

Role of MRI in staging and surgical planning and its clinicopathological correlation in patients with renal cell carcinoma

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Abstract

Background and Aims: Radiological evaluation of renal cell carcinoma (RCC) is used for non-invasive staging for better surgical planning. However, the correlation of radiological staging using magnetic resonance imaging (MRI) with histopathological findings has not been done so far. The aim of this study is to assess the role of MRI in pre-operative staging of RCC in patients undergoing radical nephrectomy and nephron sparing surgery (NSS) and correlate it with histopathological findings. **Settings and Design:** This prospective observational study was conducted from February 2015 to October 2016 at a tertiary care hospital in northern India. **Methods:** MR imaging was done on 3 Tesla MR scanner (Signa Hdx General Electrics, Milwaukee, USA). Preoperative staging was based on 2010 TNM staging system. The preoperative parameters in MRI were tumor size, detection/breach of pseudocapsule, tumor extension into perirenal fat and detection of tumor venous thrombus. The staging on MRI was compared with surgical and pathological staging. **Statistical Analysis Used:** The agreement between these three staging methods was determined using the kappa statistics (0.0-0.2, poor; 0.2-0.4, fair; 0.4-0.6, moderate; 0.6-0.8, good; 0.8-1.0, excellent). **Results:** 30 patients with suspected RCC underwent NSS (n = 10) and radical nephrectomy (n = 20). Mean tumor size was 9.66 ± 2.99 cm in the radical nephrectomy group and 4.06 ± 1.16 cm in the NSS group. There was perfect agreement between MRI, surgical and pathological staging for breach of pseudocapsule ($\kappa = 1.0$, Percentage of Agreement = 100%, $P < 0.05$). In none of the patients, MRI missed extension beyond the Gerota's fascia or presence of venous thrombus. **Conclusion:** MRI staging of RCC is an accurate predictor of the surgical and pathological stage and has the potential to become a useful tool for preoperative identification of patients with RCC who can undergo NSS.

Key words: Magnetic resonance imaging; nephron sparing surgery; radical nephrectomy

Introduction

Renal cell carcinoma (RCC) is the most common malignant tumour of the kidney, accounting for 85-90% of adult renal

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Cite this article as: Lal H, Singh P, Jain M, Singh UP, Sureka SK, Yadav RR, et al. Role of MRI in staging and surgical planning and its clinicopathological correlation in patients with renal cell carcinoma. Indian J Radiol Imaging 2019;29:277-83.

Received: 13-Apr-2019
Accepted: 08-Oct-2019

Revision: 06-Oct-2019
Published: 30-Oct-2019

Access this article online	
Quick Response Code:	Website: www.ijri.org
	DOI: 10.4103/ijri.IJRI_177_19

malignancies and 1-2% of all malignancies.^[1] The worldwide incidence of RCC is 150,000 cases annually.^[2] The percentage of incidentally discovered RCC ranges from 15-60%. These tumours are generally smaller with a lower tumour stage, and therefore have a better prognosis.^[3] Currently, nephron sparing surgery (NSS) is the preferred approach for the treatment of localized renal tumours.^[4] Other minimally invasive techniques such as radiofrequency ablation (RFA) and cryotherapy are being used increasingly for the same indication.^[5]

The goal of preoperative radiological evaluation and staging of RCC is to evaluate tumour size, tumour location, presence or absence of pseudocapsule, feeding vessels, presence and extent of any thrombus in the renal vein (RV) or inferior vena cava (IVC) and to identify invasion of perirenal fat/Gerota's fascia/adjacent organs or lymph nodes. However, it is difficult to accurately predict whether NSS would be feasible for many localized renal tumours, especially those near the renal hilum.

Multidetector CT (MDCT) is the preferred modality of imaging and staging in patients with renal mass due to wider availability, high resolution, high speed of acquisition, isotropic imaging and imaging reformatting in any plane which can provide excellent anatomical details. But MDCT examination also causes exposure to ionising radiation. Use of iodinated contrast can cause nephrotoxicity and contrast reactions which may also affect the residual renal parenchymal function after NSS. Magnetic resonance imaging (MRI) is not associated with ionizing radiation and does not require iodinated contrast agent. The Gadolinium contrast is safer than iodinated contrast for kidneys with normal glomerular filtration rate (GFR).

The purpose of this study was to assess the role of MRI in pre-operative evaluation of surgical and vascular anatomy as well as staging of RCC in patients undergoing NSS and radical nephrectomy and correlate it with histopathological findings.

Methods

This was a prospective observational study conducted at a tertiary care hospital in northern India from February 2015 to October 2016 and was approved by Institution's Ethics Committee (IEC code: 2015-26-MD-EXP, dated 11/02/2015). Patients aged 18 years and older who had suspected RCC and were planned for NSS or radical nephrectomy were included in the study. The patients who were excluded included those with contraindications for MRI (claustrophobia, pacemaker or other electromagnetic or non-MR compatible implants), cardiac conditions (unstable angina, cardiac arrhythmia and congestive heart failure), allergy to intravenous gadolinium contrast media, patients who did not undergo surgery and finally where postoperative histopathological examination revealed tumour other than RCC.

MR imaging was done on a 3 Tesla MR scanner (Signa Hdx General Electrics, Milwaukee, USA). The coil used was phased array Torso PA (Body Coil) with patient in supine position. Sequences were entirely breath-hold with field coverage of area of interest and imaging protocol included pre and post contrast sequences in axial, coronal and sagittal planes including MR angiography imaging. Gadobenate dimeglumine contrast (Multihance[®]) was used at the dose of 0.1 mmol/kg of body weight, or a contrast volume of 15 mL (maximum).

MRI image analysis

The tumour diameter was measured in three planes. The largest one was chosen to represent the tumour size. The preoperative staging was based on the 2010 TNM staging system [Table 1 and Figures 1-4].^[6] The pseudocapsule

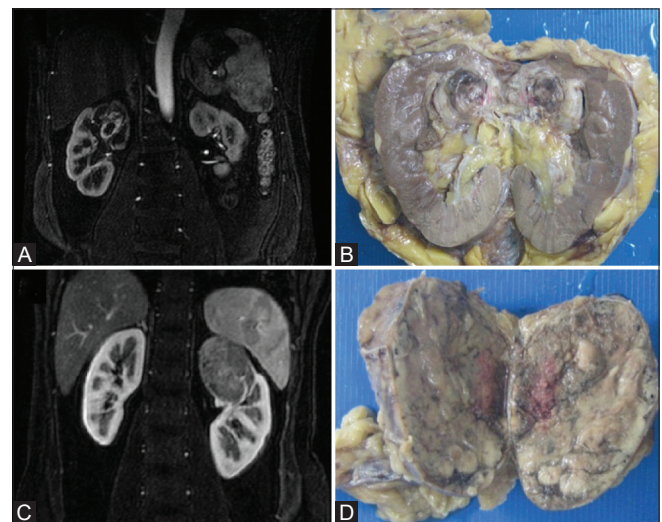


Figure 1 (A-D): Contrast MRI in coronal plane showing stage T1a tumour at the upper pole of right kidney, (A) and corresponding gross pathology specimen, (B); stage T1b tumour at the upper pole of the left kidney, (C) and corresponding gross pathology specimen, (D). Stage T2a tumour at the lower pole of the right kidney and (D) Stage T2b tumour almost entirely replacing the left kidney

Table 1: Number of cases in each stage on MRI, surgical and pathological staging

TNM stage	MRI staging (n)	Surgical staging (n)	Pathological staging (n)
T ₁	11	11	11
T _{1a}	6	7	7
T _{1b}	5	4	4
T ₂	6	6	7
T _{2a}	3	3	4
T _{2b}	3	3	3
T ₃	8	9	8
T _{3a}	5	6	5
T _{3b}	2	2	2
T _{3c}	1	1	1
T ₄	5	4	4
N ₀	21	17	25
N ₁	9	13	5

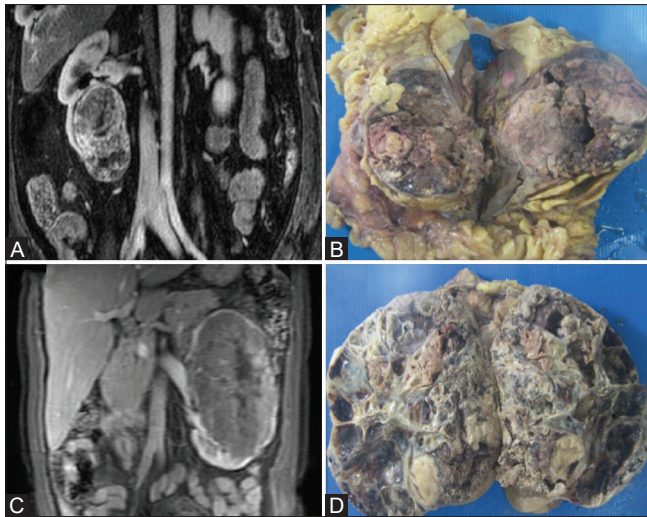


Figure 2 (A-D): Contrast MRI in coronal plane showing stage T2a tumour at the lower pole of the right kidney, (A) and corresponding gross pathology specimen, (B); stage T2b tumour almost entirely replacing the left kidney, (C) and corresponding gross pathology specimen, (D)

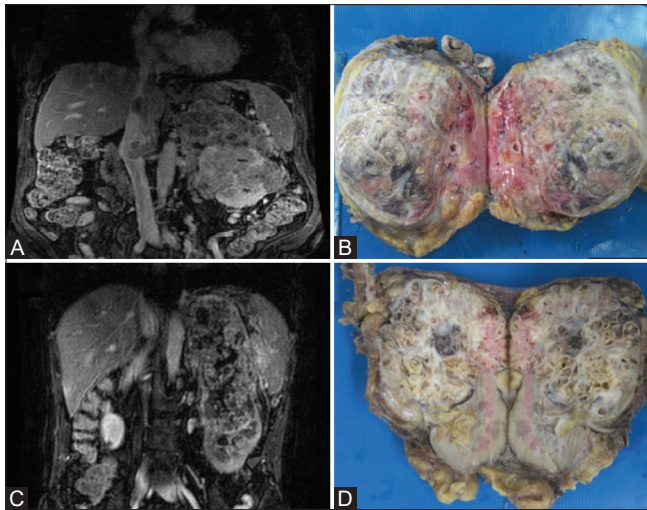


Figure 4 (A-D): (A) Contrast MRI in coronal plane showing stage T3c tumour extending into supradiaphragmatic IVC; (B) corresponding gross pathology specimen. (C) Contrast MRI in coronal plane showing stage T4 tumour extending beyond the Gerota's fascia; (D) corresponding gross pathology specimen

was also assessed for its maximum thickness, presence of breach and minimum distance from the adjacent pelvicalyceal system [Figure 5]. Perinephric fat invasion was diagnosed if the tumour-fat interface was irregular or indistinct, if thick (>5 mm) perirenal soft tissue streaks and/or nodules (≥ 5 mm) surrounded the tumour and extended into the perirenal fat and if capsular integrity was lost (disruption of the hypointense line around the kidney on T1 and T2-weighted images).

Tumour thrombus in the RV and IVC was diagnosed in case of direct continuity with the renal mass, high signal intensity, and signal heterogeneity compared with skeletal muscle on T2-weighted imaging, and contrast

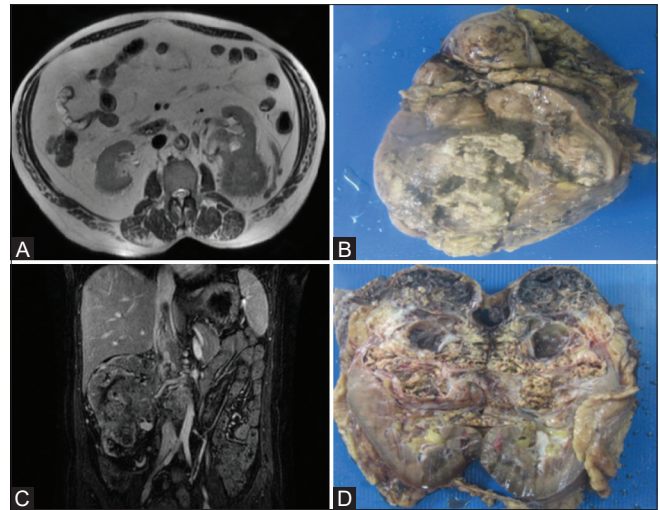


Figure 3 (A-D): (A) T2 weighted axial MR image showing stage T3a tumour involving perirenal fat. (B) Gross pathology specimen after surgery in patient shown in (A). (C) Contrast MRI in coronal plane showing stage T3b tumour extending into renal vein and infradiaphragmatic inferior vena cava (IVC). (D) Gross pathology specimen after surgery in patient shown in (C)

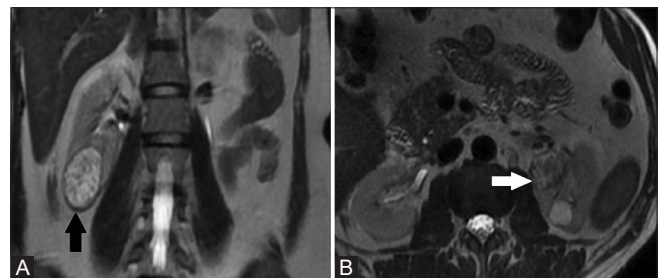


Figure 5 (A and B): (A) T2W MRI in coronal plane showing a mass at the lower pole of the right kidney. Black arrow points towards the pseudocapsule with no breach. (B) T2W MRI in axial plane showing a medially placed left renal mass. White arrow points towards breach in the pseudocapsule

enhancement. Lymphadenopathy was diagnosed if there were regional lymph nodes (nodes along the renal arteries, para-caval nodes for right-sided and para-aortic nodes for left sided RCC) which were showing diffusion restriction and/or greater than 1 cm in short axis, and/or contrast enhancement of the enlarged lymph nodes.

Statistical analysis

MRI staging was compared with surgical staging and pathological staging which was taken as the gold standard, and agreement between the staging systems was determined using the kappa statistic (0.0-0.2, poor; 0.2-0.4, fair; 0.4-0.6, moderate; 0.6-0.8, good; 0.8-1.0, excellent) using SPSS. A *P* value of 0.05 or less was considered statistically significant.

Results

A total of 30 patients with suspected RCC were finally included. Of these, 10 patients underwent NSS while

20 patients underwent radical nephrectomy. The mean age was 51.56 ± 14.74 years. There were a total of 22 males and 8 females. 24 patients had clear cell RCC, while 3 patients each had chromophobe and papillary RCC [Figure 6]. The mean size of the tumour was 9.66 ± 2.99 cm in the radical nephrectomy group and 4.06 ± 1.16 cm in the NSS group. Overall, the mean size of the tumour on MRI was 7.79 ± 3.67 cm compared to 7.35 ± 3.39 cm during surgery and 7.02 ± 3.27 on pathological examination.

There was significant agreement in detection of the pseudocapsule among the three modalities ($\kappa = 0.87$, $SE = 0.0915$, Percentage of Agreement = 93.33%, $P = 0.01$) [Table 2]. In one patient, MRI failed to detect the pseudocapsule while in another patient, MRI falsely reported a pseudocapsule compared to surgery and pathology. There was perfect agreement among all three for detecting breach of pseudocapsule ($\kappa = 1.0$, $SE = 0.0$, Percentage of Agreement = 100%, $P < 0.05$). MRI falsely reported tumour extension into the perirenal fat in 2 patients, while missing perirenal extension in one patient compared

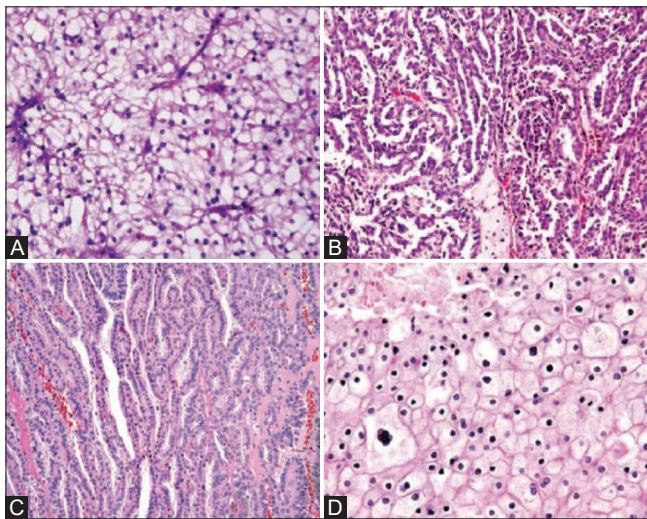


Figure 6 (A-D): Histopathological slides of renal cell carcinoma (RCC). (A) Conventional clear cell RCC. Tumour shows large uniform cells with abundant cytoplasm that is glycogen rich. (B) Papillary RCC type I. Tumour papillae are lined by short cuboidal cells with basophilic cytoplasm. Nuclei are small with few inconspicuous nucleoli. (C) Papillary RCC type II. Tumour shows papillae lined by columnar to pseudostratified cells that have striking eosinophilic cytoplasm. (D) Chromophobe RCC. Tumour cells have abundant pale flocculent cytoplasm, prominent cell membranes, perinuclear halos, and wrinkled nuclei

to surgery and pathology ($\kappa = 0.77$, $SE = 0.1256$, Percentage of Agreement = 90%, $P < 0.05$). Extension beyond the Gerota's fascia was reported in one patient on MRI in whom surgery and pathology confirmed no such extension ($\kappa = 0.87$, $SE = 0.1271$, Percentage of Agreement = 96.67%, $P < 0.05$). In none of the patients, MRI missed extension beyond the Gerota's fascia.

Venous thrombus was reported on MRI in 7 patients and all of them were found to have a thrombus during surgery as well as on pathology ($\kappa = 1.0$, $SE = 0.0$, Percentage of Agreement = 100%, $P < 0.05$). MRI did not miss any thrombus. However, one patient had a bland tumor thrombus which was confirmed on pathological examination. One patient had invasion of tumour into the ipsilateral adrenal gland which was detected preoperatively on MRI and confirmed on surgery as well as pathology, suggesting a perfect agreement. In all 20 patients undergoing radical nephrectomy as well as all 10 patients undergoing NSS, there was perfect agreement among MRI and intraoperative findings of the actual number of feeder arteries supplying the kidney/tumour. Stage wise agreement among MRI, surgery and pathology is shown in Tables 3 and 4.

Discussion

Since nephrectomy is still the only curative method in the treatment of RCC, preoperative evaluation of RCC is of great importance. Partial nephrectomy, or nephron sparing surgery (NSS), is considered the standard surgical treatment of small renal tumours.^[7] RCC of TNM class T1a without evidence of metastasis at primary staging is considered a small renal tumour: the oncologic efficacy and safety of NSS for the treatment is equivalent to radical nephrectomy.^[7] In addition, MRI is also of great importance for detection of pseudocapsule, its thickness and integrity which is particularly associated with small renal tumours and serves as a good indication for partial nephrectomy.^[8]

Both MDCT and MRI perform highly in the T-staging of local tumour extent but perform poorly in N-staging.^[9] In our study, κ test revealed excellent agreement between MRI, intraoperative staging and pathological staging which is consistent with the results of Kamel *et al.* and Spero *M et al.*^[10,11] who reported 80–85% accuracy of the MRI in staging organ confined renal cell carcinoma, as well as

Table 2: Imaging parameters on MRI and their correlation with surgical and pathological findings

	MRI findings	Surgery findings	Pathology findings	Correlation between MRI vs. Surgery (P)	Correlation between MRI vs. Pathology (P)
Mean tumour size (cm)	7.79 ± 3.67	7.35 ± 3.39	7.02 ± 3.27	0.752	0.895
Detection of pseudocapsule (yes/no)	14 cases/16 cases	14 cases/16 cases	14 cases/16 cases	0.010	0.010
Breach of pseudocapsule (yes/no)	10 cases/3 cases	10 cases/3 cases	10 cases/3 cases	< 0.001	< 0.001
Tumour extension into perirenal fat (yes/no)	9 cases/21 cases	10 cases/20 cases	10 cases/20 cases	0.015	0.015
Detection of venous tumour thrombus (yes/no)	7 cases/23 cases	7 cases/23 cases	6 cases/24 cases	< 0.001	< 0.001

Table 3: Correlation between MRI and Surgical TNM Staging

	T ₁	T ₂	T ₃	T ₄	N ₀	N ₁
κ	0.86	1.0	0.75	0.87	0.72	0.72
S.E.	0.0980	0.0	0.1335	0.1271	0.1258	0.1258
Percentage of agreement	93.33	100.00	90.00	96.67	86.67	86.67

Table 4: Correlation between MRI and Pathological TNM Staging

	T ₁	T ₂	T ₃	T ₄	N ₀	N ₁
κ	0.86	0.90	0.66	0.87	0.64	0.64
S.E.	0.0980	0.0959	0.1563	0.1271	0.1577	0.1577
Percentage of agreement	93.33	96.67	86.67	96.67	86.67	86.67

Ergen *et al.*^[12] who reported good agreement between MRI and pathological staging for T and M staging and poor for N staging.

Mean age of the patient included in our study was 51.56 years, ranging from 22 to 80 years which is in agreement with the trends.^[7] Mean of the patients in radical nephrectomy group was 55.55 years and in partial nephrectomy group was 43.60 years, which is almost a decade less. It is also noted that in Radical Nephrectomy group more numbers of patients lie toward maximum range whereas in Partial Nephrectomy Group more number of patients lie towards minimum range. Above both observations might suggest that later age of presentation is associated with more extensive tumour.

The mean tumour size measured on MRI was 7.79 cm which is marginally larger than that measured by surgeons (mean: 7.35 cm) and pathologists (mean: 7.02 cm). However, this difference was statistically insignificant. A pseudocapsule was detected in 14 cases by MRI out of which surgeons and pathologists ruled out one case. Additionally, surgeons and pathologists detected a pseudocapsule in a case which was missed on MRI. Inter investigation kappa agreement between both MRI vs. surgery and MRI vs. pathology was 0.87 which indicated excellent correlation with percentage of agreement 93.33%. Regarding the breach of pseudocapsule, there was perfect agreement between all the investigations with kappa value of 1.0 and percentage of agreement 100%. Pseudocapsule integrity is an important factor for surgical planning, as in case of an intact pseudocapsule the surgeon can simply perform an enucleation surgery resulting in maximum preservation of unaffected renal parenchyma, thus resulting in improved post-operative renal function.^[13] In our study, the mean distance of pseudocapsule from the adjacent pelvicalyceal system was zero, as in the tumour was abutting the adjacent pelvicalyceal system in all the patients.

The T-staging is determined by the tumour size and extension into perirenal fat and Gerota's fascia, invasion into ipsilateral adrenal gland, including the possibility of venous involvement comprising of renal vein, infradiaphragmatic

IVC and supradiaphragmatic IVC. For renal cell carcinoma, inter-investigation agreement in our study was excellent for T-staging: it was the best in T₂, followed by T₄, then T₁ and then T₃.

MRI over staged one T_{1a} tumour as T_{3a}; in this patient, involvement of perirenal fat was suspected. One T_{3a} tumour was also under staged as T_{1b} tumour where involvement of perirenal fat was not suspected. In the above cases, the surgeons and the pathologist did not confirm the MRI finding. The MRI findings were attributed to compression of the perirenal fat by the tumour which obscured the renal capsule making it difficult to exclude capsular invasion. Clinically, it was probably not important because both tumours were managed with radical nephrectomy. Other studies have also brought forward the challenges in distinction between RCC with and without confinement to the renal capsule on cross-sectional imaging. Catalano *et al.*^[14] diagnosed perirenal fat infiltration by MDCT on 1-mm scans with 96% sensitivity, 93% specificity, and 95% accuracy; Roy *et al.*^[15] reported 84% sensitivity, 95% specificity, and 91% accuracy in T_{3a} staging by MRI; and Ergen *et al.*^[12] concluded that MRI is a reliable method for preoperative staging of RCC. It appears that radiological distinction between confinement of RCC to the true renal capsule and extension in the perirenal fat is currently not fully reliable. Therefore, surgical planning should be individualized in patients whose cross-sectional imaging raises concern over involvement of the renal capsule and the perirenal fat.^[9,12]

One T_{2a} tumour was over staged as T_{3a} both by the radiologists as well as surgeons as extension of the tumour into renal vein was suspected by both. The pathologists found it to be a bland thrombus rather than tumour thrombus. One T_{3a} patient was also over staged as T₄ in whom tumour extension beyond the Gerota's fascia was suspected but the surgeons and the pathologist did not confirm the finding. This was due to the presence of a large renal mass abutting the surrounding organs which made it difficult to exclude extension beyond Gerota's fascia. It is important to rule out Gerota's fascia involvement as it makes the tumour locally invasive and alters surgical planning. There was no disparity noted in making decision about the invasion of ipsilateral adrenal gland and all the investigations were in perfect agreement.

Venous tumour thrombus is present in 4-10% of patients with RCC. It is important to detect the presence and extent of RV and/or IVC tumour thrombus as well as the invasion of the IVC wall preoperatively for planning subsequent surgical approach. In a small study conducted by Aslam *et al.*^[16] MRI had 100% sensitivity and 89% sensitivity in the detection of IVC wall involvement: the most reliable sign of IVC wall invasion was tumour signal both inside and outside the vessel wall, while altered signal in the vessel wall and its enhancement were nonspecific. In our study,

all seven tumours, three with RV involvement, three with RV plus IVC involvement below the diaphragm, and one with RV plus IVC involvement above the diaphragm, were correctly assessed by MRI in relation to surgery, thus with a kappa value of 1.0 and percentage of agreement 100%. But in one patient with RV thrombus, the pathologists found it to be a bland thrombus. Still, there was good correlation with respect to presence or absence of tumour thrombus on MRI in relation to pathology with kappa value of 0.90 and percentage agreement of 96.67%. With regard to the extension of tumour thrombus there was perfect agreement among all three modalities.

Regional lymph nodal involvement, classified as N-classes of the TNM system, is one of the major factors influencing the prognosis of patients with RCC: incidence of the metastasis in regional lymph nodes without distant metastasis at the same time is 10–15% and 5-year survival rate with lymph node involvement is 8–35%. Whether one uses MDCT or MRI, the commonest criterion for assigning lymph node metastasis remains size assessment.^[17] On histopathology, non-neoplastic causes of lymph node enlargement include hyperplastic or inflammatory changes related to RCC. The specificity of cross-sectional imaging for regional lymph node involvement is poor but the use of contrast agents may improve the situation. Gadolinium chelates in MRI reach lymph nodes directly via their feeding arteries and regional lymph nodes enlarged because of metastases show contrast enhancement. In addition, diffusion restriction on MRI is also a criterion for lymph node involvement. In the present study 4 cases of lymph node involvement categorized as N₀ on MRI were found as N₁ by surgeons. Furthermore, 4 cases with lymph nodes categorized as N₁ on MRI were found as N₀ by pathologists. Intraoperatively, there may be a tendency for the surgeons to assign a lymph node as N₁, especially when it is present in the region providing lymphatic drainage to the part of kidney containing the mass. In other words, the false positivity may be higher with intraoperative assessment of the lymph nodes.

In our study, regarding vascular anatomy of the kidney with tumour, perfect agreement was found between MRI and Surgery with respect to detection of number of arteries and veins supplying the kidney with tumour in all the cases. In partial nephrectomy cases, perfect agreement was found between MRI and surgery with respect to detection of the feeding artery to the tumour in all the 10 cases. Delineating the feeding artery to the tumour is of utmost importance if partial nephrectomy has been planned as it will help in preventing unnecessary vessel ligation, thus reducing chances of residual renal parenchymal ischemia, which in turn helps in preserving maximum post-operative renal function.

The present study is limited by the small number of patients. Further, the effect of preoperative imaging

characteristics on the operative variables such as the surgical approach (laparoscopic vs. open), surgical technique (radical vs. NSS), operative time and complications has not been studied. However, this is a unique study which has correlated the imaging characteristics of renal tumours with surgical and pathological characteristics and lays impetus for future research to compare the different surgical techniques based on preoperative MRI findings.

In conclusion, the present study found good agreement for MRI TNM Staging with respect to surgical and pathological findings. The use of MRI may enhance the urologist's ability to judiciously use the organ preserving surgery for patients with renal cell carcinoma.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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