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The Importance of Body Fat Composition Evaluated by Computed Tomography and Its Prognostic Significance in Patients with Testicular Cancer

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ABSTRACT

Introduction: To investigate the relationship between visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and skeletal muscle area (SMA) ratios and testicular cancer stage.

Methods: Between 2018 and 2023, 94 patients with testicular cancer were evaluated for demographic data, pathological results, and cancer stages. VAT, SAT, and SMA were measured in cm^2 using computed tomography (CT) scans. The ratios of SMA/SAT, SMA/VAT, and SAT/VAT were calculated to assess their relationships with cancer stage.

Results: A statistically significant moderate positive correlation was found between tumor stage and the VAT/SAT ratio (r=0.35, p=0.001). The mean VAT/SAT ratio was 0.64±0.43 for stage 1 tumors, 0.81±0.41 for stage 2 tumors, and 1.32±0.29 for stage 3 tumors, indicating statistically significant differences (p=0.001). Comparisons of the groups revealed that the VAT/SAT ratio was significantly higher in stage 3 tumors than in stage 1 and 2 tumors (p=0.001 and p=0.018, respectively). No significant differences were observed between stages 1 and 2. Similarly, only the VAT/SAT ratio differed significantly between localized disease and systemic disease (0.65±0.43 and 0.86±0.44, respectively, p=0.023).

Conclusion: Given that body composition parameters provide a more refined assessment of obesity than body mass index and are readily available from routine CT scans, they can serve as valuable tools for tumor staging and prognostication in patients with testicular cancer.

Keywords: Chemotherapy, computed tomography, skeletal muscle area, subcutaneous adipose tissue, testicular cancer, visceral adipose tissue

Introduction

Testicular cancer is the most commonly diagnosed cancer among males aged 15-34 years (1). The most prevalent type of cancer is the seminomatous subtype, and germ cell tumors (GCTs) account for 98% of testicular cancer cases. Regardless of tumor subtype, the prognosis remains favorable, with a five-year survival rate of 99% in localized disease, specifically reported to be 96% for stage 2 and 73% for stage 3 disease (2). Diagnosis involves clinical examination, testicular ultrasound, and assessment of tumor markers. Computed tomography (CT) scan was also performed in all patients for metastasis screening. Patients with a preliminary diagnosis of testicular tumors undergo orchiectomy for pathological diagnosis and treatment. Depending on the pathological subtype and tomography findings, some patients may require adjuvant chemotherapy or radiotherapy (1).

Body fat and muscle composition measured by CT provide important information about the metabolic status of patients. Adipose tissue functions as an active secretory organ that modulates energy equilibrium, homeostasis, inflammation, insulin resistance, angiogenesis, and fat metabolism (3,4). Changes in and dysfunction of adipose tissue are commonly observed in obesity-associated diseases, including type 2 diabetes, cardiovascular disease, breast cancer, renal cancer, and colorectal cancer (3). In consideration of fat distribution, visceral adipose tissue (VAT) is associated with a greater risk of cancer than subcutaneous adipose tissue (SAT) (5). When considering VAT activity in the context of oncogenesis, it is known to secrete adipokine, proinflammatory cytokines, and growth factors (6). In contrast, studies have found that SAT is protective and associated with better prognosis for various tumors, including prostate, colorectal, and hepatocellular carcinomas (7-9).

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In addition, skeletal muscle mass status plays an important role in predicting cancer prognosis because it is directly related to sarcopenia. Chang et al. (10) identified skeletal muscle status as an important factor in patients with hepatocellular carcinoma. Their study also showed that low skeletal muscle mass might predict relevant outcomes, with a significantly heightened risk of all-cause mortality in patients with hepatocellular carcinoma (hazard ratio: 2.04, 95% confidence interval: 1.74-2.38 (10).

The existing literature on the relationship between testicular cancer and body composition predominantly focused on changes in patients receiving adjuvant chemotherapy. During or after chemotherapy, changes in fat tissue and skeletal muscle area (SMA) directly result from the effects of chemotherapeutic agents, treatment-related inactivity, altered dietary habits, and hormonal changes (11). Previous studies have demonstrated that testicular cancer survivors often exhibit increased VAT and decreased SMA following cancer treatment (12,13). A previous study reported that treatment for testicular cancer could result in an increase in VAT and a reduction in SMA due to androgen deficiency and increased luteinizing hormone levels after treatment, which are also associated with poor prognosis and higher morbidity (12).

Although previous research has examined the relationship between adjuvant chemotherapy administered for testicular cancer and body fat distribution, the current study is the first to investigate the association between the initial tumor stage and aggressiveness. The purpose of this study was to examine the correlation between VAT, SAT, and SMA ratios and cancer stage in patients diagnosed with testicular cancer.

Methods

The Research Ethics Committee of University of Healrh Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital approved this study (approval number: 2011-KAEK-25 2023/11-06, date: 01.11.2023).

During the period from January 2018 to December 2023, 94 patients who received orchiectomy treatment at the urology clinic with a preliminary diagnosis of testicular cancer and whose pathology revealed germ cell testicular cancer were retrospectively analyzed. TNM staging was performed according to pathology results, postoperative basal tumor marker levels, and radiological examination findings.

Patients with missing tumor markers and pathology results, missing CT images, or diagnoses other than testicular cancer, those with non-germ cell subtypes, and those with extensive subcutaneous edema or intra-abdominal fluid, which could hinder the calculation of adipose volume, were not included.

Examination of CT Scans

A 128-slice multi-detector-row CT scanner (Toshiba Aquilion, Japan) was used for abdominal CT images with the following parameters: automatic tube current modulation (120 kV for tube voltage and 100-300 mAs for tube current), rotation time of 0.5 s, and table speed of 1.5-2 mm/rotation. Contrast-enhanced, thin-slice abdominopelvic CT images and a soft tissue window acquired prior to surgery were used. The SMA, VAT, and SAT of axial sections passing through the L3 vertebra plane were measured. Subsequently, the VAT/SAT, SMA/VAT, and SMA/SAT ratios were calculated. Body composition parameters were measured on CT images at the time of diagnosis before patients received any adjuvant treatment (chemotherapy or radiotherapy), thus reducing the confounding effect of chemotherapy agents on muscle breakdown. Previous studies have demonstrated that the SMA obtained passing through the L3 vertebral level is related to the total body muscle mass (14). Automatic segmentation with density adjustments was executed by utilizing the OsiriX software system (Figure 1). The Hounsfield unit (HU) cut-off values were defined as 150 to 50 HU for VAT and 190 to 30 HU for SAT. The measurements were undertaken by two radiologists.

Statistical Analysis

We used SPSS v. 25 (SPSS Inc., Chicago, IL) for statistical analyses. We assessed the normality of the data distribution using the Shapiro-Wilk test. Numerical variables were presented as mean ± standard deviation for normally distributed data and as median (interquartile range) for non-normally distributed data. We conducted statistical analyses using Student's t-test for normally distributed data and the Mann-Whitney U test for data not following a normal distribution. Categorical variables were reported as counts and percentages and compared using the chi-square test. The receiver operator characteristic (ROC) curve analysis was conducted on the VAT/SAT ratio to differentiate between local and systemic diseases. A p-value 0.05 was considered statistically significant.

Results

A total of 94 patients, with a mean age of 35.05±10.44 years, who underwent surgery for testicular cancer participated in this study. Among them, 58 (61.7%) had seminomatous GCTs and 36 (38.3%) had non-seminomatous GCTs. After radiological and biochemical examination, 51 (54.3%) patients were classified as stage 1, 37 (39.4%) as stage 2, and six (6.4%) as stage 3. There was no difference in the stage distribution between patients with and without seminomatous GCTs (p=0.177). The distribution of patients according to tumor stage is shown in Figure 2.

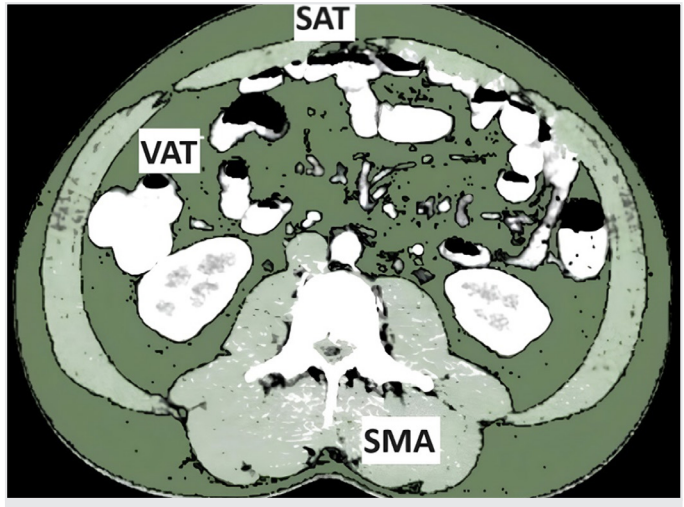

Figure 1. Axial computed tomography scan at the level of the third lumbar vertebrae in a patient with testicular cancer. Skeletal muscle area, visceral adipose tissue, and subcutaneous adipose tissue were measured semi-automatically using OsiriX software
SAT: Subcutaneous adipose tissue, VAT: Visceral adipose tissue, SMA: Skeletal muscle area

The mean tumor size was 46.8±25.3 (5-130) mm. Forty (42.6%) patients received adjuvant chemotherapy with carboplatin or bleomycin, etoposide, or cisplatin following surgery. During follow-up, 5 (5.3%) patients died, and 89 survived.

The adipose tissue composition, as measured by CT in patients with seminomatous and non-seminomatous GCTs, is presented in Table 1. Since there was no difference among the groups according to the calculated compositions and ratios, it was assumed that fat compositions were not affected by the tumor's pathological subtype in the study cohort. A moderate positive correlation was observed between tumor stage and the VAT/SAT ratio (r=0.35, p=0.001). The mean VAT/SAT ratio was 0.64±0.43 for stage 1 tumors, 0.81±0.41 for stage 2 tumors, and 1.32±0.29 for stage 3 tumors, indicating remarkable differences among the groups (p=0.001). Comparisons of the stage groups revealed that the VAT/SAT ratio was considerably higher in stage 3 than in stage 1 and 2 tumors (p=0.001 and p=0.018, respectively). There were no remarkable differences among stages 1 and 2. Similarly, only the VAT/SAT ratio differed significantly between localized disease and systemic disease (0.65±0.43 and 0.86±0.44, respectively, p=0.023). Figure 3 shows the ROC curve analysis for the VAT/SAT ratio in discriminating between local and systemic diseases at diagnosis. A VAT/SAT ratio >0.84 was able to discriminate systemic disease with a sensitivity of 55.5%, specificity of 79.6%, and area under the curve value of 0.663 (0.558-0.757).

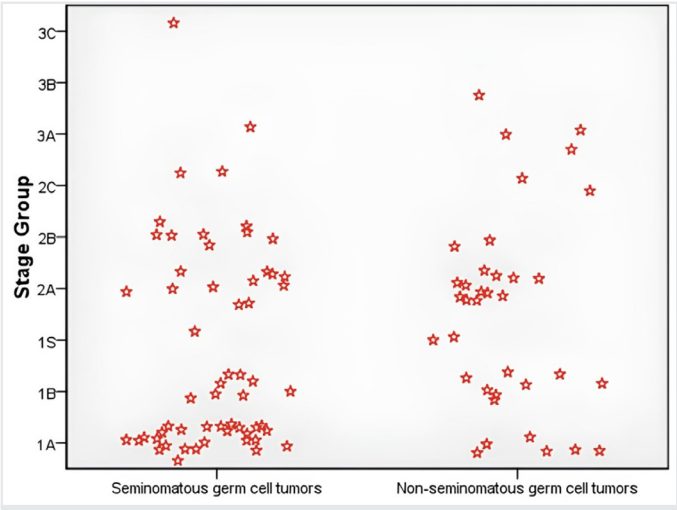

Figure 2. Distribution of seminomatous and non-seminomatous germ cell tumors by tumor stage

Table 1. Distribution of body fat composition of seminomatous and non-seminomatous germ cell tumors

	Seminomatous GCT	Non-seminomatous GCT	p
VAT (cm^2)	96±64.8	90.2±72.7	0.686
SAT (cm^2)	143.3±87.1	117±68.8	0.128
SMA (cm^2)	140.4±26.4	136.2±24	0.436
VAT/SAT	0.73±0.42	0.77±0.48	0.677
SMA/SAT	1.74±2.5	1.7±1.16	0.922
SMA/VAT	2.92±3	2.94±2.52	0.946

GCT: Germ cell tumor, VAT: Visceral adipose tissue, SAT: Subcutaneous adipose tissue, SMA: Skeletal muscle area

Tumor size and body fat composition were negatively correlated with SAT and SMA at moderate and low levels, respectively (r=-0.357, p<0.001 and r=-0.254, p=0.014, respectively). A positive moderate correlation was found between tumor size and the VAT/SAT and SMA/SAT ratios (r=0.334, p=0.001 and r=0.362, p<0.001, respectively). Only the SAT differed according to mortality status. The mean SAT values were 59.7±19.7 in patients who died and 137.4±81.4 in those who survived (p<0.001). No statistically significant differences were observed for the other measurements.

Discussion

Adipose tissue acts as an active secretory organ, modulating energy equilibrium, homeostasis, insulin resistance, and angiogenesis (3). It is well known that obesity is a pro-tumorigenic factor that may facilitate tumor development. The main inflammatory pathways are activated by adipose tissue products, initiating a series of mechanisms involving proliferation, invasion, and angiogenesis (15). In a study including 40 patients with breast cancer and a control group of 40 individuals, Schapira et al. (16) reported that individuals with visceral obesity possessed a considerably higher propensity for breast cancer compared with the control group. Similarly, in a meta-analysis examining the relationship between CRC and obesity, Dong et al. (17) identified a positive correlation between central obesity and CRC. Central obesity had the highest accuracy in predicting the risk of cancer development among the different types of obesity (17). Many mechanisms remain to be further elucidated to determine the association between central obesity and cancer development. In a study investigating the association between lung cancer and visceral obesity conducted by Hidayat et al. (18), every 10 cm increase in abdominal circumference was associated with a 10% higher propensity for lung cancer. However, cancer risk

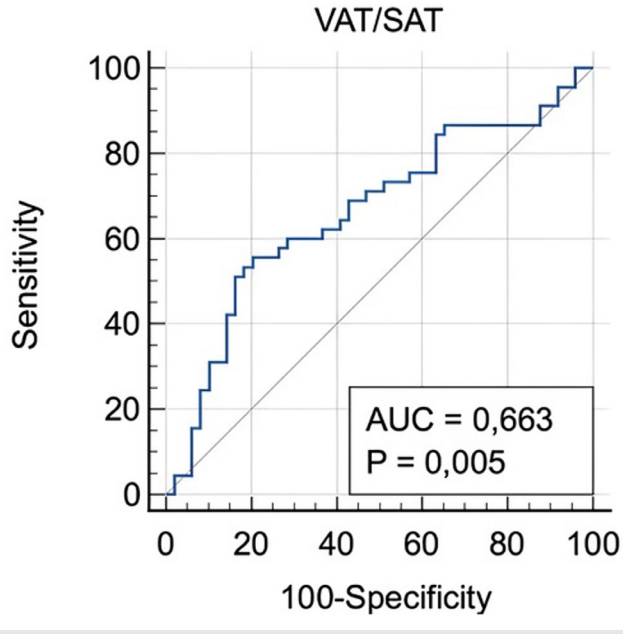

Figure 3. Receiver operating characteristic curve of the VAT/SAT ratio for discriminating between localized and systemic disease
VAT: Visceral adipose tissue, SAT: Subcutaneous adipose tissue, AUC: Area under the curve

was unrelated to body mass index (BMI), further indicating the greater importance of central obesity in cancer development (18). The assessment of body composition via CT is a comprehensive method that provides more detailed information than BMI calculation. CT allows for the separate calculation of parameters constituting body composition, namely SAT, VAT, and SMA. Moreover, it can be employed as a standard technique during follow-up.

In this study, although VAT, SAT, and SMA values alone did not show statistically significant differences, the VAT/SAT ratio increased as the stage progressed in patients with testicular cancer. Moreover, a VAT/SAT ratio >0.84 was found to indicate systemic disease, with a sensitivity of 55.5% and specificity of 79.6%.

Despite numerous studies investigating the association between central obesity and cancers such as colon, breast, and endometrial cancer, there is insufficient research on the association between testicular cancer and central obesity (3,6,17). This may be due to the younger age of patients with testicular cancer, who typically exhibit less pronounced changes in body composition. Additionally, the reduction in muscle mass in young men is likely to be less significant than that in elderly individuals with cancer. Similarly, cancer cachexia, a condition commonly expected in elderly individuals with cancer, involves a decrease in muscle mass due to age, inactivity, and cancer development. However, in testicular cancer patients, who are typically young males, the decline in muscle mass is not as pronounced as in other types of cancer, which could explain why the body compositions analyzed in our study did not change significantly. The analysis of composition ratios revealed that VAT/SAT was correlated with tumor stage and systemic disease spread, which may be related to the active role of VAT in cytokine production.

The correlation between SAT and cancer-related mortality has been investigated in only few studies. A recent study of 1,746 patients with gastrointestinal, respiratory, or renal cancer definitively established that a low SAT was strongly correlated with poor survival outcomes (19). In a study of 3,324 patients, cancer-related mortality was associated with increased VAT and SAT values (20). Similarly, SAT was significantly lower in patients with testicular cancer-related mortality in our study (59.7±19.7 and 137.4±81.4, respectively).

Considering the association between survival and body composition, no statistically significant relationship was detected. This may be attributed to the high survival rates of patients with testicular cancer and the relatively low occurrence of complications during treatment.

Study Limitations

The main limitation of this study was the lack of information about the dietary patterns and activity levels of the patients. The current study only assessed radiological fat composition upon diagnosis.

Conclusion

This study demonstrated that fat composition parameters measured by CT provide a more accurate assessment of obesity than BMI. Additionally, these parameters can be utilized to evaluate cancer stage and prognosis in patients with testicular cancer.

Ethics

Ethics Committee Approval: The Research Ethics Committee of University of Healrh Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital approved this study (approval number: 2011-KAEK-25 2023/11-06, date: 01.11.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions: Surgical and Medical Practices - D.B., A.E.; Concept - S.G.G.Ö., M.E.; Design - S.G.G.Ö., A.E.; Data Collection or Processing - S.G.G.Ö., D.B.; Analysis or Interpretation - S.G.G.Ö.; Literature Search - S.G.G.Ö.; Writing - S.G.G.Ö., M.E., A.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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