HIGH-RADIODENSITY SKELETAL MUSCLE INDEX IS THE BEST PREDICTOR OF MAJOR POSTOPERATIVE COMPLICATION IN GYNECOLOGIC CANCER

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TITLE PAGE

Title: High-radiodensity skeletal muscle index is the best predictor of major postoperative complication in gynecologic cancer

Subtitle: Muscle quality and postoperative complication

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SYNOPSIS

Identifying skeletal muscle (SM) quality is a promising strategy to understand its impact on unfavourable outcomes in oncology. SM quality was proven to be a more important risk factor for surgical complications than overall SM in women with gynecologic cancer.

ABSTRACT

Purpose: This study aimed to evaluate the influence of sarcopenia and the indicators of skeletal muscle (SM) quality on surgical outcomes in women with ovarian and endometrial cancer who underwent oncologic surgery. **Methods:** Endometrial and ovarian cancer patients admitted between 2008-2015 and who had computerized tomography (CT) images available within 45 days before surgery were enrolled in a retrospective cohort (n=250). CT images at the third lumbar vertebra were used to assess SM. Skeletal muscle index (SMI) was calculated in the range -29+150 Hounsfield Units (HU); reduced muscle attenuation (range -29 + 29HU) was classified as low-radiodensity skeletal muscle index (LRSMI). By subtracting the LRSMI area from total SMI, High-Radiodensity Skeletal Muscle Index (HRSMI) was created. Sarcopenia was defined when SMI was $\leq$38,9cm^2/m^2. Multiple logistic regression evaluated predictors of surgical complications. **Results:** Patients in lower HRSMI quartiles and in the highest quartiles of LRSMI had more surgical postoperative complication and remained more time hospitalized. Both sarcopenia and the quality indicators of SM were predictors of increased risk of surgical complication, being the HRSMI the strongest predictor.However, in a combined adjustment for HRSMI and sarcopenia, only HRSMI remained in the model as an independent predictor for surgical complication. Additionally, HRSMI was the only indicator associated with early mortality ($\leq$30 days). Conclusion: The indicators of SM quality were the most significant predictors of surgical complications. Classifying muscle quality in terms of low- or high-radiodensity area is a promising strategy to understand the impact of muscle mass quality on unfavourable outcomes in oncology.

INTRODUCTION

Surgery is considered the cornerstone of ovarian and endometrial cancer treatment[1,2,3]. The purpose of the surgery in gynecologic cancers is to establish staging, assess the extension of the disease and try to remove all visible tumors[4]. Studies have demonstrated early mortality (up to 30 days after intervention) in oncological gynecologic surgery of 0.7% for endometrial cancer[3] and 2% for ovarian cancer[1]. Postoperative prognosis is multifactorial, being determined by tumor-related factors, as well as the patient's characteristics, such as age, obesity, and presence of comorbidities[3,5,6].

Among the modifiable factors, those related to the nutritional status seem to have an important role in surgical outcomes. Obesity is associated with the increase of postoperative complication taxes, including infections and prolonged hospital stay[6,7]. On the other hand, sarcopenia - defined as loss of skeletal muscle mass and muscle strength[8] - determines worse clinical and surgical outcomes[9] and has been associated with the occurrence of surgical complications in abdominal surgeries[10], liver transplant[11], cystectomy[12] and pancreatectomy[13].

Lately, muscle quality changes have been described in different clinical conditions, including cancer[14-17]. Such changes are related to the accumulation of intramuscular fat, called myosteatosis, that seems to predict worse outcomes in oncologic patients[18]. However, there are still a few studies focusing the relationship between muscle quality and surgical complications, specially for the lack of a consensual methodology so far concerning the diagnosis of myosteatosis[15,18,19].

There aren't any studies in literature that relate sarcopenia or myosteatosis with complications in preoperative of patients with ovarian cancer. The only study that assessed the relationship between sarcopenia and surgical complications in elective surgeries of endometrial cancer did not find relevant results, possibly for the small size sample and reduced number of major surgical complications[20].

Therefore, the objective of this study was to assess sarcopenia and the quality indicators of skeletal muscle (SM) as predictive factors of surgical complications in women with ovarian and endometrial cancer subjected to curative surgery oncological.

METHODS

This retrospective cohort study recruited 250 consecutive endometrial and ovarian cancer patients who undergone elective surgery in a leading cancer treatment institute in Brazil between October 1, 2008 and December 31, 2015. Inclusion criteria were the presence of malignancy and the availability of CT scans taken up to 45 days prior to treatment. Women previously diagnosed with another type of cancer or those with synchronous tumors were excluded from the study. The study was approved by the Ethics and Research Committee of the institution, under number 466.070/2013.

The socio-demographic data and clinical information related to the oncologic treatment were collected in the electronic and physical case records and included the following: age, ethnic group, comorbidities, staging of cancer, surgical procedure details, lymphadenectomy, American Society of Anesthesiology (ASA) grade, anesthetic technique, operative blood loss, operative time, and residual disease.

Resection curability was classified as R0 (complete resection with no microscopic residual tumor), R1 (complete resection with no grossly visible tumor, but margins microscopically positive according to the pathologist) and R2 (incomplete resection with macroscopically residual tumor). Pathology data, including histological type and subtype, were obtained after surgery through histopathology reports. The staging was performed based on the International Federation of Gynecology and Obstetrics characteristic for gynecological cancer[21].

Postoperative complications were classified according to the Clavien-Dindo classification (CDC)[22]. Major complications were considered for CDC ≥3. Operative mortality was defined as occurring during hospital admission or within 30 days after discharge. Postoperative 30-days follow-up was extracted from patient´s clinical records in order to record morbidity, discharge time and mortality.

For body composition analysis, CT scans of the patients' abdomen and pelvis up to 45 days prior to oncologic surgery were used. Slices taken at the 3rd lumbar vertebra (L3) were analyzed by the same trained observer with the aid of the SliceOmatic software program 5.0 (Tomovision, Canada), which enables specific demarcation of each tissue, expressed in Hounsfield Units (HU).

In order to identify and quantify the overall skeletal muscle area, the reference radiation attenuation ranging from -29 to 150 HU was used[23]. Thus, after normalized by the square of the stature, the skeletal muscle index (SMI, cm^2/m^2) was used to classify sarcopenia, as per the cut-off point established for women (≤38.9 cm^2/m^2)[24].

Then we divided the overall skeletal muscle range into two sub-ranges: The area of skeletal muscle in the range -29 to +29 HU was denominated as low-radiodensity skeletal muscle index (LRSMI, cm^2/m^2) and the area in the range +30 to +150 HU was denominated as high-radiodensity skeletal muscle index (HRSMI, cm^2/m^2), representing the cross-sectional muscle area with low and high attenuation, respectively (figure 1).

It was thus possible to appraise SM quality assuming that the lower and higher attenuation represent the SM area with increased and reduced intramyocellular triglycerides, respectively.

Statistical analysis were performed on version 22.0 of the SPSS statistical package for Windows (Chicago, IL, USA). Data was expressed as median (range) for numeric variables, and percentage for qualitative variables. SM quality parameters were presented according to the population distribution quartiles (<Q1; ≥Q1<Q2; ≥Q2<Q3; ≥Q3). Categorical variables were compared using the chi-squared test or Fishier´s exact test as appropriate (χ^2).

Univariate logistic regression were performed to assess the association of independent variables with major surgical complication. All socio-demographic, clinical and surgical variables were tested, as well as the sarcopenia diagnosis and the three skeletal muscle parameters proposed in the present study. All variables associated with major postoperative complication with a p-value of <0.10 on univariate analysis were examined by multivariate logistic regression analysis.

The Hosmer–Lemeshow test was used to provide a goodness-of-fit for the logistic regression models (p-value > 0.05 indicates that the model does fit the data well). For all statistical analysis, a p value < 0.05 was considered statistical significant.

RESULTS

Two hundred and fifty patients were eligible for the study. Table 1 presents patient preoperative characteristics and the skeletal muscle parameters. About 65% of the patients presented some type of comorbidity, being more frequent in endometrial cancer. As to cancer staging, 50.4% were diagnosed with advanced stage (III/IV), in spite of advanced staging occurred more frequently for ovarian cancer. The presence of sarcopenia was found in 22.4% of the general population, being more frequent in patients with ovarian cancer.

In regard to clinical outcomes, 36.1% of women (n=90) presented some sort of surgical postoperative complication, which were more frequent in those with endometrial cancer. Such women also presented major complications more frequently, with higher operative mortality rates, when compared to patients with ovarian cancer (Table 2). A detailed description of the recorded postoperative complications, separeted by severity and tumor site, is available in Supplementary Table 1.

The relationship among sarcopenia, HRSMI and LRSMI to clinical and surgical outcomes are shown in Table 3. A significant association was found between diagnosis of sarcopenia and occurrence of surgical complications, as well as the severity of postoperative complications. On the other hand, HRSMI presented a significant association with all evaluated parameters. When the severity of surgical complication was analyzed, major complication was more frequent in patients that were below HRSMI quartile 1. Moreover, patients in lower HRSMI quartiles were the ones who remained longer in the hospital and all the patients below HRSMI quartile 2 died in up to 30 days after surgery. Major complication and longer postoperative length of stay were also more frequent in higher quartiles of LRSMI.

Five models of multiple logistic regression were tested for the outcome major surgical complication, taking into account the diagnosis of sarcopenia and the different parameters of SM quality (HRSMI and LRSMI) (Table 4). Considering that the groups classified according to the quartiles of distribution for SM quality could have the associated diagnosis of sarcopenia, adjusted models for sarcopenia were additionally tested for such variables.

All SM parameters were predictors of a greater risk of major surgical complication - sarcopenia, HRSMI and LRSMI. However, when SM quality parameters were adjusted by sarcopenia diagnosis, the results differed. Sarcopenia lost its predicting capacity of major surgical complication when HRSMI was considered in the model. On the contrary, when LRSMI was adjusted by the presence of the sarcopenia, the two parameters turned out to be independent predictors of the occurrence of major surgical complication. For all models, Hosmer-Lemeshow test indicated appropriate adjustment. However, best-adjusted models were those in which the diagnosis of sarcopenia was considered as an adjustment variable.

DISCUSSION

The evaluation of body composition by means of CT scans has gained visibility in the oncology setting, since it is a frequently conducted exam for diagnosis and treatment[25]. Studies assessing SM parameters and their relation with clinical outcomes in women with gynecologic cancer are still scarce in literature, especially regarding the evaluation of the muscle quality.

The word sarcopenia is used to indicate any loss of muscle tissue and functionality, as a consequence of several factors such as aging, chronic diseases - including cancer, low energy and protein intake and physical inactivity[8,26]. In a recent meta-analysis, Shachar *et al.* (2016)[9] showed that the presence of sarcopenia at diagnosis is related to shorter survival in oncologic patients.

Besides the impact on survival, studies have shown that sarcopenia is also determinant to a greater occurrence of surgical complications in patients with cancer[10,13]. Different studies indicate sarcopenia as a risk factor for the occurrence of postoperative infections[27,28,29]. This speculation is based upon the relationship between SM depletion and its consequent incapability of appropriately responding to any type of stress, including infections[28].

Kuroki *et al*. (2015)[20], analyzing sarcopenia influence in clinical and surgical outcomes of patients with endometrial cancer, concluded that sarcopenia was not a predictor of surgical complications. However, the authors did not inform the methodology used for classifying postoperative complications, and sarcopenia diagnosis was made using the median distribution of the studied population, which compromises data interpretation.

Torres *et al*. (2013)[30], assessing body composition by means of CT scans in women with ovarian cancer, concluded that sarcopenia was a strong and important predictor of length of hospital stay. Montano-Loza *et al*. (2014)[31], also reported the association among sarcopenia and length of hospital stay, differing from our findings, since in our study the diagnosis of sarcopenia was not significantly related to this outcome. On the other hand, we found that the parameters of SM quality – a decrease of HRSMI and increase of LRSMI - were related to longer length of hospital stay.

Indeed, the association of SM attenuation with cancer outcomes have been subject of recent researches[27,32,33,34]. However, these studies did not quantify the area of low- or high-radiodensity SM tissue[35,36], being the present study pioneer in such evaluation. We proposed the evaluation of intramuscular fat infiltration by means of the calculation of the area of LRSMI, different from that which has been used in literature, that generally only presents the average of muscle attenuation for comparing to clinical and surgical outcomes. We believe that the calculation of the representative area of low- and high-radiodensity SM is more appropriate to characterize muscle quality than merely classifying the individual according to the average of muscle attenuation since it allows identifying the magnitude of the SM area of increased and reduced fat infiltration, respectively.

Aubrey *et al*. (2014)[18], suggest the use of SM density range from -29 to +29 HU to identify myosteatosis, since the most accepted discriminatory range for adipose tissue and normal skeletal muscle attenuation ranges from -190 to -30 HU and from +30 to +150 HU, respectively, according to most of the authors[23].

In the present study, HRSMI and LRSMI had a significant association with either the occurrence or the surgical complication degree. It was observed that patients with a lower amount of HRSMI, as well as those with a higher amount of LRSMI, had more severe surgical complications and longer postoperative length of stay. Such data confirm recently published studies, in which SM attenuation was an independent predictor of postoperative complications, being related to frequency and severity of complications[37].

Hamaguchi *et al*., (2016)[33] also found similar results when assessing the impact of SM average attenuation on surgical complications of patients subjected to hepatectomy, observing that the presence of low average muscle attenuation in preoperative was an independent risk factor for infectious complications and major complications. The relationship between SM quality and surgical complications may be explained by the strong association between muscle quality and metabolic abnormalities, strength loss, performance worsening and functional incapability, disfavoring the patient's clinical evolution[14].

Concerning early mortality (≤ 30 days), in spite of lack of association with sarcopenia and myosteatosis, it was significantly associated to lower quartiles of HRSMI, suggesting that a high-quality SM has more impact on such outcome than the total amount of SM or the amount of fat infiltration in muscle. It is feasible that either the presence of sarcopenia or the higher amount of LRSMI could have its negative effect mitigated before a suitable minimum amount of HRSMI, that in turn, would confer a protective role for negative outcomes.

Finally, it is noteworthy that, after adjustments for confounding variables in multiple logistic regression, even though either sarcopenia or the other indicators of SM quality have been pointed out as independent predictors for major complication, the HRSMI was the strongest predictor. When HRSMI was adjusted for sarcopenia diagnosis, it lost the power of predicting the outcome in the model. Such findings reinforce our theory that compared to a proper amount of a high-radiodensity SM (that is, less likely to be infiltrated by fat), the quantitative reduction of total SM becomes a less important indicator of unfavorable outcomes.

However, since it is possible that different phenotypes related to either SM quantity or its quality may coexist (for example sarcopenia and high amount of HRSMI; sarcopenia and high amount of LRSMI; absence of sarcopenia and high amount of LRSMI), other studies that test the association of such conditions in predicting the outcomes are required.

Some limitations of the present study shall be highlighted, including its retrospective design, which caused exclusion of a great number of patients for not presenting CT scans before surgical treatment. Moreover, the surgical complications considered were those listed in medical records and may have been underestimated. We also point out the need of establishing suitable cut-off points to the proposed methodology by our research group for SM quality indicators. The lack of consensus regarding myosteatosis diagnosis limits the comparison of our results with other studies.

We can conclude that sarcopenia and the SM quality indicators (HRSMI and LRSMI) were predictors of greater risk of major postoperative surgical complication, being HRSMI the strongest predictor. Therefore, SM quality is a more important risk factor for surgical complications than muscle quantity (SMI) in women with gynecologic cancer.

These results are promising and need, however, more investigation for better understanding the impact of SM quality parameters on clinical and surgical outcomes in oncology. Future proposals include assessing such outcomes in individuals with different body composition phenotypes.

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FIGURE LEGENDS

Figure 1. Skeletal muscle classification purpose according to sub-ranges of radiodensity.

TABLES

Table 1. Patient sociodemographic, clinical and skeletal muscle parameters (n=250).

Characteristic	Total (n= 250)	Ovarian (n= 89)	Endometrial (n = 161)
Age category, y, n (%)			
<65 years	149 (59.6)	70 (78.7)	79 (49.1)
≥ 65 years	101 (40.4)	19 (21.3)	82 (50.9)
Ethnic group, n (%)			
Caucasian	147 (58.8)	53 (59.6)	94 (58.4)
Mixed	75 (30.0)	29 (32.6)	46 (28.6)
Black	28 (11.2)	7 (7.9)	21 (13.0)
Comorbidity, n (%)			
No	86 (34.4)	46 (51.7)	40 (24.8)
Yes	164 (65.6)	43 (48.3)	121 (75.2)
Comorbidity type, n (%)			
Hypertension	92 (55.8)	22 (51.2)	70 (57.4)
Diabetes	7 (4.2)	3 (7.0)	4 (3.3)
Hypertension + Diabetes	51 (30.9)	6 (14.0)	45 (36.9)
Others*	15 (9.0)	12 (27.8)	3 (2.5)
Histologic type, n (%)			
Adenocarcinoma	226 (90.4)	89 (100)	137 (85.1)
Sarcoma	24 (9.6)	0 (0)	24 (14.9)
Histologic subtype, n (%)			
Endometrioid	94 (39.3)	8 (9.5)	86 (55.5)
Serous	79 (33.1)	56 (66.7)	23 (14.8)
Others	66 (27.6)	20 (23.8)	46 (29.7)
Stage, n (%)			
I	87 (36.6)	10 (12.8)	77 (48.1)
II	31 (13.0)	8 (10.3)	23 (14.4)
III	86 (36.1)	42 (53.8)	44 (27.5)
IV	34 (14.3)	18 (23.1)	16 (10.0)
Sarcopenia, n (%)			
No	194 (77.6)	66 (74.2)	128 (79.5)
Yes	56 (22.4)	23 (25.8)	33 (20.5)
HRSMI (cm^2/m^2)			
Quartile 1	17.89	19.65	17.19
Quartile 2	22.67	23.66	21.87
Quartile 3	29.40	30.38	27.43
LRSMI (cm^2/m^2)			
Quartile 1	16.17	14.97	17.25
Quartile 2	21.40	18.91	22.30
Quartile 3	25.53	24.05	27.20
SMI, median (range)	43.5 (27.4-66.3)	43.2 (32.2-62.5)	43.7 (27.4-66.3)

*Dyslipidemia, renal insufficiency, cardiovascular disease, chronic obstructive pulmonary disease. HRSMI: High-radiodensity Skeletal Muscle Index; LRSMI: Low-radiodensity Skeletal Muscle Index; SMI: Skeletal Muscle Index. Low- and High-radiodensity skeletal muscle index were calculated using the skeletal muscle area in range -29 to +29 HU and +30 to +150 HU, respectively.

Table 2: Surgical characteristics and postoperative complications.

Characteristic	Total (n= 250)	Ovarian (n= 89)	Endometrial (n = 161)
Surgical procedure, n (%)			
Total Hysterectomy with Bilateral Salpingo-Oophorectomy	209 (83.6)	48 (53.9)	161 (100)
Salpingo-Oophorectomy	16 (6.4)	16 (18.0)	0 (0)
Total Hysterectomy with bowel resection	25 (10.0)	25 (28.1)	0 (0)
Lymphadenectomy, n (%)			
No	128 (51.2)	47 (52.8)	81 (50.3)
Yes	122 (48.8)	42 (47.2)	80 (49.7)
ASA grade, n (%)			
1	29 (11.8)	6 (7.1)	23 (14.3)
2	134 (54.7)	52 (61.9)	82 (50.9)
3	82 (33.5)	26 (31.0)	56 (34.8)
Operative time (min), n (%)			
≤ 120	36 (22.4)	11 (13.3)	47 (19.3)
121 a 240	100 (62.1)	48 (57.8)	148 (60.7)
> 241	25 (15.5)	24 (28.9)	49 (20.1)
Operative blood loss (mL), n (%)			
<500	216 (87.4)	66 (76.7)	150 (93.2)
500 - 1000	23 (9.3)	15 (17.4)	8 (5.0)
> 1000	8 (3.2)	5 (5.8)	3 (1.9)
Residual disease, n (%)			
R0 (complete resection tumor)	176 (71.5)	45 (52.3)	131 (81.9)
R1 (microscopically residual tumor)	13 (5.3)	6 (7.0)	7 (4.4)
R2 (macroscopically residual tumor)	57 (23.2)	35 (40.7)	22 (13.8)
Anesthetic technique, n (%)			
General	43 (17.4)	11 (12.8)	32 (19.9)
General + epidural	157 (63.6)	51 (59.3)	106 (65.8)
General + inhalation	19 (7.7)	3 (3.5)	16 (9.9)
Epidural	28 (11.3)	21 (24.4)	7 (4.3)
Postoperative complications, n (%)			
No	159 (63.9)	68 (76.4)	91 (43.1)
Yes	90 (36.1)	21 (23.6)	69 (56.9)
Postoperative complications (CDC), n (%)			
0-2	217 (86.8)	80 (89.9)	137 (85.1)
≥ 3	33 (13.2)	9 (10.1)	24 (14.9)
Length of stay in hospital (days), n (%)			
< 4	47 (18.9)	24 (27.0)	23 (14.4)
4 - 6	106 (42.6)	10 (44.9)	66 (41.3)
7 - 9	43 (17.3)	14 (15.7)	29 (18.1)
≥ 10	53 (21.3)	11 (12.4)	42 (26.3)
Death ≤ 30 days after operation, n (%)			
No	237 (94.8)	86 (96.6)	151 (93.8)
Yes	13 (5.2)	3 (3.4)	10 (6.2)

ASA: American Society of Anestesiology. CDC: Clavien-Dindo classification

Table 3: Association between sarcopenia, High-radiodensity Skeletal Muscle Index and Low-radiodensity Skeletal Muscle Index with clinical and surgical outcomes.

Characteristic	Total n (%)	Sarcopenia			HRSMI (Quartile)					LRSMI (Quartile)				
		No n (%)	Yes n (%)	p value*	< Q1 n (%)	≥Q1 < Q2 n (%)	≥Q2 < Q3 n (%)	≥ Q3 n (%)	p value*	< Q1 n (%)	≥Q1 < Q2 n (%)	≥Q2 < Q3 n (%)	≥ Q3 n (%)	p value*
Postoperative complications														
No	159 (63.9)	130 (81.8)	29 (18.2)	0.040	29 (18.2)	44 (27.7)	38 (23.9)	48 (30.2)	0.003	49 (30.8)	43 (27.0)	34 (21.4)	33 (20.8)	0.007
Yes	90 (36.1)	63 (70.0)	27 (30.0)		33 (36.7)	19 (21.1)	24 (26.7)	14 (15.6)		13 (14.4)	20 (22.2)	27 (30.0)	30 (33.3)	
Postoperative complications (CDC)														
0-2	217 (86.8)	174 (80.2)	43 (19.8)	0.023	42 (19.4)	55 (25.3)	58 (26.7)	62 (28.6)	0.000	59 (27.2)	57 (26.3)	49 (22.6)	52 (24.0)	0.037
≥ 3	33 (13.2)	20 (60.6)	13 (39.4)		20 (60.6)	8 (24.2)	4 (12.1)	1 (3.0)		3 (9.1)	6 (18.2)	12 (36.4)	12 (36.4)	
Length of stay in hospital (days)														
≤ 3	48 (19.2)	39 (81.3)	9 (18.8)	0.154	7 (14.6)	13 (27.1)	13 (27.1)	15 (31.3)	0.001	13 (27.1)	19 (39.6)	9 (18.8)	7 (14.6)	0.010
4 - 6	106 (42.4)	86 (81.1)	20 (18.9)		16 (15.1)	26 (24.5)	31 (29.2)	33 (31.3)		32 (30.2)	26 (24.5)	25 (23.6)	23 (21.7)	
7 - 9	43 (17.2)	34 (79.1)	9 (20.9)		13 (30.2)	12 (27.9)	10 (23.3)	8 (18.6)		9 (20.9)	5 (11.6)	10 (23.3)	19 (44.2)	
≥ 10	53 (21.2)	35 (66.0)	18 (34.0)		26 (49.1)	12 (22.6)	8 (15.1)	7 (13.2)		8 (15.1)	13 (24.5)	17 (32.1)	15 (28.3)	
Death < 30 days after operation														
No	237 (94.8)	187 (78.9)	50 (21.1)	0.079	53 (22.4)	59 (24.9)	62 (26.2)	63 (26.6)	0.000	62 (26.2)	57 (24.1)	59 (24.9)	59 (24.9)	0.068
Yes	13 (5.2)	7 (53.8)	6 (46.2)		9 (69.2)	4 (30.8)	0 (0)	0 (0)		0 (0)	6 (46.2)	2 (15.4)	5 (38.5)	

* Chi square test ($\chi 2$) or Fisher´s exact test. CDC: Clavien-Dindo classification; HRSMI: High-radiodensity Skeletal Muscle Index; LRSMI: Low-radiodensity Skeletal Muscle Index. Low- and High-radiodensity Skeletal Muscle Index were calculated using the skeletal muscle area in range -29 to +29 HU and +30 to +150 HU, respectively.

Table 4: Multiple logistic regression for severe postoperative complication according to the different skeletal muscle parameters evaluated

	OR	CI 95%	p value
Model 1[a]: Sarcopenia	3.109	1.225 – 7.891	0.017
Model 2[a]: HRSMI P50	6.542	2.259 – 18.952	0.001
Model 3[b]: HRSMI P50 adjusted for Sarcopenia			
HRSMI P50	5.669	1.899 – 6.926	0.002
Sarcopenia	2.005	0.751 – 5.352	0.165
Model 4[a]: LRSMI P50	3.146	1.220 – 8.116	0.018
Model 5[b]: LRSMI P50 adjusted for Sarcopenia			
LRSMI P50	3.633	1.345 – 9.814	0.011
Sarcopenia	3.591	1.364 – 9.452	0.010

CI: confidence interval; OR: odds ratio; HRSMI: High-radiodensity Skeletal Muscle Index; LRSMI: Low-radiodensity Skeletal Muscle Index. [a]Adjusted model for operative time, ASA, anesthetic technique, Systemic Arterial Hypertension, Diabetes Mellitus and Surgical procedure. b [a]Adjusted model for operative time, ASA, anesthetic technique, Systemic Arterial Hypertension, Diabetes Mellitus, Surgical procedure and sarcopenia. Hosmer-Lemeshow test: Model 1 - $\chi2$:12.058; p value: 0.149; Model 2 – $\chi2$: 9.506; p value: 0.301; Model 3 – $\chi2$: 5.032; p value: 0.754; Model 4 – $\chi2$: 12.472; p value: 0.086; Model 5 – $\chi2$: 6.862; p value: 0.552.

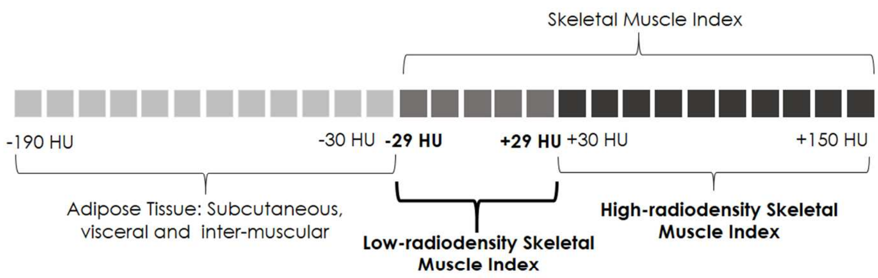

Figure 1. Skeletal muscle classification purpose according to sub-ranges of radiodensity.

338x190mm (96 x 96 DPI)

Supplementary table: Classification and description of postoperative complications according to tumor site

Clavien-Dindo classification	Postoperative Complication	Endometrial (n=51)	Ovarian (n=22)
Grade I	Postoperative wound infection	7	6
	Operative wound dehiscence	5	0
	Electrolytic changes	3	0
Grade II[a]	Pelvic fluid collections and fever	1	0
	Postoperative wound infection	0	2
	Abdominal wall dehiscence	3	2
	Cholecystitis	1	0
	Pneumonia	2	1
	Bacteremia	0	1
	Urinary tract infection	4	1
Grade IIIa[b]	Renal insufficiency not requiring dialysis	1	0
	Abdominal wall dehiscence	3	0
	Evisceration	2	0
	Paralytic ileus	1	0
Grade IIIb[b]	Intracavitary collections	1	0
	Abdominal wall hematoma	0	1
	Evisceration	1	0
	Wound dehiscense with infections	2	0
	Ureterovaginal fistulas	1	0
	Acute abdomen and lysis of Abdominal Adhesions	1	0
	Lysis of Abdominal Adhesions and peritoneotomy	0	1
Grade IVa[c]	Sepsis	5	2
	Reoperation and renal insufficiency requiring dialysis	0	1
	Sepsis and renal insufficiency requiring dialysis	2	1
	Pneumonia and pleural effusion	1	0
	Abdominal wall dehiscence and pleural effusion	0	1
	Renal insufficiency requiring dialysis	2	0
Grade IVb[d]	Sepsis and multiorgan dysfunction	1	1
	Acute respiratory distress syndrome	0	1
	Respiratory insufficiency and multiorgan dysfunction	1	0

[a] Requiring antibiotics; [b] Intervention not under general anesthesia; [c] Intervention under general anesthesia; [d] Requiring intensive care unit.