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The influence of sarcopenia on survival and surgical complications in ovarian cancer patients undergoing primary debulking surgery

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Abstract

Background: Sarcopenia, severe skeletal muscle loss, has been identified as a prognostic factor in various malignancies. This study aims to investigate whether sarcopenia is associated with overall survival (OS) and surgical complications in patients with advanced ovarian cancer undergoing primary debulking surgery (PDS).

Methods: Ovarian cancer patients (n = 216) treated with PDS were enrolled retrospectively. Total skeletal muscle surface area was measured on axial computed tomography at the level of the third lumbar vertebra. Optimum stratification was used to find the optimal skeletal muscle index cut-off to define sarcopenia ($\leq$38.73 cm^2/m^2). Cox-regression and Kaplan–Meier analysis were used to analyse the relationship between sarcopenia and OS. The effect of sarcopenia on the development of major surgical complications was studied with logistic regression.

Results: Kaplan–Meier analysis showed a significant survival disadvantage for patients with sarcopenia compared to patients without sarcopenia (p = 0.010). Sarcopenia univariably predicted OS (HR 1.536 (95% CI 1.105–2.134), p = 0.011) but was not significant in multivariable Cox-regression analysis (HR 1.362 (95% CI 0.968–1.916), p = 0.076). Significant predictors for OS in multivariable Cox-regression analysis were complete PDS, treatment in a specialised centre and the development of major complications. Sarcopenia was not predictive of major complications.

Conclusion: Sarcopenia was not predictive of OS or major complications in ovarian cancer patients undergoing primary debulking surgery. However a strong trend towards a survival disadvantage for patients with sarcopenia was seen. Future prospective studies should focus on

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interventions to prevent or reverse sarcopenia and possibly increase ovarian cancer survival. Complete cytoreduction remains the strongest predictor of ovarian cancer survival.

Keywords: Sarcopenia; Ovarian neoplasms; X-ray computed tomography; Survival; Postoperative complications; Prognosis

Introduction

Ovarian cancer is the fifth leading cause of cancer-related death among women in developed countries and claims over 150.000 lives worldwide yearly.[1] The majority of patients have abdominally metastasized disease at first presentation which resembles a 5-year survival of 17–36%.[2] Preferred treatment for patients with advanced FIGO stage (International Federation of Gynecology and Obstetrics) ovarian cancer is upfront primary debulking surgery (PDS). For patients who are considered inoperable or have estimated irresectable disease, neoadjuvant chemotherapy complemented with interval debulking surgery (IDS) provides a legitimate alternative.[3] To remove all visible tumour at surgery is pivotal as the amount of residual disease after surgery is the most influential prognostic factor contributing to ovarian cancer survival along with FIGO stage, tumour grade and performance status.[4] Additionally women with ovarian cancer often experience cancer cachexia characterised by involuntary weight loss and severe muscle wasting which can further abate their survival chances.[5] The mechanisms behind cancer cachexia and muscle depletion involve an interplay between reduced nutrient intake and abnormal metabolism incited by an excessive systemic inflammation and catabolic (tumour-related) mediators to which the host (i.e. the patient) is unable to respond properly.[6] However, cancer-related weight loss can be disguised by bulky tumour deposits or ascites and is less reliable as a measure of disease activity in ovarian cancer patients. Instead of weight measurements, measurements of body composition are now extensively being used for prognostic purposes in cancer patients. Cross-sectional computed tomography (CT) scans at the level of the third lumbar vertebra (L3) give an accurate representation of total body adipose and skeletal muscle tissue.[7–9] Severe loss of muscle mass (i.e. sarcopenia) as estimated on CT was henceforth identified as a risk factor for survival in patients with various malignancies.[10–13] In a cohort of ovarian cancer patients undergoing neoadjuvant chemotherapy and IDS, loss of skeletal muscle over time was also related to decreased survival.[14] However two earlier studies could not find a relationship between sarcopenia and survival when evaluating ovarian cancer patients treated with PDS.[15,16] The association between sarcopenia and postoperative complications is thus far unknown in ovarian cancer but has shown significance in gastrointestinal cancer.[17,18]

The data on ovarian cancer patients are scarce but there is evidence that sarcopenia could be one of the few modifiable risk factors for survival if patients with sarcopenia were to be identified timely. The reversal of sarcopenia with nutritional supplements and physical activity has been studied successfully in sarcopenic elderly.[19] Exercise might play an important role in counteracting muscle wasting through reducing the level of inflammation, increasing insulin sensitivity and modulation of muscle protein metabolism.[20,21] Although there is no direct evidence that anti-sarcopenia treatment increases survival chances in patients with advanced malignancies there is a rationale for implementing e.g. exercise therapy in oncologic patients with sarcopenia.[22] The primary objective of this study is to evaluate whether sarcopenia is associated with survival and the development of major postoperative complications in patients with advanced ovarian cancer undergoing PDS.

Patients and methods

This study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. The study protocol has been approved by the Maastricht University Medical Centre ethics committee which waived the requirement to obtain informed consent.

Eligible patients

All patients with advanced stage ovarian cancer (FIGO IIB–IV) treated with PDS between 2000 and 2015 were included in this retrospective cohort study. Patients underwent treatment in one of two specialised oncologic centres (Maastricht University or Radboud University medical centre) or in one of four general care centres in the Netherlands (Bernhoven, Rijnstate, Slingeland or St. Jansdal). The following inclusion criteria were applied: 1) an abdominal CT-scan of sufficient quality taken within two months before PDS was available, 2) relevant clinical data were retrievable from the patient's medical records and 3) follow-up data were available for at least six months post-surgery.

Primary outcome was overall survival (OS), calculated as the time between surgery and death of any cause. Survivors were censored at a fixed date no sooner than six months after inclusion of the last patient. Postoperative complications were graded using the Clavien–Dindo scale

of surgical complications.[23] We classified a Clavien–Dindo score of ≥3 as a major complication. The result of PDS was categorised into complete (no macroscopic tumour residual), optimal (largest tumour residual ≤1 cm) or incomplete (largest tumour residual >1 cm). Patients were divided into two age groups with a threshold of 65 years. A body mass index (BMI) >30 was considered obese.

Body composition analysis

Axial CT at L3 was used for evaluation of total skeletal muscle (SM), psoas muscle, intramuscular adipose tissue (IMAT), visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT). Predefined and previously validated boundaries of −30 to +150 Hounsfield Units (HU) for SM and psoas, −190 to −30 HU for IMAT and SAT, and −150 to −50 HU for VAT were used to demarcate tissue using SliceOmatic software (v5.0, Tomovision, Montreal, Canada), see Fig. 1. Surface areas in cm^2 were quantified automatically following demarcation and were standardised by height squared to compute the skeletal muscle index (SMI), psoas-index, IMAT-index, VAT-index and SAT-index in cm^2/m^2. Mean HU was calculated for SM to define the muscle radiation attenuation (MA). CT evaluation was performed by two observers (IR&JU) blinded to each other and to patient outcome. Their averaged measurements were used for statistical analysis.

Statistical analysis

We performed optimum stratification analysis on the SMI measurements to stratify patients into two groups: patients with sarcopenia and patients without sarcopenia. This method produces a p-value for each SMI cut-off and determines the optimal cut-off for sarcopenia in our population.[24] Psoas-index, IMAT-index, VAT-index, SAT-index and MA were divided into tertiles and the lowest tertile was used as cut-off for each category (with an exception for IMAT-index in which the highest tertile was used) to divide patients into a 'low' or 'high' subgroup. Baseline data between patients with and without sarcopenia were analysed with chi-squared and t-tests. Differences in OS between sarcopenic and non-sarcopenic patients were tested with the Kaplan–Meier estimate (log rank). Body composition measurements as described above, FIGO stage (<IV vs. IV), age, BMI, outcome of PDS (complete vs. optimal/incomplete), tumour grade (1 vs. 2/3), treatment centre (specialised vs. general), type of treatment (PDS vs. PDS + IDS) and development of major complications (Clavien–Dindo ≥3) were tested as effect modifiers in regression analysis adopting a backwards stepwise procedure. A proportional hazards Cox-regression model was used to evaluate relationships with OS and a binary logistic regression model was used to study predictors for the development of major complications at PDS. Hazard ratios (HR) were calculated with confidence intervals (95% CI). For univariable analysis an inclusion criterion of 10% was adopted. Significant modifiers were included in a multivariable model in a backwards stepwise procedure in which a p-value <0.05 was considered significant. For all statistical analyses SPSS v23.0 (IBM Corp, Chicago, IL) was used. Interobserver agreement for measurement of body composition variables was calculated with Pearson's correlation coefficient (r_p). Pearson's r was also used to evaluate the correlation between SMI and psoas-index.

Results

Of 280 patients deemed eligible to participate, 64 were excluded. 216 patients were included in the analyses (Fig. 2). Patient characteristics are summarised in Table 1. Mean period between CT and PDS was 21 days. Mean OS was 1714 days. Forty-three patients (19.9%) experienced a major postoperative complication. A more elaborate list of complications can be found in the Supplementary material. Sarcopenic patients had a

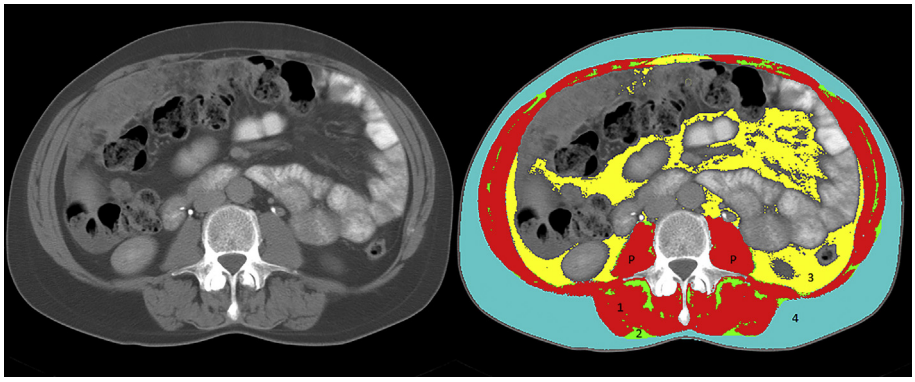


Figure 1. **Computed tomography assessment of skeletal muscle and adipose tissue with SliceOmatic software**. Preoperative axial computed tomography (CT) scan of an ovarian cancer patient. Both images are taken from the same patient. On the left a regular CT image at the level of the third lumbar vertebra. On the right an image coloured using SliceOmatic software. 1 = skeletal muscle, 2 = intramuscular adipose tissue, 3 = visceral adipose tissue, 4 = subcutaneous adipose tissue, P = psoas muscle.

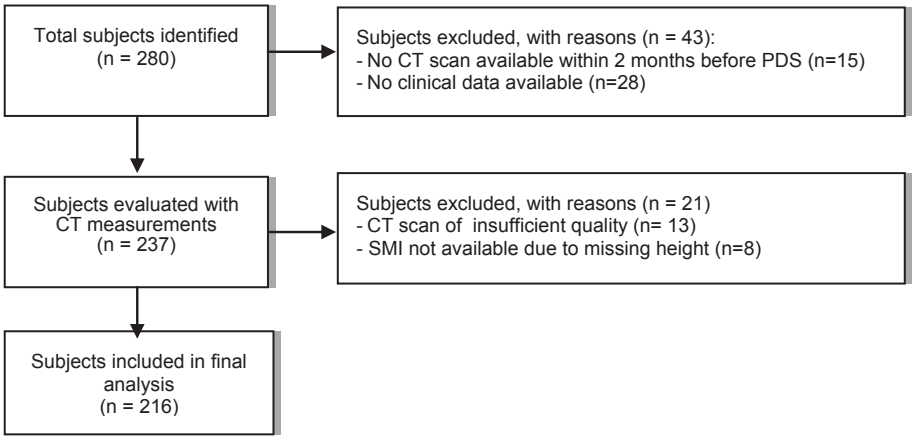


Figure 2. **Flow chart for patient inclusion**. CT; computed tomography, PDS; primary debulking surgery, SMI; skeletal muscle index.

significantly lower mean BMI compared to non-sarcopenic patients (22.7 vs. 26.0 kg/m^2, $p < 0.001$). Ascites was more prevalent in sarcopenic patients (87.1% vs. 65.7%, $p = 0.010$). Furthermore SMI, psoas-index, VAT-index and SAT-index were all significantly lower in patients with sarcopenia (all $p < 0.001$). The outcome of PDS was not significantly different between sarcopenic and non-sarcopenic patients (25.7% vs. 35.6% complete, $p = 0.346$).

Optimum stratification analysis identified an SMI $\leq$38.73 cm^2/m^2 as the most optimal cut-point for sarcopenia in our population. Using this cut-point, Kaplan–Meier analysis showed a significant survival disadvantage for patients with sarcopenia compared to patients without sarcopenia ($p = 0.010$, Fig. 3). Sarcopenia univariably predicted OS (HR 1.536 (95% CI 1.105–2.134), $p = 0.011$) but was not significant at the level of 5% in multivariable Cox-regression analysis (HR 1.362 (95% CI 0.968–1.916), $p = 0.076$, Table 2). Significant predictors for OS in multivariable Cox-regression analysis were complete PDS (HR 0.545 (95% CI 0.366–0.812), $p = 0.003$), specialised centre (HR 0.710 (95% CI 0.506–0.995), $p = 0.047$) and the development of major complications (HR 1.670 (95% CI 1.125–2.480), $p = 0.011$).

Sarcopenic patients did not develop more severe complications than non-sarcopenic patients (Table 1). Sarcopenia was also not predictive of a major complication in logistic regression analysis (Table 2). Age and low MA were univariably identified as predictors for major complications but were not significant in multivariable analysis (Table 2).

Interobserver agreement was 0.970, 0.989, 0.969, 0.997, 0.994 and 0.995 for SM, psoas, IMAT, VAT, SAT and MA respectively. Correlation between measurements of SMI and psoas-index was 0.453.

Discussion

In this study we evaluated the role of skeletal muscle measurements in prediction of OS and the development of post-surgical complications in ovarian cancer patients treated with PDS. We found a strong trend towards a survival disadvantage for patients with sarcopenia but the relationship was not significant in multivariable regression analysis. Tumour stage, completeness of PDS, treatment in a specialised centre and the development of severe post-surgical complications were stronger predictors for ovarian cancer survival. Secondly we did not establish a relationship between sarcopenia and the development of complications after PDS.

A recent meta-analysis concluded that low SMI was associated with poor OS among various tumour types.[13] Unfortunately no gynaecological malignancies were included in the meta-analysis and individual studies on ovarian cancer have not been able to confirm this association. Two retrospective studies about ovarian cancer patients undergoing PDS found no relationship between low SM and survival.[15,16] Further, in a cohort of ovarian cancer patients undergoing neoadjuvant chemotherapy and IDS an initial low SMI measurement before treatment had no prognostic relevance but a change in muscle during chemotherapy was highly predictive of OS.[14] The present study shows no significant relationship between sarcopenia and OS when corrected for other prognostic variables but does imply a tendency towards a shorter survival nonetheless as is seen in Kaplan–Meier analysis and univariable regression. It is possible that the effect of sarcopenia was substantially diminished due to the influence of other strong prognostic predictors such as the outcome of debulking surgery. Furthermore, the impact of sarcopenia on OS might become more apparent when studying a larger population, which may also explain why previously published (relatively small) studies were not able to show a connection between sarcopenia and survival.

We encountered some obstacles in this study when we were faced with the choice of a cut-point for sarcopenia. SMI cut-points of 29.6–42.1 cm^2/m^2 have been reported for female cancer patients.[13] Although the majority of studies have used a cut-point between 38.5 and 41.0 cm^2/

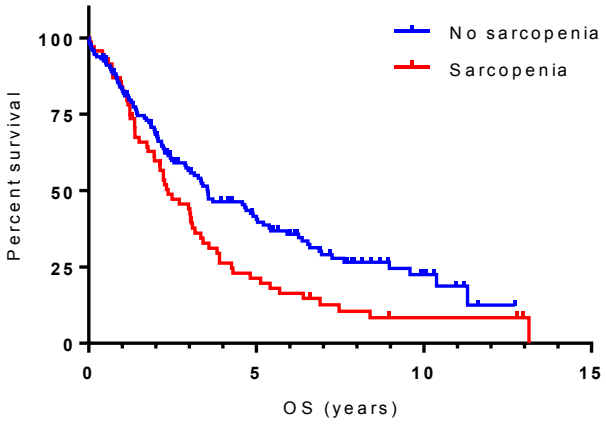
Table 1
Patient characteristics.

	All patients (n = 216)	Sarcopenia (n = 70)	No Sarcopenia (n = 146)
Patient and tumour characteristics			
Age in years, mean ± SE (range)	63.1 ± 0.8 (16–85)	64.2 ± 1.4 (27–85)	62.5 ± 1.1 (16–85)
Body mass index in kg/m^2, mean ± SE	24.9 ± 0.3	22.7 ± 0.4[a]	26.0 ± 0.3[a]
FIGO tumour stage, n (%)			
II	12 (5.6)	1 (1.4)	11 (7.5)
III	161 (74.5)	50 (71.4)	111 (76.0)
IV	43 (19.9)	19 (27.1)	24 (16.4)
Tumour grade, n (%)			
1	16 (7.4)	4 (5.7)	12 (8.2)
2	47 (21.8)	12 (17.1)	35 (24.0)
3	133 (61.6)	50 (71.4)	83 (56.8)
Unknown	20 (9.3)	4 (5.7)	16 (11.0)
Presence of ascites, n (%)	157 (72.7)	61 (87.1)[a]	96 (65.8)[a]
Measurements			
SMI in cm^2/m^2, mean ± SE (cut-point)	41.99 ± 0.39 (38.73)	35.73 ± 0.28[a]	44.98 ± 0.34[a]
Psoas-index in cm^2/m^2, mean ± SE (cut-point)	5.34 ± 0.08 (4.65)	4.64 ± 0.10[a]	5.68 ± 0.10[a]
IMAT-index in cm^2/m^2, mean ± SE (cut-point)	5.28 ± 0.22 (3.51)	4.75 ± 0.34	5.54 ± 0.28
VAT-index in cm^2/m^2, mean ± SE (cut-point)	27.11 ± 1.45 (13.22)	19.68 ± 1.87[a]	30.66 ± 1.88[a]
SAT-index in cm^2/m^2, mean ± SE (cut-point)	62.40 ± 2.29 (44.52)	47.65 ± 2.84[a]	69.47 ± 2.94[a]
MA in HU, mean ± SE (cut-point)	36.64 ± 0.62 (33.67)	37.06 ± 1.14	36.43 ± 0.73
Surgical outcome			
Outcome PDS, n (%)			
Complete	70 (32.4)	18 (25.7)	52 (35.6)
Optimal	51 (23.6)	18 (25.7)	33 (22.6)
Incomplete	95 (44.0)	34 (48.6)	61 (41.8)
Blood loss in mL, mean ± SE	1438 ± 119	1614 ± 231	1350 ± 137
Length of hospital stay in days, mean ± SE	14.2 ± 0.8	15.3 ± 1.6	13.6 ± 0.9
Re-admitted within 30 days, n (%)	13 (6.0)	5 (7.5)	8 (5.7)
Clavien–Dindo complications scale, n (%)			
Grade 0 (No complications)	121 (56.0)	36 (51.4)	85 (58.2)
Grade I (Any deviation from normal postoperative course)	14 (6.5)	4 (5.7)	10 (6.8)
Grade II (Requiring pharmacological treatment)	33 (15.3)	14 (20.0)	19 (13.0)
Grade III (Requiring invasive intervention)	22 (10.2)	7 (10.0)	15 (10.3)
Grade IV (Life-threatening requiring ICU)	15 (6.9)	6 (8.6)	9 (6.2)
Grade V (Death)	6 (2.8)	2 (2.9)	4 (2.7)
Unknown	5 (2.3)	1 (1.4)	4 (2.7)
Treatment, n (%)			
PDS	154 (71.3)	47 (67.1)	107 (73.3)
PDS + secondary IDS after chemotherapy	62 (28.7)	23 (32.9)	39 (26.7)
Treatment centre, n (%)			
General care centre	99 (45.8)	33 (47.1)	66 (45.2)
Specialised oncologic centre	117 (54.2)	37 (52.9)	80 (54.8)
30-day mortality, n (%)	7 (3.2)	2 (2.9)	5 (3.4)
OS in days, mean ± SE	1714 ± 117	1309 ± 162[a]	1887 ± 147[a]

SE; standard error, FIGO; International Federation of Gynecology and Obstetrics, SMI; skeletal muscle index, IMAT; intramuscular adipose tissue, VAT; visceral adipose tissue, SAT; subcutaneous adipose tissue, MA; muscle radiation attenuation, HU; Hounsfield Units, PDS; primary debulking surgery, IDS; interval debulking surgery, ICU; intensive care unit, OS; overall survival.

[a] Indicates significant difference between "Sarcopenia" and "No sarcopenia" ($p < 0.05$, independent-samples T-test, chi-squared test or log rank test).

m^2 for females, this has still resulted in a very heterogeneous reported incidence of 15–74% patients classifying as sarcopenic.[13] Cancer type and stage, interpersonal variation of muscle mass, obesity and ethnicity can all influence SMI and to define a single 'gold standard' cut-point for sarcopenia is virtually impossible.[25,26] We revised previous oncologic studies but cut-points for gynaecological cancer patients specifically were non-existent. In our opinion cut-points designed for and applied to gastrointestinal cancer patients were less applicable to our population since these cancers have a stronger relationship with nutrition and metabolism in general. Although gynaecological tumours and urological tumours have differences in presentation, pathology and prognosis, they both do not affect nutrient uptake and metabolism directly. Due to a lack of other suitable comparable cancers we investigated cut-points used in populations with urological cancers. Psutka et al. studied patients with renal cell cancer and urothelial cancer and found a relationship between sarcopenia and survival when using an SMI cut-point of 39 cm^2/m^2.[11,27]



Number of subjects at risk (%)

	0 yr	1 yr	2 yr	5 yr	10 yr
No Sarcopenia	146 (100)	117 (80)	90 (62)	44 (30)	10 (7)
Sarcopenia	70 (100)	57 (81)	40 (57)	14 (20)	4 (6)

Figure 3. **Kaplan–Meier survival analysis**. OS; overall survival. Log rank estimate: p = 0.010.

The cut-point of 39 cm^2/m^2 in these studies was chosen in accordance with guidelines defined by an international consensus group.[6] However, this guideline dates back to 2011 and was strongly based on the outcome of a study investigating respiratory and gastrointestinal tumours in an obese population.[28] Due to the absence of a suitable existing cut-point for ovarian cancer patients we used optimum stratification to determine the optimal cut-point for sarcopenia in our own cohort. To investigate if a different sarcopenia cut-point would influence the relationship with OS we performed a post-hoc analysis using two alternative cut-points: 1) 39 cm^2/m^2 from the existing literature on urological tumours and 2) the lowest tertile SMI from our own population which was 38.87 cm^2/m^2. These cut-points were very close to the cut-point of 38.73 cm^2/m^2 used in this study and expectedly did not have a substantial impact on outcome. Both alternative cut-points resulted in a significant univariable but not multivariable relationship between sarcopenia and OS although they also showed a strong tendency towards a relation. In fact, all cut-points between 37.90 and 40.25 showed univariable significant relationships with OS for our population.

Interobserver agreement between the two observers was very strong (r_p 0.969–0.997). Quantification of skeletal muscle and adipose tissue with SliceOmatic software is highly reproducible. Although the mean VAT- and SAT-index were significantly lower in patients with sarcopenia compared to patients without sarcopenia, neither measurements of adipose tissue were predictive of OS or complications. The psoas-index weakly correlated with the SMI and was not predictive of survival or complications thus we strongly advise against using it as substitute for the SMI. Aust et al. previously identified MA as a prognostic factor for OS in ovarian cancer patients.[16] We could not establish this relationship in our population.

From our results we can conclude that sarcopenia does not predict the development of major complications after PDS for ovarian cancer. This is in agreement with the only other ovarian cancer study that evaluated sarcopenia in relation to surgical complications.[15] However researchers in other cancer types have been able to connect

Table 2
Regression analysis studying the relationship of clinical and body composition variables with overall survival (left) and major complications (right).

Variables	1. Outcome: overall survival				2. Outcome: major complication (Clavien–Dindo ≥3)			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.007 (0.994–1.020)	0.312			1.045 (1.012–1.080)	0.007[a]	1.035 (0.999–1.073)	0.054
Age ≥65 years	1.031 (0.750–1.418)	0.850			1.682 (0.850–3.328)	0.135		
BMI	0.982 (0.940–1.027)	0.429			1.030 (0.948–1.120)	0.485		
Obesity (BMI ≥30)	1.062 (0.558–2.021)	0.854			0.784 (0.270–2.278)	0.655		
FIGO stage IV	1.600 (1.097–2.333)	0.015[a]	1.420 (0.965–2.091)	0.075	1.240 (0.555–2.768)	0.600		
High grade tumour	1.084 (0.758–1.551)	0.657			0.801 (0.383–1.675)	0.556		
Complete PDS	0.490 (0.333–0.721)	<0.001[a]	0.545 (0.366–0.812)	0.003[a]	0.734 (0.351–1.536)	0.412		
Specialised centre	0.622 (0.451–0.859)	0.004[a]	0.710 (0.506–0.995)	0.047[a]	1.175 (0.597–2.314)	0.641		
Sarcopenia (SMI ≤38.73)	1.536 (1.105–2.134)	0.011[a]	1.362 (0.968–1.916)	0.076	1.131 (0.558–2.291)	0.733		
Low MA	1.417 (1.011–1.984)	0.043[a]	NS	NS	2.318 (1.169–4.595)	0.016[a]	1.623 (0.755–3.486)	0.215
Low psoas-index	1.062 (0.760–1.483)	0.725			1.071 (0.530–2.167)	0.848		
High IMAT-index	0.921 (0.648–1.308)	0.645			1.047 (0.512–2.144)	0.899		
Low VAT-index	1.105 (0.792–1.541)	0.556			0.734 (0.351–1.536)	0.412		
Low SAT-index	1.038 (0.744–1.449)	0.826			0.844 (0.409–1.742)	0.646		
PDS + IDS	1.387 (0.988–1.947)	0.058[a]	NS	NS	–	–		
Major complication (Clavien–Dindo ≥3)	1.555 (1.059–2.282)	0.024[a]	1.670 (1.125–2.480)	0.011[a]	–	–		

HR; hazard ratio, CI; confidence interval, BMI; body mass index, FIGO; international federation of obstetrics and gynecology, SMI; skeletal muscle index, MA; muscle radiation attenuation, IMAT; intramuscular adipose tissue, VAT; visceral adipose tissue, SAT; subcutaneous adipose tissue, PDS; primary debulking surgery, IDS; interval debulking surgery CD; Clavien–Dindo, NS; not significant and therefore not included in final model.

[a] Indicates significant p-value (p < 0.10 for univariable analysis and p < 0.05 for multivariable analysis).

sarcopenia to the risk of surgical complications although the results are inconsistent. We hypothesize that this difference may be (partially) explained by the aggressiveness of the surgical procedure. The extensiveness of surgery is possibly more limited in ovarian cancer patients than for instance in patients undergoing resections for gastrointestinal malignancies. When it is apparent that a patient with ovarian cancer will have to undergo extensive surgery including splenectomy, (partial) hepatectomy, and/or multiple resections of large or small bowel, patients are often primarily treated with neoadjuvant chemotherapy.[3,29] In this way the risk of complications during a possible interval debulking is decreased with an expected decrease of tumour burden. Patients undergoing more extensive surgery are also more likely to develop severe complications which could explain why a relationship between sarcopenia and complications might be more prominent in other cancer types because the complication rate is higher.

Due to the retrospective nature of our study we encountered a substantial amount of irretrievable data which explains why 64 patients from the original cohort were excluded. We would also have liked to analyse the influence of performance status on sarcopenia and survival but this information was unfortunately missing in over 50% of patients.

Conclusion

Sarcopenia was not predictive of overall survival or major surgical complications in ovarian cancer patients undergoing primary debulking surgery. Other prognostic factors were stronger predictors for survival. However we did see a strong trend towards a survival disadvantage for patients with sarcopenia. Previous investigations have shown that loss of skeletal muscle during chemotherapy was related to decreased survival in ovarian cancer and the measurement of muscle change might be more important than a single measurement before treatment.[14] Sarcopenia seems to play a noticeable role in ovarian cancer. Whether sarcopenia can be modified with therapy is still unknown. Nutritional and exercise interventions have been found to improve muscle function in sarcopenic elderly.[19] However, readily implementable anti-sarcopenia protocols for cancer patients are unfortunately not yet available. Future prospective studies should focus on investigation of the metabolic phenotype of patients with sarcopenia and to assessing whether interventions (e.g. nutritional support, anti-inflammatory medication and physical exercise) have an effect in cancer patients. For the time being it remains pivotal however to achieve complete cytoreduction during ovarian cancer debulking surgery as this has shown to be the strongest predictor of overall survival.

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Conflict of interest statement

Iris J.G. Rutten, Jorne Ubachs, Roy F.P.M. Kruitwagen, David P.J. van Dijk, Regina G.H. Beets-Tan, Leon F.A.G. Massuger, Steven W.M. Olde Damink and T. Van Gorp have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ejso.2016.12.016.

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