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Percentiles for body composition parameters based on computed tomography in patients with endometrial cancer

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ABSTRACT

Objectives: The aim of this study was to provide the percentiles of distribution of body composition parameters according to cancer staging and body mass index (BMI) stratum, as well as to identify the contribution of age, BMI, and cancer staging in the variation of the different parameters of body composition in a population of patients with endometrial cancer.
Methods: We enrolled 545 patients who had pretreatment computed tomography images, which were used to assess total skeletal muscle (SM); low- and high-radiodensity SM; visceral, subcutaneous, and intramuscular adipose tissue; and mean skeletal muscle radiodensity (SMD). All the body composition parameters were normalized by the square of the stature. They were then presented on average and at the 5th, 50th and 95th percentiles. The correlation of these parameters with age, BMI, and cancer stage was tested, and then a multiple linear regression analysis was performed. $P \leq 0.05$ was accepted as statistically significant.
Results: BMI was associated with body fat parameters and low-radiodensity SM index; cancer stage was associated with SM index, mean SMD, and high-radiodensity SM index.
Conclusion: This study provides age, stage, and BMI specific percentiles for body composition parameters, which allowed an in-depth interpretation of how such body compartments, especially the low/high SM sub-ranges, varies according to these stratification variables.

Introduction

Despite the convincing evidence that overweight is associated with a higher incidence of several types of cancer, the association between body mass index (BMI) and cancer prognosis is still inconsistent [1–4], possibly due to its inability to differentiate muscular and adipose tissue [5,6]. Therefore, more accurate measures of body composition can improve the prognostic evaluation in oncology [7,8].

Literature has shown that the cross-sectional areas of skeletal muscle (SM) and adipose tissue, assessed by a single computed tomography (CT) slice, at the level of third lumbar vertebra (L3), are strongly correlated to lean and body fat mass [9–11]. Moreover, CT provides quantitative and qualitative SM measurements through area and radiodensity measurements, respectively. The decline of skeletal muscle index (SMI) characterizes myopenia [12], and the low skeletal muscle radiodensity (SMD) is an indirect indicator of fat infiltration in SM, or myosteatosis [13].

These two muscular abnormalities can occur in any class of BMI [14,15] and are also often observed during aging [16,17]. In cancer patients, in addition to the metabolic and inflammatory mechanisms, which predispose to sarcopenia, the prevalence of overweight and obesity is increased [18]. Thus, the coexistence of these two conditions has become increasingly frequent as excess of weight is one of the determining factors of increased lipids content in the SM [19,20]. On the other hand, body fat can mask muscle loss, which in turn, when undiagnosed and untreated, impairs cancer treatment response [21].

Both quantitative and qualitative SM measurements have been widely studied and are considered a prognostic factor in cancer [22–24]. However, despite its emergent use, one of the methodological challenges is to uncover the physiologic, prognostic, and statistical interactions between muscle and adiposity [1]. The interpretation of body composition parameters becomes complex because reference values are lacking, even for healthy population [25]. There are few studies that evaluated the percentile distribution of body composition parameters in healthy population [26], of which only one used CT measurements at the L3 level [27]. To our

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knowledge, there are no studies that described such parameters in a cancer population.

On the basis of the aforementioned considerations, the purpose of this study was to provide the percentiles of distribution of body composition parameters according to the cancer stage, age and BMI stratum, as well as to identify the contribution of age, BMI, and staging in the variation of the different parameters of body composition in a population of patients with endometrial cancer.

Methods

This cross-sectional study included women with a diagnosis of endometrial cancer, confirmed by histologic report, who were referred to a leading cancer treatment institute in Brazil between October 1, 2008 and December 31, 2017. Of these women, those who had CT images at the time of L3 before treatment or up to 15 d after the start of the first therapy were included. Patients who underwent some type of previous cancer treatment, with synchronous tumors, previous history of cancer, or who did not have height reported in their medical records were excluded from the study.

Data were collected in the physical and electronic case records, and comprised age, comorbidities, clinical and histopathologic information (histologic type, histologic subtype, tumor grade and cancer stage), as well as weight and height, which were collected within a period of 30 d before or after the CT exam.

The staging was performed based on the International Federation of Gynecology and Obstetrics characteristics for gynecologic cancer [28]. BMI was calculated based on weight and height and then classified according to the criteria of the World Health Organization [29]. For the statistical analysis, the patients were grouped into three BMI categories: ≤24.99 kg/m^2 (normal weight), 25–29.99 kg/m^2 (overweight), and ≥30 kg/m^2 (obesity) [29]. Thus, patients with BMI <18.50 kg/m^2 (n =15) were included in the category BMI ≤24.99 kg/m^2.

Body composition was assessed using the transverse CT image at the L3 level that most clearly exhibited both vertebral transverse processes. Images must comprise the following quality characteristics: no artifacts, no cutoff of muscle, and clear differentiation between muscle and surrounding tissue. All body composition parameters were measured with SliceOmatic software program version 5.0 (Tomovision, Chemin Milletta, Magog, Canada). The software enables specific demarcation of each tissue, expressed in Hounsfield units (HU). All images were evaluated by the same trained observer and checked by a second observer.

SM assessment included psoas muscle, paraspinals, quadratus lumborum, transversus abdominus, internal and external obliques, and rectus abdominus. For identification and quantification of body composition parameters, the following radiodensity ranges were used:

- SM: −29 to +150 HU [9];
- Low-radiodensity (LR)SM: −29 to +29 HU [13];
- High-radiodensity (HR)SM: +30 to +150 HU [24]; and
- Visceral adipose tissue: −150 to −50 HU [9].
- Subcutaneous and intramuscular adipose tissue: −190 to −30 HU [9].

The areas (cm^2) of the respective tissue regions were computed automatically by summing the given tissues' pixels and multiplying by the pixel surface area. Subsequently, all parameters were normalized by the square of the stature [30] and presented in square centimeters per square meter (cm^2/m^2). In addition to low- and high-radiodensity SM area, we also assessed the mean SMD.

Statistical analysis

Statistical analysis was performed with the aid of SPSS version 22 (IBM, Chicago, IL, USA). The categorical variables were expressed as proportions and stratified between adults and older adults (≥65 y of age). Associations between categorical variables were analyzed using the χ^2 test or Fisher's exact test.

Adherence to the normal curve was tested and a normal distribution was identified for all numeric variables. Such variables were expressed as the mean and SD; and at the 5th, 50th, and 95th percentiles. Mean differences between two and three or more groups were tested by Student's *t* test and analysis of variance, followed by the post hoc Bonferroni test, respectively. Age, BMI, and cancer stage were correlated to the body composition parameters by simple linear regression analysis. Both variables were then tested in a multiple model for each body composition parameter. Residual diagnostic plots were used to check the linear relationship assumptions and whether the residuals were normally distributed. For all statistical analysis, $P < 0.05$ was considered statistically significant.

The study was approved by the ethics and research committee of the Brazilian National Cancer Institute.

Results

The study population consisted of 545 women with endometrial cancer. The clinical-pathologic features are presented in Table 1. Mean age was 64.5 ± 9.8 y (ranging from 22 to 95 y) and 51.4% (n = 280) were >65 y. The majority of the population presented some type of comorbidity, with systemic arterial hypertension being the most frequent (58.6%). Epithelial histologic type and endometrioid histologic subtype were the most prevalent, both in those <65 and those >65 y of age. The mean BMI was 29.80 ± 7.22 kg/m^2, and 73.4% (n = 393) were overweight or obese.

Percentile distribution of the body composition parameters, stratified by age, BMI and cancer stage, are presented in Table 2. Regardless of age or percentile stratum (Supplementary Tables 1 and 2), SMI and LRSMI increased gradually with the increase of BMI. However, HRSMI and mean SMD did not show substantial changes concerning BMI ranges. When evaluating the percentiles of SM parameters (SMI, HRSMI, and LRSMI), slightly lower values were observed in advanced stages.

Regarding the parameters of body fat mass (visceral adipose tissue index [VATI], subcutaneous adipose tissue index [SATI], and intramuscular adipose tissue index [IMAT]), higher values were observed in the higher classes of BMI, whereas lower values were found for advanced cancer stages (III and IV).

Table 3 shows the mean comparison of body composition parameters according to cancer stage and BMI. Except for HRSMI and mean SMD, the mean of all other body composition parameters increased as BMI increased, with a significant difference ($P < 0.001$) between each BMI stratum. HRSMI did not differ between BMI ranges and, for patients with normal weight and overweight, mean SMD was similar, differing only among obese women ($P < 0.001$). Only HRSMI and SATI had significantly different means according to the cancer stage. Lower mean HRSMI was observed in the advanced stage, with significant difference between those in the normal weight stratum. Similarly, a lower mean of SATI was observed in stages III and IV, with a significant difference between patients with BMI >30 kg/m^2. No interactions were observed between BMI and staging for any parameter of body composition ($P > 0.102$).

According to the multiple linear regression models, BMI presented the greatest explanatory power for body fat parameters, especially SATI. Age and staging seems to have a lower influence on these parameters when compared with BMI, whereas age was positively correlated to these parameters and staging showed a negative correlation. R^2 >0.7 was observed for the SATI model, indicating a high explanatory power of stage, BMI and age model for these compartments (Table 4).

For SM parameters, cancer stage presented a greater explanatory power when compared with BMI and age, except for the LRSMI, which seems to be more influenced by BMI. For all SM parameters, R^2 presented lower values, with the highest R^2 obtained for LRSMI (R^2 = 0.420); therefore, indicating that the model considering only BMI, age and staging is not sufficient to properly explain muscle parameters (Table 4).

Discussion

The literature provides sufficient evidence that obesity is a risk factor for endometrial cancer and this association has a dose–response relationship, with the incidence of endometrial cancer increasing as BMI increases [4,31,32]. Although endometrial cancer commonly occurs in older women, corroborating our findings, it also has been diagnosed in younger women [33]. The main cause of this change in the epidemiologic pattern is related to the obesity

Table 1
Clinical-pathologic characteristics of the population (n= 545)

Characteristics	Total (n = 545) n (%)	<65 y of age (n = 265) n (%)	≥65 y of age (n = 280) n (%)	*P*-value*
Comorbidity				0.001
Yes	415 (76.1)	179 (67.5)	236 (84.3)	
No	130 (23.9)	86 (32.5)	44 (15.7)	
Comorbidity type				0.363
SAH	243 (58.6)	106 (59.2)	137 (58.1)	
Diabetes mellitus	15 (3.6)	9 (5)	6 (2.5)	
SAH and diabetes mellitus	142 (34.2)	56 (31.3)	86 (36.4)	
Others†	15 (3.6)	8 (4.5)	7 (3)	
Histologic type				0.013
Epithelial tumors	474 (87)	230 (86.8)	244 (87.1)	
Mesenchymal tumors	21 (3.9)	16 (6)	5 (1.8)	
Mixed epithelial and mesenchymal tumors	50 (9.2)	19 (7.2)	31 (11.1)	
Histologic subtype				0.022
Endometrioid	275 (59)	145 (64.4)	130 (53.9)	
Serous	85 (18.2)	31 (13.8)	54 (22.4)	
Mixed	66 (14.2)	33 (14.7)	33 (13.7)	
Clear cell	29 (6.2)	9 (4)	20 (8.3)	
Others	11 (2.4)	7 (3.1)	4 (1.7)	
Tumor grade				0.003
1	81 (16.1)	50 (20.1)	31 (12.1)	
2	127 (25.1)	71 (28.5)	56 (21.9)	
3	297 (58.8)	128 (51.4)	169 (66)	
Stage				0.267
I	197 (40.3)	90 (36.9)	107 (43.7)	
II	55 (11.2)	28 (11.5)	27 (11)	
III	133 (27.2)	66 (27)	67 (27.3)	
IV	104 (21.3)	60 (24.6)	44 (18)	
BMI (kg/m^2)				
≤24.99	143 (26.7)	67 (25.8)	76 (27.5)	
25–29.99	165 (30.8)	89 (34.2)	76 (27.5)	0.238
≥30	228 (42.5)	104 (40)	124 (44.9)	

BMI, body mass index; SAH, systemic arterial hypertension
*χ^2 test or Fisher's exact tests.
†Dyslipidemia, renal insufficiency, cardiovascular disease, chronic obstructive pulmonary disease.

epidemic [34,35]. Such epidemic also resulted in other changes, such as an increased incidence of more aggressive histologic subtypes, besides endometrioid subtype [36].

In addition to obesity, diabetes mellitus and systemic arterial hypertension, are also risk factors for endometrial cancer. Women with hypertension may have a 61% increased risk for developing endometrial cancer; however, further studies are needed to elucidate the possible effect of risk modification by age, BMI, and diabetes [37].

In the aging process, a complex set of changes occurs in parallel in muscle and adipose tissue. Changes in the body composition of those >65 y of age are mainly characterized by increase of fat mass related to the fat-free mass [38]. The present findings corroborate such evidence as patients >65 y of age presented a significantly lower SMI compared with patients <65 y of age. This loss of muscle tissue is called *primary sarcopenia*, as it is a physiologic process of senescence [39].

In addition to the reduction of muscle mass, the aging process is characterized by fatty infiltration of SM [16,17]. Despite being physiologic in advanced age, this excess of muscle triacylglyceride, or myosteatosis, is considered a pathologic phenomenon, and it has been observed in individuals with obesity, diabetes, insulin resistance, and cancer [13,19,40,41]. Obesity [42], hyperglycemia [43], and senescence [44–46] lead to changes in mitochondrial functioning. Consequently, fatty acids are directed to mitochondria to esterification and storage, rather than oxidation, resulting in the accumulation of ectopic fat [47]. This mitochondrial dysfunction is one of the hypotheses postulated on triggers of myosteatosis [48,49]. However, even with its increasing clinical relevance, the biological mechanisms and its determinants have not been well understood to date [50].

Myosteatosis, represented in the present study by LRSMI and mean SMD, determines the decrease of muscle radiodensity in imaging tests, such as CT. Thus, the higher the fat content, the lower SMD [13]. The low radiodensity of SM is an important factor related to muscle quality. It has emerged as a possible predictor of muscle function and metabolic status [41,50], and an important prognostic factor in patients with cancer. Furthermore, it seems to be a superior indicator to predict clinical outcomes when compared with SM mass alone [21,24]. All muscular quality parameters assessed in the present study (HRSMI, LRSMI, and mean SMD) presented a significant mean difference between adults <65 and those >65 y of age (data not shown).

The changes in body composition due to senescence can be explained by the fact that those >65 y of age tend to gain more weight, with redistribution of fat to the abdominal region, reflecting in the increase of visceral adipose tissue [51]. Although cancer stage was not associated with VATI and IMATI in our regression models, the reporting reference values of adipose tissue stratified by subcutaneous, visceral, and intramuscular adipose tissue broaden the view on adiposity, mainly in its metabolic implications. Obesity-related carcinogenesis mechanisms postulate that visceral adipose tissue increases the risk for cancer by promoting chronic subclinical inflammation. Additionally, increasingly robust evidence shows the biological complexity of adiposity, and it is hypothesized that the risks for carcinogenesis attributed to excess of adipose tissue are, in part, more due to fat distribution than to total fat itself [52].

The present findings also corroborate previous studies that reported that lean body mass increased with increasing BMI [53] and that patients with high BMI also had greater muscle mass on absolute scale (kg) [54]. It is assumed that individuals with greater body weight require greater muscle mass for movement, so they

Table 2
Percentile (5th, 50th, and 95th) distribution and mean ± SD of body composition parameters for BMI and cancer stage

			Percentile		
Parameters	n	Mean ± SD	5th	50th	95th
SMI					
Total	545	44.14 ± 8.68	31.20	43.20	60.38
Age (y)					
<65	265	45.17 ± 8.41	31.41	44.80	60.32
≥65	280	43.17 ± 8.83	30.33	41.97	60.47
BMI (kg/m^2)					
<24.99	143	38.27 ± 6.18	28.20	38.27	48.58
25–29.99	165	43.00 ± 6.61	32.18	42.62	53.71
>30	228	48.85 ± 8.73	36.34	47.67	63.80
Cancer stage					
I–II	252	46.14 ± 8.44	34.55	44.87	63.17
III–IV	237	42.95 ± 8.61	30.19	42.17	58.99
HRSMI					
Total	545	21.68 ± 8.18	9.06	21.03	36.49
Age (y)					
<65	265	24.56 ± 8.17	10.80	24.07	38.52
≥65	280	18.96 ± 7.21	7.66	18.64	30.96
BMI (kg/m^2)					
<24.99	143	20.21 ± 7.13	7.67	20.41	31.20
25–29.99	165	22.37 ± 8.19	10.75	21.90	36.02
>30	228	22.24 ± 8.73	8.40	20.84	38.26
Cancer stage					
I–II	252	22.99 ± 8.19	10.56	22.17	37.62
III–IV	237	21.37 ± 8.07	9.39	20.59	35.93
LRSMI					
Total	545	22.46 ± 6.78	11.41	22.46	34.12
Age (y)					
<65	265	20.62 ± 6.67	10.56	20.38	31.10
≥65	280	24.21 ± 6.43	14.21	23.91	36.50
BMI (kg/m^2)					
<24.99	143	18.06 ± 6.21	8.76	17.11	29.28
25–29.99	165	20.64 ± 5.53	12.36	20.46	31.53
>30	228	26.61 ± 5.61	17.49	26.53	37.18
Cancer stage					
I–II	252	23.15 ± 6.88	11.52	23.24	34.44
III–IV	237	21.57 ± 6.73	10.81	21.66	33.45
Mean SMD					
Total	545	27.64 ± 8.44	13.27	27.46	41.31
Age (y)					
<65	265	30.88 ± 8.36	16.69	30.67	45.05
≥65	280	24.57 ± 7.31	11.90	24.32	37.30
BMI (kg/m^2)					
<24.99	143	29.58 ± 9.35	13.27	29.00	45.33
25–29.99	165	28.81 ± 7.99	16.62	28.69	41.36
>30	228	25.68 ± 7.81	12.13	25.88	39.54
Cancer stage					
I–II	252	28.22 ± 8.35	13.34	28.19	41.36
III–IV	237	28.02 ± 8.37	14.89	27.89	41.64
VATI					
Total	545	50.16 ± 29.75	7.03	46.49	100.16
Age (y)					
<65	265	47.40 ± 28.70	5.66	43.39	94.34
≥65	280	52.78 ± 30.52	8.78	48.08	105.89
BMI (kg/m^2)					
<24.99	143	23.32 ± 17.87	2.33	19.32	58.93
25–29.99	165	46.50 ± 21.56	15.99	41.56	89.32
>30	228	70.31 ± 26.27	29.38	69.66	116.48
Cancer stage					
I–II	252	55.01 ± 29.51	10.65	52.78	103.61
III–IV	237	43.78 ± 28.81	4.68	39.93	97.74
SATI					
Total	539	105.29 ± 52.40	32.73	95.86	205.52
Age (y)					
<65	259	104.36 ± 53.98	36.17	90.40	207.41
≥65	280	106.16 ± 50.97	30.61	98.65	205.23
BMI (kg/m^2)					
<24.99	142	57.72 ± 28.10	18.33	54.66	110.66
25–29.99	164	88.89 ± 27.78	51.30	85.80	128.52
>30	224	148.07 ± 44.34	86.02	145.08	225.69
Cancer stage					

(*continued*)

Table 2 (*Continued*)

Parameters	n	Mean ± SD	Percentile		
			5th	50th	95th
I–II	247	117.40 ± 50.79	49.04	106.10	207.77
III–IV	236	93.16 ± 49.66	23.34	84.39	192.82
IMATI					
Total	545	9.54 ± 5.66	2.51	8.27	20.21
Age (y)					
<65	265	8.16 ± 5.28	2.06	6.95	17.32
≥65	280	10.84 ± 5.71	3.33	9.99	22.44
BMI (kg/m^2)					
<24.99	143	6.02 ± 3.69	1.58	5.34	15.23
25–29.99	165	8.15 ± 4.10	3.30	7.37	15.90
>30	228	12.75 ± 5.98	4.54	12.07	23.91
Cancer stage					
I–II	252	10.10 ± 5.36	2.85	9.18	20.56
III–IV	237	8.67 ± 5.69	2.25	7.51	18.71

BMI, body mass index; HRSMI, high-radiodensity skeletal muscle index; IMATI, intramuscular adipose tissue index; LRSMI, low-radiodensity skeletal muscle index; SATI, subcutaneous adipose tissue index; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index; VATI, visceral adipose tissue index

are expected to have more muscles than leaner individuals [54]. LRSMI, as well as SMI, was increased in the higher strata of BMI. BMI, in turn, was the strongest predictor for LRSMI in the multiple linear regression. Studies over time have demonstrated that the high amount of intramuscular triacylglycerides is related to higher BMI [19,55]. Also, it has been discussed that low muscle radiodensity precedes the development of sarcopenia, considering the studies reporting that the increase in lipid content occurs before the decline of muscle mass [56,57].

In the present study, we highlight that SM loss occurs independently of body weight or body fatness. In the oncology setting, sarcopenia may be present in all BMI strata [58]. Providing reference values for body composition parameters in patients with cancer is warranted, as muscle loss related to aging is lower (1–1.4%/y) [59,60] than the observed in patients undergoing chemotherapy, for whom SM loss has been reported ≤7.3%/100 d, depending on the protocol [61].

When obesity coexists with sarcopenia, the association of two negative conditions worsens the cancer prognosis [8,62]. Thus, detecting these abnormalities early could propel multidisciplinary interventions.

Patients in advanced stages of cancer had significantly lower means of HRSMI compared with those in the initial stages. The same behavior was observed for the SMI, with a trend toward significance. Xiao et al. [26] also observed lower SMI in stages II and III compared with stage I in patients with colorectal cancer. Although SMI and LRSMI increased with the increase in BMI, HRSMI did not change. Therefore, it is suggested that the increase of SM in overweight individuals occurs as a result of an increase in low-radiodensity muscle. This finding has high clinical relevance as previous studies have already demonstrated that muscle quality parameters were better predictors of outcomes than simply the muscular amount [24,63,64]. Additionally, some authors recommend specific cutoff points for SMI according to BMI stratum, without considering that the increase in BMI among overweight individuals may occur as a function of a potentially dysfunctional muscle tissue [14]. Using SM cutoffs according to BMI classification should be investigated in the future, in the light of the present results.

Table 3
Comparison of means of body composition parameters according to staging and BMI and their interaction (n = 482)

Parameters	BMI (kg/m^2)	Cancer stage		*P*-value BMI	*P*-value Stage	*P*-value BMI × Stage
		I–II	III–IV			
SMI	<24.99	$39.82^{a} \pm 5.26$	$38.22^{a} \pm 6.52$			
	25–29.99	$43.82^{b} \pm 5.20$	$42.45^{b} \pm 7.75$	0.000	0.056	0.973
	>30	$49.62^{c} \pm 9.13$	$48.44^{c} \pm 8.48$			
HRSMI	<24.99	$22.85^{A} \pm 6.51$	$19.78^{B} \pm 7.28$			
	25–29.99	$23.29^{A} \pm 7.27$	$22.15^{A} \pm 8.93$	0.320	0.044	0.417
	>30	$22.87^{A} \pm 9.24$	$22.35^{A} \pm 7.90$			
LRSMI	<24.99	$16.^{97a} \pm 6.58$	$18.43^{a} \pm 6.26$			
	25–29.99	$20.52^{b} \pm 5.34$	$20.30^{a} \pm 5.58$	0.000	0.734	0.297
	>30	$26.75^{c} \pm 5.57$	$26.09^{b} \pm 6.03$			
Mean SMD	<24.99	$32.57^{a} \pm 9.12$	$28.96^{a} \pm 9.49$			
	25–29.99	$29.71^{a} \pm 7.55$	$28.82^{a} \pm 7.99$	0.000	0.085	0.112
	>30	$25.91^{b} \pm 7.89$	$26.36^{a} \pm 7.82$			
VATI	<24.99	$23.38^{a} \pm 18.60$	$21.51^{a} \pm 17.15$			
	25–29.99	$43.57^{b} \pm 18.82$	$46.58^{b} \pm 23.12$	0.000	0.334	0.102
	>30	$72.32^{c} \pm 25.72$	$64.86^{c} \pm 26.93$			
SATI	<24.99	$63.77^{aA} \pm 21.37$	$55.89^{aA} \pm 32.41$			
	25–29.99	$88.26^{bA} \pm 21.71$	$89.08^{bA} \pm 33.47$	0.000	0.034	0.132
	>30	$152.20^{cA} \pm 42.61$	$137.38^{cB} \pm 44.27$			
IMATI	<24.99	$5.52^{a} \pm 3.31$	$6.09^{a} \pm 3.87$			
	25–29.99	$8.32^{b} \pm 4.18$	$7.72^{a} \pm 3.87$	0.000	0.710	0.579
	>30	$12.96^{c} \pm 5.15$	$12.21^{b} \pm 6.91$			

BMI, body mass index; HRSMI, high-radiodensity skeletal muscle index; IMATI, intramuscular adipose tissue index; LRSMI, low-radiodensity skeletal muscle index; SATI, subcutaneous adipose tissue index; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index; VATI, visceral adipose tissue index.
Factorial analysis of variance followed by the post hoc Bonferroni test. Lowercase letters compare the BMI classes. Capital letters compere the stage I–II and III–IV.

Table 4
Association between BMI, age, and staging to each body composition parameter according to the multiple linear regression models

Parameters	R^2	*P*-value	Non-standard β-coefficient	95% CI	T-test	*P*-value
SMI (n = 480)						
Model	0.347	0.000				
Stage			−0.671	−1.199 to −0.143	−2.497	0.013
BMI			0.644	0.554 to 0.734	13.993	0.000
Age			−0.146	−0.211 to −0.082	−4.450	0.000
HRSMI (n = 478)						
Model	0.229	0.000				
Stage			−1.076	−1.608 to −0.544	−3.977	0.000
BMI			0.055	−0.034 to 0.144	1.214	0.225
Age			−0.374	−0.439 to −0.308	−11.182	0.000
LRSMI (n = 480)						
Model	0.420	0.000				
Stage			0.316	−0.085 to 0.717	1.547	0.123
BMI			0.585	0.516 to 0.653	16.735	0.000
Age			0.217	0.168 to 0.266	8.702	0.000
Mean SMD (n = 482)						
Model	0.237	0.000				
Stage			−0.875	−1.439 to −0.310	−3.043	0.000
BMI			−0.278	−0.373 to −0.183	−5.760	0.000
Age			−0.390	−0.459 to −0.321	−11.089	0.000
VATI (n = 478)						
Model	0.460	0.000				
Stage			−0.698	−2.323 to 0.926	−0.845	0.399
BMI			2.737	2.457 to 3.017	19.182	0.000
Age			0.406	0.207 to 0.604	4.011	0.000
SATI (n = 471)						
Model	0.702	0.000				
Stage			−2.688	−4.807 to −0.568	−2.492	0.013
BMI			5.985	5.615 to 6.355	31.764	0.000
Age			0.064	−0.194 to 0.322	0.488	0.626
IMATI (n = 480)						
Model	0.418	0.000				
Stage			−0.046	−0.360 to 0.268	−0.287	0.774
BMI			0.434	0.380 to 0.488	15.805	0.000
Age			0.185	0.147 to 0.223	9.503	0.000

BMI, body mass index; HRSMI, high-radiodensity skeletal muscle index; IMATI, intramuscular adipose tissue index; LRSMI, low-radiodensity skeletal muscle index; SATI, subcutaneous adipose tissue index; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index; VATI, visceral adipose tissue index.

To date, there are no reference values, for either healthy or oncologic populations, for body composition parameters determined by CT. However, it is known that several factors may contribute to alter these parameters, such as sex, age [14,54,65–67], and ethnicity [68,69]. Although ethnicity is described in the literature as having a potential influence on body composition [68], this variable was not addressed in the present study. We acknowledge this limitation, and we suggest that this variable should be evaluated in future studies. Other limitations of the present study included its retrospective nature, which led to the exclusion of a large number of patients because they did not have CT or had poor-quality images CT. Additionally, data from only one type of tumor were used, from a single reference center, which made it difficult to extrapolate the results to other populations.

To our knowledge, this was the first study to provide reference values for body composition parameters in a cancer population. These results allow a broadening of the comprehension regarding the interaction between age, BMI, and cancer stage in body composition parameters, using a method of high accuracy and reproducibility [70]. The assessment of SM in two sub-ranges, of high and low radiodensity, enabled us to explore in more detail the behavior of the SM mass according to the variables analyzed. Additionally, the use of body composition parameters normalized by stature allowed the comparison between different individuals or groups, who differ in height, and also creates an analytical framework for future studies [30].

Conclusion

The present study described the percentile distribution of the body composition parameters for patients with endometrial cancer. Percentile values were established for adults <65 and >65 y of age, in addition to specific values for BMI classes and cancer stage. BMI was associated with adipose tissue parameters and LRSMI, whereas cancer stage was associated with SMI, mean SMD, and HRSMI. The reference values presented in the present study can contribute to the interpretation of the data originated from CT and can be used further to categorize individuals in different phenotypes of body composition. It is suggested that future studies associate tumor-related characteristics with body composition parameters for better comprehension of distribution of muscle and adipose tissues at different cancer sites and histologic types, and, thus, to develop specific strategies in the prevention and treatment of cancer.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.nut.2020.110873.

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