

Renal cell carcinoma T staging: Diagnostic accuracy of preoperative contrast-enhanced computed tomography

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Abstract. Renal cell carcinoma (RCC) accounts for 1-2% of all malignancies and is the most common renal tumor in adults. Imaging studies are used for diagnosis and staging. Tumor-Node-Metastasis staging strongly affects prognosis and management, while contrast-enhanced computed tomography (CECT) is regarded as a standard imaging technique for local and distant staging. The present study aimed to evaluate the accuracy of CECT for the preoperative staging of RCC by using surgical and pathological staging as the reference methods. This single-center prospective study was conducted between October 2019 and November 2021. The preoperative abdominal CT scans of patients suspected of having RCC were reviewed. Imaging data were collected, including tumor side and size, and perinephric fat invasion. Intraoperative notes were recorded, including the operation type, perinephric fat invasion, renal vein (RV) or inferior vena cava (IVC) tumor extension, and surrounding organ invasion. Pathological data were collected on tumor size, RCC type, presence of clear margins, presence of renal capsule or perinephric fat invasion, renal sinus or pelvicalyceal system (PCS) invasion, segmental or main RV extension, and the involvement of Gerota's fascia and nearby organs. Preoperative CECT revealed that 42 out of 59 tumors had a greater maximum diameter than the pathological specimen, with an overall disparity of 0.25 cm.

The specificity of CT for the detection of tumor invasion of the perinephric and renal sinus fat and PCS was 95%, and the sensitivity ranged from 80 to 88%. CT had an 83% sensitivity and a 95% specificity in detecting T4 stage cancer, with a 100% specificity for adrenal invasion. The concordance between radiographic and histological results for RV and IVC involvement was high, with specificities of 94 and 98%, and sensitivities of 80 and 100%, respectively. Overall accuracy for correct T staging was 80%. In conclusion, CECT is accurate in the local T staging of RCC, with high sensitivity and specificity for estimating tumor size and detecting extension to nearby structures and venous invasion.

Introduction

Renal cell carcinoma (RCC) consists of a heterogeneous group of tumors originating from renal tubular epithelial cells and is one of the 10 most frequently occurring cancer types in the world; it accounts for 2% of all cancer diagnoses and cancer-associated deaths worldwide (1). RCC is the most common malignant tumor of the kidney, accounting for 85-90% of all renal cancer cases and 1-2% of all malignancies (2). According to pathological features, mutational analysis and syndromic correlations, RCC has been classified into several subtypes: Clear cell carcinoma (70-90%), papillary RCC (10-15%) and chromophobe RCC (3-5%). Classifying the subtype of RCC has clinical significance in prognosis and therapeutic interventions (3). Despite improvements in diagnosis, mainly improved imaging modalities and the incidental detection of a number of tumors by imaging tests for unrelated complaints, nearly 30% of all patients with RCC are diagnosed with a metastatic illness (4). Contrast-enhanced computed tomography (CECT) is the modality of choice for the preoperative characterization and staging of renal tumors, and for follow-up of an RCC that has been kept under active surveillance or treated non-operatively. Native scan, arterial 'corticomedullary' phase, parenchymal 'nephrographic' phase and pelvicalyceal 'excretory' phase are all essential techniques, and three-plane reconstruction is suggested in all patients (5). Tumor size and local T staging have been shown

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to be independent predictors of outcome, with higher T stages portending a poorer survival rate; for example, the 5- and 10-year disease-free survival rates after surgery for T1, T2, T3a, T3b and T3c tumors are ~95 and 91%, 80 and 70%, 66 and 53%, 52 and 43%, and 43 and 42%, respectively (5,6). In local T staging of RCC (Table I), T1 and T2 are solely determined by tumor size in the absence of invasion of surrounding structures (7). The importance of local T staging also matters for the operational approach; for T1a tumors, partial nephrectomy (PN) or tumor enucleation has become standard, while for larger tumors, PN is considered (if suitable), but is not yet conventional (8). Staging a tumor as T3a reduces overall tumor-related survival rates by 4-6 times, requires radical nephrectomy and doubles the chance of distant metastases (~16% for T2 and 34% for T3) (9,10). Preoperative detection of the invasion of the renal vein (RV) or its segments (T3a), the infradiaphragmatic inferior vena cava (IVC) (T3b), the supradiaphragmatic IVC or the IVC wall (T3c) is crucial, as this will impact the operation plan and require a multidisciplinary approach that includes cardiothoracic and hepatobiliary teams. In some cases when distant metastasis is present, only cytoreductive surgery is performed (11).

The current study aimed to evaluate the accuracy of CECT for the preoperative staging of RCC by using surgical and pathological staging as reference methods.

Patients and methods

Study population. This is a single-center prospective study conducted between October 2019 and November 2021 at the Radiology Center of Sulaimani Teaching Hospital in Sulaimani, Iraq. It was performed for individuals who had a renal mass and were diagnosed with RCC based on clinical and imaging studies. The age of the patients ranged from 31 to 80 years, with a median age of 52 years and a mean age of 56.1 years. Among the patients, 35 (59.32%) were male and 24 (40.68%) were female.

Ethical approval. The study was approved by the Arab Board Scientific Committee of the Iraqi Ministry of Health (approval no. 22-2018). All participants gave verbal and written informed consent for the participation in the CECT, as well the publication of CECT data and that of surgical and pathological data.

Inclusion and exclusion criteria. Adult patients with renal masses who had optimal CECT, a pathology report confirming RCC and adequate local T staging (within 3 weeks of surgery, containing native, nephrographic and delayed phase images, and thin slices reformatted in coronal and sagittal sections) were included in this study. The exclusion criteria included the following: i) Patients in the pediatric age group, as most of the renal tumors in this age group are Wilm's tumors, and RCC is rarely encountered; ii) tumors radiologically suspected to be RCC, but subsequently proved to be a non-RCC tumor; iii) tumors radiologically consistent with AML, transitional cell carcinoma or lymphoma; and iv) tumors radiologically suspected to be RCC, but without pathological confirmation.

Radiological evaluation. Patients with suspected RCC had their preoperative abdominal CT scans reviewed. The study

included native, nephrographic and excretory phases with non-ionic intravenous (IV) contrast. The contrast material routinely used for these scans was Low Osmolar Contrast Media administered at a rate of 2-4 ml/sec through an automated IV injector at a dose of 1-1.5 ml/kg.

The scan region extended from the diaphragm to the symphysis pubis. CECT was performed with a thickness of 5 mm in the axial plane, then reconstructed to a 1-2 mm thickness, and reformatted to the coronal and sagittal planes.

Imaging data were collected, including tumor side and size (largest tumor diameter in any plane), and perinephric fat invasion. The latter was diagnosed when there was fat stranding in addition to an irregular tumor edge, angular lobulation, and nodular extension or obvious tumor invasion towards Gerota's fascia, but without reaching it.

In the early stages, the excretory phase was reviewed for perinephric fat stranding and the invasion of the pelvicalyceal system (PCS) and renal sinus fat. Other parameters that were assessed included tumor extension into the major RV or its segmental branches, IVC extension or wall invasion in the nephrographic and excretory phases, and the invasion of Gerota's fascia (clear invasion by thickening and breaching, or contact >1 cm).

Invasion of the adrenal gland and other surrounding organs was determined by loss of the fat plane and contact (>1 cm) in all planes, loss of the fat plane between the tumor and the organ with local change in enhancement or texture, or obvious tumor extension into the organ. Lastly, the radiologic T stage was recorded according to the Tumor-Node-Metastasis (TNM) staging system (Table I) (5,6).

Operative and pathological evaluation. Intraoperative notes were recorded, including the operation type, perinephric fat invasion, RV or IVC tumor extension, and surrounding organ invasion. Pathological data were collected on tumor size, RCC type, presence of clear margins, preservation of renal capsule or perinephric fat invasion, renal sinus or PCS invasion, segmental or main RV extension, and involvement of Gerota's fascia or nearby organs.

Data entry and statistical analysis. The collected data were organized in Microsoft Excel 2016 (Microsoft Corporation) for better classification, and statistical analysis was performed using STATA version 15 (StataCorp LP) and Microsoft Excel. Descriptive statistics (mean, frequency, percentage) and analytical statistics (P-value) were calculated for related data. Fisher's exact test was used for the comparison of categorical data (as >20% of the cells contained count numbers of <5), and unpaired the t-test was calculated for comparison of the numerical data. The association between two variables was measured by Pearson's correlation. $P \leq 0.05$ was considered to indicate a statistically significant difference.

Results

In the current study, 59 patients with RCC were included. The average age \pm standard deviation of the patients was 56.24 ± 12.70 . Table II shows the distribution of the tumors by sex, side and pole of the kidney, and type of operation.

Table I. Primary renal cell carcinoma staging (T staging).

T category	T criteria
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor <7 cm in greatest dimension, limited to the kidney
T1a	Tumor <4 cm in greatest dimension, limited to the kidney
T1b	Tumor >4 cm but <7 cm in greatest dimension, limited to the kidney
T2	Tumor >7 cm in greatest dimension, limited to the kidney
T2a	Tumor >7 cm but <10 cm in greatest dimension, limited to the kidney
T2b	Tumor >10 cm, limited to the kidney
T3	Tumor extends into major veins or perinephric tissues. But not into the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a	Tumor extends into the renal vein or its segmental branches, the pelvicalyceal system, or the perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor extends into the vena cava below the diaphragm
T3c	Tumor extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)

The average tumor size in the radiological and pathological staging was 6.72 and 6.47 cm, respectively; however, the mean difference in tumor size between the radiological and pathological findings was not statistically significant (mean difference, 0.25 cm; 95% CI, -1.22 to 1.72; $t=0.34$; $P=0.734$).

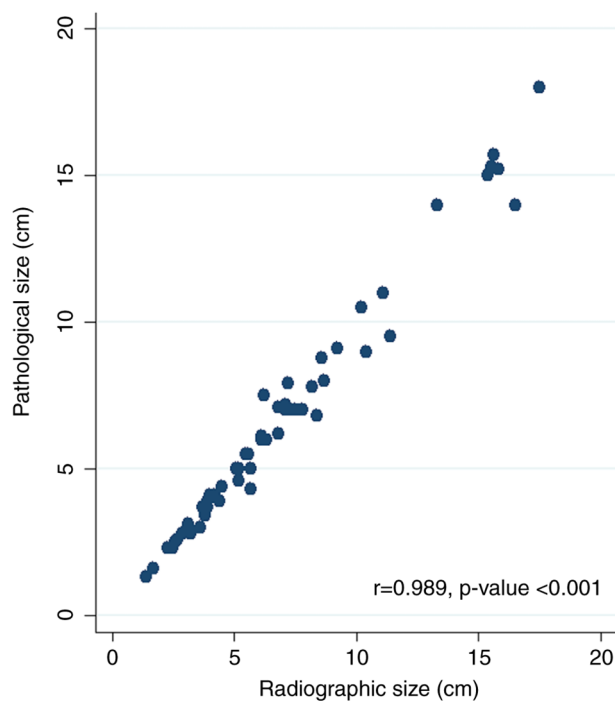
Overall, the pathological measurements revealed that 71.19% ($n=42$) of the tumors were smaller, 11.89% ($n=7$) were of the same size and 16.94% ($n=10$) were larger than the radiological measurements. The scatter plot shows a positive linear correlation between the pathological and radiological tumor sizes ($r=0.989$; $P<0.001$; Fig. 1).

Fig. 2 demonstrates one of the criteria for perinephric fat invasion, namely, a nodular extension from the tumor to the perinephric fat (T3a). Fig. 3 shows an enhanced filling defect in the right main renal vein in the arterial and nephrographic phases without extension to the IVC.

CECT accurately detected perinephric fat invasion in 12 out of 15 cases and excluded invasion in 42 out of 44 pathologically negative cases. CECT was able to detect PCS and sinus fat invasion in 15 out of 17 pathologically proven

Table II. Baseline characteristics in patients with renal cell carcinoma.

Base-line characteristics	n (%)
Sex	
Male	35 (59.32)
Female	24 (40.68)
Side	
Right	32 (54.24)
Left	27 (45.76)
Pole of kidney	
Upper	11 (18.64)
Middle	12 (20.34)
Lower	17 (28.81)
Upper and middle	10 (16.95)
Lower and middle	6 (10.17)
Diffuse involvement	3 (5.08)
Type of operation	
Radical nephrectomy	37 (62.71)
Partial nephrectomy	19 (32.20)
Enucleation of mass	2 (3.39)
No operation	1 (1.69)

Figure 1. Plot showing Pearson's correlation coefficient between radiological tumor size and pathological tumor size ($n=59$; $P<0.001$).

patients, while excluding invasion in 40 out of 42 negative cases (Table III).

Regarding renal vein invasion, CECT detected 8 out of 10 pathologically proven patients and excluded 46 out of 49 negative cases. CECT detected both cases of IVC invasion and excluded 56 out of 57 pathologically negative cases. Furthermore, four out

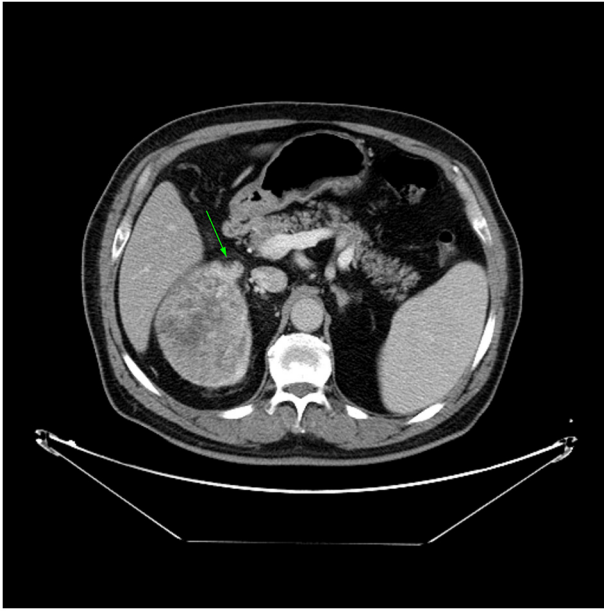


Figure 2. Perinephric fat invasion. Right-sided renal cell carcinoma with an enhancing nodule from the anterior part of the tumor invading the perinephric fat (stage T3a), as indicated by the arrow.



Figure 3. Computed tomography scan of a right-sided RCC showing expansion and an enhancing filling defect in the right renal vein (stage T3a), as indicated by the arrow. The patient had von-Hippel-Lindau disease; there were two pancreatic lesions (serous cystadenomas) and a contralateral nephrectomy had been performed previously due to RCC. RCC, renal cell carcinoma.

of five cases of Gerota's fascia invasion were diagnosed radiologically, and 52 out of 54 patients were accurately excluded. Adrenal invasion was diagnosed in 1 out of 2 cases, while all 57 pathologically negative cases were excluded using CECT (Table IV).

Table V clarifies the important parameters by which radiologists decide RCC local staging. In this table, a comparison between the radiological suspicion of invasion and pathological true invasion has been performed. These points are important

Table III. Sensitivity, specificity and predictive values of detecting invasion of perinephric fat, PCS and sinus fat using contrast-enhanced computed tomography.

Parameter	Perinephric fat invasion	PCS or sinus fat extension
Sensitivity, %	80.00	88.23
Specificity, %	95.45	95.23
PPV, %	85.71	88.23
NPV, %	93.33	95.23

PCS, pelvicalyceal system; PPV, positive predictive value; NPV, negative predictive value.

to radiologists to calculate the sensitivity and specificity of CT scans for detecting invasion of these structures.

Table VI provides an overall view of the present study results, summarizing the sensitivity, specificity, predictive values and accuracy of contrast-enhanced computed tomography for local T staging. This data enables other specialists who work on RCC (e.g., urologists, oncologists and nephrologists) to understand the accuracy of CT scans in the local staging of RCC.

Discussion

When used properly, a CT scan is considered a highly accurate measure (100% sensitivity and 95% specificity) for detecting renal masses. According to previous studies, CT scans can detect and stage renal masses with up to 91% accuracy, making them the imaging modality of choice (12,13). The current study found that the mean pathological diameter of the tumors was less than the radiological mean diameter (6.47 vs. 6.72 cm), with a mean difference of 0.25 cm. This size discrepancy, in which radiological size is larger, is well known from previous studies. Choi *et al* (14) reported a 0.17-cm discrepancy. Chen *et al* (15) observed a 0.22-cm discrepancy. Meanwhile, Nazim *et al* (12) found a 0.38-cm discrepancy. The reduction in tumor size observed on pathological examination has been attributed to a decrease in the blood volume in a highly vascular renal tumor following ligation or blockage of the renal artery (16). The reduction in tumor size may also be due to the use of 10% buffered formalin for pathological specimen fixation. Pathological size is an important indicator of the prognosis of patients. However, radiological size estimation is an essential component for selecting the appropriate treatment in RCC (12).

The involvement of perinephric fat tissue is a critical element in therapeutic planning. In fact, perirenal fat tissue infiltration alters the surgical technique from conservative to radical nephrectomy (13). One of the most challenging aspects of staging renal tumors is detecting perinephric fat invasion, which causes tumors of any size to be classified as T3a. Catalano *et al* (13) demonstrated perinephric fat invasion with a sensitivity and specificity of ~96 and 93%, respectively. El-Hefnawy *et al* (17) observed a specificity of 80%, while

Table IV. Sensitivity, specificity and predictive values of detecting invasion of the renal vein, IVC, Gerota's fascia and adrenal gland using contrast-enhanced computed tomography.

Parameter	Renal vein invasion	IVC extension	Gerota's fascia invasion	Adrenal gland direct invasion
Sensitivity, %	80.00	100.00	80.00	50.00
Specificity, %	93.87	98.25	96.30	100.00
PPV, %	72.72	66.70	66.67	100.00
NPV, %	95.83	100.00	98.11	98.30

IVC, inferior vena cava; PPV, positive predictive value; NPV, negative predictive value.

Table V. Association of radiological detection of types of invasion with pathological assessment.

Type of invasion	Radiological, n (%)	Pathological, n (%)	P-value
Renal vein invasion			0.002
Segmental branch	8 (13.56)	7 (11.86)	
Main renal vein	3 (5.08)	3 (5.08)	
No invasion	48 (81.36)	49 (83.05)	
IVC extension			0.002
Infradiaphragmatic invasion	2 (3.39)	1 (1.69)	
IVC wall invasion	1 (1.69)	1 (1.69)	
No extension	56 (94.92)	57 (96.61)	
Surrounding organ invasion other than adrenal gland			<0.0001
Liver	2 (3.39)	1 (1.69)	
Colon	1 (1.69)	1 (1.69)	
Abdominal muscle	1 (1.69)	1 (1.69)	
Diaphragm	1 (1.69)	1 (1.69)	
Psoas	1 (1.69)	0 (0.00)	
Tail of pancreas	1 (1.69)	0 (0.00)	
No	52 (88.14)	55 (93.22)	

IVC, inferior vena cava.

Sokhi *et al* (10) reported a sensitivity and specificity of 83 and 76%, respectively. Liu *et al* (18) showed a sensitivity and specificity of 32 and 86%, respectively. The current study found a sensitivity and specificity of 80 and 95%, respectively, which was somewhat higher than previous studies. These values depend on the criteria for perinephric fat invasion, which varied among the studies. In the present study, perinephric fat stranding was considered as perinephric fat invasion in addition to other features, such as perinephric nodules, an irregular tumor edge and angular lobulation.

Using two phases (non-contrast and nephrographic), Sokhi *et al* (10) found renal sinus fat invasion sensitivity and specificity to be 71-88 and 71-79%, respectively. In the current study, PCS and renal sinus fat invasion were detected by CECT with higher sensitivity and specificity (88 and 95%, respectively) when compared with prior studies. The higher sensitivity and specificity of the present study can be attributed to the use of additional excretory phases, which

are effective in differentiating PCS compression or invasion. Perinephric and renal sinus fat invasion are the most difficult to diagnose with CT imaging, as perinephric fat stranding unrelated to tumor invasion, a large tumor size, a previously unhealthy kidney, and the presence of microscopic and radiologically undetectable invasion all complicate interpretation. Sinus fat invasion is also difficult to differentiate from compression (10,19).

Accurate preoperative assessment of invasion and the extent of tumor thrombi in the RV and IVC is essential for a surgeon to determine the right surgical strategy for thrombectomy and to reduce the risk of perioperative tumoral embolism (20). RV can be radiologically assessed for invasion when there is a hypodense filling defect that is continuous with the tumor or an extended RV with an intraluminal lesion, and the result becomes more specific when it is enhanced (10,21). Tumors can be classified as stage pT3a due to renal vein infiltration, renal sinus invasion or extra-

Table VI. Sensitivity, specificity, predictive values and accuracy of contrast-enhanced computed tomography for local T staging.

Stages	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %	P-value
T1a	90.00	97.44	94.74	95.00	94.92	<0.001
T1b	75.00	91.49	69.23	93.48	88.14	<0.001
T2a	60.00	98.15	75.00	96.36	94.92	0.002
T2b	100.00	100.00	100.00	100.00	100.00	0.017
T3a	69.23	95.65	81.82	91.67	89.83	<0.001
T3b	100.00	98.28	50.00	100.00	98.31	0.034
T3c	100.00	100.00	100.00	100.00	100.00	0.017
T4	83.33	96.23	71.43	98.08	94.92	<0.001

PPV, positive predictive value; NPV, negative predictive value.

capsular extension, which can be small and thus difficult to detect on CT (2). In the study by Sokhi *et al* (10), a renal vein invasion with a specificity of 91-93%, but a sensitivity of 59-69%, was reported. Bradley *et al* (22) discovered renal vein involvement with a sensitivity and specificity of 84 and 98%, respectively. The sensitivity and specificity of the current study were 80 and 94%, respectively. Karlo *et al* (23) noted that the tumor edge touching the sinus fat was an accurate CT sign of branch RV invasion. Sokhi *et al* (10) also demonstrated that the presence of suspected sinus fat invasion, numerous perinephric septa, stranding or vascularity, and thickened perirenal fascia, especially in the case of a necrotic and irregular tumor edge, should alert the radiologist to perform a more proper examination of the renal veins.

IVC extension, like RV tumor extension, is described when there is an enhancing filling defect within the IVC or a non-enhancing lesion continuous with the renal tumor. Whether the extension is infra- or supra-diaphragmatic does not appear to affect the prognosis, but the invasion of the IVC wall greatly reduces survival rate (20,24). For IVC extension and invasion, magnetic resonance imaging (MRI) demonstrated great accuracy, up to 100% (25). However, MRI is only used as a problem-solving tool in indeterminate cases. Türkvtan *et al* (20) reported IVC invasion with 100% accuracy. Nazim *et al* (12) showed a sensitivity and specificity of 100 and 97%, respectively. The sensitivity and specificity for detecting IVC invasion in the current study were 100 and 98%, respectively.

The T3a stage is the most difficult to define precisely. Reznek (25) calculated the sensitivity and specificity for T3a stage diagnosis to be 46 and 98%, respectively. In an investigation by El-Hefnawy *et al* (17), T3a sensitivity and specificity were found to be 51 and 80%, respectively. The overall sensitivity and specificity for T3 in the current study were 80 and 97%, respectively, while the sensitivity and specificity for T3a were 69.2 and 95.6%, respectively.

Gerota's fascia invasion and expansion are difficult to distinguish. The studies by Reznek (25) and Tsili and Argyropoulou (26) discussed the difficulty of Gerota's fascia infiltration without mentioning the accuracy of CT or MRI (25,26). Bradley *et al* (22) showed that thickening of Gerota's fascia had a sensitivity and specificity of 52 and

90%, respectively. The sensitivity and specificity of the present study were 80 and 96%, respectively.

The absence of barrier planes between renal cancer and the surrounding structures raises the possibility of neighboring organ invasion (stage T4) (17). Direct expansion of RCC beyond Gerota's fascia and into adjacent organs is difficult to identify without a proven localized change in attenuation within the diseased organ (20). Larger tumors touching adjacent organs make it challenging to determine whether invasion is evident radiologically (22). The study by Reznek (25) claimed that organ invasion should be suggested only when there is enlargement or alteration in density, but did not discuss CECT accuracy; however, the study did report an MRI accuracy for organ invasion of ~97% (25). In the current study, radiological invasion of surrounding organs employing the selected criteria provided a sensitivity of 100%, a positive predictive value of 57% and a specificity of 95%.

According to the study by Liu *et al* (18), the overall accuracy of T staging is 75%. El-Hefnawy *et al* (17) reported an overall T staging accuracy of 65%. Türkvtan *et al* (20) demonstrated an accuracy of 89% in a study of 57 cases. In an investigation by Kim *et al* (27), an accuracy of about 87% in 144 cases was reported. The overall local T staging accuracy of the current study was estimated to be at least 80%. These differences might be attributed to the number of patients included in the study, as well as the imaging characteristics employed for local staging.

Despite the advantages of the current study, it also has crucial limitations, as it was a single-center study and it had a small sample size.

In conclusion, CECT is accurate in the local T staging of RCC, with a high sensitivity and specificity regarding the assessment of tumor size, extension to nearby structures and venous invasion.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The research was registered in the Research Registry (registration number: researchregistry7516) and is available at the following link: https://www.researchregistry.com/browse-the-registry/#home/?view_2_search=7516&view_2_page=1.

Authors' contributions

SHT, FHK, and RJR performed the radiological assessments and confirm the authenticity of all the raw data. FHK contributed to manuscript drafting. LAA pathologically examined the specimens, was a major contributor to the study conception and revised the manuscript. SMF and AMS were major contributors to the study conception, and the revision and final revision of the manuscript. FHF and DHR contributed to the conception and the design of the study. IA and RB analyzed and interpreted the data. SSF, BAA and SHM collected patient data and thoroughly revised the content of the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was approved by the Arab Board Scientific Committee of the Iraqi Ministry of Health (approval no. 22-2018). Written informed consent was obtained from all the patients.

Patient consent for publication

The representative patient in Figs. 2 and 3 provided consent for the publication of diagnostic images and data.

Competing interests

The authors declare that they have no competing interests.

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