Original Research Paper

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Radio-Diagnosis

ACCURACY OF MULTIDETECTOR CT IN PREOPERATIVE STAGING OF RENAL CELL CARCINOMA.

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ABSTRACT **Background:** Renal cell carcinoma (RCC) is the most frequent malignancy of the kidney, accounting for 85–90% of adult renal malignant tumours and 1–2% of all malignancies. This study aims at evaluating the accuracy of MDCT in pre-operative staging of renal cell carcinoma. **Methods:** The study population included 48 patients with RCC who underwent partial/radical nephrectomy from 2019 to 2021. Image interpretations were done by a radiologist. Categorical variables were expressed in frequency and percentage. Numerical variables were presented using frequency and percentage. Diagnostic measures such as sensitivity, specificity, positive predictive value, negative predictive value, accuracy and agreement were calculated. A p-value of <0.05 was considered to be statistically significant. **Results:** Consistency between MDCT and histopathologic staging was moderate for T staging (kappa= 0.5) and excellent for M staging (kappa= 1.00). Thirty two of 48 tumours were correctly staged, fifteen were over staged and one was under staged by MDCT. The sensitivity and specificity of MDCT in detecting perinephric fat invasion were 55.6% and 87.2%, in detecting pelvicalyceal system invasion were 100% and 74.5%, in detecting renal vein invasion were 100% and 97.78%, in detecting sinus fat invasion were 85.71% and 64.71%, in detecting IVC thrombosis were 100%, in detecting adrenal gland invasion/involvement beyond adrenal gland were 100% and 97.87%, in detecting distant metastasis were 100%, respectively. Our study did not have patients with nodal metastasis and supradiaphragmatic IVC thrombosis. **Conclusion:** MDCT with a dynamic contrast protocol is able to delineate RCC with high accuracy. However, a great portion of tumours were over staged by MDCT because of overestimation of tumour size and poor visualization of infiltration of the perinephric fat. In addition, nodal metastatic lesion evaluation relies on node size only and remains a difficult task.

KEYWORDS : Renal Cell Carcinoma; preoperative staging of renal cell carcinoma.

INTRODUCTION

Renal cell carcinoma is the most frequent malignant neoplasm of the kidney, accounting for 85–90% of adult renal malignant tumors and 1–2% of all malignancies[1].The majority of RCC cases are incidentally diagnosed during imaging, usually with ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI).

Current guidelines[2] propose nephron-sparing surgeries (partial nephrectomy or ablation) for Stage T1a renal cell carcinomas (RCC), although the indications are expanding[3].With Stage T1b (4–7 cm) tumors and even Stage T2 RCCs, successful surgical sessions have been documented. Stage T1 and T2 tumors are determined by tumor diameter (T1a, 4 cm; T1b, 4–7 cm; T2a, 7–10 cm; and T2b, 10 cm) in the most recent TNM iteration. Invasion of the renal sinus or perinephric fat is included to the definition of stage T3a RCC[4].

Renal vein invasion without caval involvement was down staged from Stage T3b to Stage T3a, while adrenal invasion was advanced from Stage T3a to Stage T4. With T3a tumors, size is still not a deciding criterion, and some renal masses less than 7 cm in diameter will be locally aggressive. Unrecognized sinus invasion may explain the recurrence of cancer in some cases of presumed T1 RCCs.[5,6] Centrally placed masses often demonstrate local invasion with positive surgical resection margins after partial nephrectomy[7,8].

Stage T3b is defined as extension of tumor into the vena cava below the diaphragm while T3c is extension of tumor into the vena cava above the diaphragm However, in previous studies, CT staging has been variably accurate for RCCs, and staging inaccuracies are said to be most common with Stage T3a disease. This study aims at evaluating the accuracy of Multi Detector Computed Tomography (MDCT) in pre-operative staging of renal cell carcinoma.

Methods

Selection And Description Of Study Participants:

After obtaining approval from the Thesis Protocol Review Committee (Scientific, Ethical & Financial), Amrita Institute of Medical Sciences, this study was carried out.

Study Design: Cross-sectional validational study.

Study Duration: 18 months starting from the date of acceptance of protocol of the thesis.

Study Setting: Department of Radio-diagnosis and Imaging, Department of Uro-oncology, Amrita Institute of Medical Sciences, Kochi.

Study Population: Patients referred from the uro oncology department from 2019 to 2021 for multiphase CT in renal mass protocol in the department of Radio-Diagnosis of Amrita Institute of Medical Sciences research center, Kochi.

Inclusion Criteria

All patients who had triphasic enhanced abdominal MDCT study done at our institution prior to partial /radical nephrectomy were included.

Exclusion Criteria

Patients with

- Benign cystic lesions (BOSNIAK I, II, IIF)
- pre-operative arterial embolization.
- Improper/incomplete imaging.

Sample Size

Based on the accuracy of MDCT for TNM staging as 89% observed in earlier publication conducted by Türkvatan et al [16]and with 95% confidence and 10% relative error, the minimum sample size came to 48.

CT examination of the patients with RCC who underwent partial /radical nephrectomy from 2019 to 2021 were reviewed. The patients were included in the study according to inclusion and exclusion criteria and multiple parameters were analyzed.

Technical Information:

Primary Objective

To evaluate the diagnostic accuracy of MDCT for pre-operative staging of renal cell carcinoma using updated TNM classification (2017).

Technique

All CT examinations were performed in multidetector (MDCT)256 iCT PHILIPS. CT examination includes four phases: a plain scan, corticomedullary phase, (arterial) nephrogenic phase (venous)and IVP phases. Contrast-enhanced images were obtained after IV administration of mixture of 80 ml of contrast and 20 ml of saline. Nonionic iodinated contrast medium (iobitridol, Xenetix 350, Guerbet) was used. Both dose modulation and automatic current settings were used. The data was reconstructed, analyzed, and interpreted in Philips's workstations.

Statistics

Statistical analysis was carried out using IBM SPSS 20. (SPSS Inc,

Chicago, USA). Descriptive statistics were expressed as mean ± SD for continuous variables and frequency and percentage for categorical variables. To test the statistical significance of the difference in the mean or median comparison of numerical variables between groups, Independent sample t test was applied for parametric data and Mann Whitney U test was applied for non parametric data. To test the statistical significance of the comparison of CT parameters with gold standard (Histopathology), McNemars test was used with validity parameters such as sensitivity, Specificity, Predictive Value Positive, Predictive value Negative and Accuracy. A p value < 0.05 was considered as statistically significant.

RESULTS

Out of the total 48 patients with RCC, 36 were males and the remaining were females. Maximum number of patients were noted in the 50-59 year age group (31.2%) and least in the more than 70 years age group (6.2 %).

The most common histological type was the clear cell variant, accounting for 81.2% of the total. Papillary cell carcinoma was the second most common sub type (10.4%). The Chromophobe variant was the next most common, accounting for 4.2 percent of the population. Sarcomatoid and tubulocystic variants were the least common, accounting for 2.1% of all cases.

Out of the 48 patients, 29(60.41%) underwent partial nephrectomy and the remaining 19(39.5%) had radical nephrectomy.

The mean tumor diameters were 2.778 cm(T1a), 4.736cm(T1b), 8.75 cm(T2a), 7.6 cm(T3a), and 10 cm(T3b). The p value was more than 0.05 for all the stages and overall there was no statistical difference in the tumor size between CT and histopathology.

Out of the 9 patients with perinephric fat invasion, CT accurately detected 5(10.4%) cases. Five patients were over staged and 4 patients were under staged. There is a no statistically significant difference between CT and histopathology in detection of PNF invasion (p value-1.0) with sensitivity 55.6%, specificity 87.2%, PPV 50%, NPV 89.5% having histopathology as gold standard. Based on Cohen's kappa analysis (0.410) there is almost fair agreement between CT and histopathology in detection of PNF invasion.

One patient(2.1%) who had invasion of PCS as per HPE was correctly diagnosed. 12(25%) patients were over staged. There is statistically significant difference between CT and histopathology in detection of PCS invasion (p value <0.001) with sensitivity 100%, specificity 74.52%, PPV 7.7%, NPV 100% having histopathology as gold standard. Based on Cohen's kappa analysis (0.108) there is only slight agreement between CT and histopathology in detection of PCS invasion.

All the patients with RVI were accurately diagnosed. One (2.1%) patient was over staged. There is no statistically significant difference between CT and histopathology in detection of RVI invasion (p value-1.000) with sensitivity 100%, specificity 97.78%, PPV 75%, NPV 100% having histopathology as gold standard. Based on Cohen's kappa analysis (0.846) there is an almost perfect agreement between CT and histopathology in detection of renal vein invasion.

Out of 14 patients with SFI, 12(25%) were correctly picked up in CT. 12(25%) patients were falsely diagnosed with SFI. There is statistically significant difference between CT and histopathology in detection of SFI (p value-0.013) with sensitivity 85.71%, specificity 64.71%, PPV 50%, NPV 91.67% having histopathology as gold standard. Based on Cohen's kappa analysis (0.417) there is a moderate agreement between CT and histopathology in detection of SFI.

Two(4.2%) patients with infra diaphragmatic IVC invasion were correctly diagnosed. None of them were over staged. There is no statistically significant difference between CT and histopathology in detection of IDIVC thrombosis (p value-1.00) with sensitivity, specificity, PPV, NPV and accuracy of 100% having histopathology as gold standard. Based on Cohen's kappa analysis (1.000) there is an almost perfect agreement between CT and histopathology in detection of IDIVC thrombosis. None of the patients had supra diaphragmatic IVC involvement

In our study, all of the 5 cases with enlarged lymph nodes were characterized as reactive hyperplasia in HPE. The presence of primary tumor necrosis or venous thrombosis is related to greater occurrence of reactive lymphadenopathy, resulting in increased false- positive cases for the 10-mm threshold. Our study had a specificity of 89.58%.

One patient with lung metastases was diagnosed effectively giving it a sensitivity, specificity and accuracy of 100%.

Only one (2.1%) patient had tumour extension beyond gerota's fascia in histopathology which was correctly diagnosed in CT. One (2.1%) patient was over staged as T4 in CT. There is no statistically significant difference between CT and histopathology in detection of adrenal invasion/invasion beyond gerota's fascia (p value-1.00) with sensitivity 100%, specificity 97.87%, PPV 50%, NPV 100% and accuracy of 97.92% having histopathology as gold standard. Based on Cohen's kappa analysis (0.657) there is a substantial perfect agreement between CT and histopathology in detection of detection of adrenal invasion/invasion beyond gerota's fascia.

MDCT In Staging Of Renal Cell Carcinoma (TNM Staging)

CT correctly detected 10/18 patients in T1a, four out of 11 patients in T1b, one out of 2 patients in T2a and T4, 13 out of 14 patients in T3a, both the patients in T3b (2/2). There is statistically significant difference between CT and histopathology in detection of T staging (p value<0.001). Based on Cohen's kappa analysis (0.508) there is a moderate agreement between CT and histopathology in detection of T staging.

None of the patients had nodal metastasis in our study as per histopathology. Five were falsely diagnosed to have nodal metastasis due to their increased size. CT had a specificity of 89.58% and NPV 100% with histopathology as gold standard.

One patient (2.1%) with lung metastases was diagnosed effectively giving it a sensitivity, specificity PPV, NPV and accuracy of 100%. There is statistically significant difference between CT and histopathology in detection of metastasis (p value-<0.001). Based on Cohen's kappa analysis (1.000) there is an almost perfect agreement between CT and histopathology in detection of metastatic disease.

DISCUSSION

A. Tumoral Size Staging

Clinical tumour size is one of the primary components in the TNM staging system and is an important prognostic marker. Radiological tumor size evaluation is necessary for choosing the appropriate surgical management.

The mean tumor diameters were 2.778 cm(T1a), 4.736cm(T1b), 8.75 cm(T2a), 7.6 cm(T3a), and 10 cm(T3b). The p value was more than 0.05 for all the stages and overall there was no statistical significant difference in tumor size between CT and histopathology.

B. Involvement Of Perinephric Fat

Evaluation of tumor into the perinephric space is difficult even with MDCT and three- dimensional technology as perinephric fat stranding is non-specific and can be due to edema, vessel engorgement or previous inflammation. In our study out of 9 HPR proven cases of perinephric fat invasion, CT correctly detected 5 cases. Five tumors with thickened bridging septa in the perinephric fat were over staged as T3a disease in the present study. Four tumors with microscopic invasion were under staged due to a lack of perinephric fat stranding. It had a sensitivity, specificity and accuracy of 55.6 %, 87.2% and 81.2% respectively in detecting perinephric fat invasion. Despite being specific in detecting neoplastic infiltration of the perinephric fat, the sensitivities were low.

CT has been found to be 32–64 % [9,10] accurate in identifying perinephric fat, with sensitivity of 46 %(99%) and specificity of 98 percent[11] in previous study performed by Johnson et al. In a study conducted by Yinghua et al, the sensitivity and specificity of MDCT in detecting perinephric fat invasion were 32.26% and 85.87%[10].

C. Involvement Of Pelvicalyceal System

Invasion was seen in only one patient (2%) as per histopathology. Twelve patients were over staged as they were closely indenting the calyceal system. It had a sensitivity, specificity and accuracy of 100 %, 74.5 % and 75 % respectively.

A study done previously by Goldin et al[13] compared the distance from the tumor to the calyceal system measured on CT images with the

actual distance observed in specimens and found that the CT-measured distance showed high sensitivity but low specificity for detection of CSI, suggesting that CT findings of a relationship between renal tumors and the CS are overestimated. This may explain the increased false positivity in our study.

D. Invasion Of Renal Vein/IVC:

RCC has a tendency to spread as tumor thrombus into the tributaries of the renal veins, ultimately reaching the main renal vein, the IVC, the hepatic veins, and sometimes into the right atrium. The presence and extent of tumor thrombus must be precisely described for planning of surgery. Those with tumor thrombus situated inferior to the diaphragm will just need a laparotomy, whereas patients with supradiaphragmatic extension will need a thoracoabdominal surgical approach. In our study all 3 cases with renal vein invasion were correctly diagnosed. One false positive case was seen due to filling defect caused by streaming of contrast medium. The sensitivity, specificity and accuracy were 100%, 97.78%, 97.92%

Two patients with infra diaphragmatic IVC invasion were correctly diagnosed. The sensitivity, specificity and accuracy were 100%.

In previous study conducted by Johnson et al[11] the sensitivity of CT in detecting venous invasion (renal vein & IVC) was 78%, with a specificity of 96%.

None of the patients had supradiaphragmatic IVC infiltration in our study.

E. Invasion Of Sinus Fat

Renal sinus is the central fat containing space that is located in the medial border of the kidney. It contains major branches of renal vessels and calyces of the collecting system. Sinus fat invasion had a remarkable impact on overall survival rate in RCC patients without nodal or distant metastasis[5]. It is a common finding in T3a. Sinus fat was involved in a total of 14 patients out of which 12 were correctly diagnosed in CT. Two patients with sinus fat invasion were under staged in CT. On the other hand, 12 patients without sinus fat invasion were over staged by CT. The sensitivity, specificity and accuracy were 85.7%, 64.7 % and 70.8% respectively. Sokhi et al[12] described the fat invasion with a sensitivity of 71–88% and specificity of 71–79%. According to Kim et al., tumour size more than 50 mm was by far the most predictive factor of renal sinus invasion [14]. MDCT had a high sensitivity but a low positive predictive value in identifying renal sinus fat invasion in a work by Bolster et al[15].

F. Lymph Node Involvement:

Lymph nodes are the third most common site of metastasis after lungs and bones.

Renal hilar, para-aortic and aortocaval nodes having a short axis diameter of more than 10 mm were considered to be metastatic. In our study, all of the 5 cases with enlarged lymph nodes were characterized as reactive hyperplasia. The presence of primary tumor necrosis or venous thrombosis is related to greater occurrence of reactive lymphadenopathy, resulting in increased false-positive cases for the 10-mm threshold. Our study had a specificity of 89.58%. Johnson et al described the sensitivity and specificity of nodal metastasis to be 83% and 88% [11].

I. Metastasis

The lung, bone, brain, and liver are the most common sites of RCC organ metastasis. The metastatic lesions are most likely hypervascular. Patients with metastatic disease still benefit from radical nephrectomy paired with systemic immunotherapy, thus detecting visceral metastases is critical. In our study one patient with lung metastases was diagnosed effectively giving it a sensitivity, specificity and accuracy of 100%. In a previous study conducted by Liu et al, MDCT's sensitivity and specificity for detecting distant metastases were 100 percent and 99.67 percent [10], respectively.

G. Invasion Of Adrenal Gland/Extension Beyond Gerota's Fascia

The diaphragm, psoas, quadratus lumborum, and erector spinae muscles have all been found to be directly invaded by the tumor. Infiltration of tumor in the liver, colon, pancreas, or spleen and adrenal have been described previously. The absence of fat planes between the tumor and these organs were considered indicative of tumor invasion. In our study it had a sensitivity, specificity and accuracy of 100%, 97.87% and 97.92% respectively. Only one patient has tumour extension beyond gerota's fascia in histopathology which was correctly diagnosed in CT. One patient with histopathological T3a was overstaged as T4 in CT because of the suspicious loss of fat plane between the liver capsule and the tumor in CT. The sensitivity and specificity of MDCT in detecting adrenal gland/adjacent organ invasion were found to be 60% and 95.79% [10] in a study conducted by Liu et al.

Table 1.1 Comparison Of CT vs HPR In T Staging.

T Staging - CT	T Staging - HPE						Kappa	To-tal	p value
	T1a	T1b	T2a	T3a	T3b	T4			
T1a	10 (20.8%)	1(2.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	11(22.9%)	0.508	<0.001
T1b	0 (0%)	4 (8.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4(8.3%)		
T2a	0 (0%)	0 (0%)	1(2.1%)	0 (0%)	0 (0%)	0 (0%)	1(2.1%)		
T3a	8 (16.7%)	6 (12.5%)	1(2.1%)	13(27.1%)	0 (0%)	0 (0%)	28(58.3%)		
T3b	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2(4.2%)	0 (0%)	2(4.2%)		
T4	0 (0%)	0 (0%)	0 (0%)	1(2.1%)	0 (0%)	1(2.1%)	2(4.2%)		
Total	18 (37.5%)	11(22.9%)	2(4.2%)	14(29.2%)	2(4.2%)	1(2.1%)	48(100%)		

Table 1.2 Comparison Of CT With HPR For Nodal Invasion.

CT	HPE		Total	p value
	Yes (%)	No (%)		
Yes	-	5(10.4%)	5(10.4%)	-
No	-	43(89.6%)	43(89.6%)	
Total	-	48(100%)	48(100%)	

Table 1.3 Comparison Of CT vs HPR In M Staging

CT	HPE		Total	p value	kappa
	Yes (%)	No (%)			
Yes	1(2.1%)	0(0%)	1(2.1%)	<0.001	1.000
No	0(0%)	47(97.9%)	47(97.9%)		
Total	1(2.1%)	47(97.9%)	48(100%)		

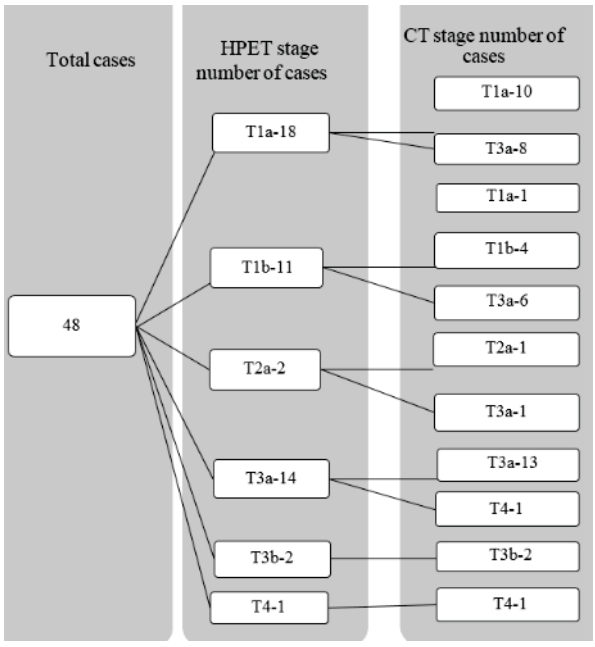

Figure 1.1 Diagram Depicting The Distribution Of The Total Number Of Cases Among Various Stages In HPR And The Split-up Of How These Cases Were Staged In The Corresponding CT.

Limitation

Majority of the patients belonged to earlier stages and hence our study does not adequately discuss the utility of CT in advanced stages. This led to the statistical parameters being overestimated in T3 and T4 stages.

CONCLUSION

Overall MDCT with multiphase protocol helps in delineating the extent of RCC. However, in many instances, MDCT over staged a large number of tumors due to overestimation of perinephric fat and sinus fat invasion. In evaluating the invasion of pelvicalyceal system, filling defect in IVP phase is the more reliable finding rather than mere indentation of PCS by the tumor. Furthermore, evaluating nodal metastasis is difficult because it is based solely on node size. Overall CT has a moderate agreement with HPE in T staging and an almost perfect agreement in M staging. Our study included more number of patients in T1, T2 and T3 and hence it is better applicable to early stages.

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