestinal cancers. Ann Surg Oncol 2017;24:2241–51.
[14] Blauwhoff-Buskermolen S, Versteeg KS, de van der Schueren MA, den Boer-Willems MM, et al. Prognostic value of computed tomography in patients with colorectal cancer with synchronous liver metastases. J Clin Oncol 2016;34:1339–44.
[15] Boer BC, de Graaff F, Brusse-Keizer M, Bouman DE, Slump CH, Slee-Van der Luijt AJ, et al. Skeletal muscle mass and quality as risk factors for postoperative outcome after open colo rectal cancer. Int J Colorectal Dis 2016;6:1117–24.
[16] Bowden J, Williams L, Simms A, Price A, Campbell S, Fallon M, et al. Prediction of 90 day and overall survival after chemoradiotherapy for lung cancer: role of performance status and body composition. Clin Oncol 2017;29:576–84.
[17] Bronger H, Hedrich P, Hafplermeier A, Mets S, Noel P, Kechtle M, et al. Sarcopenia in advanced serious ovarian cancer. Int J Gynecol Canc 2017;27:2281–8.
[18] Coelen RJ, Wiggers JK, Nio CY, Besselink MG, Busch OR, Gouma DJ, et al. Preoperative computed tomography assessment of skeletal muscle mass is an independent prognostic biomarker of advanced urothelial carcinoma. PLoS One 2015;10:e0139749.
[19] Choi M, Oh S, Lee I, Oh S, Won D. Sarcopenia is negatively associated with long-term outcomes in locally advanced rectal cancer. J Cachexia Sarcopenia Muscle 2017;9:53–9.
[20] Choi Y, Oh DY, Kim TY, Lee KH, Han SW, Im SA, et al. Skeletal muscle depletion predicts survival of patients with advanced biliary tract cancer undergoing palliative chemotherapy. Oncotarget 2017;8:79491–52.
[21] Choi M, Oh S, Lee I, Oh S, Won D. Sarcopenia is negatively associated with long-term outcomes in locally advanced rectal cancer. J Cachexia Sarcopenia Muscle 2017;9:53–9.
[22] Choi Y, Oh DY, Kim TY, Lee KH, Han SW, Im SA, et al. Skeletal muscle depletion predicts the prognosis of patients with advanced pancreatic cancer undergoing palliative chemotherapy, independent of body mass index. PLoS One 2015;10:e0139749.
[23] Coelen RJ, Wiggers JK, Nio CY, Besselink MG, Busch OR, Gouma DJ, et al. Preoperative computed tomography assessment of skeletal muscle mass is valuable in predicting outcomes following hepatectomy for perihilar cholangiocarcinoma. HPB (Oxford) 2015;17:520–8.
[24] Cooper AB, Slack R, Fogelman D, Holmes HM, Petzel M, Parker N, et al. Characterization of anthropometric changes that occur during neoadjuvant therapy for potentially resectable pancreatic cancer. Ann Surg Oncol 2015;22:2416–23.
[25] Dalal S, Hui D, Bidaut L, Lem K, Del Fabbro E, Crane C, et al. Relationships among body mass index, longitudinal body composition alterations, and survival in patients with locally advanced pancreatic cancer receiving chemoradiation: a pilot study. J Pain Symptom Manag 2012;44:181–91.
[26] DeLany DJ, Judge SM, George M, TJ, Sarosi GA, Thomas RM, Behrens KE, et al. A clinically applicable muscular index predicts long-term survival in resectable pancreatic cancer. Surgery 2017;161:930–9.
[27] Deluche E, Leobon S, Desport J, Venat-Bouvet L, Usseglio J, Tubiana-Mathieu N. Impact of body composition on outcome in patients with early breast cancer. Support Care Canc 2018;26:861–8.
[28] Ebadi M, Martin L, Ghosh S, Field C, Lehrer R, Baracos V, et al. Subcutaneous adiposity is an independent predictor of mortality in cancer patients. Br J Cancer 2011;104:1177–84.
[29] Fujikawa N, Nakagawa H, Kudo Y, Tateishi R, Taguri M, Watadani T, et al. Sarcopenia, intramuscular fat deposition, and visceral adiposity independently predict the outcomes of hepatocellular carcinoma. J Hepatol 2015;63:113–20.
[30] Fukushima H, Yokoyama M, Nakamichi Y, Tobisu K, Koga F. Sarcopenia as a prognostic biomarker of advanced urothelial carcinoma. PLoS One 2015;10:e015895.
[31] Fukushima H, Nakatani Y, Katoaka M, Tobisu K, Koga F. Prognostic
significance of sarcopenia in patients with metastatic renal cell carcinoma. J Urol 2016;195:26–32.

[42] Fukuji H, Nakamura Y, Kataoka K, Tokish K, Koga F. Prognostic significance of sarcopenia in upper trach utruchal carcinoma patients treated with radical nephroureterectomy. Cancer Med 2016;5:2213–20.

[43] Go S, Park M, Song H, Kim H, Kang M, Lee H, et al. Prognostic impact of sarcopenia in locally advanced rectal cancer patients with diffuse large B-cell lymphoma treated with neoadjuvant chemotherapy. J Hematol Oncol 2014;7:87.

[44] Grossberg AJ, Chamchod S, Fuller CD, Mohamed AS, Heukelom J, East J, et al. Sarcopenia predicts outcomes following neoadjuvant chemotherapy in patients with colorectal liver metastases? HPB (Oxford) 2015;17:438–46.

[45] Malieszki G, Currie AC, Athanasiou T, Johns N, Anyamene N, Glynne-Jones R, et al. Influence of body composition profile on outcomes following colorectal cancer surgery. Br J Surg 2015;102:572–80.

[46] Martin L, Birdsell L, Macdonald N, Reimann T, Claudinin M, McCargar L, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. J Clin Oncol 2013;31:1359–47.

[47] McCorley S, Black D, Horgan P, McMillan D. The relationship between tumour stage, systemic inflammation, body composition and survival in patients with colorectal cancer. Clin Nutr 2013;32:1279–85.

[48] Meza-Junco J, Montano-Lopez AJ, Baracos VE, Prado CM, Bain VG, Beaumont C, et al. Sarcopenia as a prognostic index of nutritional status in concurrent cirrhosis and hepatocellular carcinoma. J Clin Gastroenterol 2013;47:914–20.

[49] Miyake M, Morizawa Y, Horii S, Marugami N, Iida K, Ohashi K, et al. Integrative assessment of pretreatment inflammation-, nutrition-, and muscle-based prognostic markers in patients with muscle-invasive bladder cancer undergoing radical cystectomy. J Urol 2015;194:1171–7.

[50] Naganuma A, Hoshino T, Suzuki Y, Uehara D, Kudo T, Ishibara H, et al. Association between skeletal muscle depletion and sorafenib treatment in male patients with hepaticcellular carcinoma: a Retrospective Cohort Study. Acta Med Okayama 2017;71:291–9.

[51] Naganuma A, Hara T, Shibata Y, Matsumoto T, Nakamura H, Ninomiya S, et al. Sarcopenia is an independent prognostic factor in male patients with diffuse large B-cell lymphoma. Ann Hematol 2015;94:2043–53.

[52] Nault JC, Pigeur F, Nelson AC, Costentin C, Telska L, Katafah S, et al. Visceral fat area predicts survival in patients with advanced hepatocellular carcinoma treated with tyrosine kinase inhibitors. Dig Liver Dis 2015;47:869–76.

[53] Ninomiya G, Fuji T, Yamada S, Yabusaki N, Suzuki K, Iwata N, et al. Clinical impact of sarcopenia on prognosis in pancreatic ductal adenocarcinoma: a retrospective cohort study. Int J Cancer 2017;9:45–51.

[54] Nishikawa H, Nishijima N, Enomoto H, Sakamoto A, Nasu A, Komekado H, et al. Prognostic significance of sarcopenia in patients with hepatocellular carcinoma undergoing sorafenib therapy. Oncol Lett 2017;14:1637–47.

[55] Okumura S, Kaido T, Hamaguchi Y, Fujimoto Y, Masui T, Mizumoto M, et al. Impact of preoperative quality as well as quantity of skeletal muscle on survival after resection of pancreatic cancer. Surgery 2015;157:1088–98.

[56] Okumura S, Fujimoto Y, Kida T, Kobayashi A, Iida T, Miyaishi A, et al. Impact of the preoperative quantity and quality of skeletal muscle on outcomes after resection of extrapleural biliary malignancies. Surgery 2015;165:821–33.

[57] Otsuka S, Kido T, Hamaguchi Y, Kobayashi A, Shirai H, Fujimoto Y, et al. Impact of skeletal muscle mass, muscle quality, and visceral adiposity on outcomes following resection of intraperitoneal cholangiocarcinoma. Ann Surg Oncol 2017;24:1037–45.

[58] Peiper M, Asari R, Kristo I, Rieder E, Tammann D, Ba-Salamah A, et al. Are sarcopenia, obesity and sarcopenic obesity predictive of outcome in patients treated with targeted therapy? Br J Cancer 2015;112:1806–8.

[59] Psutka SP, Carrasco A, Schmit GD, Moynagh MR, Boorjian SA, Frank I, et al. Sarcopenia in patients with bladder cancer undergoing radical cystectomy: impact on cancer-specific and all-cause mortality. Cancer 2014;120:2910–8.

[60] Psutka SP, Boorjian SA, Schmit GD, Frank I, Carrasco A, et al. Mortality after radical cystectomy: impact of obesity versus adiposity after adjusting for skeletal muscle wasting. J Urol 2015;193:1507–13.

[61] Psutka SP, Boorjian SA, Moynagh MR, Schmit GD, Costello BA, Thompson D, et al. Decreased skeletal muscle mass is associated with an increased risk of...
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et al. Unraveling the relationship between mortality, hyponatraemia, inflammation and malnutrition in hemodialysis patients: results from the international MONDO initiative. Eur J Clin Nutr 2016;70:779–84.

[111] Jin S, Lu Q, Su C, Pang D, Wang T. Shortage of appendicular skeletal muscle is an independent risk factor for mortality in peritoneal dialysis patients. Perit Dial Int 2017;37:78–84.

[112] Kim J, Kim S, Oh J, Lee J, Shin J, Kim H, et al. Impact of sarcopenia on long-term mortality and cardiovascular events in patients undergoing hemodi-
alysis. Korean JIntern Med 2019;34:599–607.

[113] Kittusukulpan P, Chertow GM, Carrero JJ, Delgado C, Kayser GA, Johansen KL. Sarcopenia and its individual criteria are associated in part with mortality among patients on hemodialysis. Kidney Int 2017;92:238–47.

[114] Lin T, Peng C, Hung S, Tarrq D. Body composition is associated with clinical outcomes in patients with non-dialysis-dependent chronic kidney disease. Kidney Int 2018;93:689–97.

[115] Paudel K, Visser A, Burke S, Samad N, Fan SL. Can bioimpedance mea-
surements of lean and fat tissue mass replace subjective global assessments in peritoneal dialysis patients? J Ren Nutr 2015;25:480–7.

[116] Rosenberger J, Kissova V, Majernikova M, Straussova Z, Boldizsár J. Body composition monitor assessing malnutrition in the hemodialysis population independently predicts mortality. J Ren Nutr 2014;24:2–7.

[117] Abad S, Sotomayor G, Vega A, Perez de Jose A, Verdales U, Jofre R, et al. The phase angle of the electrical impedance is a predictor of long-term survival in dialysis patients. Nefrologia 2011;31:670–6.

[118] Barros A, Costa BE, Mottin CC, d’Avila DD. Depression, quality of life, and body composition in patients with end-stage renal disease: a cohort study. Clin Nutr 2015;34:70–7.

[119] Vega A, Abad S, Macias N, Aragoncillo I, Santos A, Galan I, et al. Low lean tissue mass is an independent risk factor for mortality in patients with stages 4 and 5 chronic kidney disease. Nephrology 2017;22:563–9.

[120] Wilson FP, Xie D, Anderson AH, Leonard MB, Reese PP, Delafontaine P, et al. Urinary creatinine excretion, biochemical impedance analysis, and clinical outcomes in patients with CKD: the CRIC study. Clin J Am Soc Nephrol 2014;9:2005–103.

[121] Wu H, Tseng S, Wang W, Chen H, Lee L. Association between obesity and muscle mass and mortality in dialysis. Intern Med J 2017;47:1282–91.

[122] Androgra L, Sharma D, Amouda A, Abramowitz M, Sarcopenia, obesity, and mortality in US adults with and without chronic kidney disease. Kidney Int Rep 2017;2:201–11.

[123] Honda H, Quresha A, Axcellon J, Heimburger O, Sulinman M, Barany P, et al. Obese sarcopenia in patients with end-stage renal disease is associated with increased inflammation and undergoing radical nephrectomy: a retrospective multi-institutional study. Int J Clin Pract 2017;22:136–44.

[124] Fukasawa H, Kaneko M, Niwa H, Matsuayma T, Yasaki H, Kumahagi E, et al. Lower thigh muscle mass is associated with all-cause and cardiovascular mortality in elderly hemodialysis patients. Eur J Clin Nutr 2014;68:1472–7.

[125] Locke J, Carr J, Nair S, Terry J, Reed R, Smith G, et al. Abdominal lean mass is associated with lower mortality among kidney waitlist candidates. Clin Transplant 2017;31. https://doi.org/10.1111/ctr.12911.

[126] Nishikawa H, Enomoto H, Ishii A, Ishwa Y, Miyamoto Y, Ishii N, et al. Comparison of prognostic impact between the child-pugh score and skeletal muscle mass for patients with liver cirrhosis. Nutrients 2017:9:595.

[127] Miyamoto H, Ymita Y, Nishikawa H, Enomoto H, Miyamoto T, Ihara M, et al. Clinical utility of bioimpedance analysis in liver cirrhosis. J Hepatobiliary Pancreat Sci 2017;24:409–16.

[128] Golse N, Bucur P, Ciocio O, Pittua G, Sa Cunha A, Adam R, et al. A new definition of sarcopenia in patients with cirrhosis undergoing liver transplantation. Liver Transplant 2017;23:143–54.

[129] Haniu T, Shirai M, Ohnishi S, Miyazaki T, Ieda T, Toshi K, et al. Rapid skeletal muscle wasting predicts worse survival in patients with liver cirrhosis. Hepatology 2017;66:1023–31.

[130] Jeon YJ, Wang JH, Ock SY, Xu W, Lee JD, Lee JH, et al. Newly developed sarcopenia as a prognostic factor for survival in patients who underwent liver transplantation. PloS One 2015;10:e0145986.

[131] Masuda T, Shirabe K, Ishimura T, Yashiki T, Hayashi M, Ishizu T, Szejoe Y, et al. Sarcopenia is a prognostic factor in living donor liver transplantation. Liver Transplant 2014;20:401–7.

[132] Montano-Loza A, Angulo F, Meza-Junco J, Prado C, Sawyer M, Beaumont C, et al. Sarcopenic obesity and myosteatosis are associated with higher mortality in patients with cirrhosis. Aliment Pharmacol Ther 2010;32:68–77.
mortality in patients with cirrhosis. J Cachexia Sarcopenia Muscle 2016;7: 126–35.

[143] Nishiwaki H, Enomoto H, Isih I, Awata Y, Miyamoto Y, Ishii N, et al. Prog- nostic significance of low skeletal muscle mass compared with protein-energy malnutrition in liver cirrhosis. Hepatol Res 2017;47:1042–52.

[144] Shirai H, Kadoi T, Hamaguchi Y, Yao S, Kobayashi A, Okumura S, et al. Preoperative low body mass index has a strong negative effect on pulmonary function in patients undergoing living donor liver transplantation. Nutrition 2018;45:1–10.

[145] Tandon P, Mey M, Irwin I, Mm GM, Gramlich L, Bain VG, et al. Severe muscle depletion in patients on the liver transplant wait list is a predictor of independent and incidental prognostic value. Liver Transplant 2012;18:1209–16.

[146] Yadav A, Chang YH, Carpenter S, Silva AG, Rakela J, Aqel BA, et al. Relationship between sarcopenia, six-minute walk distance and health-related quality of life in liver transplant candidates. Clin Transplant 2015;29:134–41.

[147] Carey EJ, Lai JC, Wang CW, Dasarathy S, Lobach I, Montano-Loza AJ, et al. Severe muscle mass and risk of death in an elderly population. Nutr Metabol Cardiovasc Dis 2016;26:505.

[148] Toss F, Wiklund P, Nordstrom P, Nordstrom A. Body composition and mortality in elderly people. Eur J Geriatr Pharmacol 2017;17:691–6.

[149] Spahilari A, Mukamal KJ, Isih I, Awata Y, Miyamoto Y, Ishii N, et al. Prog- nostic significance of low skeletal muscle mass compared with protein-energy malnutrition in liver cirrhosis. Hepatol Res 2017;47:1042–52.

[150] Shirai H, Kadoi T, Hamaguchi Y, Yao S, Kobayashi A, Okumura S, et al. Preoperative low body mass index has a strong negative effect on pulmonary function in patients undergoing living donor liver transplantation. Nutrition 2018;45:1–10.

[151] Tandon P, Mey M, Irwin I, Mm GM, Gramlich L, Bain VG, et al. Severe muscle depletion in patients on the liver transplant wait list is a predictor of independent and incidental prognostic value. Liver Transplant 2012;18:1209–16.

[152] Yadav A, Chang YH, Carpenter S, Silva AG, Rakela J, Aqel BA, et al. Relationship between sarcopenia, six-minute walk distance and health-related quality of life in liver transplant candidates. Clin Transplant 2015;29:134–41.

[153] Carey EJ, Lai JC, Wang CW, Dasarathy S, Lobach I, Montano-Loza AJ, et al. Severe muscle mass and risk of death in an elderly population. Nutr Metabol Cardiovasc Dis 2016;26:505.
Aahlín EK, Tranø G, Johns N, Horn A, Soreide JA, Fearon KC, et al. Risk factors, complications and survival after upper abdominal surgery: a prospective cohort study. BMC Surg 2015;15:83.

Leeper C, Lin E, Hoffman M, Fombona A, Zhou T, Kutch M, et al. Computed tomography abbreviated assessment of sarcopenia following trauma: the CAAS measurement predicts 6-month mortality in older adult trauma patients. J Trauma Acute Care Surg 2016;80:805–11.

Rangel E, Rios-Diaz A, Uyeda J, Castillo-Angeles M, Cooper Z, Olufajo O, et al. Sarcopenia increases risk of long-term mortality in elderly patients undergoing emergency abdominal surgery. J Trauma Acute Care Surg 2017;83:1179–86.

Shibahashi K, Sugiyama K, Kashiura M, Hamabe Y. Decreasing skeletal muscle as a risk factor for mortality in elderly patients with sepsis: a retrospective cohort study. J Intens Care 2017;5:8.

Wagner D, Buttro S, Kim Y, Gani F, Xu L, Margonis GA, et al. Clinical and morphometric parameters of frailty for prediction of mortality following hepatopancreaticobiliary surgery in the elderly. Br J Surg 2016;103:83–92.

Yoo T, Lo WD, Evans DC. Computed tomography measured psoas density predicts outcomes in trauma. Surgery 2017;162:377–84.

Boutin RD, Bamrungchart S, Bateni CP, Beavers DP, Beavers KM, Meehan JP, et al. CT of patients with hip fracture: muscle size and attenuation help predict mortality. Am J Roentgenol 2017;208:W208–15.

Dirks RC, Edwards BL, Tong E, Schaeven B, Turrentine FE, Shada A, et al. Sarcopenia in emergency abdominal surgery. J Surg Res 2017;207:13–21.

Wallace JD, Calvo RY, Lewis PR, Brill JB, Shackford SR, Sise MJ, et al. Sarcopenia as a predictor of mortality in elderly blunt trauma patients: comparing the masseter to the psoas using computed tomography. J Trauma Acute Care Surg 2017;82:65–72.

Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition, prevalence, etiology, and consequences. International working group on sarcopenia. J Am Med Dir Assoc 2011;12:249–56.

Morley JE, Abbatecola AM, Argiles JM, Baracso V, Bauer J, Bhasin S, et al. Sarcopenia with limited mobility: an international consensus. J Am Med Dir Assoc 2011;12:403–9.

Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci 2014;69:547–58.

Zhuan CL, Shen X, Zou HB, Dong QT, Cai HY, Chen XL, et al. EWGSOP2 versus EWGSOP1 for sarcopenia to predict prognosis in patients with gastric cancer after radical gastrectomy: analysis from a large-scale prospective study. Clin Nutr 2020;39:2301–10.

Martin L, Birdsall L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. J Clin Oncol 2013;31:1539–47.

Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol 2008;9:629–35.

Williams BA, Mandrekar JA, Mandrekar SJ, Cha SS, Furth AF. Finding optimal cutoffs for continuous covariates with binary and time-to-event outcomes. Mayo Foundation; 2006. Technical Report Series #79. Rochester, MN, USA.