REVIEW

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Sarcopenia and ovarian cancer survival: a systematic review and meta-analysis

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Abstract

Background Sarcopenia is the loss of skeletal muscle mass and function that occurs with advancing age and certain diseases. It is thought to have a negative impact on survival in cancer patients. Routine computed tomography imaging is often used to quantify skeletal muscle in cancer patients. Sarcopenia is defined by a low skeletal muscle index (SMI). Skeletal muscle radiation attenuation (SMRA) is used to define muscle quality. The primary aim of this meta-analysis was to study the association between sarcopenia or SMRA and overall survival (OS) or complications in patients with ovarian cancer.

Methods Medline, Embase, CINAHL, and PEDro databases were searched from inception to 15 February 2019. Studies evaluating the prognostic effect of SMI and SMRA on ovarian cancer survival or surgical complications were included. Risk of bias and study quality were evaluated with the Quality in Prognosis Studies Instrument (QUIPS) according to the modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.

Results The search strategy yielded 4262 hits in all four databases combined. Ten and eight studies were included for qualitative and quantitative analysis, respectively. Meta-analysis revealed a significant association between the SMI and OS [0.007; hazard ratio (HR): 1.11, 95% confidence interval (CI): 1.03–1.20]. SMRA was also significantly associated with OS ($P < 0.001$; HR: 1.14, 95% CI: 1.08–1.20). Association between the SMI and surgical complications had borderline statistical significance (0.05; HR: 1.23, 95% CI: 1.00–1.52). The risk of bias assessed with QUIPS was high in all studies. The quality of the evidence was very low.

Conclusions Whereas our meta-analysis indicated that a low SMI and low SMRA are associated with survival in ovarian cancer patients, the low quality of the source data precludes drawing definitive conclusions.

Keywords Sarcopenia; Ovarian cancer; Cachexia; Survival; Meta-analysis

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Introduction

Despite intensified treatment and staging procedures, long-term survival (10–15 years) of women with epithelial ovarian cancer has not improved in the last 25 years. The observed improvements in 5 year overall survival (OS) reflect a more prolonged disease control rather than a better chance of cure.[1] Attempts to improve the management of ovarian cancer are focused on overcoming chemotherapy resistance and intraperitoneal chemotherapy, immunotherapy, and personalized medicine.[2–5] With regard to personalized medicine, efforts are being made to explore new therapeutic targets, and the patients' physical ability to receive treatment is an important accompanying factor to be considered. This physical

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ability is partially reflected by the patients' muscle mass. Low muscle mass or sarcopenia has been identified as a prognostic factor in several malignancies including pancreatic,[6] hepatic, biliary tract, gastrointestinal,[7] and urothelial cancer.[8,9]

Sarcopenia is frequently encountered in the elderly but also in patients with heart failure, chronic renal failure, malnutrition, chronic obstructive pulmonary disease, and cancer.[10,11] Cancer-related sarcopenia is part of a syndrome called cancer cachexia,[12] which results from a negative protein and energy balance driven by abnormal metabolism and reduced food intake. Because the pathophysiology is not yet fully understood, therapeutic options remain limited.[13] The diagnosis of cancer cachexia is based on body weight loss alone or a combination of loss of body weight and muscle mass.[12] Diagnosing cachexia in ovarian cancer patients can be challenging because weight loss is often masked by accumulation of ascites. In ovarian cancer patients, it is therefore more reliable to quantify skeletal muscle instead of weight loss. Dual-energy X-ray absorptiometry, bio-impedance analysis, magnetic resonance imaging, and computed tomography (CT) are available methods to perform this quantification. Magnetic resonance imaging and CT scanning are considered the gold standard for the quantification of skeletal muscle mass.[10,14] Skeletal muscle mass, as assessed by CT scan analysis, is a prognostic factor independent of body mass index.[15] Because ovarian cancer patients undergo CT scan imaging for routine diagnostic purposes, it has become the most frequently used method for quantifying skeletal muscle mass and quality in this population. Sarcopenia is often defined by the skeletal muscle index (SMI), which is the total muscle area as observed on the CT scan corrected for height. Skeletal muscle radiation attenuation (SMRA) is defined by the mean Hounsfield unit value of the skeletal muscle and has been used as a measure of muscle quality. The Hounsfield unit value is a quantitative scale for describing radiodensity and is used in CT scanning.

Skeletal muscle index and SMRA have been quantified in several cohorts of ovarian cancer patients,[16–26] with the purpose of identifying a potential association between skeletal muscle mass or quality and survival. Because some of these studies have reported associations between SMI or SMRA and survival/complications while others have not, we aimed to summarize and integrate their findings to provide a complete overview of all available literature on this subject. This meta-analysis is the first to provide a quantitative and qualitative assessment of SMI and SMRA related to ovarian cancer survival and development of complications.

Materials and methods

Electronic search

This analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[27] An independent search of the Medline (via OvidSP), Embase (via OvidSP), CINAHL (via EBSCO), and PEDro databases was carried out. The search was completed on 15 February 2019. Reviews, case reports, opinion articles, conference abstracts, and non-published data were excluded.

Study selection

Studies that met the following criteria were included for quantitative meta-analysis: (i) studies of patients with ovarian cancer; (ii) studies that associated SMI or SMRA with OS or complication rate; (iii) skeletal muscle was quantified by CT scan; and (iv) studies that reported hazard ratios (HRs), odds ratios (ORs) or event counts, and 95% confidence intervals (CIs) for survival or complications. Studies reporting insufficient data for calculating HR, OR, and 95% CI were excluded. Two researchers (J. U. and J. Z.) performed an independent search of the databases and selected abstracts. They were blinded to each other's results. Agreement upon selected abstracts was reached afterwards. Both researchers then independently screened full-text articles and came to agreement for inclusion after each made their individual selection. All databases were screened from inception up to 2019 (see *Appendices* S1 and S2 for full electronic search and used terms). In the case of duplicate studies or reports, the most recent version was included.

Data extraction

Data extraction was also performed independently by the two researchers. The following data were retrieved: first author name, year of publication, type of study, number of patients included, mean/median population age, disease stage, method of quantifying skeletal muscle mass, cut-off point for SMI or low SMRA, prevalence of SMI and low SMRA, and associated HR or OR with 95% CI for OS and associated HR or OR for complications. HRs and ORs were extracted from univariate and multivariate analyses or calculated from event counts.

Quality assessment

Risk of bias for individual studies was assessed with the Quality in Prognosis Studies (QUIPS) Risk of Bias Assessment Instrument for Prognostic Factor Studies.[28,29] The QUIPS tool has several domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. All domains consist of several criteria of which the combined rating produces a classification of high, moderate, or low risk. All domains were scored by the two individual researchers. The overall risk of bias was considered low if $\leq$2 domains were rated a moderate risk of bias and all others were rated a

low risk of bias. The overall risk of bias was considered moderate if >2 domains were rated a moderate risk of bias and all others were rated a low risk of bias. The overall risk of bias was considered high if ≥1 domain was rated a high risk of bias, irrespective of all other domains. Consensus was reached after classification by the individual researchers. The quality of the overall quantitative outcome of this meta-analysis was determined with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool, which objectively assesses outcomes based on different domains using a scoring system. Outcomes are allocated a score based on study design, which can be downgraded if certain criteria for quality are not met. This results in an objective score with a GRADE rating ranging from 1 (very low quality; little confidence in the estimate; the true prognosis is likely to be substantially different from the estimate) to 4 (high quality; very confident that the true prognosis lies close to that of the estimate).[30,31]

Data handling and statistical analysis

Meta-analyses were performed in Review Manager (RevMan v5.3, 2014; The Cochrane Collaboration, Copenhagen, Denmark), and results were displayed in forest plots. HRs for survival and ORs for surgical complications were either retrieved or calculated from the included studies. HRs and ORs were calculated with an indirect variance estimation as proposed by Parmar *et al*.[32] A fixed effects model was used because effects were not expected to substantially vary between studies because the methodologies were highly homogeneous. Results were considered statistically significant at $P < 0.05$. Statistical heterogeneity, or inconsistency, was assessed using the χ^2 and I^2 tests. An $I^2 \geq 65\%$ and a *P*-value for the χ^2 test below 0.10 was considered a violation of the assumption of homogeneity.

Results

Search results/included studies

The search of four databases yielded 4262 hits. After the automatic removal of 66 duplicates, 4196 titles and abstracts were screened by two independent researchers (J. U. and J. Z.). After screening abstracts and titles and reaching agreement, 38 full-text articles were considered for inclusion. After a full-text review of the 38 articles, 10 remained for qualitative analysis. Out of these 10 articles, eight remained for quantitative analysis. The selection process and reasons for exclusion are shown in *Figure* 1. A manual review of the references yielded no extra inclusions. All included studies were published from 2013 onwards. Study characteristics are summarized in *Table* 1.

Included studies

All eight included studies for quantitative analysis were of a retrospective nature. Six out of the eight included studies evaluated SMI and its association with OS in ovarian cancer, comprising a total of 1198 patients.[16–20,22] Four studies evaluated SMRA and its association with OS in ovarian cancer, comprising a total of 975 patients.[17,18,20,22] Three studies evaluated SMI and its association with short-term postoperative morbidity, comprising a total of 407 patients.[17,23,24]

All studies were published in international peer-reviewed journals. Skeletal muscle mass was quantified on an axial CT scan at the third or fourth lumbar level. The SMI or SMRA was calculated from total muscle area as determined from the lumbar CT scan in all studies, except one that used the core muscle index (CMI; psoas muscle area) for quantification.[24] See Appendix S4 for an overview of how skeletal muscle was defined on CT scan. Two studies were not included for quantitative analyses: one that analysed phase angle with bio-impedance analysis instead of with CT,[25] and the other did not determine a cut-off for defining sarcopenia but analysed muscle mass as a continuous variable.[21]

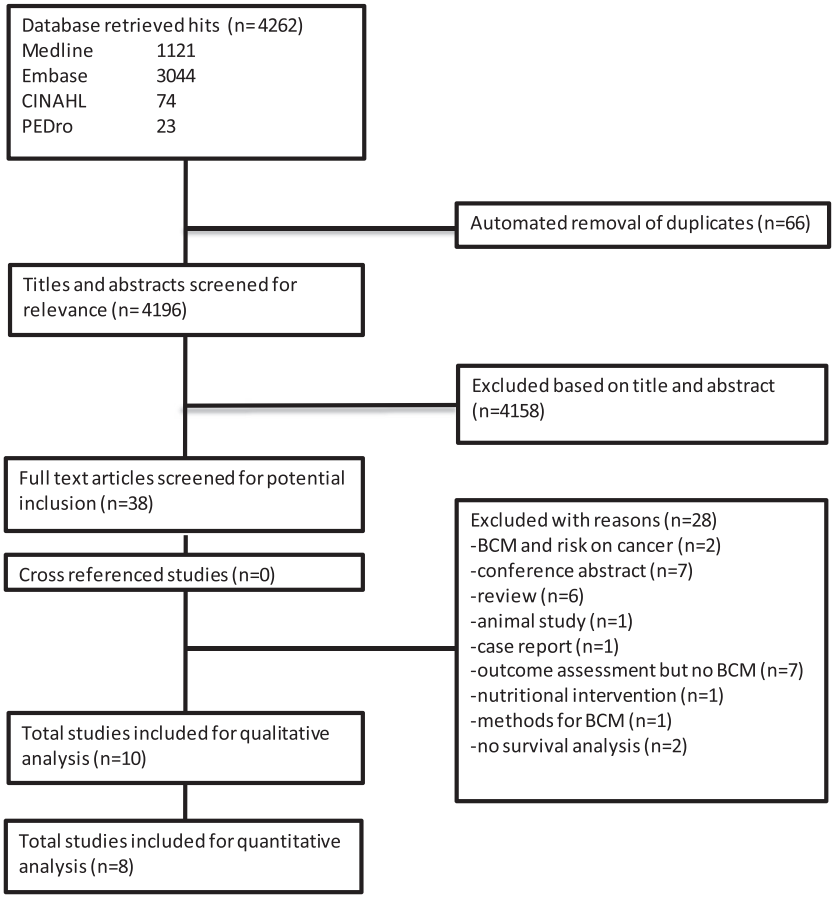
Patient characteristics

All patients underwent primary or interval debulking surgery combined with adjuvant or neo-adjuvant chemotherapy. One study included patients with endometrial and ovarian cancer. For this meta-analysis, only the cohort of ovarian cancer patients was included.[23] FIGO (International Federation for Gynecologic Oncology) stage across all studies ranged from I to IV. The distribution of patients according to FIGO stage was as follows: I, *n* = 106 (6.8%); II, *n* = 55 (3.5%); III, *n* = 968 (62%); and IV, *n* = 433 (27.7%).

Skeletal muscle index, skeletal muscle radiation attenuation, and overall survival

The meta-analysis of the univariate data of the influence of the SMI on OS is depicted in *Figure* 2. The overall effect of sarcopenia on OS was significant (0.007; HR: 1.11, 95% CI: 1.03–1.20). Statistical consistency between the compared HRs and 95% CIs was evaluated with the χ^2 and I^2 tests, which returned a χ^2 0.15 and an I^2 of 38%, indicating methodological homogeneity, or consistency, between studies. The fixed effects model was deliberately chosen because the methodologies for measuring SMI and its association with OS used in the studies were homogeneous; however, use of the random effects model would not have influenced the results (0.03; HR: 1.12, 95% CI: 1.01–1.24). In meta-analysis of the multivariate data (fixed effects), there was also a significant association between SMI and OS (0.02; HR: 1.17, 95% CI:

Figure 1 Flow diagram depicting the selection process for studies. BCM, body composition measurement.



1.03–1.33) (*Figure* 3). A χ^2-test *P*-value of 0.31 and an I^2 of 14% indicated consistency between studies for this association.

The meta-analysis of univariate data of the influence of low SMRA on OS is depicted in *Figure* 4. The overall effect of low SMRA on OS was significant ($P < 0.001$; HR: 1.14, 95% CI: 1.08–1.20). Again, the fixed effects model was chosen; however, a random effects model would not have influenced the results ($P < 0.001$; HR: 1.15, 95% CI: 1.08–1.22). A χ^2-test *P*-value of 0.34 and an I^2 of 11% indicated consistency. The meta-analysis of the multivariate data (fixed effects) revealed a significant association between SMRA and OS (0.001; HR: 1.13, 95% CI: 1.06–1.20) (*Figure* 5), while tests for consistency yielded a χ^2 0.07 and an I^2 of 62%.

Sarcopenia and surgical complications

The meta-analysis of the effect of a low SMI on the development of surgical complications is depicted in *Figure* 6. The overall effect of low SMI vs. high SMI was borderline significant (0.05; HR: 1.23, 95% CI: 1.00–1.52). A fixed effects model was chosen, but using a random effects model would not have changed the outcome (0.10; HR: 1.26, 95% CI: 0.95–1.67). Studies showed statistical consistency (χ^2 0.17; I^2 of 43%).

Risk of bias and GRADE assessment

According to the QUIPS checklist, all included studies had an overall high risk of bias. An overview per domain can be found in *Appendix* S3. According to the GRADE rating, quality of the outcome was considered 'very low' for the reliability of all associations. The findings are summarized in *Table* 2. The reason for downgrading 'indirectness' was because of the use of different assessments of SMI in the surgical complications cohort (total SMI vs. CMI). Indirectness was defined as the correspondence of the population of interest with the population included for analysis. Imprecision was detected in the forest plot on the influence of SMI on OS. Imprecision was defined as an insufficient sample size of included studies and very wide CIs in meta-analysis, crossing the null in ≥50% cases.

Table 1 Study characteristics and main findings

Author	Year	Country	Study design	*n*	Age[a]	Disease stage (FIGO)	Measurement	SMI cut-point (cm^2/m^2)	SMRA (HU) cut-point	Prevalence of sarcopenia (%) (based on SMI)	Qualitative/ quantitative	QUIPS score	Outcome (OS/ complications)	Main outcome
Torres	2013	USA	Retrospective	83	68.4	IIIc–IV	CT based 3rd lumbar level	n.a.	n.a.	n.a.	Qualitative	High	OS	Total muscle mass is not predictive for survival. Lower subcutaneous fat and intramuscular fat is associated with poor OS and longer hospital stay
Aust	2015	Austria	Retrospective	140	60	I–IV	CT based 3rd lumbar level	41	39	28.9	Quantitative	High	OS	Low SMRA is associated with poor OS; SMI is not associated with poor OS
Rutten	2016	Netherlands	Retrospective	123	66.5	II–IV	CT based 3rd lumbar level	41.5	n.a.	50.4	Quantitative	High	OS	Longitudinal loss of SMI is associated with poor OS; low baseline SMI is not associated with poor OS
Kumar	2016	USA	Retrospective	296	64.6	IIIc–IV	CT based 3rd lumbar level	39	36.4	39	Quantitative	High	OS	Low SMRA is associated with poor OS; SMI is not associated with poor OS
Bronger	2017	Germany	Retrospective	105	65	III–IV	CT based 3rd lumbar level	38.5	n.a.	11	Quantitative	High	OS	Low SMI is associated with poor OS
Rutten	2017	Netherlands	Retrospective	216	62.5	II–IV	CT based 3rd lumbar level	38.73	36	32	Quantitative	High	Both	Low SMI is not associated with poor OS or surgical complications. Low SMRA is not associated with OS
Conrad	2018	USA	Retrospective	102	55	III–IV	CT based 4th lumbar level	2.8 (CMI)	n.a.	54	Quantitative	High	Both	Low SMI combined with hypoalbuminaemia is associated with worse OS. Low SMI is not associated with complications
Paula de Silva	2018	Brazil	Retrospective	89	n.r.	I–IV	CT based 3rd lumbar level	38.9	Quartiles	25.8	Quantitative	High	30 days of mortality and complications	Low SMI and skeletal muscle quality are associated with development of surgical complications
Ataseven	2018	Germany	Retrospective	323	60	IIIb–IVb	CT based 3rd lumbar level	38.5 39 41	32	29.4 33.7 47.1	Quantitative	High	OS	Low SMRA is associated with OS; low SMI is not associated with OS
Uccella	2018	Italy	Retrospective	70	58.5	IIIc–IV	Phase angle (BIA)	n.a.	n.a.	n.a.	Qualitative	High	Complications	Low phase angle is associated with surgical complications

BIA, bio-electrical impedance analysis; FIGO, International Federation for Gynecologic Oncology; HU, Hounsfield units; *n*, no. of included patients; n.a., not applicable; n.r., not reported; OS, overall survival; SMI, skeletal muscle index; SMRA, skeletal muscle radiation attenuation.
[a]Mean or median as reported.

Figure 2 Meta-analysis of univariate data: the effect of low skeletal muscle index on survival. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error.

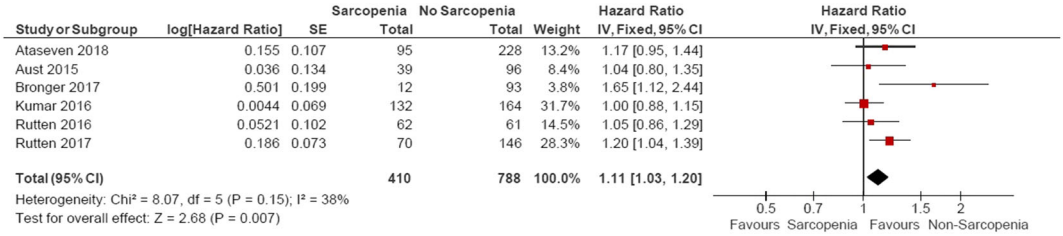


Figure 3 Meta-analysis of multivariate data: the effect of low skeletal muscle index on survival. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error.

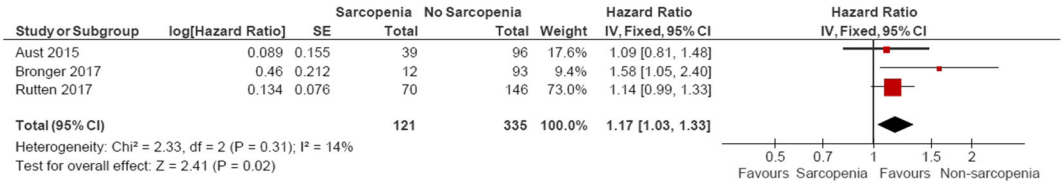


Figure 4 Meta-analysis of univariate data: the effect of low muscle attenuation on overall survival. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error; SMRA, skeletal muscle radiation attenuation.

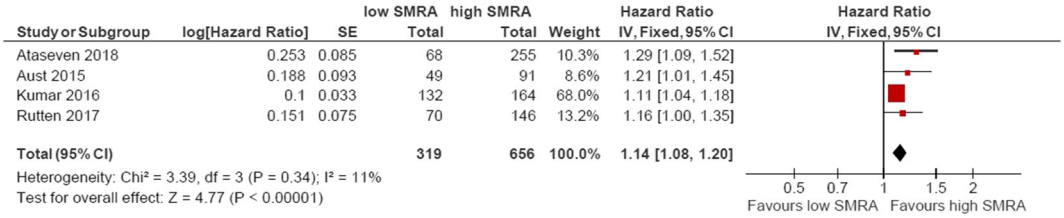


Figure 5 Meta-analysis of multivariate data: the effect of low muscle attenuation on overall survival. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error; SMRA, skeletal muscle radiation attenuation.

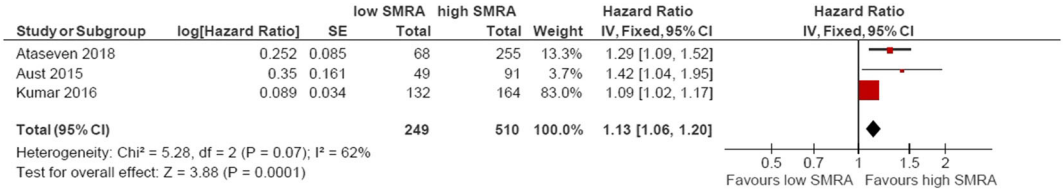


Figure 6 Meta-analysis: effect of low skeletal muscle index on surgical complications. CI, confidence interval; df, degrees of freedom; IV, inverse variance; SE, standard error. Conrad *et al.* assessed core muscle index instead of skeletal muscle index.

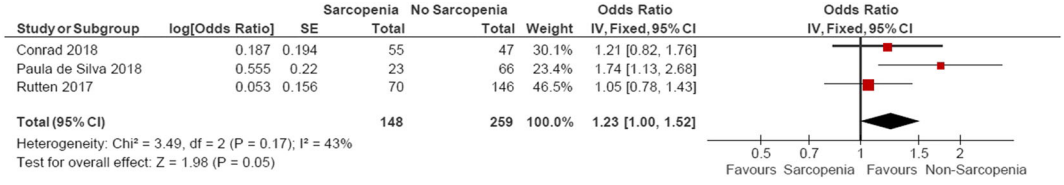


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Table 2 The influence of SMI or SMRA on ovarian cancer OS or complication rate

GRADE assessment of outcome				GRADE factors							
	Participants (studies)	Estimated effect size (95% CI)	Phase	Study limitations	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Effect size	Dose effect	GRADE assessment
Primary outcome												
OS based on SMI	1198 (6)	1.11 (95% CI: 1.03–1.20)	1	x	x	✓	✓	x	n.a.	n.a.	n.a.	Very low (+)
OS based on SMRA	979 (4)	1.14 (95% CI: 1.08–1.20)	1	x	x	✓	✓	✓	n.a.	n.a.	n.a.	Very low (+)
Secondary outcome												
Complications based on SMI	407 (3)	1.23 (95% CI: 1.00–1.52)	1	x	x	✓	x	✓	n.a.	n.a.	n.a.	Very low (+)

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool is judged per outcome and rationale for overall GRADE score is given. Phase 1 exploratory studies start with a moderate score of three points (+++). Because all included studies consisted of observational studies (phase 1), authors allocated each outcome category three points to start with. Study limitations encompassed (i) no clearly defined cut-off, (ii) definition of the outcome was not clearly defined, and (iii) time period for measurement of outcome was not clearly stated in ≥50% of studies. Risk of bias was assessed with the QUIPS tool. Inconsistency was defined by an $I^2 \geq 65\%$ and *P*-value <0.10 and 95% CI and estimate points of effect found on both sides of null line. Indirectness was defined by the correspondence of population of interest to the population included for analysis. Imprecision was defined by insufficient sample size and very wide confidence intervals, crossing the null in ≥50% cases. Number of included studies was too low for assessment of publication bias. 95% CI, 95% confidence interval; n.a., not applicable; OS, overall survival; SMI, skeletal muscle index; SMRA, skeletal muscle radiation attenuation; ✓, no serious limitation; x, serious limitation; xx, very serious limitation. Outcome: +, very low; ++, low; +++, moderate; ++++, high.

Discussion

This meta-analysis shows that SMI and SMRA are associated with OS in ovarian cancer patients in both univariate and multivariate analyses. The magnitude of the observed effect in our meta-analysis of multivariate data is likely to be lower than that reported in other studies, because those studies that did not find a significant association between SMI[16,20,22] and/or SMRA[17] and survival in univariate analysis did not report multivariate outcomes. The association between SMI and surgical complications was borderline significant in meta-analysis of the univariate data, and meta-analysis of the multivariate data could not be performed because it was only reported in one study.[23]

Sarcopenia prevalence estimated by SMI in the included studies of our meta-analysis of ovarian cancer cases has a wide range from 11 to 54%; one important reason for which may be related to the use of different cut-offs for assessing sarcopenia (38.5–41.5 cm^2/m^2). Sex-specific cut-offs for defining sarcopenia have previously been made using optimum stratification methods.[15,33] Optimum stratification methods are based on log-rank statistics. They solve the threshold value of a continuous covariate (SMI) that best separates patients with and without sarcopenia with respect to time to an event outcome.[34] Although cut-offs for women of 38.5 cm^2/m^2 for respiratory tract and GI cancer[33] and 41 cm^2/m^2 for lung and GI cancer[15] are the most widely used, cut-offs used in ovarian cancer studies vary. A meta-analysis of 38 studies of different malignancies (no ovarian cancer patients) by Shachar *et al*.[8] revealed a range in sarcopenia prevalence of 11–69%. Because the cut-off used to define sarcopenia will directly influence the outcome of associations made between SMI and OS or complication rate, it is vital that a consensus is arrived at. Frequently, cohorts are divided based upon tertiles, quartiles, or standard deviations to discriminate between sarcopenic and non-sarcopenic patients. This seems an acceptable method for comparing patients suffering from more severe sarcopenia with non-sarcopenic patients. In the current cohort, we observed that studies with lower cut-offs, between 38.5 and 38.73 cm^2/m^2, were more likely to report a prognostic effect of sarcopenia.[17,19] In future assessments of sarcopenia and ovarian cancer survival, we propose the use of tertiles, quartiles, or a relatively low cut-off (<38.5 cm^2/m^2) to distinguish sarcopenic from non-sarcopenic patients. These measurements should preferably be combined with muscle function assessment according to the recommendations of several international working groups on sarcopenia.[10,11,14,35]

Longitudinal changes in SMI are also used to assess the development of sarcopenia.[16,19] However, surgery and subsequent recovery considerably affect skeletal muscle mass. One week of bed rest has been shown to lead to a substantial decrease in muscle mass.[36] Nevertheless, because sarcopenia is a dynamic process, the prognostic value of changes in

skeletal muscle mass seems greater than assessment of baseline measurements only. One study of end-stage pancreatic cancer patients undergoing chemotherapy did find an association between decreasing skeletal muscle mass and survival.[6] In another cohort of pancreatic cancer patients receiving chemotherapy, in which the prevalence of sarcopenia was very high and the median OS was very short, longitudinal decrease of fat and muscle mass was associated with worse OS.[37] In a very large cohort study of stage I–III colorectal cancer patients, a decline in muscle mass was also associated with shorter survival.[38] So far, only two studies have examined longitudinal changes in SMI in ovarian cancer: one study of end-stage patients undergoing surgery found no correlation between decreasing skeletal muscle mass and survival,[19] while the other examining patients receiving neo-adjuvant chemotherapy concluded that longitudinal decrease in the SMI was predictive for survival.[16]

The present meta-analysis is the first to report a quantitative assessment of SMI and SMRA and their clinical outcomes in ovarian cancer. The strength of this meta-analysis is that only ovarian cancer patients whose SMI or SMRA was assessed with a lumbar CT scan were included, creating a homogeneous cohort. A weakness is the fact that included studies used different cut-off points to define sarcopenia, leading to heterogeneity in the reported sarcopenia prevalence. The CMI or psoas muscle index was used for the assessment of skeletal muscle in one included study[24]; however, as the psoas muscle can be affected by spinal pathology, it may be unsuitable for assessing skeletal muscle. Moreover, the psoas represents only a small area of total lumbar skeletal muscle and is difficult to measure accurately, making it an unreliable substitute for the total lumbar skeletal muscle area.[39,40] Although the contrast phase used for the CT scan does not majorly influence SMI values,[41,42] it does greatly affect SMRA. Because the contrast phase is not mentioned by any of the studies assessing SMRA, this is a potential shortcoming. Overall, quality of the evidence as assessed with the GRADE checklist was very low. Additionally, all studies in this meta-analysis were of a retrospective nature. Because all studies were methodologically homogeneous, a fixed effects model was chosen for the meta-analysis. However, use of a random effects model would not have changed the outcome for OS. As assumptions of homogeneity were not violated, subgroup analyses were not performed. All the individual studies were found to have a 'high risk of bias' according to evaluation with the QUIPS tool. We did not assess publication bias using a funnel plot as there were fewer than 10 included studies.[43] Publication bias arises when small studies with negative results remain unpublished, and although publication bias was not assessed, it may be substantial. Based on this meta-analysis, SMI and SMRA measured by axial CT scanning at the third or fourth lumbar level currently have little utility as reliable prognostic factors in ovarian cancer.

Conclusions

Although SMI and SMRA appear to be associated with shorter survival in ovarian cancer patients, the lack of standardized cut-offs for assessing its prevalence hampers the interpretation of this association and its strength. A consensus on standardized cut-off values to define sarcopenia in patients with ovarian cancer needs to be found. Because physical exercise interventions have potential in preventing sarcopenia and improving physical function in cancer patients, future studies should incorporate information on muscle strength and nutritional assessments.

Ethical standards

All authors certify that they comply with the ethical guidelines for authorship and publishing as laid down by the *Journal of Sarcopenia Cachexia and Muscle*.[44]

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1. Full electronic search performed in multiple international databases.
Appendix S2. Search strategy.
Appendix S3. Quality in prognostic studies (QUIPS).
Appendix S4. Axial CT-scan at the third lumbar level. Skeletal muscle is defined in red. The surface area of the skeletal muscle yields a value in squared centimetres (cm2). The skeletal muscle index (SMI in cm2/m2) is derived from skeletal muscle area by dividing it with the squared height of the subject (m2). Skeletal muscle radiation attenuation (SMRA) is defined by the mean Hounsfield value of the total skeletal muscle area in red. Picture is taken from Rutten et.al. JCSM, 2017.

Conflict of interest

None declared.

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