MDCT IN PREOPERATIVE EVALUATION OF PATIENTS WITH RENAL CELL CARCINOMA WITH HISTOPATHOLOGICAL CORRELATION
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HOW TO CITE THIS ARTICLE:
C. Arpita. "MDCT in Preoperative Evaluation of Patients with Renal Cell Carcinoma with Histopathological Correlation". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 36, September 07, 2015; Page: 5772-5781, DOI: 10.18410/jebmh/2015/793

ABSTRACT: PURPOSE: To evaluate the diagnostic accuracy of multidetector computed tomography (MDCT) for preoperative staging of renal cell carcinoma (RCC) using the AJCC 7th edition 2010 TNM (tumor, node, metastasis) classification. MATERIALS AND METHODS: In a retrospective study, a total of 30 patients with renal cell carcinoma were preoperatively assessed for tumor staging using multidetector-row CT. The scanning protocol of MDCT consisted of unenhanced and contrast-enhanced scans during corticomedullary, nephrographic and excretory phases. MDCT and histopathological staging were performed using the 2010 TNM staging system. A single blinded reader evaluated the CT scans independently who reviewed the scan on multi planar reconstructions. The results of MDCT were compared with the histopathological results. Agreement between the two staging methods was evaluated using the kappa (κ) statistics. RESULTS: Agreement between MDCT and surgical-histopathologic staging was very good for T staging (κ = 0.851), good for N staging (κ = 0.40), and excellent for M staging (κ = 1.00). Agreement between MDCT and surgical-histopathologic staging was good for perinephric invasion (κ = 0.8783) and perfect for tumor thrombus (κ = 1.00). MDCT was able to correctly identify and localize the extension of the tumor thrombus in all 4 patients. In the evaluation of nodal involvement, twenty six patients were correctly staged (87%), 4 patients (13%) were overstaged. CONCLUSION: MDCT with a dynamic contrast enhancement protocol is an accurate method for preoperative staging of RCC. MDCT with multiplanar reconstruction capability enables a reliable detection and characterization of the tumor, but the involvement of lymph nodes by tumor is still difficult to predict because it is based on node size criterion only. KEYWORDS: Renal cell carcinoma, Tumor staging, Multidetector Computed Tomography.

INTRODUCTION: Renal cell carcinoma (RCC) is the eighth most common malignancy affecting adults. Renal cell carcinoma accounts for 2%-3% of all visceral malignancies\(^1\)\(^,\)\(^2\) and for 85-90% of all malignant renal tumors in adults.\(^1\) Although radical surgery is the only efficient and curative treatment both in localized and advanced RCC, surgical techniques have evolved over the years. Less invasive surgical techniques, such as laparoscopic and nephron-sparing surgery are used in the treatment of renal tumors.\(^3\) In preoperative staging of RCC, the aim of any imaging study is to adequately evaluate tumor size, localization, and organ involvement, to reliably predict the presence and extent of any thrombus of the inferior vena cava, and to identify invasion of adjacent organs or lymph nodes, or distant metastases.

MDCT uses a high-resolution protocol for image evaluation with the aim of providing all anatomic and pathologic information necessary to correctly stage the disease process.
The purpose of the present study was to evaluate the accuracy of MDCT for preoperative staging of RCC using the 2010 TNM classification, by taking histopathologic staging as the reference method.

MATERIALS AND METHODS:

PATIENTS: We retrospectively reviewed the MDCT examinations of 30 patients (22 men and 8 women; age range, 24–83 years; mean age, 53 years) with 30 histologically verified RCCs, performed between January 2006 to Dec. 2012 at Tata Memorial Hospital, Mumbai. In accordance with the guidelines of our institutional review board for retrospective studies, informed consent and formal approval were not obtained.

EXAMINATION TECHNIQUE: Helical CT was performed using an MDCT scanner ((GE Light speed Ultra, General Electrical Medical Systems, Milwaukee, Wisconsin, USA). In all patients, following phases were acquired: an unenhanced scan from the renal calcifications, and intra tumoral fat; followed by contrast enhanced phase to evaluate the enhancement characteristics of the tumor, relation with renal cortex and renal arteries, and to assess renal venous drainage; and an excretory delayed phase to evaluate the relationship between the tumor and the collecting system. The excretory phase scans were acquired from the upper pole of the kidneys to the bladder. Unenhanced scanning was performed using the following parameters: collimation, 4.0 × 2.5mm; slice thickness, 5mm; reconstruction interval, 5mm; 130mAs; and 120kVp. Contrast-enhanced scanning was performed using the following parameters: collimation, 4×1mm; slice thickness, 1.25mm; reconstruction interval, 1mm. All patients received an injection of a standard dose of 80 mL of non-ionic iodinated contrast peripheral venous access (Generally an antecubital vein) at a flow rate of 2-3 mL/sec; the start delay was 40–60 sec for the parenchymal venous phase. The excretory phase was acquired 5 min after the start of the injection. The bolus injection technique was used to administer contrast material with an automated injector. The CT images were analyzed on a dedicated workstation with 3D rendering software.

IMAGE EVALUATION: CT scan examinations were reviewed by a single radiologist who was unaware of the histopathological results. All tumors were staged according to the 2010TNM staging system (Table 1). Tumor staging included the following parameters: tumor location; tumor diameter (The largest of anterioposterior, and transverse planes was defined as the radiological size), invasion of perinephric fat (determined by the presence of small hyperdense strands and nodules surrounding the lesion); involvement of the adrenal gland or satellite lesions within the Gerota’s fascia; presence and extent of tumor thrombus, lymph node involvement and visceral metastasis. Renal hilar, paraaortic, paracaval, retrocaval and aortocaval lymph nodes with short-axis diameter >1 cm were considered to be positive. Nodes showing necrosis and perinodal spread were also considered positive.
STASTITICAL ANALYSIS: The results from MDCT assessment of tumor staging were compared with the results from the surgical and histopathological evaluation, which served as the reference standard. Agreement between the two staging systems was determined using the kappa statistic (0.00–0.20, poor; 0.20–0.40, fair; 0.40–0.60, moderate; 0.60–0.80, good; and 0.80–1.00, excellent).

RESULTS:
Surgical Findings: Thirty patients underwent unilateral radical nephrectomy. Thirty renal cell carcinomas were seen in 30 patients. Twenty tumors were in the right kidney, and 10 in the left. Histopathology was evaluated in all 30 patients with renal cell carcinoma, revealing the following tumor cell types: clear cell (n = 22), papillary (n = 6), chromophobe (n=2). The mean tumor size was 7.6 cm (range, 3–17.5 cm). In 18 patients (60%), tumor was confined within the renal capsule (stages T1 and T2) and there was no infiltration into perinephric fat. Renal vein or inferior vena cava thrombosis was detected in 4 patients (13.3%). Lymph node involvement (renal hilar, paraaortic, aorto caval or paracaval lymph nodes) was found in 6 (20%) patients.

All tumors were staged according to 2010 TNM staging system. Histopathologic examination of the surgical specimens revealed that 11 tumors were stage T1 (37%), 10 were stage T2 (33%), nine were stage T3 (30%).

In the evaluation of lymph node involvement and distant metastases, 24 tumors (80%) were stage N0, six were stage N1 (20 %), 25 were stage M0 (83%), and 5 were stage M1 (16%).
MDCT Findings:

**T Staging:** In retrospective image analysis, all 30 tumors were identified with MDCT. The mean radiographic size of all included tumors was ~ 7.6 cm. Assessment of the MDCT images revealed 9 of 30 renal cell carcinomas (30%) were stage T1, 9 were stage T2 (30%), 12 were stage T3 (40%). Twenty seven out of the thirty tumors were correctly staged by MDCT, with an overall accuracy of 90%.

Three tumors were over staged with MDCT. In these patients, MDCT showed evidence of perinephric spread, but no infiltration of tumor cells was seen on pathology.

MDCT was able to identify correctly and localize the extension of the tumor thrombus in all of 4 patients with 100% diagnostic accuracy. Direct continuity with the renal tumor, and enhancement after administration of contrast medium were considered features of tumor thrombus.

**N Staging:** In the evaluation of lymph node involvement (renal hilar, paraaortic, aorto caval, retrocaval and paracaval lymph nodes) 20 patients (67%) were staged N0, 10 (33%) were staged N1. Twenty six patients were correctly staged (87%), 4 patients (13%) were over staged. In 4 patients with false-positive diagnoses of metastatic lymph node involvement by MDCT, the lymph nodes were larger than 1 cm but were characterized as reactive hyperplasia on pathology.

**M Staging:** Five patients (16%) had metastatic disease, and all of them were correctly staged by MDCT. The common site of metastases was the lung (66%) and axial skeleton (33%). MDCT detected all six lesions with 100% diagnostic accuracy.

**MDCT and Histopathologic Staging:** Agreement between MDCT and surgical-histopathologic staging was very good for T staging (k = 0.851), good for N staging (k = 0.40), and perfect for M staging (k = 1.00).

Agreement between MDCT and surgical-histopathologic staging was good for perinephric invasion (k = 0.8783) and perfect for tumor thrombus (k = 1.00).

| Histopathologic | MDCT   | Total |
|-----------------|--------|-------|
|                 | T1     | T2    | T3    | T4    |       |
| T1              | 9      | 0     | 2     | 0     | 11    |
| T2              | 0      | 9     | 1     | 0     | 10    |
| T3              | 0      | 0     | 9     | 0     | 9     |
| T4              | 0      | 0     | 0     | 0     | 0     |
| **Total**       | 9      | 9     | 12    | 0     | 30    |

Table 2: Histopathology and multidetector computed tomography (MDCT) staging of tumors (T)
DISCUSSION: Accurate staging at the time of diagnosis is essential to determine prognosis and formulate a therapeutic plan. With a reported accuracy of 91%, MDCT remains the most widely available and single most effective modality for staging renal cell carcinoma. The T component of the TNM classification for staging of RCC is the most important variable in predicting prognosis and survival. It is determined primarily by the size, extent of the tumor and the presence and extent of venous involvement. Evaluating the spread of the tumor into perinephric fat, and differentiation between T1/T2 and T3a stages is the most difficult aspect of T staging of RCC with spiral CT. Perinephric stranding does not reliably indicate tumoral spread, and is found in about 50% of patients with localized T1 and T2 tumors. It is caused by edema, vascular engorgement, or previous inflammation. The presence of an enhancing nodule in the perinephric fat, considered the most reliable finding of perinephric invasion, has high specificity (98%) but low sensitivity (46%). In this study twenty seven out of the thirty tumors were correctly staged by MDCT, with an overall accuracy of 90%. Three tumors were over staged with MDCT. In these patients, MDCT showed evidence of perinephric spread, but no infiltration of tumor cells was seen on pathology.
It can be concluded that the assessment of perinephric fat infiltration continues to be a problem, even with MDCT.

As renal cell carcinoma has a propensity to extend into the venous system, accurate preoperative evaluation for the presence and extent of the tumor thrombus in the renal vein and inferior vena cava is important for the surgeon to plan the appropriate surgical approach for thrombectomy, and to minimize the risk of intraoperative tumoral embolism. MDCT is accurate in detection of tumor thrombus and delineating its superior extent into inferior vena cava. In our study, MDCT correctly identified and localized the extent of the tumor thrombus in all of 4 patients with 100% diagnostic accuracy.

One of the most important prognostic factors in RCC is lymph node (LN) involvement. Life expectancy decreases considerably when nodal metastases are present, with the overall 5-yr survival rate ranging from 11% to 35%. The incidence of lymph-node metastases in renal cancer ranges from 13% to >32%, and this incidence increases with the stage of the tumor. Identification of lymph node involvement using a threshold of 1 cm remains a significant problem. Use of this criterion is neither sensitive nor specific for lymph node involvement. A cutoff value of 1 cm as the upper limit for normal nodes reveals a false-negative finding of 10% because micrometastases cannot be identified. Nodal enlargement may be caused by reactive hyperplasia, which is often associated with extensive tumoral necrosis or venous thrombosis, and may represent a reactive immune response.

In the present study twenty six patients were correctly staged (87%), 4 patients (13%) were over staged. The false-positive diagnoses of metastatic lymph node involvement by MDCT were larger than 1 cm, but were characterized as reactive hyperplasia on pathology.

RCC commonly metastasizes to the lungs and mediastinum, bones, and liver. Metastatic disease at presentation varies with the patient series but typically occurs in about one in 10 patients. Prognosis is influenced by the extent of disease at diagnosis, with a 5-year survival rate in the absence of metastases exceeding 50%; in the presence of distant metastases, the 5-year survival rate decreases to 10%. In this study, five patients (16%) had metastatic disease, and all of them were correctly staged by MDCT. The common site of metastases was the lung (66%) and axial skeleton (33%). MDCT detected all six lesions with 100% diagnostic accuracy.

CONCLUSION: The multiplanar and three-dimensional reconstruction capability of MDCT provides good delineation and characterization of the RCC tumor, including evaluation of the presence and extent of renal venous involvement. A major limitation of MDCT in staging of tumors was differentiation of T1 and T2 tumors from T3a tumors because of poor visualization of infiltration of the perinephric fat. Involvement of lymph nodes by tumor remained difficult to predict because the criterion of node size >1 cm was neither sensitive nor specific for nodal metastases.

Thus MDCT is the single most effective imaging modality for the diagnosis and staging of renal cell carcinoma. It is the only imaging test needed prior to surgical management in majority of patients. It provides unparalleled capabilities for the detection, staging, and management of primary renal cell carcinoma.
CECT images show a 10x 12 cm heterogeneously enhancing mass in the right kidney. Perinephric stranding, tumor thrombus in the right renal vein (RRV) and inferior vena cava (IVC). Numerous perinephric collaterals are also seen secondary to right renal vein thrombosis.
CECT images show a 8x9cm heterogeneously enhancing mass in the right kidney. Associated renal cysts are also seen.

Enlarged metastatic paracaval, retrocaval and aortocaval nodes are seen, few of which are necrotic and show perinodal spread.

![Fig. 4a, 4b & 4c: Renal Cell Carcinoma in the left kidney stage T3a N1M1](image)

CECT shows an 8.5x7 cm heterogeneously enhancing mass in the left kidney. Perinephric fat invasion is noted. A necrotic metastatic lymph node with is present in the aortocaval region. Metastatic lytic destruction of the right iliac bone and right sacral ala noted.

![Fig. 5a & 5b: Renal Cell Carcinoma in the right kidney stage T3aN1M0](image)

CECT show a 13.5x10 cm heterogeneously enhancing mass in the right kidney. Perinephric fat stranding is noted. Few enlarged para caval, retro caval and aorto caval nodes were seen, which appeared metastatic.

Histopathological correlation showed no perinephric invasion and the nodes were reactive. (PT2N0).
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Date of Submission: 23/08/2015.
Date of Peer Review: 24/08/2015.
Date of Acceptance: 02/09/2015.
Date of Publishing: 07/09/2015.