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ORIGINAL ARTICLE

Perirenal fat Hounsfield units: not only for renal stones but also for renal cell carcinoma

Unidades Hounsfield de grasa perirrenal: no solo para los cálculos renales, sino también para el carcinoma de células renales

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Abstract

Objective: *We aimed to evaluate the role of attenuation values of perirenal fat calculated by computed tomography (CT) in differentiating aggressive renal masses.* **Methods:** *The data of 83 patients with histologically confirmed local stage renal cell carcinoma (RCC), who were treated with nephrectomy in our center, and 78 control group cases were analyzed. All measurements including renal mass volume, abdominal subcutaneous fat area and subcutaneous fat area pelvic subcutaneous fat area, and perirenal fat thickness and Hounsfield unit (perirenal fat tissue thickness [PFT]-hounsfield unit of perirenal fat [PFHU]) were performed on CT by the same radiologist.* **Results:** *In the statistical analysis of PFT and PFHU measurements between the groups, fat thickness was found to be lower in the patient group compared with the control group. However, hounsfield unit measurements were statistically significantly higher in the patient group ($p < 0.0001$). A cutoff value of –98.1 for the PFHU can identify the patient group with a sensitivity of 89.2% and a specificity of 84.6% (area under the curve = 0.9; 95% confidence interval: 0.86-0.95 $p < 0.0001$). In the multivariate logistic regression analysis, a PFHU ≥ –98.1 was independently associated with RCC after accounting for clinical and radiologic parameters.* **Conclusion:** *We believe that measurement of the HU values of perirenal adipose tissue with the CT may be useful in differentiating aggressive renal masses and therefore in determining the appropriate treatment selection.*

Keywords: *Computed tomography. Hounsfield. Kidney. Perirenal fat. Renal cell carcinoma.*

Resumen

Objetivo: *Evaluar el papel de los valores de atenuación de la grasa perirrenal calculados por tomografía computarizada (TC) en la diferenciación de masas renales agresivas.* **Métodos:** *Se analizaron los datos de 83 pacientes con carcinoma de células renales en estadio local confirmado histológicamente, que fueron tratados con nefrectomía en nuestro centro, y de 78 casos del grupo control. Todas las mediciones, incluido el volumen de masa renal, el área de grasa subcutánea abdominal y pélvica (SFA_A-SFA_P), el espesor de la grasa perirrenal y las unidades Hounsfield (PFT-PFHU), fueron realizadas en TC por el mismo radiólogo.* **Resultados:** *En el análisis estadístico de las mediciones de PFT y PFHU entre los grupos se encontró que el espesor de la grasa era menor en los pacientes en comparación con los controles. Sin embargo, las mediciones de las unidades Hounsfield fueron mayores, con significación estadística, en el grupo de pacientes ($p < 0.0001$). Un valor de corte de –98.1 para la PFHU puede identificar el grupo de pacientes con una sensibilidad del 89.2% y una especificidad del 84.6% (AUC = 0.9; IC 95%: 0.86-0.95; $p < 0.0001$). En el análisis de regresión logística multivariado, una PFHU ≥ –98.1 se asoció de manera independiente con el carcinoma de células renales después de tener en cuenta los parámetros clínicos y radiológicos.*

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Conclusiones: *Creemos que la medición de los valores de unidades Hounsfield del tejido adiposo perirrenal con TC puede ser útil para diferenciar masas renales agresivas y, por tanto, para determinar la selección del tratamiento adecuado.*

Palabras clave: *Tomografía computarizada. Unidades Hounsfield. Riñón. Grasa perirrenal. Carcinoma de células renales.*

Introduction

Renal cell carcinoma (RCC) is the most common solid lesion in the kidney and accounts for approximately 90% of all renal malignancies and is associated with the highest mortality[1,2]. The three main subtypes with specific histopathologic and genetic features are clear cell RCC (ccRCC), papillary RCC (pRCC types I and II), and chromophobe cell RCC (chRCC)[3]. The diagnosis of early stage RCCs is increased with the widespread use of imaging methods.

There is numerous epidemiologic evidence showing that long-term obesity is one of the major causes of some types of cancers, such as breast, colon, esophageal, pancreatic, and renal cancers[4]. Although the exact etiology of RCC remains unclear, the association of obesity with RCC development was reported in some previous studies[5,6]. In addition, perirenal fat may promote migration of the ccRCC cells[7]. A recent study showed that renal neoplasms were more common in patients with a high perirenal fat tissue thickness (PFT) than in those with a low PFT[8]. It is also reported that the density of the perirenal fat is a negative factor for the progression-free survival of localized renal cancer[9].

The hounsfield unit (HU) measurement on computed tomography (CT) is routinely performed in clinical practice to define the hardness and composition of kidney stones and to predict the outcome of the stone treatment[10-12]. It is known that CT has high sensitivity and specificity in the diagnosis and extension of renal tumors[13]. In patients with suspected RCC undergoing routine abdominal CT imaging, the HU can be easily measured and reported without the need for extra procedures. Detection of the radiologic and histopathologic association of the high PFT and high perirenal fat density (hounsfield unit of perirenal fat [PFHU]) with renal masses may help in planning appropriate treatment at the right time.

Methods

Patients and data collection

Patients, who were treated with partial or radical nephrectomy between January 2020 and December 2023 in two centers of University of Health Sciences, were included in the study. Those, whose pre-operative CT images were unavailable, who underwent the surgery in another hospital, and whose tumor location may have affected the subcutaneous fat thickness (SFT) measurement (posterior in the renal hilus) were excluded. Individuals, who were under 45 or over 80 years of age, had experienced a previous intra-abdominal surgery, had a history of kidney stones, a malignancy other than RCC, and infection around the kidney, and had incomplete data were excluded. Numbers of patients with pRCC and chRCC subtypes were insufficient for statistical analysis, and therefore, they were also excluded. A total of 100 cases were picked randomly and included as the control group among the participants who underwent a CT imaging for screening in the above-mentioned time period at our center and had similar descriptive characteristics such as age, gender, body mass index (BMI), and comorbidities. A total of 22 individuals, who had a history of intra-abdominal surgery or kidney stones, and had kidney stones, malignancy or infection around the kidney in the admission were excluded. The study was completed with a total of 83 patients with clinically and histologically confirmed local stage ccRCC and 78 patients are the control group (Fig. 1).

Age at the diagnosis, BMI, tumor location (right and left kidney), and the presence of systemic diseases (hypertension and diabetes mellitus) were retrospectively obtained from medical records. T stage based on the American Joint Committee on Cancer (T1vs. T2), Fuhrman grade, RCC subtype, histological necrosis, and presence of sarcomatoid component were reported by our uropathologist[14]. All measurements including the renal mass volume, abdominal subcutaneous fat area (SFA_A), pelvic subcutaneous fat area (SFA_P), PFT, and PFHU were performed on CT by the same radiologist Dr. Esin Derin-Çiçek (third author).

Regional Ethic Committee (Hamidiye-BAEK 20/268) reviewed and approved the study protocol and the study's protocol was in accordance with by the 1964 Declaration of Helsinki and its later changes. All participants included in the study obtained informed consent form.

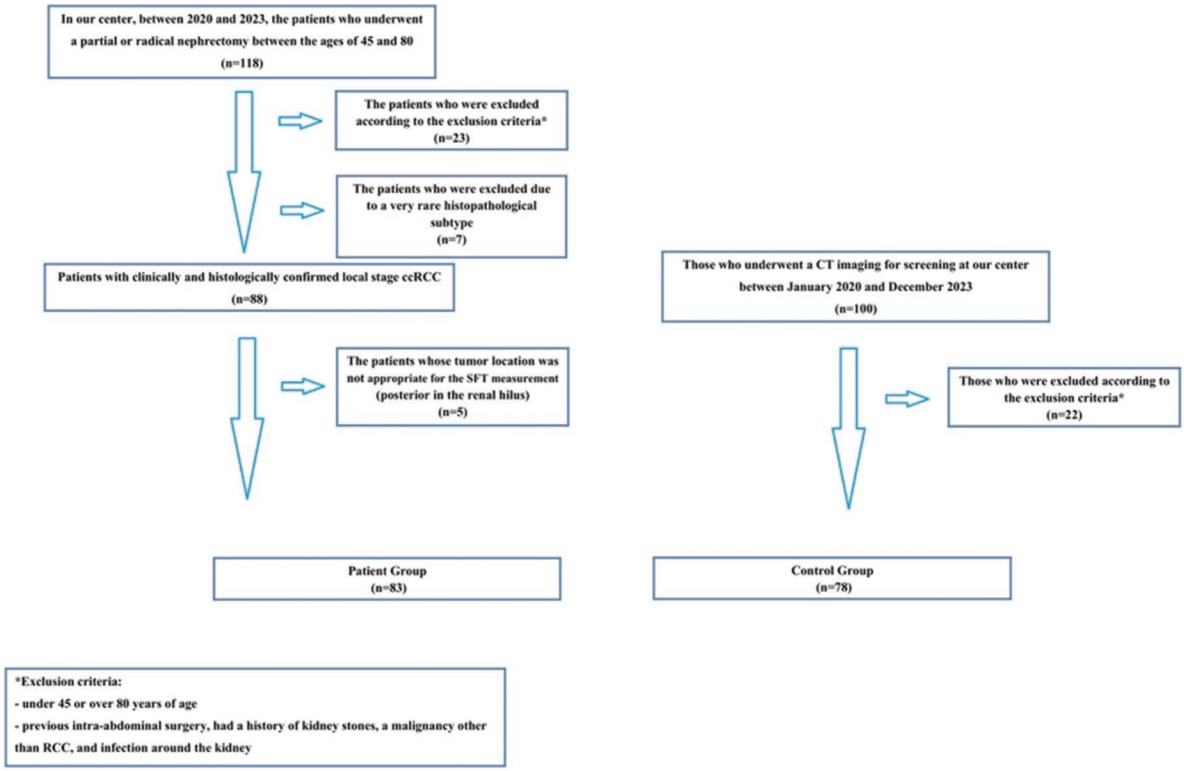

Figure 1. *Flowchart of patients who met inclusion/exclusion criteria for the study.*

The measurement of the SFA, PFT, and PFHU

A non-contrast CT scan of abdomen (Optima 660 SE, GE Healthcare/Aquilion Lightning Ultra Helical CT, Canon Medical) was performed for all individuals in the preoperative period. The SFA_A and SFA_P (Fig. 2) calculations were consistent with those reported in the previous studies[15,16]. First, the border between the visceral and subcutaneous compartment was defined manually along with the contour of the abdominal muscular wall at the umbilical level. Then, to identify the fat containing pixels, an image display window width between −195 and −45 HUs was utilized. A software analysis program (RAD-X® PACS software, Simplex, Ankara, Turkey) evaluated the values of the SFA_A and SFA_P automatically.

The PFT and PFHU were also calculated with the same method as in the previous studies[8,16]. In the CT images, the linear ruler tool of the software was used to measure the distance from the posterior surface of the kidney to the external edge of the iliopsoas at the renal hilum level (Fig. 3). The same radiologist Dr. Esin Derin-Çiçek (third author), who was unaware of the clinical and pathological data, assessed the all preoperative scans.

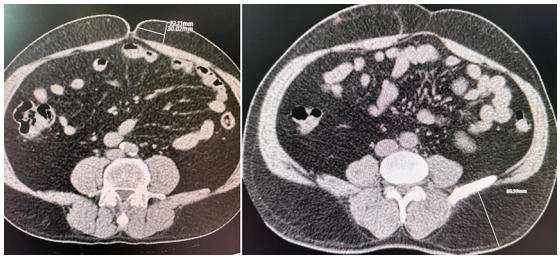

Figure 2. A: *evaluation of the subcutaneous fat area of the abdomen.* **B:** *evaluation of the subcutaneous fat area of the pelvis.*

Statistical analysis

IBM Statistical Package for the Social Sciences Statistics 22 program was used for statistical analysis of the findings. The conformity of the parameters to normal distribution was evaluated by Kolmogorov–Smirnov test. In addition to descriptive statistical methods (minimum, maximum, mean, standard deviation, median, and frequency), t-test was used for comparisons of quantitative data between two groups

Figure 3. *The evaluation of the perirenal fat thickness and perirenal fat hounsfield unit.*

for normally distributed parameters and Mann-Whitney U test was used for comparisons of non-normally distributed parameters between two group receiver operating characteristics (ROC). Chi-square and Fisher's Exact test were used to compare qualitative data. Spearman's rho correlation analysis, ROC for discrimination, and logistic regression analysis for effect were used to analyze the relationships. Analysis of covariance was performed to control/refine the SFA values. Significance was evaluated at $p < 0.05$ level.

Results

The study was conducted with a total of 161 patients, 59 (36.7%) women and 102 (63.3%) men, aged between 45 and 79 years. The mean age was 58.5 ± 8.56 years. The cases were evaluated in two groups as "Patient" (n = 83) and "Control" (n = 78). There was no statistically significant difference between the two groups in terms of descriptive characteristics ($p > 0.05$; Table 1).

The pre-operative SFA_A and SFA_P measurements were not statistically significantly different between the groups ($p > 0.05$). In the pre-operative PFT measurement analysis in both groups, fat thickness was found to be lower in the patient group compared with the control group; however, this difference was not statistically significant ($p > 0.05$). In separate comparisons of both kidneys, fat thickness was found to be lower in the patient group than in the control group according to the PFT (PFT_R) measured in the right kidney and the PFT (PFT_L) measured in the left kidney; however, these differences were not statistically significant ($p > 0.05$). After eliminating the effect of the SFA_A and SFA_P values in our study, the PFT measurements were re-evaluated between the two groups; however, no statistically significant difference was found ($p > 0.05$; Table 1).

The analysis of the pre-operative PFHU measurements revealed higher perirenal fat densities in the patient group compared with the control group; this difference was statistically significant ($p < 0.0001$). In separate comparisons for both kidneys, perirenal fat densities were found to be higher in the patient group than in the control group according to the analysis of the PFHU ($PFHU_R$) measured in the right kidney and the PFHU ($PFHU_L$) measured in the left kidney; these

Table 1. Demographic data and the radiological measurements of the participants among the groups

Data and measurements	Patient (mean) (%)	Control (mean) (%)	Total (mean) (%)	p
Age	59.10 ± 9.29	57.87 ± 7.71	58.50 ± 8.56	0.451[1]
Sex				
Male	54 (65)	102 (63)	48 (61)	0.643[1]
Female	29 (35)	59 (37)	30 (39)	
BMI				
< 25	37 (45)	72 (45)	35 (45)	0.97[1]
≥ 25	46 (55)	89 (55)	43 (55)	
HT				
+	46 (55)	80 (50)	34 (44)	0.133[1]
–	37 (45)	81 (50)	44 (56)	
DM				
+	24 (29)	40 (25)	16 (20)	0.218[1]
–	59 (71)	121 (75)	62 (80)	
SFA_A	25.65 ± 8.79	25.10 ± 7.49	25.38 ± 8.17	0.671[2]
SFA_P	61.96 ± 16.28	59.61 ± 13.64	60.82 ± 15.06	0.325[2]
PFT	16.31 ± 9.12	17.78 ± 7.07	17.02 ± 8.2	0.256[2]
PFT_R	15.53 ± 9.41	16.58 ± 7.01	16.04 ± 8.33	0.423[2]
PFT_L	17.09 ± 10.05	18.99 ± 8.07	18.01 ± 9.17	0.187[2]
PFHU	–92.63 ± 6.43	–103.63 ± 7.03	–97.96 ± 8.68	0.0001[2]*
$PFHU_R$	–92.88 ± 8.55	–103.03 ± 8.06	–97.8 ± 9.73	0.0001[2]*
$PFHU_L$	–92.38 ± 8.47	–104.24 ± 7.99	–98.13 ± 10.14	0.0001[2]*

[1]Mann-Whitney U-test.
[2]t-test.
*p < 0.05.
BMI: body mass index; HT: hypertension; DM: diabetes mellitus; SFA: subcutaneous fat area; SFA_A: subcutaneous fat area of abdomen; SFA_P: subcutaneous fat area of pelvis; PFT: perirenal fat thickness; PFT_R: perirenal fat thickness of right kidney; PFT_L: perirenal fat thickness of left kidney; PFHU: kounsfield unit of perirenal Fat; $PFHU_R$: hounsfield unit of right kidney perirenal fat; $PFHU_L$: hounsfield unit of left kidney perirenal fat.

Table 2. Histopathologic data of the patient group

Characteristics	Tumor Location		p
	L (%)	R (%)	
T Stage			
1	36 (64)	20 (36)	0.059[1]
2	5 (42)	7 (58)	
3	5 (33)	10 (67)	
Fuhrman Grade			
1	7 (64)	4 (36)	0.587[1]
2	26 (51)	25 (49)	
3	13 (62)	8 (38)	
Tumor necrosis			
+	15 (71)	6 (29)	0.088[1]
–	31 (50)	31 (50)	
Sarcomatoid component			
+	1 (50)	1 (50)	0.99[2]
–	45 (56)	36 (44)	

[1]Ki-Kare test.
[2]Fisher's exact test.

differences were statistically significant (p < 0.0001; Table 1).

The histopathologic data of the patient group are shown in table 2. According to T staging, the rates of stage 1, 2, and 3 were 67.5%, 14.5%, and 18%, respectively. Fuhrman grades 1, 2, and 3 were 11%, 51%, and 21%, respectively. Tumor necrosis was positive in 21% of patients and sarcomatoid component was positive in 2.5%. T stages, Fuhrman grades, tumor necrosis, and presence or absence of the sarcomatoid component were not significantly different in the analysis of the tumor formation sides (left/right) (p > 0.05) (Table 2).

In the analysis of radiologic measurements (Table 3), there was no statistically significant difference between the right and left kidney for the SFA_A, SFA_P, and PFHU values in the patient group (p > 0.05). There was a statistically significant difference between the PFT_L and PFT_R in both patient and control groups (p < 0.0001). In the patient group, the measurement of the tumor side and in the control group and the mean of the measurements of the right and left sides were taken for further comparison. While the difference in the PFT measurements between the two groups was not statistically significant, the difference in the PFHU measurements was statistically significant (p = 0.0001).

The PFHU measurement was found to be highly differentiative for the patient group, the cutoff point was set as –98.1 and the participants were divided into two groups. Those with a PFHU value < –98.1 had 6.7 times more risk than those with a PFHU value < –98.1 (Exp(B) = 6.725; 95% confidence ınterval [CI] 4.2-10.6 p < 0.0001). A cutoff value of –98.1 for the PFHU can identify the patient group with a sensitivity of 89.2% and a specificity of 84.6% (area under the curve = 0.9; 95% CI: 0.86-0.95 p < 0.0001) (Fig. 4). In multivariate logistic regression analysis, a PFHU ≥ –98.1 was independently associated with RCC after clinical and radiological parameters were added to the analysis.

Discussion

The relationship between ccRCC, the most common histologic subtype of RCC, and obesity has been emphasized in previous studies[16,17]. Obesity is highly associated with an increased risk of RCC development; therefore, it is considered to be one of the best known etiologic factors of RCC[5,6]. A high BMI appears to be associated with poor survival outcomes in both

Table 3. Data on radiological measurement

Outcomes	L	R	p
SFA_A	26.05 ± 9.14	25.15 ± 8.45	0.647[1]
SFA_P	61.71 ± 16.64	62.27 ± 16.05	0.877[1]
PFT			
Patient	17.09 ± 10.05	15.53 ± 9.41	0.04[2]*
Control	18.99 ± 8.07	16.58 ± 7.01	0.001[2]*
PFHU			
Patient	−92.38 ± 8.47	−92.88 ± 8.55	0.685[2]
Control	−104.24 ± 7.99	−103.03 ± 8.06	0.172[2]

[1]t-test.
[2]paired sample t-test.
*$p < 0.05$.
SFA_A: subcutaneous fat area of abdomen; SFA_P: subcutaneous fat area of pelvis; PF%rirenal fat thickness; PFHU: hounsfield unit of perirenal fat.

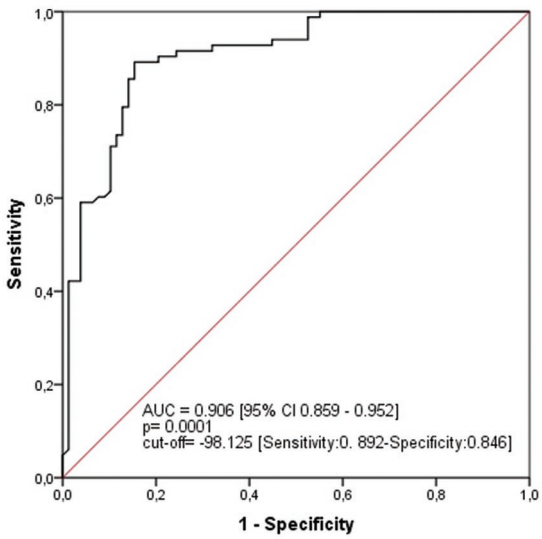

Figure 4. *Cutoff point determination for perirenal fat thickness hounsfield unit in radiologic imaging of renal cell carcinoma.*

non-metastatic and metastatic RCC[18,19]. There are also studies on the role of body composition indices measured on cross-sectional imaging, such as sarcopenia and fat accumulation, in the prognosis of RCC[20,21].

Visceral and subcutaneous fat thickness measurements are quantitative methods calculated on CT. These measurements, which have been emphasized recently, may provide more objective results than BMI. The visceral fat, which increases with age, has been shown to increase the risk of metabolic diseases as well as prostate cancer (PCa) in men[22]. Another study showed that PCa patients with higher periprostatic fat levels had more aggressive PCa[23]. In studies on RCC, Zhu et al. reported a positive correlation between the percentage of visceral adipose tissue and the Fuhrman tumor grade[24]. Huang et al. revealed that high visceral fat accumulation played a positive role on the progression of ccRCC[16]. On the contrary, there are also studies reporting that high visceral fat deposition is associated with relatively long cancer-specific survival in RCC patients[15].

Perirenal fat accumulation is an ectopic fat accumulation and has been reported to be associated with high diastolic blood pressure, diabetes mellitus, metabolic syndrome, and chronic renal failure[25,26]. In 2012, Okhunov et al. revealed that perirenal fat accumulation was an important predictor of ccRCC histopathology[8]. They showed that WNT signaling pathway-related factors secreted from perirenal adipose tissue affected the oncogenic pathways critical for ccRCC (migration of ACHN and CaKi-2 cells) and promoted the progression of local ccRCC to locally advanced (T3 stage) disease[7]. Huang et al. reported that the high PFT was associated with lower progression-free survival for ccRCC in both sexes[16]. In our study, we compared the images of histologically confirmed ccRCC patients with those of control group participants who were equivalent to them in terms of descriptive characteristics such as age, gender, BMI, and comorbidity (we measured the PFT using the technique described by Okhunov et al. and Huang et al., due to the lack of any standardized measurement method). The PFT was lower in the patient group compared with the control group; however, this difference was not statistically significant. The PFT was again compared by separating the right and left kidneys according to the side of the cancerous kidney, and again the PFT was found to be lower in the patient group. The PFT measurements were re-evaluated by eliminating the effect of the SFA_A and SFA_P values; however, again, no statistically significant difference was found. The PFT measurements for both genders were compared again separately; no significant difference was found between the PFTs for male and female genders in all cases and in the control group. However, the mean PFT measurement of women in the patient group was statistically significantly lower (13.2 ± 7.9, 17.9 ± 9.3; $p = 0.023$).

So far, most studies on the perirenal fat have focused on the thickness and volume of the adipose tissue[16,27]. However, several experimental studies suggest that the fat quality (HU) measurements may also be important[28,29]. They have shown that a lower HU is associated with an adipose tissue containing higher levels of lipid content and the range of HU typically

attributed to fat is in the range of −195 to −45[27]. The fat depots with higher lipid content and lipolytic activity can cause endothelial dysfunction and high insulin resistance[30]. These studies also suggest that adipocyte hypertrophy is associated with vascularity; decreased perfusion may lead to hypoxia and inflammation in adipose tissue[31].

In characterization of the renal masses, the CT still remains as the first-line imaging modality[32]. Based on the above mentioned studies, we think that the perirenal fat tissue density (PFHU), which can be easily measured by non-contrast CT, may be associated with RCC independently of the abdominal adipose tissue. In our study, the mean PFHU value of the RCC group was significantly higher than that of the control group (−92.6 ± 6.4 vs. −103.6 ± 7; p = 0.0001). Right and left kidney measurements were also compared and similar results were obtained. In our study, gender-specific PFHU was also evaluated; the mean PFHU value for males was found to be higher (denser) in both the patient group and the control group, but this difference was not significant. According to the results of our study, those with a PFHU value < −98.1 were 6.7 times more likely to have RCC than those with a PFHU value > −98.1. In multivariate logistic regression analysis, a PFHU ≥ −98.1 was independently associated with RCC after accounting for clinical and radiologic parameters.

The main limitations of our study are its retrospective nature, relatively small sample size and the lack of survival analysis. Second, only histologically confirmed localized ccRCC patients were included in this study, as the numbers of patients with other histological subtypes were not sufficient for statistical study. Third, our study may not include different ethnic groups. However, to our knowledge, our study is the first to examine the association between the PFHU and ccRCC, in English literature.

Conclusion

Although potential mechanisms for the association of the perirenal adipose tissue thickness with RCC are known, its exact role remains unclear. We suggest that the measurement of the perirenal adipose tissue HU by CT may be useful in differentiating the aggressive renal masses and therefore in determining the appropriate treatment selection. The effects of the PFT and PFHU need to be clarified by further research.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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