Pre-operative staging of renal cell carcinoma: Spiral CT versus pathological considerations.

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Abstract

Background: Renal cell carcinoma (RCC) is the commonest renal malignancy, comprising 85-90% of all malignant renal tumours and represents 3% of all adult malignancies. The prognosis of RCC depends on the size, stage, and grade of the tumor. CT has proved to be the most important imaging technique for the evaluation of renal lesions and the preoperative staging of renal cell carcinomas.

Objective: The aim of our study was to evaluate the accuracy of spiral CT in the preoperative assessment of patients with renal cell carcinoma correlated with histopathological findings.

Patients and methods: Between February 2008 and September 2009, a prospective study included 40 patients (age range, 36–66 years; 28 men, 12 women) with solid renal masses. All the patients were diagnosed by CT as having renal cell carcinoma, underwent total nephrectomy & proved to be renal cell carcinoma at histopathlogical examination. In all patients, initial CT images were obtained without administration of contrast Material, 100ml of Intravenous contrast material was administered, a repeated scan was done 120 seconds after contrast injection, both scans should covered the entire volume of the abdomen. Percentage of the parameters used in the study was calculated. Diagnostic accuracy of CT in staging renal cell carcinoma was calculated.

Results: The study included 40 patients (28 men, 12 women) with solid renal masses. Tumor size ranged from 1.7 to 6.5 cm (mean size, 3.1 cm). All the patients showed evidence of contrast enhancement by about 47HU. Thirty seven patients (92.5%) show heterogeneous enhancement while only 3 patients (7.5%) show homogenous enhancement. Calcification was seen in 10 patients (25%). A pseudocapsule was present in 16 patients. Lymph node (LN) involvement with adenopathies larger than 1 cm in diameter was found in 7 patients (17.5%), only one patient (2.5%) show false negative diagnosis, the over all diagnostic accuracy of LN detection was 83%. Renal vein or inferior vena cava thrombosis was detected in 8 patients (20%), diagnostic accuracy was 87.5%. The overall diagnostic accuracy of CT in staging renal cell carcinoma was 90% (36 out of 40).

Conclusions: CT is an excellent imaging technique for the evaluation of solid renal masses and the preoperative staging of renal cell carcinomas. CT has some difficulty in differentiating T3a from T2. CT has a limited ability to identify lymph node involvement by malignancy because it is still based on only size criteria, with 10 mm as the limiting size for normal nodes.

Keywords: Spiral CT, pre-operative staging, renal cell carcinoma.

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Introduction

Renal cell carcinoma is the commonest renal malignancy, comprising 85-90% of all malignant renal tumours and represents 3% of all adult malignancies [1-5].

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It occurs bilaterally in 2–5% of cases [1, 6, 7], and is the eighth most common malignancy, accounting for 3% of newly diagnosed neoplasms [1]. Most cases arise spontaneously, peaks in the 5th to 7th decades, with a male predominance [1, 5, 8], and a male to female ratio of approximately 2.5:1 [2]. Today, most newly diagnosed RCCs are discovered incidentally during imaging performed for non urologic symptoms [5, 9].

Investigators have also concluded that renal cell carcinoma is not a single disease but, rather, a group of several disease entities [1, 10]. According to the First International Workshop on Renal Cell Carcinoma held by the World Health Organization, renal cell carcinoma can be classified into conventional (i.e., clear cell) renal carcinoma, papillary renal carcinoma, chromophobe renal carcinoma, collecting duct renal carcinoma, and unclassified renal carcinoma [11-13].

The prognosis of renal cell carcinoma depends on the size, stage, and grade of the tumor [14]. The stage of a renal cell carcinoma at the time of treatment correlates directly with its prognosis [15]. The tumor stage is the most important factor affecting the prognosis and survival rate. Tumor type also affects survival, with aggressive anaplastic renal cell carcinomas having a worse prognosis compared to clear cell carcinoma [16-19]. An accurate diagnostic assessment of the extent of a renal cell carcinoma is valuable for determining the therapeutic approach, which may include partial or radical nephrectomy, possibly with tumor thrombectomy or resection of infiltrated adjacent organs [20].

Computed Tomography (CT) has proved to be the most important imaging technique for the evaluation of renal lesions and the preoperative staging of renal cell carcinomas [21, 22], with accuracy ranging between 72 and 90% [1, 2]. The role of preoperative imaging is to define the tumor, detect and delineate the extent of venous involvement if any, as well detect the presence of local and distant metastases [23]. Furthermore, with the use of helical CT, it is possible to analyze the dynamic enhancement pattern of the tumor [24].

The two most common staging systems that have been used for renal cell cancer staging are the Robson and TNM classification. Tumor staging for renal cell carcinoma has been incorporated into the TNM system of the UICC in 1997, which has been modified in 2002 (Table 1) [1, 16-19, 23].

Table 1: TNM classification and staging system of renal cell carcinoma (UICC, 2002)

T-classification	
T1	Confined to kidney, T1a < 4 cm, T1b < 7 cm
T2	Confined to kidney, >7 cm
T3	Confined to Gerota's fascia
T3a	Extending to ipsilateral adrenal or perirenal fat
T3b	Extending to renal vein or IVC below diaphragm
T3c	Extending to IVC above diaphragm
T4	Extending beyond Gerota's fascia
N-classification	
N0	No regional lymph node metastasis
N1	Metastasis in one regional lymph node
N2	Metastasis in more than one regional lymph node

Nx	Regional lymph nodes cannot be evaluated		
M-classification			
M0	No distant metastasis		
M1	Distant metastasis		
Mx	**Distant metastasis cannot be evaluated**		
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IV	T4	N0, N1	M0

Patients and methods

Between February 2008 and September 2009, a prospective study was done at Al-Kadhimyia teaching hospital, Baghdad, Iraq. The study included 40 patients (age range, 36–66 years; 28 men, 12 women; male: female ratio is 2.3:1) with solid renal masses.

Tumor size ranged from 1.7 to 6.5 cm (mean size, 3.1 cm). All the patients were diagnosed by CT as having renal cell carcinoma, underwent total nephrectomy and proved to be renal cell carcinoma at histopathlogical examination.

All the patients have an ultrasound examination that reveals the presence of a solid renal mass, being refereed to CT.

Examinations were performed with the CT unit (Somatom plus4; siemens medical system, Germany). In all patients, initial CT images were obtained without administration of contrast material. In this examination the site and the density of the lesion were noticed. Two large pour IV canula were inserted into each antecubital vein, manual injection of 100ml of Intravenous contrast material (iohexole, Omnipaque 350, Schering, Berlin, Ireland) was administered, a repeated CT scan was done 120 seconds after contrast injection (nephrographic phase (NP)), both scans should have covered the entire volume of the abdomen. During this perfusion phase, uniform contrast enhancement of the renal parenchyma was achieved. The NP mainly reflected the advanced distribution of contrast material in the renal interstitial space and the filtered contrast material entering the loops of Henle and the collecting tubules. In this phase the fallowing parameters were assessed: the size of the tumor, degree of contrast enhancement, and pattern of enhancement (heterogeneous or homogenous), presence of calcification, and presence of pseudo-capsule, perinephric involvement, LN enlargement, renal vein or inferior vena cava thrombosis, tumor extension into the ipsilateral adrenal gland.

Percentage of the above parameters was calculated. Diagnostic accuracy of CT in staging renal cell carcinoma was also calculated.

Results

Tumor size ranged from 1.7 to 6.5 cm (mean size, 3.1 cm). The entire patient underwent radical nephrectomy & proved to be renal cell carcinoma.

All patients included in the study showed a solid mass on unenhanced CT, with mean attenuation of 38HU (mean 30-54HU).

After IV contrast all the patients showed evidence of contrast enhancement by about 47HU. Thirty seven of our patients (92.5%) show evidence of heterogeneous enhancement while only 3 patients (7.5%) show homogenous enhancement. Calcification was seen in 10 patients (25%).

A pseudocapsule was present in 16 patients. Peri-nephric extension was seen in 18 patients. Adrenal glands were involved in 3 patients (7.5%).

Lymph node involvement with adenopathies larger than 1 cm in diameter was found in 7 patients (17.5%), only one patient (2.5%) showed false negative diagnosis, the over all diagnostic accuracy of LN detection was 83%.

Renal vein or inferior vena cava thrombosis was detected in 8 patients (20%), diagnostic accuracy was 87.5%.

Tumor extension beyond Gerota's fascia was observed in 5 patients (12.5%) (3 show evidence of liver metastases, & 2 patients show multiple lung metastases at follow-up examination).

CT showed that: 6 patients (15%) were stage I, 10 (25%) were stage II, 19 (47.5%) were stage III, 5 (12.5%) were stage IV.

Histopathological examination showed that: 6 patients (15%) were stage I, 14 (35%) were stage II, 15 (37.5%) were stage III, 5 (12.5%) were stage IV.

The overall diagnostic accuracy of CT in staging renal cell carcinoma was 90% (36 out of 40).

Figures 1 & 2 show examples of CT images of different patients having RCC at different stages of the disease.

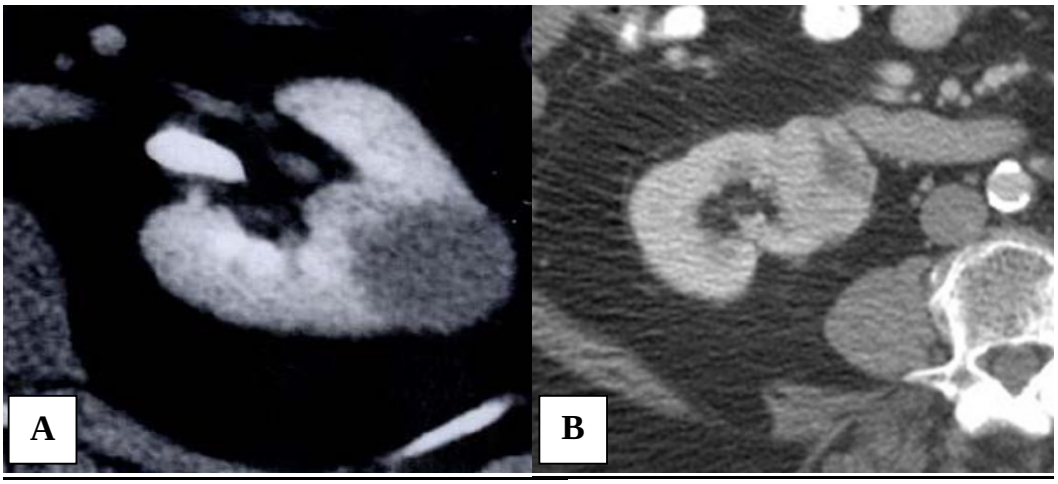

Figure1: A: 46 year old male with RCC of the Lt. Kidney (stage I) which is proved at histopathological examination. **B:** 45 year old male patient with RCC of right kidney shows evidence of perinephric extension (T3a), which was confirmed at histopathological examination.

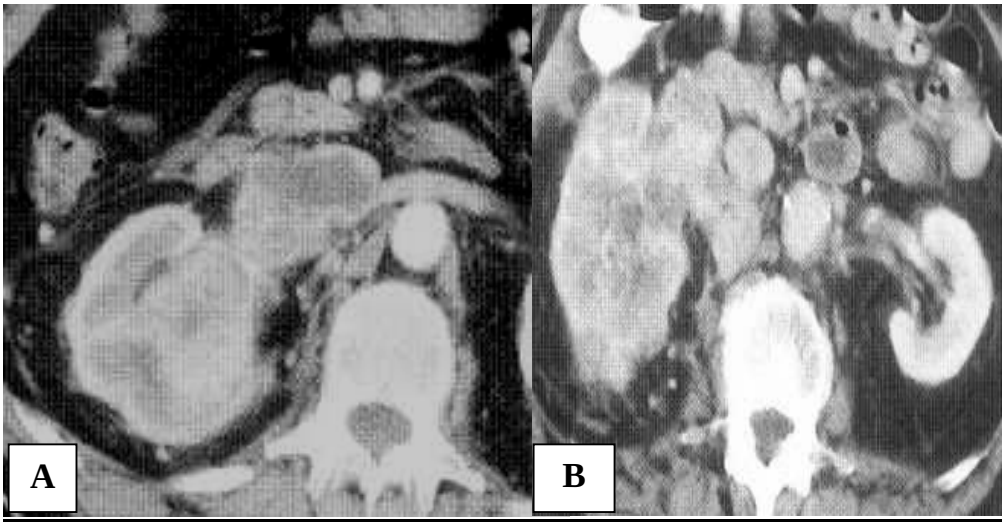

Figure1: A: 55year old male with RCC of the Rt. Kidney showing thrombosis of the Rt. Renal vein. **B:** 60 year old male patient with RCC of right kidney shows evidence of extra-renal extension and para-aortic LN enlargement.

Discussion

The prognosis of renal cell carcinoma depends on the size, stage, and grade of the tumor [14]. Improvement in imaging modalities continues to have a large impact on the diagnosis and treatment of solid renal masses [25]. CT has proved to be the most important imaging technique for the evaluation of renal lesions and the preoperative staging of renal cell carcinomas [21, 22]. Spiral CT eliminates respiratory misregistration [26], and so is useful in evaluating renal lesions because the entire lesion is imaged free of skip areas and even small features can be depicted. Similarly, spiral CT might be useful in assessing contrast enhancement, considered by some the most important feature of small renal lesions [27, 28].

Most renal cell cancers are solid, with attenuation values of more than 20HU on unenhanced CT images [1]. In our study all patients showed solid mass on unenhanced CT, with mean attenuation of 38HU (mean 30-54HU).

The most important criterion used in differentiating surgical from non surgical renal masses is the determination of enhancement. Renal mass enhancement is dependent on multiple factors, including the amount and rate of the contrast material injection, the imaging delay, and the nature of the tissue within the mass. Obviously, tumors that are very vascular will enhance considerably, while hypovascular tumors will enhance to a lesser degree, some tumors will enhance heterogeneously [29]. Enhancement of more than 20HU indicates malignancy [1], in our study all the patients showed evidence of contrast enhancement of the renal mass by more than 47HU & this result was comparable to that seen by Jeong Kon Kim et al [30], where the tumors that enhanced more than approximately 44 H in the excretory phase were likely to be conventional renal carcinoma. Thirty seven of our patients (92.5%) showed evidence of heterogeneous enhancement while only 3 patients (7.5%) showed homogenous enhancement, these results were comparable to that seen by Jeong Kon Kim et al [8].

In the current study calcification was seen in 10 patients (25%). In general, intratumoral calcification is not an uncommon finding in RCCs and may be seen in about 30% of cases [6, 31, 32]. Calcification was associated with a better prognosis and is more frequently seen in papillary and chromophobe renal carcinomas [25].

CT showed that a pseudocapsule was present in 16 patients & Peri-nephric extension was seen in 18 patients, 4 cases were over-staged as stage III disease on CT which later were proved to be stage II or stage I disease on histopathological examination i.e there is difficulty in differentiating T3a from T2 or T1 cases. The presence of pseudocapsule or its infiltration by a significant amount of tumoral tissue is a specific sign, which, nevertheless, cannot always and easily be recognized [33, 34].

The probable cause of the misinterpretation was the presence of perinephric edema (that was erroneously related to previous inflammatory processes), vascular engorgement, or fibrosis [1, 33]. Perinephric spread of tumor has been reported as the most common cause of under- and overstaging of renal cell carcinoma on CT [33]. Renal cell carcinoma also acquires a collateral or parasitic blood supply which is often visible in the perinephric space and may be mistaken for tumour extension through the capsule [2]. Fortunately, preoperative differentiation of stages II and III tumor is not essential for determining the therapeutic approach, which would be the complete resection of the kidney including the perinephric fat tissue in either case [35], and this show little prognostic difference [2]. Currently, however, nephron-sparing surgery (partial nephrectomy) is increasingly being offered under certain circumstances. These include situations where there is only one functioning kidney and/or where the tumour is small (less than 4 cm diameter) and localised, especially if there is a possibility of a more benign pathology such as an oncocytoma. In these patients it becomes much more important to attempt accurate differentiation between stage II and III [2]. With the recent surgical developments, this sign represents in some centers the main limitation for a conservative, possibly laparoscopic approach, which is feasible in stage I or II when no evidence of perinephric fat invasion is present [36]. In fact, the infiltration of perirenal fat tissue modifies the surgical approach from conservative to radical nephrectomy [15, 35,37].

Adrenal glands were involved in 3 of our patients (7.5%). The overall incidence of adrenal metastases is between 1.2% and 8.5%, CT with normal appearing ardenal glands has a high negative predictive value for adrenal involvement with metastases, but a positive CT is not always due to malignancy, as adrenal adenomas are more commonly seen even in patients with underlying extra-adrenal malignancy [38, 39].

CT has a limited ability to identify lymph node involvement; the diagnosis of malignancy with regard to lymph node involvement is still based only on size criteria, with 10 mm as the limiting size for normal nodes [1, 40]. Enlargement above 2 cm diameter is almost always due to metastases [2]. In this study Lymph node involvement with adenopathies larger than 1 cm in diameter was found in 7 patients (17.5%), Lymph node metastases occur in about 15% of patients in the absence of other metastases [41]. In our study only one patient (2.5%) showed false negative diagnosis and this result was approximate to that seen in the previously reported studies [1,40] where 4% of lymph nodes had a false-

negative finding because micro-metastases could not be identified. There is also a variable false-positive rate due to nodal enlargement caused by reactive hyperplasia, this is more common when tumour necrosis or tumour thrombus is present [1, 2]. The reported accuracy of conventional CT in lymph node involvement was between 83% and 89% [1, 2, 40] and this was similar to our study which showed the diagnostic accuracy of LN detection to be 83%. Nevertheless, it has been recently shown that there is no clinical benefit in performing regional lymph node dissection in patients with no suspected adenopathy before surgery or in those patients with lymph nodes smaller than 10 mm [42].

The evaluation of renal vein and inferior vena cava thrombosis is crucial for treatment planning; in fact, if tumor thrombus spreads into the inferior vena cava, the exact extent of the thrombus is essential for planning the correct surgical approach [25]. Thrombus is seen as a filling defect within the vein. Isolated renal vein enlargement is an unreliable sign because it can be caused by increased blood flow secondary to tumour hypervascularity [1]. In our study renal vein or inferior vena cava thrombosis was detected in 8 patients (20%) and this result was approximately similar to that seen in previously reported study where approximately 23% of renal cell carcinomas invade the renal veins and 7% invade the inferior vena cava [43]. The diagnostic accuracy was 87.5% where only one patient had false positive CT diagnosis of renal vein thrombosis. The reported accuracy for detection of renal vein and inferior vena cava involvement using CT is 72-88% [23, 44].

Tumor extension beyond Gerota's fascia was observed in 5 patients (12.5%) (3 showed evidence of liver metastases, and 2 patients showed multiple lung metastases at follow-up examination). Staging of renal cell carcinoma also requires assessment of the lungs and liver where metastases can be found. Metastatic lesions to the liver may be, like the primary tumor, hypervascular [31].

The overall diagnostic accuracy of CT in staging renal cell carcinoma was 90% (36 out of 40), and this was comparable with that seen in the previously reported literatures where the accuracy ranging between 72 and 90% [1, 2, 45].

In Conclusions CT :

1. is an excellent imaging technique for the evaluation of solid renal masses and the preoperative staging of renal cell carcinomas.
2. has some difficulty in differentiating T3a from T2.
3.has a limited ability to identify lymph node involvement by malignancy because it is still based on size criteria only, with 10 mm as the limiting size for normal nodes.

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