How accurate is radiological imaging for perirenal fat and renal vein invasion in Renal Cell Carcinoma ?

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Abstract

Objective: To evaluate the accuracy of radiological staging, especially renal venous and perirenal fat invasion, in renal cell carcinoma (RCC). Material & Methods: Data of 4823 renal tumor patients from Renal Tumor Database of Association of Uro-oncology in Turkey were evaluated. Of 4823 patients, 3309 RCC patients had complete radiological and histopathological data were included to this study. The Pearson Chi-squared test ($\chi 2$) was used to compare radiological and histopathological stages. Results: The mean (SD) age of 3309 patients was 58 (12.3). Preoperative radiological imaging was performed using computed tomography (CT) (n=2510, 75.8%) or magnetic resonance imaging (MRI) (n=799, 24.2%). There was a substantial concordance between radiological and pathological staging (κ=0.52, $p<0.001$). Sensitivities of radiological staging in stage I, II, III and IV were 90.7%, 67.3%, 27.7% and 64.2%, respectively. The sensitivity in stage III was lower than the other stages. Sub-analysis of stage IIIa cases revealed that, for perirenal fat invasion and renal vein invasion, sensitivity values were 15.4% and 11.3%, respectively. Conclusions: There was a substantial concordance between radiological (CT and/or MRI) and pathological T staging in RCC. However, this is not true for T3 cases. Sensitivity of preoperative radiological imaging in patients with pT3a tumors is insufficient and lower than the other stages. Consequently, preoperative imaging in patients with T3 RCC has to be improved, in order to better inform the patients regarding prognosis of their disease.

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What is already known about this topic?

Radiological evaluation with computerized tomography (CT) and/or magnetic resonance imaging (MRI) is used to characterize renal mass and its TNM stage.

What does this article add?

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Introduction

Renal Cell Carcinoma (RCC) is the most frequent malignant tumor of the kidney in adults and its incidence has been increasing globally (1). Radical or partial nephrectomy is the standard surgical treatment of RCC. Both the surgical procedure and approach are decided according to the stage of cancer and the tumor features such as location, size and centrality. Prognostic factors of RCC are classified into anatomical, histological, clinical, and molecular by European Association of Urology (EAU) Guidelines on RCC. The anatomical prognostic factors consist of the criteria in the TNM classification system (2). Radiological evaluation with computerized tomography (CT) and/or magnetic resonance imaging (MRI) is used to characterize renal mass and its TNM stage. This information is then used for treatment planning and patient counselling.

Multi-phasic contrast-enhanced CT of abdomen and chest is recommended for the diagnosis and staging of RCC by EAU Guidelines on RCC. The Guidelines also recommend MRI because of some advantages such as better evaluation of venous involvement, avoidance of intravenous CT contrast medium and reduction of radiation (2). CT staging for RCC has been variably accurate, and staging inaccuracies, usually understaging (most common with Stage T3a disease) in previous studies has been reported (3,4). Two large studies reported that patients upstaged from clinical stage T1 to pathologic stage T3a RCC showed shorter survival outcomes than those without upstaging (5,6). Therefore, accuracy of radiological staging is very important for the management of patients with RCC. The aim of the present study is to investigate the accuracy of radiological staging of RCC in every stage and especially in pT3a cases.

Material and Method

Data of 4823 patients who underwent radical or partial nephrectomy for renal tumors during the period from 2000 to 2019 was obtained from Turkish Urooncology Association-Urologic Cancer Database-Kidney (TUOA UroCaD-K) by using Research Electronic Data Capture (REDCap) (7,8) in Turkey. Of 4823 patients, 3309 RCC patients were found to have complete radiological and histopathological data and were included to this study. Exclusion criteria were incomplete radiological and/or histopathological data, other malignant or benign renal tumors except RCC, incomplete demographic data, patients less than 18 years of age and

patients who were performed other procedures without surgical resection such as radiofrequency ablation and microwave ablation. Radiological and pathological stages of the patients were recorded according to TNM 2017 classification system. Radiological evaluations were made with CT and/or MRI.

Statistical analysis

The Pearson Chi-squared test ($\chi 2$) was used to compare radiological and pathological stages. The concordance between the radiological and pathological stages was evaluated by using the κ statistic, which is a measure of agreement between observers that corrects for chance agreement. The grade of concordance has been defined as 'fair', for a of 0–0.2, moderate for 0.21–0.45, substantial for 0.46–0.75 and almost perfect for 0.76–0.99 [9]. Statistical analysis was performed using SPSS software package version 22.0 (Statistical Package for Social ScienceTM, Chicago, IL, USA) and $p < 0.05$ was considered to indicate statistical significance.

Results

The mean (SD) age of study population was 58 (12.3). Of our patients, 2176 (65.8%) were male and 1133 (34.2%) were female. Radical and partial nephrectomies were performed in 2099 (63.4%) and 1210 (36.6%) patients, respectively. CT and MRI were performed in 2510 (75.8%) and 799 (24.2%) patients, respectively. The demographic and surgical data of the patients are given in Table 1. There was a substantial concordance between radiological and pathological staging (κ=0.52, $p<0.001$) (Table 2). Sensitivity, specificity, negative and positive predictive values and accuracy rates of radiologic staging for pathologic stage are shown in table 3. The sensitivity in stage III was lower than the other stages ($p<0.05$). Sub-analysis of stage IIIa cases revealed that, for perirenal fat invasion and renal vein invasion, sensitivity values were 15.4% and 11.3%, respectively. Out of 383 radiological stage III cases, concordant pathology was found in 185 (48.3%). Of 2658 radiologically localized tumors (stage I or II), 464 (17.5%) identified as up-staged to stage III after nephrectomy (Table 2). Positive surgical margins (PSM) were found in 39 (8.4%) of 464 up-staged patients and 23 (12.4%) of 185 concordant pathology cases ($p=0.08$).

Discussion

More than 50% of patients with RCC are diagnosed incidentally by abdominal ultrasound or non-enhanced CT for other medical reasons (10,11). Radiological T stage of a renal cancer is a major factor in predicting prognosis and survival in these patients. Some studies have reported that multi-phasic CT or MRI for the diagnosis of RCC have accuracy of up to 90% (12-14). In this study, using a large sample size, we also showed that there was a substantial concordance between radiological and pathological staging in Turkey. In addition, the results showed that CT (75.8%) is being used three times more commonly than MRI (24.2%) for the diagnosis and staging of RCC. The reason why urologists prefer CT rather than MRI for renal imaging may be due to the fact that CT is less time consuming and cheaper than MRI, and the urologists are more familiar with CT images rather than MRI images.

Although the accuracy of CT and MRI in the diagnosis and staging of RCC is generally high, the sensitivity and specificity values are found to be lower in T3 cases compared to other stages (15). Renard et al., retrospectively, investigated the diagnostic accuracy of CT in predicting pT3a RCC in 96 cases (15). Renal sinus fat infiltration, peri-nephric fat infiltration and renal venous wall involvement were assessed by two radiologists specialized in urological imaging and compared with the histopathologic staging. The authors found that assessment of renal tumor extension into perinephric fat remained a difficult task, leading to reduced accuracy in T3a staging. Similarly, the results of our study showed that the diagnostic accuracy of CT or MRI in stage III RCC was lower than other stages. The importance of these findings is that in all RCC types prognosis worsens with stage (2), and this is also true for stage III cases compared to those with stage I and II tumors. Chevinsky et al. reported pathological stage T3a as a poor prognostic factor in RCC regardless of tumor size and also demonstrated that there was an increased rate of risk of recurrence with perinephric fat invasion compared to those with pT1/T2 tumors (16). Therefore, radiologic under-staging in pT3a cases, will underestimate the risk of cancer recurrence and survival rates, and the patient will be misinformed regarding prognosis of his/her tumor during patient counselling before surgery.

Although, both renal vein invasion and perirenal fat invasion are classified as T3a disease, it was reported in recent studies that patients with pT3aN0M0 RCC with renal vein invasion have a significantly poorer prognosis than those with fat invasion (17). In TNM sub-group analysis of Stage III, we found that the sensitivities of perirenal fat and renal vein invasions were 15.4% and 11.3%, respectively. Although these values are very low compared to values reported in other studies (15), other studies also showed that peri-nephric fat and renal vein invasion in RCC are difficult to evaluate radiologically (5). By using the Surveillance Epidemiology and End Results registries Srivastava et al. reported that from the patients undergoing partial nephrectomy, the estimated proportion up-staged to pT3a was 9.5%, and 19.5% for cT1b, and cT2, respectively (5). In our study, incidence of up-staging from localized stages to stage III was 17.5%, which is consistent with the results reported in literature. Therefore, preoperative imaging in patients with stage III RCC has to be improved. Advanced MRI techniques such as diffusion weighted and perfusion-weighted imaging are being explored for renal mass assessment and staging (18).

Presence of PSM on final pathology creates uncertainty in terms of further management options. Some have performed an immediate or delayed nephrectomy whereas others followed patients without complete nephrectomy (19,20). The incidence of PSM ranges from 0–10.7% in literature and the rate of PSM may be influenced by tumour stage, fat invasion and tumor grade (19,20). Bansal et al, by looking at the partial nephrectomy patients included in the Canadian Kidney Cancer information system database, reported that higher stage ([?]T3) and grade were associated with a higher risk of PSM (19). In our study, PSM rate was 8.4% in patients up-staged from localized tumor to pathologically stage III and 12.4% in radiologically stage III cases with concordant pathology (p=0.08). As there is no statistically significant difference between these two rates, during surgery one should also be as cautious as possible in radiologically localized disease in order not to have a PSM.

The present study is limited by its retrospective nature. In addition, central pathological and radiological review could not be performed. Patients were included from different centres and therefore the quality of radiologic and pathologic evaluation is probably variable. However, the aim of our study was to evaluate the accuracy of radiological staging of RCC in daily routine urology practice, rather than assessment of radiological techniques or surgical procedures. So, we did not perform any comparison between radiological techniques, surgical procedures or centers.

There was a substantial concordance between radiological (CT and/or MRI) and pathological T staging in RCC. However, this is not true for stage T3 cases. The reason is that, it is difficult to evaluate peri-nephric fat and renal vein invasion radiologically. Therefore, the sensitivity of preoperative radiological imaging in patients with pT3a tumors is insufficient and lower than the other stages. Consequently, preoperative imaging in patients with T3 RCC has to be improved, in order to better inform the patients regarding prognosis of their disease.

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Ethical standards

The Local Ethics Committee approved the study protocol.

Conflict of interest

There are no conflicts of interest to be stated for the corresponding author and all co-authors.

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TABLES

Table 1. The demographic and surgical data of all the patients.

		N (%)	Mean ± SD (min-max)
Age (years)	Age (years)	3309 (100)	58.04 ± 12.26 (18-99)
Tumor size (cm)	Tumor size (cm)	3309 (100)	5.89 ± 3.60 (1-37)
Sex	Male Female	2176 (65.8) 1133 (34.2)	
Surgical procedure	Radical nephrectomy Partial nephrectomy	2099 (63.4) 1210 (36.6)	
Surgic al approach	Open Laparoscopic	2611(78.9) 698 (21.1)	
Radiological technique	CT MRI	2510 (75.8) 799 (24.2)	

CT: Computer Tomography, MRI: Magnetic Resonance Imaging

Table 2. Concordance of the stages between radiological and patological staging.

	Pathological Staging	**Pathological Staging**	**Pathological Staging**	**Pathological Staging**	**Pathological Staging**
	Stage I (n=1904)	Stage II (n=401)	Stage III (n=669)	Stage IV (n=335)	κ=0.52 p<0.001

		Pathological Staging	**Pathological Staging**	**Pathological Staging**	**Pathological Staging**	**Pathological Staging**
Radiological staging	Stage I (n=2157)	1726 (80%)	81 (3.7%)	306 (14.2%)	44 (2.1%)	
	Stage II (n=501)	46 (9.2%)	270 (53.9%)	158 (31.5%)	27 (5.4%)	
	Stage III (n=383)	110 (28.7%)	39 (10.2%)	185 (48.3%)	49 (12.8%)	
	Stage IV (n=268)	22 (8.2%)	11 (4.1%)	20 (7.5%)	215 (80.2%)	

Table 3. Sensitivity, specificity, negative and positive predictive values and accuracy rates of radiologic staging

		Sensitivity %	**Specificity %**	Negative predictive value %	Positive predictive value %	Accuracy %
Pathological staging	Stage I	90.7	69.3	84.5	80.0	81.6
	Stage II	67.3	92.1	95.3	53.9	89.1
	Stage III	27.7	92.5	83.5	48.3	79.4
	Stage IV	64.2	98.2	96.1	80.2	94.8

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