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The Relationship Between Abdominal Adiposity Parameters and Renal Cell Carcinoma: A Volumetric Study Using All Computed Tomography Slices

Abdominal Yağ Parametreleri ve Renal Hücreli Karsinom Arasındaki İlişki: Tüm Bilgisayarlı Tomografi Kesitlerinin Kullanıldığı Hacimsel Çalışma

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ABSTRACT Objective: To investigate a possible relationship between abdominal adiposity parameters and the presence of renal cell carcinoma (RCC), and between these adiposity parameters and various histopathological tumor findings. **Material and Methods:** A total of 48 patients (31 males and 17 females, mean age: 60.17±13.39 years) with RCC and 50 control subjects (32 males and 18 females, mean age: 60.26±7.71 years) were enrolled. The medical data and the abdominopelvic computed tomography (CT) examinations of the study groups were retrospectively reviewed. The abdominal adiposity parameters, including visceral adipose tissue (VAT) volume, subcutaneous adipose tissue (SAT) volume, total adipose tissue (TAT) volume, visceral adipose tissue index (VATI), subcutaneous adipose tissue index (SATI), and VAT-to-SAT ratio, were calculated using specialized software. We also noted histopathological features of the tumors. **Results:** We found significantly higher SAT volume and SATI in the RCC group in comparison with the control group ($p=0.024$ and $p = 0.001$, respectively). The VAT volume and VATI were significantly lower in the patient group, compared to the control group ($p = 0.001$ for both). There was no statistically significant relationship between VAT-to-SAT ratio and the presence of RCC. No statistically significant relationship between abdominal adiposity parameters and histopathological tumor features was detected ($p > 0.05$). **Conclusion:** We designed a volumetric study of all slices of abdominopelvic CT examination by using specialized software. As far as we know, this study is the first volumetric study to investigate those relationships. Volumetric adipose tissue measurements may be more accurate than area measurements and can easily be performed during abdominopelvic CT examination, which is the routine imaging modality for RCC patients.

Keywords: Abdominal adipose tissue; renal cell carcinoma; pathology; subcutaneous adipose tissue; visceral adipose tissue; computed tomography

ÖZET Amaç: Abdominal yağ parametreleri ile renal hücreli karsinom (RHK) varlığı ve bu adipozite parametrelerinin tümörün histopatalojik bulguları ile arasındaki olası ilişkiyi araştırmak. **Gereç ve Yöntemler:** RHK' sı bulunan 48 hasta (31 erkek ve 17 kadın, ortalama yaş: 60,17±13,3 yıl) ve 50 kontrol hastası (32 erkek ve 18 kadın, ortalama yaş: 60,26±7,71 yıl) olmak üzere toplam 98 hasta çalışmaya dahil edildi. Çalışma gruplarının tıbbi kayıtları ve opaklı abdominopelvik bilgisayarlı tomografi (BT) tetkikleri retrospektif olarak değerlendirildi. BT tetkiklerinde, visseral yağ doku (VYD) hacmi, subkutan yağ doku (SYD) hacmi, total yağlı doku (TYD) hacmi, VYD indeks (VYDİ), SYD indeks (SYDİ) ve VYD/SYD oranlarını içeren abdominal yağ parametreleri özel bir yazılım kullanılarak hesaplandı. Ayrıca var olan tümörlerin histopatolojik özellikleri kaydedildi. **Bulgular:** RHK grubunda istatistiksel olarak anlamlı şekilde kontrol grubuna göre daha yüksek SYD hacmi ve SYDİ değerleri bulundu (sırasıyla p=0,024 ve p=0,001). Hasta grupta VYD hacmi ve VYDİ değerleri ise kontrol grubuna göre daha düşüktü (her ikisi için de p=0,001). VYD/SYD oranı ile RHK varlığı arasında anlamlı ilişki yoktu (p>0,05). Ayrıca değerlendirilen abdominal yağ parametreleri ve tümörlerin histopatolojik özellikleri arasında da anlamlı bir ilişki saptanmadı (p>0,05). **Sonuç:** Özel bir yazılım kullanarak tüm abdominopelvik BT kesitlerinin dahil edildiği hacimsel bir çalışma dizayn ettik. Bildiğimiz kadarıyla, bu çalışma tanımlanan ilişkileri araştıran ilk hacimsel çalışmadır. Hacimsel yağlı doku ölçümleri daha önceki çalışmalarda kullanılmış olan ve sadece birkaç kesit esas alınarak yapılan alansal ölçümlerden daha doğru olabilir ve RHK hastalarında rutin görüntüleme modalitesi olan abdominopelvik BT ile kolaylıkla yapılabilir.

Anahtar Kelimeler: Abdominal yağ doku; renal hücreli karsinom; patoloji; subkutan yağ doku; visseral yağ doku; bilgisayarlı tomografi

Obesity and cancer are two of the most important health problems worldwide, and their rates are increasing. Obesity is known to be associated with increased risk for cardio-metabolic diseases, including type 2 diabetes mellitus, cardiovascular disease, and metabolic syndrome.[1,2] Moreover, the relationship between obesity and several types of cancer, including breast, esophageal, colorectal, and renal cancer, has also been shown.[3] Classically, obesity has been accepted as whole-body fat and has been quantified using the body mass index (BMI). More recently, however, the concept of fat compartments has become evident, and they have all been shown to have varying degrees of pathogenic influence.[4]

Adipose tissue is anatomically distributed in varying proportions throughout the human body, and the pattern of distribution changes based on many factors such as race, ethnicity, genotype, sex, age, diet, physical activity, hormone levels, and medications.[5-7] Two compartments of body fat tissue with different metabolic characteristics are traditionally identified: subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT). Although both of these adipose tissue types are important, particular attention has been given to VAT because of its association with various medical problems.[8] Recently, VAT has been accepted as the primary mediator of inflammatory messaging in diabetes, immune modulation, and cardiovascular disease, and is considered an important pathogenic factor of metabolic syndrome.[9]

Renal cell carcinoma (RCC) is the eighth most common malignancy in adults and the most common one in the kidney.[10] The lifetime risk of RCC is 1.56% for US residents.[11] Obesity, smoking and hypertension are the most well-known risk factors and each demonstrates strong associations with RCC.[12,13] The association between obesity and RCC has been studied.[14,15] In a large scale study, a 71% increased risk of RCC was found in morbidly obese individuals (BMI≥35), compared with normal weight individuals (BMI<25).[11] Moore et al. and Awakura et al. also showed a positive correlation between obesity and RCC.[16,17] However, obesity is a gross term and most authors believe that such generality is insufficient to understand the exact relationship between adiposity and RCC. Delineating fat tissue compartments may provide a more detailed and accurate understanding of this relationship.

Computed tomography is one of the most accurate radiological methods for assessing abdominal adipose tissue, and it has the ability to directly measure visceral adiposity.[18,19] Such specific measurements have been suggested to be more useful than BMI.[20] Area measurements obtained from one or two CT slices were used in most studies evaluating VAT. However, the results obtained by only a few CT slices and derived from area measurements vary partly because of measuring technique differences.[21] These measurements can be more accurately conducted volumetrically by using specialty computer programs.

In medical literature, there are a very limited number of studies investigating the relationship between RCC and abdominal adiposity parameters.[22-24] However, in all of them, measurements were performed from one or two nonstandard CT slices at different body levels accepted as representing all of the abdominal fat tissue volume. In the present study, we investigated a possible relationship between volumetric abdominal adiposity measurements and the presence of RCC, and between these adiposity parameters and various histopathological tumor findings.

MATERIAL AND METHODS

PATIENT SELECTION

Review board approval (Kecioren Training and Research Hospital Clinical Research Review Board, 2012-KAEK-15, 22.11.2017) was obtained and this retrospective study was conducted in accordance with the principles of the Declaration of Helsinki. The medical data and abdominopelvic CT examinations were reviewed for consecutive patients with newly diagnosed RCC who were operated on in our hospital and a control group similar in age and gender distributions between January 2014 and October 2017. In total, 64 RCC patients and their medical data were evaluated. Patients were excluded from the study if any of the following criteria applied: pa-

tients with recurrent RCC (n=2); patients who had previous surgery for any other abdominal cancer or a major surgery that could affect abdominal adipose tissue (n=1); those who had emergency surgery for tumor-related complications (n=3); and patients with CT examinations performed in another center (n=10). Finally, 48 patients (31 males, 17 females) with histopathologically proven RCC who met the criteria were enrolled in the study. In all cases, the final histopathological diagnosis was made by partial or total resection.

The control group was selected consecutively from patients who underwent abdominopelvic CT examination for reasons other than abdominal cancer during the same time period as the RCC patients. The age and gender distributions of the control group were similar to those of the patient group. The patients who had had major abdominal surgery or who were diagnosed with any abdominal cancer by the current CT were excluded from the control group. In total, 50 cases (32 males and 18 females) were included in the control group, and the same abdominal adipose tissue measurements mentioned above were conducted on them as well.

CT PROTOCOL AND ANALYSIS

Prior to surgical resection, all of the CT examinations were performed with 64- and 320-row detector systems belonging to the same brand (Aquilion; Toshiba Medical Systems, Otawara, Japan). Enhanced CT images of the axial plane in the portal venous phase were acquired after using a standard oral agent (50 ml, 76% amidotrizoate meglumine, sodium amidotrizoate) and intravenous non-ionic contrast agents (mean: 80 ml), and multi-planar reformatted images (sagittal and coronal) were created from the initial scan. The scanning parameters were as follows: tube current 150-200 mAs; tube voltage 120 kV/ slice thickness 0.5-3 mm; rotation time 0.75 ms; and total scan time 12.8 s.

The abdominopelvic CT images of 48 patients and 50 control patients were retrieved from the picture archiving and communication system of our hospital and analyzed for abdominal adipose tissue parameters with an FDA-approved software program (Vitrea 2 Vital v4.1.8.0, Vital Images, Inc., Minnetonka, MN, USA) which was successfully used in some previous studies.[25,26] All CT images of the soft tissue window between the esophageal hiatus in the diaphragm and the level of the symphysis pubis were used, and abdominal adipose tissue volumes were calculated by using the "organ selection tool" option of the software (Figure 1). Visceral adipose tissue is defined as deep adipose tissue, including the mesenteric, subperitoneal, and retroperitoneal fat and excluding paraspinal muscles and the vertebral column. Subcutaneous fat tissue is defined as adipose tissue superficial to the abdominal wall musculature and the back muscles. After the region of interest was selected as a representative area in the visceral adipose tissue, the program derived a subtracted image showing only the visceral adipose tissue. Two radiologists checked the images formed by the software for any mistakes, correcting and reforming the images in consensus when necessary. Images were manually edited in each section by using the edit tool to avoid including non-fat tissue such as solid organs, intestines, vessels, and skeletal tissue. Then, using the subtracted 3D volume images created, the VAT volume was automatically calculated in milliliters by the program. A similar process was applied for the SAT. The VAT and SAT volumes were added together to measure the TAT volume. All measurements were taken by two radiologists in consensus. Because all the images formed by the software were used for measurements, estimated calculations, such as adding or multiplying by pixel surface area, were not used; thus, adipose tissue volumes were real-life calculations.

HISTOPATHOLOGICAL ANALYSIS

The histopathological data of the RCC patients retrieved from the medical archive of the hospital were evaluated for tumor location (right or left kidney), histological type (clear cell, chromophobe, or papillary), grade (1 to 4), size, renal capsule invasion, perirenal fat involvement, lymphovascular tissue invasion, renal vein involvement, renal sinus invasion, presence of sarcomatoid component, and tumor necrosis. Nephrectomy type (radical or partial) was also noted.

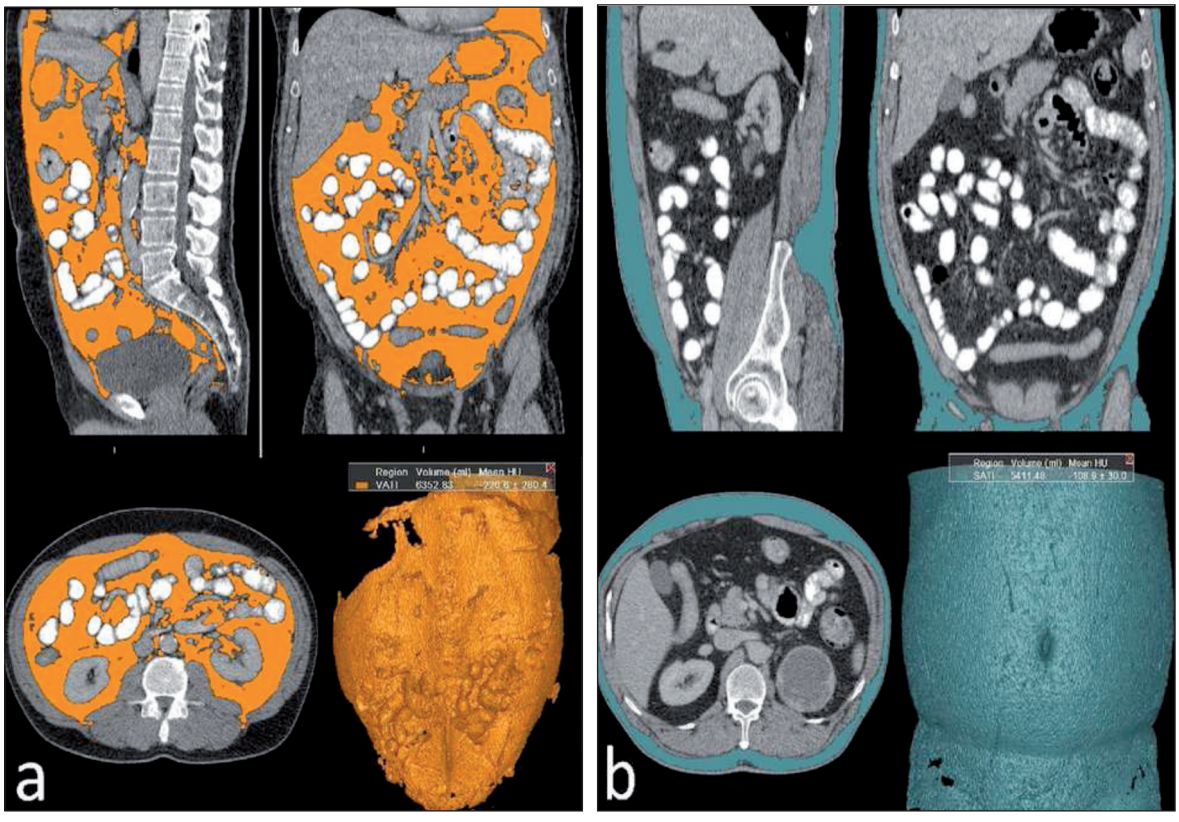

FIGURE 1 a-b: Abdominal adipose tissue measurements by using specialized software. Images (a) and (b) demonstrate the distribution of visceral (orange) and subcutaneous (blue) adipose tissues determined by the software in the sagittal, coronal, and axial projections. The lower right pictures in both images are the volume-rendered images showing the amount of visceral and subcutaneous abdominal adipose tissue, respectively, in milliliters.

STATISTICAL ANALYSIS

Statistical analysis was done using Statistical Package for Social Sciences 20.0 software (SPSS 20.0 for Mac). Descriptive statistics of nominal samples were expressed with numbers and percentiles. Descriptive statistics of scale samples were expressed as mean ±standard deviation (minimum–maximum). Kolmogorov Simirnov, Shapiro-Wilk, Kurtosis, and Skewness Tests were used to assess variable normalization. The Independent Sample T Test was used to compare two independent scale parameters with normal distribution. The Mann-Whitney U Test was used to compare two independent scale parameters without normal distribution. The Chi Square Test was used to compare independent nominal parameters. The Pearson Correlation Test was used to correlate two scale samples. Probability of $p < 0.05$ was accepted as statistically significant.

RESULTS

A total of 98 cases were enrolled in this study. The patient and control groups comprised 48 and 50 cases, respectively. Among these cases, the patient group consisted of 31 (64.6%) males and 17 (35.4%) females, and the control group was comprised of 32 (64%) males and 18 (36%) females. The mean ages were 60.17±13.39 (33-88 years) and 60.26±7.71 (49-73 years) in the patient and control groups, respectively. No statistically significant difference was found between the two groups regarding age ($p=0.966$) and gender ($p=0.952$) distribution. The demographic features of the study groups are shown in (Table 1).

The VAT, SAT, and TAT volumes were the main measurements, and they were calculated using the specialized software. The VAT index (VATI=VAT/TAT), SAT index (SATI=SAT/TAT)

TABLE 1: Some demographic features and calculated abdominal adipose tissue parameters of the study groups. The last column (p value) shows the statistical relationship between these variables and the study groups.

Some demographic features and adipose tissue measurements	Patient group (n= 48)	Control group (n= 50)	*p value
Age (mean±sd) (year)	60.17±13.39	60.26±7.71	0.966
Gender			
Female (%)	17 (35.4%)	18 (36%)	0.952
Male (%)	31 (64.6%)	32 (64%)	
VAT (mean±sd ml)	4073.56±2084.09 (543-9590)	8063.84± 2812.98 (2563-17055)	**0.001**
SAT (mean±sd ml)	6712.29± 3818.19 (881-21844)	5324.1±1878.15 (730-8687)	**0.024**
TAT (mean±sd ml)	10785.85±4713.16 (2004- 25261)	12705.56±3564.97 (5020- 20650)	**0.025**
VATI	0.38±0.15 (0.13-0.76)	0.65± 0.10 (0.42-0.87)	**0.001**
SATI	0.61±0.15 (0.23-0.86)	0.34± 0.10 (0.12-0.57)	**0.001**
VAT-to-SAT ratio	0.76±0.58 (0.15-3.17)	0.70±0.30 (0.17- 1.67)	0.577

VAT: Visceral Adipose Tissue; **SAT:** Subcutaneous Adipose Tissue; **TAT:** Total Adipose Tissue; **VATI:** VAT index (VAT/TAT); SAT index (SAT/TAT).
* Mann Whitney U and Independent Sample t Tests.

values, and VAT-to-SAT ratio derived from the main measurements were also calculated. Those abdominal adipose tissue parameters and their statistical relationships with the study groups are shown in (Table 1).

No correlation was found between the VAT, SAT, TAT volumes, SATI, VATI, VAT- to-SAT ratio and the ages of the participants in the study groups (p=0.69, 0.87, 0.44, 0.74, 0.74, 0.37 in general, p=0.860, 0.739, 0.727, 0.835, 0.835, 0.480 in the patient group, and p=0.29, 0.50, 0.29, 0.46, 0.46, 0.73 in the control group, respectively).

We did not find any statistically significant correlation between abdominal adiposity parameters and gender in our study group (p value was 0.06 for VAT, 0.58 for SAT, 0.48 for TAT, 0.109 for VATI and SATI, and 0.112 for VAT-to-SAT ratio).

The relationship between abdominal adipose tissue parameters and RCC was the main subject of this study. We found significantly higher SAT volumes and SATIs in the RCC group when compared with the control group (p=0.024 and p=0.001, respectively). Additionally, the VAT volumes and VATIs were significantly lower in the patient group when compared with the control group (p= 0.001 for both). There was no statistically significant relationship between VAT-to-SAT ratio and the presence of RCC in the study groups. The detailed measurements and their relationships with the patient and control groups are shown in (Table 1).

In the second phase of the study, we investigated the possible relationship between abdominal adipose tissue parameters and histopathological tumor findings, such as tumor location (right or left kidney), histological type (clear cell, chromophobe, or papillary), grade (1 to 4), size, renal capsule and perirenal fat involvement, lymphovascular tissue, renal vein involvement, renal sinus invasion, presence of sarcomatoid component, tumor necrosis, and nephrectomy type (radical or partial). The distribution of the histopathological tumor features is presented in (Table 2).

We did not find any statistically significant relationship between the abdominal adipose tissue parameters and RCC histopathological features in our study groups. The results of the detailed statistical analyses between abdominal adipose tissue parameters and histopathological tumor features are shown in (Table 3).

DISCUSSION

In the current study, we used a specialized software program to measure adipose tissue volumes located in different abdominal compartments. These measurements were performed involving the entire ab-

TABLE 2: Detailed histopathological features of the renal cell carcinomas and their distributions in the patient group.

Histopathological features	Patient group (n= 48)
Tumor Location	
Right kidney (%)	25 (52%)
Left kidney (%)	23 (48 %)
Tumor Size (mean±sd mm)	53.04±29.8
Histological Type	
Clear cell (%)	35 (73%)
Chromofobe (%)	9 (18.7%)
Papillary (%)	4 (8.3%)
Histological Grade	
Grade 1 (%)	1 (2.1%)
Grade 2 (%)	14 (29.2%)
Grade 3 (%)	19 (39.6%)
Grade 4 (%)	6 (12.5%)
Missing (%)	8 (16.6%)
Renal Capsule Invasion	
No (%)	27 (58.3%)
Yes (%)	21 (41.7%)
Perirenal Fat Invasion	
No (%)	40 (83.3%)
Yes (%)	8 (16.7%)
Lymphovascular Invasion	
No (%)	39 (56.8%)
Yes (%)	9 (43.2)
Renal Vein Invasion	
No (%)	37 (77.1%)
Yes (%)	11 (22.9%)
Renal Sinus Invasion	
No (%)	33 (68.7%)
Yes (%)	15 (31.3%)
Sarcomatoid Component	
No (%)	45 (93.8%)
Yes (%)	3 (6.2%)
Tumor Necrosis	
No (%)	31 (64.6%)
Yes (%)	17 (35.4%)
Nephrectomy Type	
Partial (%)	16 (33.3%)
Radical (%)	32 (66.7%)

domen from the level of the esophageal hiatus to the symphysis pubis, and all the CT slices were used for volumetric calculations. Nemoto et al. first reported the type of software and concluded it was feasible for calculating visceral fat volumes in a reasonable time with high accuracy.[27] By using similar software, we avoided estimation calculations such as adding or multiplying by pixel surface area. Thus, we were able to calculate real-life adipose tissue volumes, which would not be possible using the area measurements used in most previous cancer studies.[8,12,24,28,29] By using this method, we were able to calculate even thin subdiaphragmatic/perihepatic/perisplenic adipose tissue. To the best of our knowledge, this study is the first to utilize real-life abdominal adipose tissue volumes in RCC patients created using all the CT slices rather than area measurements.

Abdominopelvic CT is the routine imaging modality for most abdominal cancers and has been used worldwide for years. The ability to acquire high-resolution images of the abdominal organs and, at the same time, evaluate bone tissue accurately in cancer patients is the main advantage. CT is also the preferred imaging modality for evaluating adipose and skeletal tissue, due to its excellent resolution. It is a practical and precise method to directly quantify body composition in both adult and pediatric populations.[24,30] There are many studies in literature regarding quantification of body fat using CT. However, in most of those studies, one or two CT slices thought to reflect all adipose abdominal tissue were used for the measurements. Those studies advocate that a single slice from a specific abdominal level can represent the whole VAT. However, the studies on which those previous studies are based have some limitations, such as small sample size and the use of MR imaging instead of CT.[30,31] Additionally, most studies using VAT area to reflect whole VAT volume measured various abdominal levels. In Japan, VAT at the level of the umbilicus is typically used in diagnostic criteria for metabolic syndrome.[32] Mourtzakis et al. used VAT measurements obtained from the L3 level on MR images.[30] Shen et al. reported that the VAT area 10 cm above the L4-5 vertebral interspace in men and 5 cm above in women has greater power to represent VAT volume.[31] Other studies have used many different levels such as umbilicus, L3, and L3-4 vertebral space, etc.[20,22,24,33-35] Due to these discrepancies regarding VAT measurements

TABLE 3: Results of the statistical analyses between abdominal adipose tissue parameters and the histopathological tumor features.

	*p value					
	Abdominal Adipose Tissue Measurements					
Histopathological Features	**VAT**	**SAT**	**TAT**	**VATI**	**SATI**	**VAT/SAT**
Tumor Location	0.051	0.69	0.59	0.61	0.61	0.24
Tumor Size	0.68	0.85	0.98	0.7	0.7	0.79
Histological type	0.77	0.82	0.98	0.73	0.73	0.42
Histological Grade	0.14	0.81	0.4	0.4	0.4	0.75
Renal Capsule Invasion	0.27	0.69	0.42	0.19	0.19	0.09
Perirenal Fat Invasion	0.38	0.65	0.98	0.74	0.74	0.96
Lymphovascular Invasion	0.33	0.35	0.23	0.34	0.34	0.12
Renal Vein Invasion	0.82	0.71	0.69	0.55	0.55	0.49
Renal Sinus Invasion	0.38	0.82	0.57	0.55	0.55	0.77
Sarcomatoid Component	0.76	0.75	0.9	0.67	0.67	0.43
Tumor Necrosis	0.26	0.79	0.48	0.65	0.65	0.97
Nephrectomy Type	0.35	0.63	0.98	0.23	0.23	0.43

VAT: Visceral Adipose Tissue; **SAT:** Subcutaneous Adipose Tissue; **TAT:** Total Adipose Tissue; **VATI:** VAT index (VAT/TAT); **SAT index** (SAT/TAT).
Tumor location: Right kidney or left kidney; **Histological type:** Clear cell, chromofobe or papillary; **Histological grade:** Grade 1, 2, 3 or 4); **Nephrectomy type:** Partial or radical.
* Mann Whitney U and Independent Sample t Tests.

in the literature, in the present study we chose the volumetric method to measure VAT volume, utilizing a specialized program that uses all abdominopelvic CT slices.

Our main investigation was a possible relationship between abdominal adipose tissue parameters and the presence of RCC. We detected statistically significant lower VAT volumes and VATIs in the patient group compared to the control group. Most previous studies about visceral fat and RCC have been conducted on clinical features and oncologic outcome, including the disease stage, prognosis, survival, or perioperative outcomes, and none mentioned SAT and other adiposity indexes derived from main measurements, such as VATI, SATI or VAT-to-SAT ratio, as our study did. There are very few studies about specific abdominal obesity parameters and RCC.[8,22-24] Naya et al. reported a greater VAT area in patients with stage 1 RCC disease than in patients with more advanced disease.[22] Keehn et al. showed that VAT area may be associated with worsening tumor grades in patients with small-volume RCC. Park et al. reported that a higher VAT percentage in RCC patients correlated to higher disease stage.[23,24]

In the present study, we also detected higher SAT volume and SATI in RCC patients compared to the control group. If SAT and SATI are assessed as components of general obesity, the statistically-significant higher values measured in our patient group are similar to previous studies regarding the relationship between obesity and RCC. However, as far as we know, there is no study in medical literature specifically evaluating subcutaneous fat and its relationship with RCC.

We also examined a possible relationship between abdominal adipose tissue parameters and some histopathological RCC features involving tumor location, histological subtype, histological grade, tumor size, renal capsule invasion, perirenal fat involvement, lymphovascular tissue invasion, renal vein involvement, renal sinus invasion, the presence of a sarcomatoid component, and tumor necrosis. We did not find any statistically significant relationship between abdominal adiposity parameters and these histopathological features. In medical literature, only a limited number of studies have been conducted on this subject. In their 487-case study, Wang et al. reported that an increased visceral fat area was associated with clear

cell RCC.[36] Park et al. showed high histological tumor grade correlated to a higher VAT percentage in RCC patients.[24] As far as we know, this study is the first to investigate a possible relationship between abdominal adipose tissue parameters and such a wide spectrum of histopathological findings in any cancer.

Although which kind of obesity affects renal carcinogenesis is not clear and has been under-explored, insulin resistance and certain growth factors, including sex steroids, insulin-like growth factor and biochemical markers such as adiponectin, may be the major culprits.[15] A positive correlation between obesity and the clear-cell type of RCC, which is the major histological subtype, is well-known.[33] On the other hand, an association between obesity and clinical features of RCC, such as survival, appears to be much more complex. However, this complex situation may be due to reverse causation, selection bias, or other forms of bias, rather than true biological association.[35] The complex pathophysiology of the relationship between abdominal adipose tissue and RCC, and the discrepancies regarding adipose tissue measurements in the medical literature have prevented a clear picture and this can be the reason of our contradictory results compared to the previous studies. We could not find any causality in the inverse correlation except the different measurement method. However, we enrolled 48 histopathologically-proven RCC patients, as well as an age-, gender-, and number-matched control group to overcome selection bias. FDA-approved specialized software and a manual editing system were used for abdominal adipose tissue measurements to prevent miscalculations. Unlike previous studies that used area abdominal adipose tissue calculations from limited CT slices, we formed a measurement method nearest to real life. The novel findings of our study may be a step toward further large-scale studies regarding this subject, which is open to new challenges.

Our study has several limitations. The small sample size and retrospective design are the most important ones. Not knowing how long the patients have had RCC before the initial diagnosis is also a major limitation because, in this time interval, abdominal adipose tissue quantities could have been affected. We did not pay attention to endocrine problems any participants may have had, such as diabetes mellitus, and these conditions might have also affected adipose tissue amounts. Not knowing the weights of the participants in the patient and control groups can be counted as a limitation that may have affected statistical results. To overcome this limitation, we selected the control group from consecutive age- and sex-matched patients who applied to our radiology department.

CONCLUSION

This study investigated the possible relationship between abdominal adipose tissue quantities and the prevalence and histopathological features of RCC. We designed a volumetric study by using specialized software and aimed to overcome possible disadvantages of area measurement, which cannot reflect the amount of adipose tissue in the entire abdomen. We detected lower VAT volumes in RCC patients, which is in contrast to previous studies in the literature. Because all RCC patients routinely undergo abdominopelvic CT, we believe that volumetric adipose tissue measurements can be easily done using specialized programs. They may be more accurate than area measurements. This different measurement method may have caused the unusual result our study revealed about the relationship between VAT and RCC, which was contrary to what is generally known in literature. However, further studies must be conducted for making this subject clear.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sinan Akay;* ***Design:*** *Sinan Akay, Turgay Ebiloğlu, Engin Kaya;* ***Control/Supervision:*** *Sinan Akay, Mustafa Taşar;* ***Data Collection and/or Processing:*** *Sinan Akay, Mehmet Ersen, Uğurcan Balyemez;* ***Analysis and/or Interpretation:*** *Sinan Akay, Mehmet Ersen, Uğurcan Balyemez;* ***Literature Review:*** *Mehmet Ersen, Uğurcan Balyemez, Sinan Akay;* ***Writing the Article:*** *Sinan Akay, Uğurcan Balyemez, Turgay Ebiloğlu;* ***Critical Review:*** *Mustafa Taşar, Turgay Ebiloğlu, Engin Kaya;* ***References and Fundings:*** *Sinan Akay, Turgay Ebiloğlu;* ***Materials:*** *Sinan Akay, Turgay Ebiloğlu, Engin Kaya.*

REFERENCES

1. Feinleib M. Epidemiology of obesity in relation to health hazards. Ann Intern Med. 1985;103(6 Pt 2):1019-24. [Crossref]
2. Reynolds DW, Stagno S, Stubbs KG, Dahle AJ, Livingston MM, Saxon SS, et al. Inapparent congenital cytomegalovirus infection with elevated cord IgM levels. Casual relation with auditory and mental deficiency. N Engl J Med. 1974;290(6):291-6. [Crossref]
3. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371(9612):569-78. [Crossref]
4. Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. Obes Rev. 2010;11(1):11-8. [Crossref]
5. Wu CH, Yao WJ, Lu FH, Yang YC, Wu JS, Chang CJ. Sex differences of body fat distribution and cardiovascular dysmetabolic factors in old age. Age Ageing. 2001;30(4): 331-6. [Crossref]
6. Kanaley JA, Sames C, Swisher L, Swick AG, Ploutz-Snyder LL, Steppan CM, et al. Abdominal fat distribution in pre-and postmenopausal women: the impact of physical activity, age, and menopausal status. Metabolism. 2001;50(8):976-82. [Crossref]
7. Evans EM, Van Pelt RE, Binder EF, Williams DB, Ehsani AA, Kohrt WM. Effects of HRT and exercise training on insulin action, glucose tolerance, and body compositionin older women. J Appl Physiol (1985). 2001;90(6): 2033-40. [Crossref]
8. Shuster A, Patlas M, Pinthus JH, Mourtzakis M. The clinical importance of visceral adiposity: a critical review of methods for visceral adiposetissue analysis. Br J Radiol. 2012;85(1009):1-10. [Crossref]
9. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005;365(9468): 1415-28. [Crossref]
10. Bazan F, Busto M. [Imaging renal cell carcinoma]. Radiologia. 2014;56(1):61-75. [Crossref]
11. Macleod LC, Hotaling JM, Wright JL, Davenport MT, Gore JL, Harper J, et al. Risk factors for renal cell carcinoma in the VITAL study. J Urol. 2013;190(5): 1657-61. [Crossref]
12. Navai N, Wood CG. Environmental and modifiable risk factors in renal cell carcinoma. Urol Oncol. 2012;30(2):220-4. [Crossref]
13. Weikert S, Ljungberg B. Contemporary epidemiology of renal cell carcinoma: perspectives of primary prevention. World J Urol. 2010;28(3):247-52. [Crossref]
14. Stewart SB, Freedland SJ. Influence of obesity on the incidence and treatment of genitourinary malignancies. Urol Oncol. 2011;29(5):476-86. [Crossref]
15. Wilson KM, Cho E. Obesity and kidney cancer. Recent Results Cancer Res. 2016;208: 81-93. [Crossref]
16. Moore LE, Wilson RT, Campleman SL. Lifestyle factors, exposures, genetic susceptibility, and renal cell cancer risk: a review. Cancer Invest. 2005;23(3): 240-55. [Crossref]
17. Awakura Y, Nakamura E, Ito N, Yamasaki T, Kamba T, Kamoto T, et al. Influence of body mass index on prognosis of Japanese patients with renal cell carcinoma. Urology. 2007;70(1):50-4. [Crossref]
18. Borkan GA, Gerzof SG, Robbins AH, Hults DE, Silbert CK, Silbert JE. Assessment of abdominal fat content by computed tomography. Am J Clin Nutr. 1982;36(1):172-7. [Crossref]
19. Yoshizumi T, Nakamura T, Yamane M, Islam AH, Menju M, Yamasaki K, et al. Abdominal fat: standardized technique for measurement at CT. Radiology. 1999; 211(1):283-6. [Crossref]
20. Moon HG, Ju YT, Jeong CY, Jung EJ, Lee YJ, Hong SC, et al. Visceral obesity may affect oncologic outcome in patients with colorectal cancer. Ann Surg Oncol. 2008;15(7):1918-22. [Crossref]
21. Rickles AS, Iannuzzi JC, Mironov O, Deeb AP, Sharma A, Fleming FJ, et al. Visceral obesity and colorectal cancer: are we missing the boat with BMI? J Gastrointest Surg. 2013;17(1): 133-43. [Crossref]
22. Naya Y, Zenbutsu S, Araki K, Nakamura K, Kobayashi M, Kamijima S, et al. Influence of visceral obesity on oncologic outcome in patients with renal cell carcinoma. Urol Int. 2010;85(1):30-6. [Crossref]
23. Keehn A, Srivastava A, Maiman R, Taylor J, DiVito J, Ghavamian R, et al. The relationship between visceral obesity and the clinicopathologic features of patients with small renal masses. J Endourol. 2015;29(3):372-6. [Crossref]
24. Park YH, Lee JK, Kim KM, Kook HR, Lee H, Kim KB, et al. Visceral obesity in predicting oncologic outcomes of localized renal cell carcinoma. J Urol. 2014;192(4): 1043-9. [Crossref]
25. Yuan X, Zhang J, Quan C, Tian Y, Li H, Ao G. A simplified whole-organ CT perfusion technique with biphasic acquisition: preliminary investigation of accuracy and protocol feasibility in kidneys. Radiology. 2016; 279(1):254-61. [Crossref]
26. Kwon J, Barrera JE, Jung TY, Most SP. Measurements of orbital volume change using computed tomography in isolated orbital blowoutfractures. Arch Facial Plast Surg. 2009;11(6):395-8. [Crossref]
27. Nemoto M, Yeernuer T, Masutani Y, Nomura Y, Hanaoka S, Miki S, et al. Development of automatic visceral fat volume calculation software for CT volume data. Obes. 2014;2014: 495084. [Crossref]
28. Jeong TG, Kim JW, Lee SY, Park HS, Han HS, Hwang DY. Inverse correlation between cancer size and abdominal obesity in colorectal cancer cases. Asian Pac J Cancer Prev. 2016;17(8):4025-30.
29. Park SW, Lee HL, Doo EY, Lee KN, Jun DW, Lee OY, et al. Visceral obesity predicts fewer lymph node metastases and better overall survival in colon cancer. J Gastrointest Surg. 2015;19(8):1513-21. [Crossref]
30. Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab. 2008;33(5):997-1006. [Crossref]

31. Shen W, Punyanitya M, Wang Z, Gallagher D, St-Onge MP, Albu J, et al. Visceral adipose tissue: relations between single-slice areas and total volume. Am J Clin Nutr. 2004;80(2):271-8. [Crossref]

32. Kanaya AM, Harris T, Goodpaster BH, Tylavsky F, Cummings SR; Health, Aging, and Body Composition (ABC) Study. Adipocytokines attenuate the association between visceral adiposity and diabetes in older adults. Diabetes Care. 2004;27(6):1375-80. [Crossref]

33. Ebadi M, Martin L, Ghosh S, Field CJ, Lehner R, Baracos VE, et al. Subcutaneous adiposity is an independent predictor of mortality in cancer patients. Br J Cancer. 2017;117(1):148-55. [Crossref]

34. Lee JY, Lee HS, Lee DC, Chu SH, Jeon JY, Kim NK, et al. Visceral fat accumulation is associated with colorectal cancer in postmenopausal women. PLoS One. 2014;9: e110587. [Crossref]

35. Hagiwara M, Miyajima A, Hasegawa M, Jinzaki M, Kikuchi E, Nakagawa K, et al. Visceral obesity isa strong predictor of perioperative outcome in patients undergoing laparoscopic radical nephrectomy. BJU Int. 2012;110(11 Pt C):E980-4. [Crossref]

36. Wang HK, Song XS, Cheng Y, Qu YY, Zhang SL, Dai B, et al. Visceral fat accumulation is associated with different pathological subtypes of renal cellcarcinoma (RCC): a multicentre study in China. BJU Int. 2014;114(4):496-502. [Crossref]