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ORIGINAL ARTICLE/ORİJİNAL MAKALE

The impact of visceral fat-to-muscle ratio on prognosis in patients with endometrial cancer

Endometrium kanseri hastalarında viseral yağ dokusu-kas oranının prognoza etkisi

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ABSTRACT

Aim: Obesity increases the risk of endometrial cancer (EC) by 2-5 times compared to non-obese individuals. This study investigates the relationship between radiological measurements of skeletal muscle, visceral, and subcutaneous fat tissue, and their association with clinical features and survival in EC patients.

Material and Method: This retrospective study included 109 EC patients who underwent primary surgery between 2014-2024, with preoperative CT/MR imaging and BMI data available. Measurements of visceral fat area (VFA), subcutaneous fat area (SFA), and skeletal muscle area (SMA) were taken at the L3-L4 vertebral level. Ratios of VFA/SMA, total fat area/SMA (TFA/SMA), and skeletal muscle index (SMI) were calculated. Associations between these metrics, clinical features, and survival outcomes were analyzed.

Results: The mean age was 61.5 years, with a BMI of 35.24; 74.3% were obese (BMI > 30). Mean disease-free survival was 96.1 months, and overall survival was 92.9 months. Advanced age and higher cancer stage correlated with recurrence and mortality. Higher SMA was associated with lower cancer stages, while lower SMA correlated with stages III-IV (p = 0.036). However, no significant differences in disease-free or overall survival were observed across groups.

Conclusions: Skeletal muscle area inversely correlates with cancer stage, indicating a potential protective effect. Obesity-related metrics (VFA, SFA, TFA) showed no significant impact on survival. Further studies are needed to explore underlying mechanisms and clinical relevance.

Keywords: Adiposity, Body composition, Endometrial cancer, Obesity, Visceral fat

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ÖZET

Amaç: Obezite, EK gelişimini obez olmayan hastalara göre 2-5 kat artıran önemli bir risk faktörüdür. Obeziteyi tanımlamakta genellikle vücut kitle indeksi (VKİ) kullanılır. Ancak bu ölçüt; kiloya yağ, kas ve kemiklerin etkisini ayırt etmekte yetersiz kalır. Bu çalışmadaki amaç; viseral ve subkutan yağ dokusu ile birlikte iskelet kasının radyolojik ölçümlerinin, endometrium kanserli hastalarda klinik özellikler ve prognoz ile ilişkisinin incelenmesidir.

Yöntem: Retrospektif yapılan bu çalışmaya 2014-2023 yılları arasında primer cerrahisi merkezimizde yapılmış ve endometrial karsinom tanılı, preoperatif BT/MR görüntülerine ve VKİ verilerine erişilen 109 hasta dahil edilmiştir. L3-L4 seviyesinden alınan tek aksiyel kesitte, viseral, subkutan yağ ve iskelet kası alanı ayrı ayrı ölçülmüştür. Bu ölçümler kullanılarak, viseral yağ alanı-kas oranı, toplam yağ alanı-kas oranı ve iskelet kas indeksi hesaplanmıştır.

Bulgular: Hastaların tanı anında ortalama yaşı 61,5, ortalama VKİ, 35,24 idi. Dört hastadan üçünün (%74,3) obez (VKİ>30) olduğu görüldü. Yapılan analizlerde ortalama hastalıksız sağkalım 96,1, toplam sağkalım 92,9 ay olarak bulundu. Tanı yaşı ve evre arttıkça rekürrens riskinin ve mortalitenin arttığı görülmüştür. Obezite ilişkili radyolojik ölçümler (SYA, VYA, TYA, İKA) ve bunlar kullanılarak hesaplanan oranların (VYA/İKA, TYA/İKA, SMI) yüksek ve düşük olmak üzere iki gruba bölünmüştür ve klinik özellikler ve sağkalım açısından karşılaştırılmışlardır. İskelet kas alanı yüksek olan hastaların genellikle daha düşük evreli olduğu, iskelet kas alanı düşük olan hastaların yüksek evreli (evre III-IV) olduğu saptanmıştır (p=0,036). Bu gruplar arasında hastalıksız ve toplam sağkalım açısından anlamlı farklılık görülmemiştir.

Sonuç: Obezite ve endometrium kanseri ilişkisinin altında yatan hücresel mekanizmaların aydınlatılması, bunların klinik sonuçlarının ve tedavi protokollerine etkisinin anlaşılabilmesi için ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Adipozite, Endometrium kanseri, Obezite, Viseral yağ dokusu, Vücut bileşenleri

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INTRODUCTION

According to data from the World Health Organization (WHO), uterine cancers are the second most common gynecological malignancy among women in both developed and developing countries (1). Several significant risk factors contribute to the pathogenesis of endometrial cancer (EC), with prolonged unopposed exposure to endogenous or exogenous estrogen being among the most critical. Obesity is a major risk factor, increasing the likelihood of EC development by 2–5 times compared to non-obese individuals (2). The risk attributed to obesity may be partially explained by the fact that adipose tissue is the primary source of estrogen in the postmenopausal period (3)but whether risk varies by use of postmenopausal hormone therapy (HT. Other mechanisms underlying obesity-associated carcinogenesis include pro-inflammatory cytokines secreted by visceral adipose tissue, which promote endometrial proliferation and tumorigenesis (4). Additionally, increased visceral fat is associated with insulin resistance and hyperinsulinemia, and insulin itself has tumorigenic effects (5).

Body mass index (BMI) is commonly used to define obesity. However, BMI cannot differentiate the contributions of fat, muscle, and bone to body weight, making it an inadequate measure of body composition and fat distribution (6). Other anthropometric measurements, such as waist circumference and waist-to-hip ratio, also fail to distinguish between subcutaneous and visceral fat. Individuals with increased visceral fat due to mesenteric, omental, and retroperitoneal fat accumulation have a higher risk of developing Type 2 diabetes and cardiovascular diseases (4). These individuals are also more prone to developing breast, colorectal, and esophageal cancers compared to those with less visceral fat (7). Visceral adipose tissue (VAT) has distinct cellular, molecular, and endocrine functions compared to subcutaneous fat, which may make it an alternative predictive factor for obesity in patients with EC (8). VAT and subcutaneous adipose tissue (SAT) quantified as areas, referred to as visceral fat area (VFA) and subcutaneous fat area (SFA), respectively; provide more specific insights into fat distribution. The total fat area (TFA) is determined as the sum of visceral and subcutaneous fat areas. Similarly, skeletal muscle area (SMA) represents the total cross-sectional area of skeletal muscles, while the skeletal muscle index (SMI) normalizes SMA by body surface area to provide a standardized measure of muscle mass.

Although previous studies have demonstrated the physiological relationship between adipose and muscle tissue with EC, the clinical significance of these relationships remains unclear. This study aims to investigate the relationship between radiological measurements of VFA, SFA, as well as SMA, and the clinical characteristics and prognosis of patients with EC. It also seeks to evaluate the clinical significance of body composition parameters beyond simple measures of weight and BMI as indicators of obesity.

MATERIAL AND METHOD

Patient Selection

This study included 109 patients diagnosed with endometrial carcinoma who underwent total abdominal, laparoscopic, or robotic hysterectomy with bilateral salpingo-oophorectomy, ± omentectomy, ± pelvic and para-aortic lymphadenectomy, and had preoperative CT or MRI imaging available at Istanbul Medipol University Mega Hospitals Complex between April 2014 and December

2023. Retrospective data collection was conducted for these patients. Pathology reports were used to obtain data on stage, grade, lymphovascular space invasion (LVSI), and lymph node involvement. Tumor grade was classified according to FIGO guidelines as Grade 1, 2, or 3 for endometrioid types, and as non-endometrioid types for other histologies. Imaging studies conducted within one month before or six weeks after surgery were considered valid for inclusion. BMI was calculated using the height and weight recorded at the time of diagnosis.

Patients were excluded from the study if they met any of the following criteria: lack of preoperative imaging studies, absence of preoperative BMI measurements, primary surgery not performed at the study center, presence of concurrent malignancies.

Ethical Approval

This study was approved by the Ethics Committee of Istanbul Medipol University under approval number 692.

Image analysis

Preoperative imaging data were obtained from the hospital's Picture Archiving and Communication System (PACS, GE Medical Systems, United Kingdom). Previous studies have demonstrated that measurements of abdominal fat and muscle tissues using both computed tomography (CT) and magnetic resonance imaging (MRI) are reliable and valid (9–12)the impact of obesity on clinical and histological phenotype is poorly understood. This study explored abdominal fat volumes and fat distribution quantified by computed tomography (CT. Measurements performed on both MRI and CT images of the same patient showed high similarity and correlation, supporting their reliability and validity as documented in literature (13–18) along with related conditions such as metabolic syndrome, which is strongly associated with this epidemic. Novel and innovative methods to assess relevant obesity-related biomarkers are needed to determine the clinical significance, allow for surveillance and intervene if appropriate. Aggregations of specific types of fat, specifically hepatic and visceral adiposity, are now known to be correlated with these conditions, and there are a variety of imaging techniques to identify and quantify their distributions and provide diagnostic information. These methods are particularly salient for metabolic syndrome, which is related to both hepatic and visceral adiposity but currently not defined by it. Simpler non-specific fat measurements, such as body weight, abdominal circumference and body mass index are more frequently used but lack the ability to characterize fat location. In addition, non-alcoholic fatty liver disease (NAFLD.

Using the Syngo.Via software package (Siemens Healthcare, Germany), a single experienced radiologist manually measured subcutaneous fat, visceral fat, and muscle tissue areas from a single axial slice at the L3-L4 vertebral level, based on parameters established in previous studies (19). VAT was differentiated from intestinal loops, intra-abdominal structures, and abdominal wall muscles. SAT was measured separately from the abdominal wall and paraspinal muscles. SMA was calculated by encompassing all muscles in the cross-sectional slice. TFA was determined as the sum of visceral and subcutaneous fat areas. All measurements were recorded in square centimeters (cm^2).

The SMI was calculated by dividing the skeletal muscle area measured at the L3-L4 level by

the square of the patient's height(20,21). The visceral fat-to-skeletal muscle ratio (VFA/SMA) was determined by dividing the VFA by the SMA, and the total fat-to-skeletal muscle ratio (TFA/SMA) was calculated by dividing the TFA by the SMA. An example cross-sectional image of these measurements is shown in Figure 1.

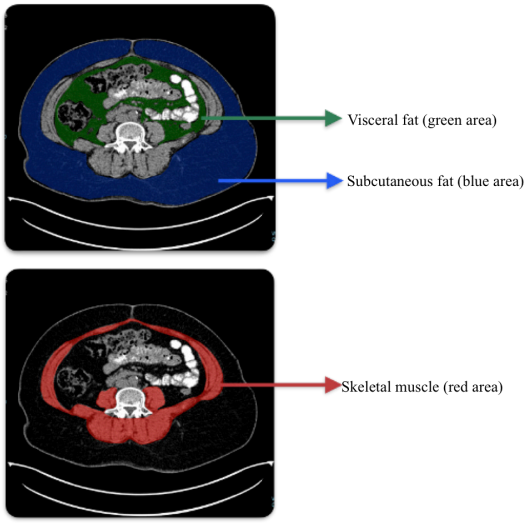

Figure 1. Areas marked on abdominal segment

Statistical Analysis

The data analysis was conducted using the SPSS software package (Version 28.0; Armonk, NY, IBM Corp.). Qualitative variables were expressed as frequencies and percentages, while quantitative variables were described using the mean, standard deviation, median, and interquartile range (1st and 3rd quartiles). Comparisons of categorical variables between groups were performed using the Pearson chi-square test, Fisher's exact chi-square test, or the Fisher-Freeman-Halton test, as appropriate. The normality of quantitative variables was assessed with the Kolmogorov-Smirnov test, and homogeneity of variances was evaluated using Levene's test. For comparing means between two independent groups, the Student's t-test was employed, while the Mann-Whitney U test was used for median comparisons. To examine factors influencing survival durations related to recurrence and mortality risks, univariate and multivariate Cox regression analyses were performed. Variables with a p-value < 0.25 in univariate analysis were included in the multivariate analysis for further evaluation. Kaplan-Meier survival curves were generated to illustrate survival outcomes, and the level of statistical significance was set at $p < 0.05$. Disease-free survival was defined as the interval from surgery to the first clinically confirmed recurrence or, in the absence of recurrence, the date of last follow-up. Overall survival was defined as the time from surgery to death attributable to the disease.

RESULTS

Demographic and Clinical Characteristics

The clinical characteristics of the patients (n=109) at the time of diagnosis, along with parameters related to body composition, are detailed in Tables 1 and 2. At the time of diagnosis, the mean age of the patients was 61.5 years, and the mean BMI was 35.24 kg/m². A significant proportion of the patients (74.3%) were obese (BMI >30). The majority of the sample (85.3%) consisted of postmenopausal women, and nearly 80% of the patients had either diabetes or hypertension. In terms of surgical approach, 66 patients underwent minimally invasive procedures, while 43 patients were operated on via laparotomy. Lymphadenectomy was performed in approximately 90% of the patients. Most patients were diagnosed at FIGO Stage I (66.1%) and had endometrioid histological subtype (75.2%). Non-endometrioid histological subtypes, including serous, clear cell, carcinosarcoma, and other rare types, were grouped together and accounted for 27 patients. Over half of the patients (58.7%) did not exhibit LVSI. Advanced-stage disease (Stage III-IV) was

observed in 30 patients, and recurrence was documented in 13 patients. Among patients with recurrence, 3 cases involved pelvic recurrence, 4 cases abdominal recurrence, and 6 cases distant metastases. Neoadjuvant therapy (chemotherapy or radiotherapy) was administered to 4 patients, while 74 patients received adjuvant therapy.

The average values for body composition parameters were as follows: VFA: 134.61 cm^2, SFA: 369.32 cm^2, TFA: 503.94 cm^2, SMA: 131.74 cm^2. The calculated ratios and indices were: VFA/SMA: 1.01, TFA/SMA: 3.80, SMI: 52.65

Table 1. Demographic and clinical characteristics of patients

	n (%)
DM/HT	
None	23 (21,1)
DM or HT	86 (78,9)
Menopausal status	
Pre/perimenopausal	16 (14,7)
Postmenopausal	93 (85,3)
Parity	
Nulliparous	13 (11,9)
≥1	96 (88,1)
BMİ	
<30	28 (25,7)
≥30	81 (74,3)
Histological subtype & grade	
Endometrioid grade 1	24 (22,0)
Endometrioid grade 2	42 (38,5)
Endometrioid grade 3	16 (14,7)
Non-endometrioid	27 (24,8)
FIGO Stage	
I	72 (66,1)
II	7 (6,4)
III	24 (22,0)
IV	6 (5,5)
Lymphovascular invasion (LVSI)	
Var	45 (41,3)
Yok	64 (58,7)
Surgery type	
Laparotomy	43 (39,4)
Minimally invasive	66 (60,6)
Lymphadenectomy	
Yes	98 (89,9)
No	11 (10,1)
Adjuvant treatment	
None	35(32,1)
Radiotherapy	28 (25,6)
Chemotherapy	9 (8,2)
Chemotherapy + Radiotherapy	28 (25,6)
Immunotherapy	9 (8,2)
Neoadjuvant treatment	
None	105 (96,3)
Chemotherapy / Radiotherapy	4 (3,7)
Recurrence	
No	96 (88,1)
Yes	13 (11,9)

Table 2. Demographic characteristics and radiological measurements of body compositions of the patients

	Mean ± Standard Deviation
Age, years	61,50 ± 9,48
BMI, kg/m^2	35,24 ± 7,48
Visceral fat area (VFA), cm^2	134,61 ±58,50
Subcutaneous fat area (SFA), cm^2	369,32 ±140,80
Total fat area (TFA), cm^2	503,94±169,97
Skeletal muscle area (SMA), cm^2	131,71±22,64
Visceral fat/skeletal muscle (VFA/SMA)	1,01 ±0,40
Total fat/skeletal muscle (TFA/SMA)	3,80 ± 1,04
Skeletal muscle index (SMI), cm^2/m^2	52,65 ± 9,10

Survival Analysis

This study aimed to investigate the factors influencing survival in EC. Analysis revealed that the mean disease-free survival (DFS) was 96.1 months, and the mean overall survival (OS) was 92.9 months. The results of univariate and multivariate analyses are presented in Table 3.

Key findings indicate that as age at diagnosis and stage increase, the risk of recurrence and mortality also rises. However,

obesity-related radiological measurements, including SFA, VFA, TFA, and SMA, as well as the ratios derived from these measurements (VFA/SMA, TFA/SMA and SMI), were found to have no significant impact on either DFS or OS based on this analysis.

Radiological measurements (SFA, VFA, TFA, and SMA) and their calculated ratios (VFA/SMA, TFA/SMA, and SMI) were used to divide patients into two groups for each parameter: those below and above the median values. These groups were compared in terms of several clinical and demographic characteristics, including: age, menopausal status, parity, comorbidities (diabetes mellitus/hypertension), histological grade, FIGO staging, LVSI, recurrence. Analyses were performed to assess the relationships between these characteristics and the radiological measurements, and p-values were calculated to determine statistical significance. The p-values for these comparisons are presented in Table 4.

Table 3. Survival analysis

	Disease-free survival (DFS)			Overall survival (OS)		
	Univariate	Multivariate		Univariate	Multivariate	
	p-value	p-value	HR	p-value	p-value	HR
Age	**<0,001**	**0,038**	1,074	**<0,001**	**<0,001**	1,170
BMI	0,671			0,219	0,528	1,512
DM/HT	0,729			0,270		
Menopausal status	0,299			0,295		
Parity	0,521			0,339		
Histological grade	0,197	0,878	1,110	**<0,001**	0,015	10,779
FIGO stage	**<0,001**	**0,003**	16,025	**<0,001**	**<0,001**	31,362
Adjuvant treatment	**0,002**	0,190	1,374	0,231		
Neo-adjuvant treatment	**0,077**			**<0,001**	**0,015**	11,603
Subcutaneous fat area	0,293			0,352		
Visceral fat area	0,831			0,756		
Total fat area	0,348			0,503		
Skeletal muscle area	0,363			0,871		
VFA/SMA	0,331			0,745		
TFA/SMA	0,050	0,163	1,648	0,408		
Skeletal muscle index (SMI)	0,380			0,788		

Table 4. Comparison of parameters of patients with radiological measurements

	BMI	SFA	VFA	TFA	SMA	VFA/SMA	TFA/SMA	SMI
	p	*p*	*p*	*p*	*p*	*p*	*p*	*p*
Age	0,691	0,416	0,996	0,262	0,102	0,948	0,714	0,173
Menopausal status	0,917	0,287	0,616	0,229	0,917	0,968	0,200	0,569
DM/HT	0,873	0,680	0,261	0,931	0,527	0,776	0,629	0,952
Parity	0,273	0,305	0,795	0,170	0,200	0,130	0,477	0,870
Histological grade	0,521	0,953	0,880	0,749	0,678	0,758	0,413	0,967
FIGO stage	0,700	0,950	0,107	0,725	**0,036**	0,384	0,935	0,326
LVSI	0,098	0,135	0,909	0,057	**0,041**	0,909	0,336	**0,023**
Recurrence	0,616	0,870	0,741	0,688	0,273	0,395	0,637	0,305

For the groups divided based on radiological measurements, no significant differences were observed regarding age, menopausal status, comorbidities, parity, histological grade, staging, LVSI, or recurrence. However, a notable finding was that patients with higher SMA were more likely to be in lower stages (Stage I), whereas those with lower SMA were more commonly in higher stages (Stage III-IV) ($p = 0.036$). Similarly, when patients were grouped based on SMA and SMI, significant associations were found with LVSI, with $p = 0.041$ and $p = 0.023$, respectively.

Radiological measurements of body composition and their calculated ratios were divided into two groups based on their median values (high and low). Kaplan-Meier survival curves for these groups, illustrating DFS and OS, are presented in Figures 2 and 3, respectively, along with the results of the log-rank test. The analyses showed no significant differences between the high and low groups in terms of either disease-free survival or overall survival.

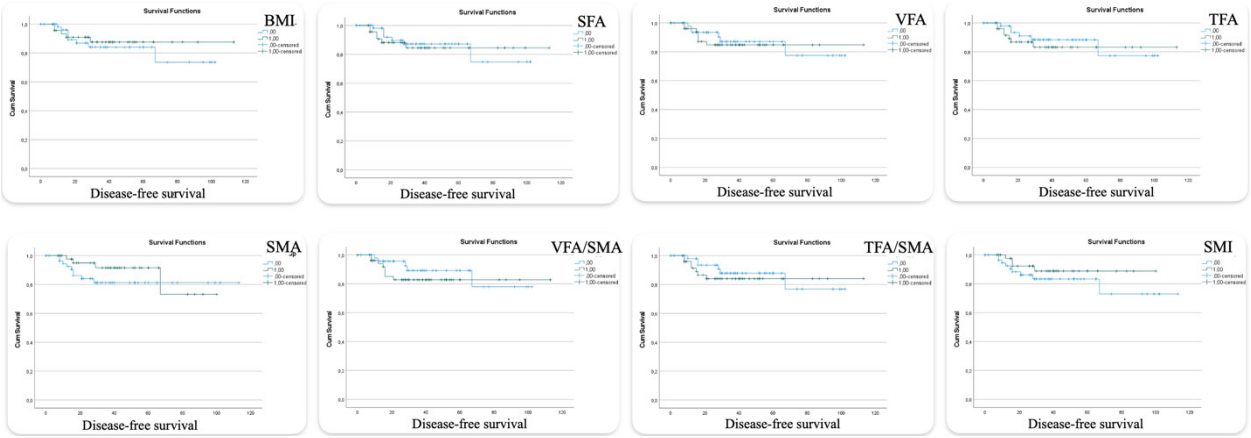

Figure 2. Kaplan-Meier survival curves and log-rank tests, disease-free survival values are shown

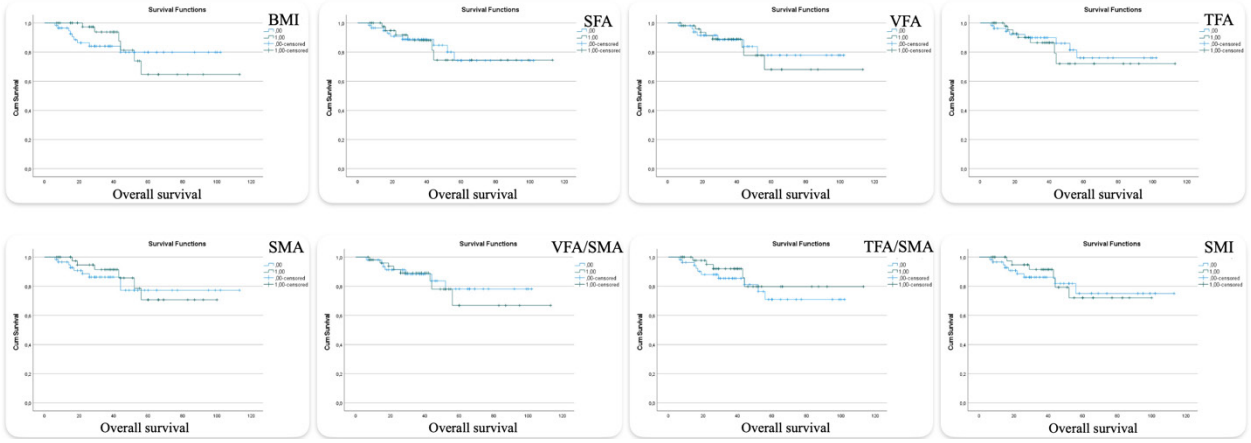

Figure 3. Kaplan-Meier survival curves and log-rank tests, overall survival values are shown

DISCUSSION

Key findings of this study showed that advanced age at diagnosis and higher FIGO stage were associated with increased risks of recurrence and mortality. However, radiological measurements of obesity-related parameters (SFA, VFA, TFA, SMA) and the ratios derived from these measurements (VFA/SMA, TFA/SMA, SMI) had no significant impact on DFS or OS. When grouped by median values, no significant differences were found in terms of clinical features, except that patients with higher SMA

were predominantly at lower stages (Stage I), while those with lower SMA were more likely to be at higher stages (Stage III-IV).

While age as an independent prognostic factor is debated, many studies have associated advanced age with poorer survival outcomes and higher clinical failure rates (22). Similarly, in our study, univariate and multivariate analyses revealed that age significantly affected both DFS and OS.

Numerous studies have explored the relationship between obesity and cancer from molecular, clinical, and radiological perspectives. A meta-analysis of over a thousand studies concluded that obesity increases the risk of 13 different types of cancer and is among the leading preventable causes of cancer, alongside smoking (23,24). The relationship between EC and obesity has also been extensively studied, with various researchers examining the prognostic value of radiological indicators of adiposity (25).

For instance, Buckley et al. studied 83 patients with high-grade endometrial cancer and found that patients with a higher VFA/SFA (visceral fat/subcutaneous fat) ratio (>0.45) had shorter DFS and OS. These patients exhibited a fivefold increase in recurrence risk and mortality, with no significant differences in BMI, stage, histological grade, or surgical type (26). Similarly, Donkers et al. observed shorter survival durations in high-grade EC patients with a high percentage of visceral fat (27)but mainly included grade 12 EC.\nObjective: To evaluate body fat distribution and its relation to outcome in high-grade endometrial cancer.\nMethods: Retrospective study in women diagnosed with high-grade EC between February 2006 and August 2017 at the Royal Cornwall Hospital who had abdominal CT-scan as part of routine diagnostic work-up. Subcutaneous abdominal fat volumes and visceral abdominal fat volumes were quantified based on CT-scan measurements, and visceral fat percentage calculated.\nResults: A total of 176 patients with high-grade EC were included. The median age was 70 years and median BMI was 29.4 kg/m2. The majority of patients had non-endometrioid endometrial cancer (NEEC; 62 %. Our study differed by including patients with all histopathological grades, not just high-grade tumors.

Studies exploring the immunopathological relationship between adiposity and cancer, such as Mauland et al.'s work in Norway, found no significant association between volumetric fat measurements and survival in univariate Cox analysis, although low visceral fat percentage was linked to poorer survival. Mauland's study associated high BMI and fat-related parameters with low-grade endometrioid tumors and progesterone receptor positivity but found no link with estrogen receptors (9). Unlike their use of volumetric measurements, our study relied on area-based measurements.

In another study, Ye et al. examined 200 Chinese patients and found that a high percentage of visceral fat was associated with lymph node metastasis, Grade 3 disease, and LVSI. Patients with high visceral fat percentages were also older and exhibited extrauterine spread. Although BMI correlated with total adiposity, it showed no significant relationship with VFA percentage (28).

A recent study from Turkiye, Çelik et al. focused on VAT and VAT index in predicting survival outcomes in EC. Unlike our study, they excluded skeletal muscle metrics. Their findings showed that higher VAT index values are significantly associated with increased cancer-specific mortality, although no meaningful

relationship was found with progression-free survival or tumor characteristics. Nonetheless, Çelik et al. provided valuable insights into the independent impact of visceral fat distribution on EC outcomes, advocating for the use of VAT-based metrics over BMI in predicting patient prognosis (29).

The clinical significance of visceral fat varies by cancer type. For instance, increased visceral fat is associated with better survival in gastric cancer but poorer survival in pancreatic, colorectal, and cervical cancers (30,31). Nattenmüller et al. compared all gynecologic malignancies (cervical, tubo-ovarian, and endometrial cancers) using densitometric measurements from CT scans. They found that body composition parameters had no significant impact on OS in univariate analyses, a finding supported by multivariate analyses. However, they observed that increased muscle mass was protective against mortality (32). Similarly, Ham et al. identified visceral fat/muscle ratio as an independent prognostic factor for tubo-ovarian cancers, while subcutaneous fat, total fat, and sarcopenia were not significant (33). They demonstrated that L3-level visceral fat measurements are more reliable for assessing survival in such cancers. Our study also utilized L3-L4 level measurements as a reference point.

Sarcopenia, characterized by age-related decreases in muscle mass and function, has been associated with increased mortality and poor prognosis in various cancers. In EC, the clinical significance of sarcopenia remains debated. However, the concept of "sarcopenic obesity," which combines increased fat mass with decreased muscle mass, has gained prominence in recent years. This condition exacerbates cancer prognosis by combining the independent risks of obesity and sarcopenia (34). SMI, calculated by dividing the skeletal muscle area at the L3 level by the square of the patient's height (cm^2/m^2), is a key measure of sarcopenia. In our study, low SMI was associated with LVSI, and patients with higher SMA were predominantly in earlier stages, while those with lower SMA were in advanced stages (Stage III-IV). Aydın et al. similarly underline the significance of body composition, suggesting correlations between these parameters and disease outcomes. The shared emphasis on body composition highlights its growing relevance in understanding EC prognosis, but methodological differences, such as the imaging levels and parameters assessed, offer unique perspectives (35).

The presence of a radiological parameter to assess high-risk patients at diagnosis could be beneficial for treatment planning. Prospective studies evaluating the response of these measurements to treatment would be valuable in advancing the field. Awareness of body composition in EC patients could guide recommendations for medical or surgical interventions, nutrition, and exercise strategies aimed at reducing visceral fat and preserving muscle mass, thereby improving outcomes (36). It is essential to investigate the clinical implications to develop therapies targeting the microenvironment generated by adipose tissue (37).

Limitations of this study include its retrospective design, single-center nature, and small sample size. Missing data for some patients reduced the sample size and statistical power. Prospective studies with larger cohorts are needed to validate these findings and explore the long-term effects of changes in body composition on cancer outcomes.

Our study focused only on the patient's weight and fat distribution at diagnosis. Understanding

the impact of lifetime weight and fat distribution changes on cancer development would require more complex, long-term studies. Further research is needed to explore how weight fluctuations over time contribute to cancer progression (38).

Our hypothesis aimed to demonstrate that obesity is a more complex risk factor than BMI alone can capture. The results suggest that the underlying pathological mechanisms are indeed more complex and that their clinical implications remain incompletely understood. Further large-scale studies are required to elucidate the cellular mechanisms underlying the relationship between obesity and EC, as well as to evaluate the impact of these findings on clinical outcomes and treatment protocols.

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Authorship Contributions Conception and design: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ, Acquisition of data: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ, Analysis and interpretation of data: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ, Drafting of the manuscript: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ,Critical revision of the manuscript: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ, Statistical analysis: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ, Administrative technical or material support: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ, Supervision: ZAS, NZY, ÖP, HKA, SEE, MŞ, İAÖ,

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