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Multiphasic CT enhancement patterns of various renal neoplasms: usefulness and correlations with histopathology

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Abstract

Background: CT scan plays a major role in diagnosis of renal cancers and characterizing its different subtypes.

Aim: Our study aimed to study the diagnosed or suspicious renal mass lesions with Multi detector computed tomography and obtain information regarding their enhancement pattern in various phases of CT scan with emphasis on HU density and correlation with histo-pathological findings.

Methods and Material: Approximately 60 patients with diagnosed or suspicious renal masses were included in the study and images were examined with emphasis on enhancement patterns and density in Hounsefield units (HU) in different phases of study. The diagnosis was then correlated with the histo-pathological findings.

Results: In our study including 60 renal cell carcinoma lesions (RCC), most of them were clear cell RCC; and other types included papillary, chromophobe, and oncocytoma variants. About 5 lesions showed diagnosis other than renal cell carcinoma. Clear cell RCC showed more enhancement in arterial phase (51.5-147.5 HU) than unenhanced phase (26-104 HU) and de enhancement in venous phase (40-122 HU). Papillary RCC showed maximum enhancement in venous phase (66-117.5 HU) than unenhanced (26-99 HU) and arterial phases (55-76 HU). The pattern of enhancement in context to HU density in various subtypes of RCC vary and in comparison to clear cell RCC, each type shows variable density [Table 2].

Conclusions: Density in Hounsefield units on CT scan within the mass lesion in various phases reflects the pattern of enhancement of the mass and hence can give a clue about the type of the mass lesion.

Keywords: renal mass, CT scan, enhancement, density, hounsefield unit

Introduction

Renal cell carcinoma (RCC) is the most frequent type of renal malignancy (fifth most common) in adults. It accounts for 2% of all adult malignancies and 85% of all malignant tumours of the kidney [1]. The incidence varies from 6.0 - 8.0 per 100,000 of the population [1]. A great number of such lesions are incidentally found owing to easy and widespread use of imaging techniques these days. Imaging plays a major role in proper characterization and aids in choosing proper management. Ultrasound is the basic imaging modality to primarily diagnose renal simple cysts and to differentiate them from further complex cysts and solid lesions which require CT scan or MRI for characterization. We have tried to establish the importance of CT scan as a modality of choice for detection, characterization, staging of such lesions and to correlate the CT scan findings in the form of Hounse filed (HU) density in various phases with pathological findings.

Material and Method

Our present retrospective cross-sectional study comprised of 60 patients who underwent CT scan with diagnosed or suspicious renal masses at Department of Radio-diagnosis, Institute of Kidney Disease and Research Centre, Dr H L Trivedi Institute of transplantation Sciences, Ahmedabad, Gujarat. All of them underwent CT Urography or CT angiography on Siemens Somatom 64 Slices CT scanner with Injection of Iohexol in 60 mg/kg dose with prior written consent. About 70 – 100 ml bolus of 300-400mg/ml contrast at the rate of 3.5 mL/sec followed by 20 ml saline at rate of 2.8 mL/sec was infused. The region included was from dome of diaphragm up to termination of common iliac arteries. Slice thickness was 5 mm and the scans were reconstructed at 0.6 mm thickness. Unenhanced, Arterial, venous and excretory phases were obtained at 0 seconds, 10 seconds, 60 seconds and 7 to 10 minutes respectively. Non enhanced images were examined for presence, size, shape and position of kidney and presence of any calculus. Renal lesions under investigations were also identified on unenhanced scans and presence of hemorrhage, calcification or necrosis was looked for. Presence of fat density lesion which implied the lesion to be angiomyolipoma (AML) were excluded. Arterial phase of contrast enhanced study was used to confirm the site, size and type of lesion, presence of any associated parenchymal abnormality and peri-nephric extension. The enhancement pattern was identified as homogeneous or heterogeneous visually. The density in HU was measured at the region visibly enhancing the most with circle ROI of diameter approximately 0.5 cm^2. Three or four such measurements were taken at different sites. Vascular information was also obtained in this phase in the form of number of arteries supplying tumour bearing

kidney. Venous phase was used to identify the enhancement pattern and again HU density was taken in same manner as in arterial phase. Conscious effort was done to keep the site of measurement constant. Renal veins draining the tumour bearing kidney were examined for the number and presence of thrombus. IVC was also examined for presence and extent of thrombus. Excretory phases were used to detect the presence of involvement of PC system if any. The extent of enhancement was also measured in HU in delayed excretory phases to evaluate any delayed enhancement patterns. Arterial and venous supply were also examined in a Multi planar and curved planar reformations (MPR and CPR), maximum intensity projection (MIP), and volume rendering (VR) techniques which were used for post processing of images.

Results

In present retrospective study, including 60 patients (44 males and 16 females) with age ranging from 23 to 88 years (mean 55.8 years); 33 lesions (55%) involved right kidney and 24 lesions (24%) involved left kidney and 3 (5%) lesions were bilateral. About 12 lesions (19%) showed presence of calcification and 6 lesions (9%) had presence of internal necrosis. About 3 lesions (4%) had central scar [Table 1]. About 34 (53.96%) mass bearing kidneys had single supplying renal artery and 19(30.15%) of them had more than one. About 42 (66.67%) of mass bearing kidneys were drained by single renal vein and about 11 (17.46%) had more than one of them. About 52 lesions (82.53%) shows no evidence of associated renal vein or Inferior vena cava (IVC) thrombus. About 5 lesions (8.33%) had thrombus in draining renal vein and 3 lesions (5%) had thrombus in renal vein as well as in IVC. On histology correlations, about 45 (71.42%) were clear cell renal cell carcinoma (ccRCC); about 5 (7.93%) lesions were papillary renal cell carcinoma, 1 (1.58%) lesion was chromophobe variant of renal cell carcinoma and 3 (4.76%) lesions were oncocytoma. About 5 lesions (7.93%) showed diagnosis than renal cell carcinoma. Clear cell renal cell carcinoma showed more enhancement in arterial phase (51.5-147.5 HU) than unenhanced phase (26-104 HU) and de enhancement in venous phase (40-122 HU) [Figure 1]. Papillary renal cell carcinoma showed maximum enhancement in venous phase (66-117.5 HU) than unenhanced (26-99 HU) and arterial phases (55-76 HU) [Figure 2]. Oncocytoma showed typical central scar and more enhancement in arterial phase (77-98 HU) than unenhanced phase (40 – 75HU) and venous phase (70-81 HU). Presence of central non enhancing scar makes the diagnosis of oncocytoma very clear [Figure 3]. Chromophobe renal cell carcinoma showed maximum enhancement in arterial phase (75-121 HU) than unenhanced phase (29- 92 HU) and venous phases (47-102 HU). The pattern of enhancement in context to HU density in various subtypes of RCC vary and in comparison to cc RCC, each type of RCC shows variable density. However due to considerable variation in the number of each type of RCC in our data, no significant correlation between the enhancement pattern of papillary and chromophobe type of RCC with clear cell RCC could be achieved [Table 2].

Table 1: Patient and Lesion Characteristics

Characteristics	All Lesions	Clear Cell RCC	Papillary RCC	Chromophobe RCC	Oncocytoma	Others
Sex						
Male	44	31	4	1	3	5
Female	16	15	1		0	0
Mean Age (Y)	55.88	55.08	66.8	64	64.33	45.6
Range Age (Y)	23 - 80	25 - 76	50 - 80	64 - 64	23 - 72	60 - 70
Mean Lesion Size (cm)						
Left	7.12	7.17	-	-	5.6	6.84
Right	7.19	7.3	5.8	6.6	-	-
Range (cm)	2.4 - 20.6	2.4 - 20.6	3.8 - 16.1	5.2 - 5.2	4.2 - 7.3	5.5 - 7.7
No. of Lesions	63	48	6	1	3	5
Calcification within Lesion	12	9	1	1	0	1
Necrosis Within Lesion	6	5	1	0	0	0
Central Scar	3	0	0	0	3	0
Pathologic Tumor Stage						
T1a	5	5	0	0	NA	NA
T1b	17	16	1	0	NA	NA
T2a	4	4	0	0	NA	NA
T2b	4	3	1	0	NA	NA
T3a	12	10	1	1	NA	NA
T3b	6	5	1	0	NA	NA
T3c	0	0	0	0	NA	NA
T4	1	1	0	0	NA	NA

Table 2: Multiphasic Attenuation: Distinguishing Clear Cell Renal Cell Carcinoma (cc RCC) from other Renal Lesions.

Imaging Phase	Clear Cell RCC (n=48)	Papillary RCC (n=6)	Chromophobe RCC (n=1)	Oncocytoma (n=3)	Others (n=5)
Unenhanced	50.08 (26.5 - 104.5)	54.13 (27 - 104.5)	59.5 (59.5 - 59.5)	74.5 (45 - 91)	41.66 (35 - 49.5)
p vs clear cell RCC		0.639	0.512	0.008	0.197
Arterial	84.07 (51.5 - 122.5)	76.88 (66-98.5)	72 (72 - 72)	66.36 (49.5 - 90)	97.07 (96.5 - 97.5)
p vs clear cell RCC		0.471	0.537	0.057	0.252
Venous	80.43 (40.5 - 147)	77 (55 - 117.5)	98 (98 - 98)	81.6 (77.5 - 85.3)	67.86 (51.5 - 81)
p vs clear cell RCC		0.699	0.277	0.899	0.091

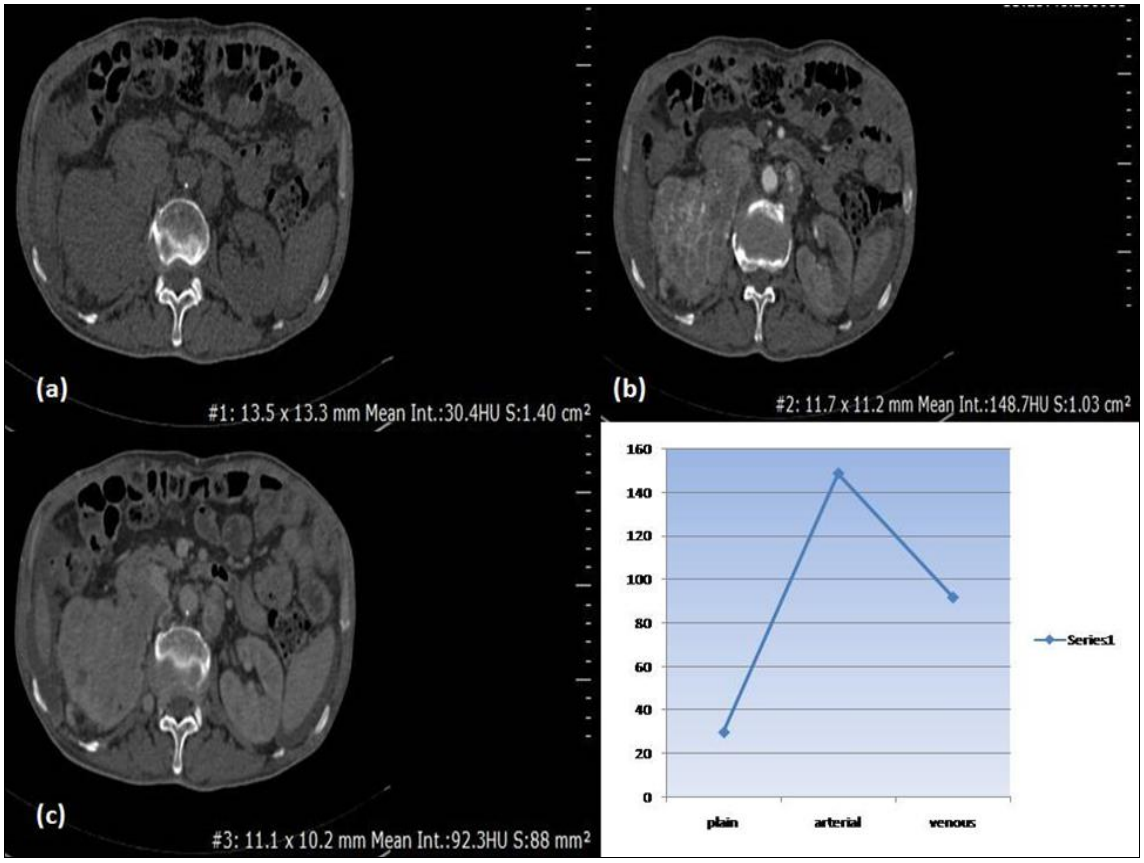

Fig 1: MDCT scan showing mass lesion involving almost whole of right kidney in pre contrast (a), arterial (b) and venous (c) phases with a graph depicting enhancement in HU density in all phases. The mass lesion shows heterogenous marked enhancement in arterial phase with de enhancement in venous phase. Histological diagnosis was clear cell renal cell carcinoma.

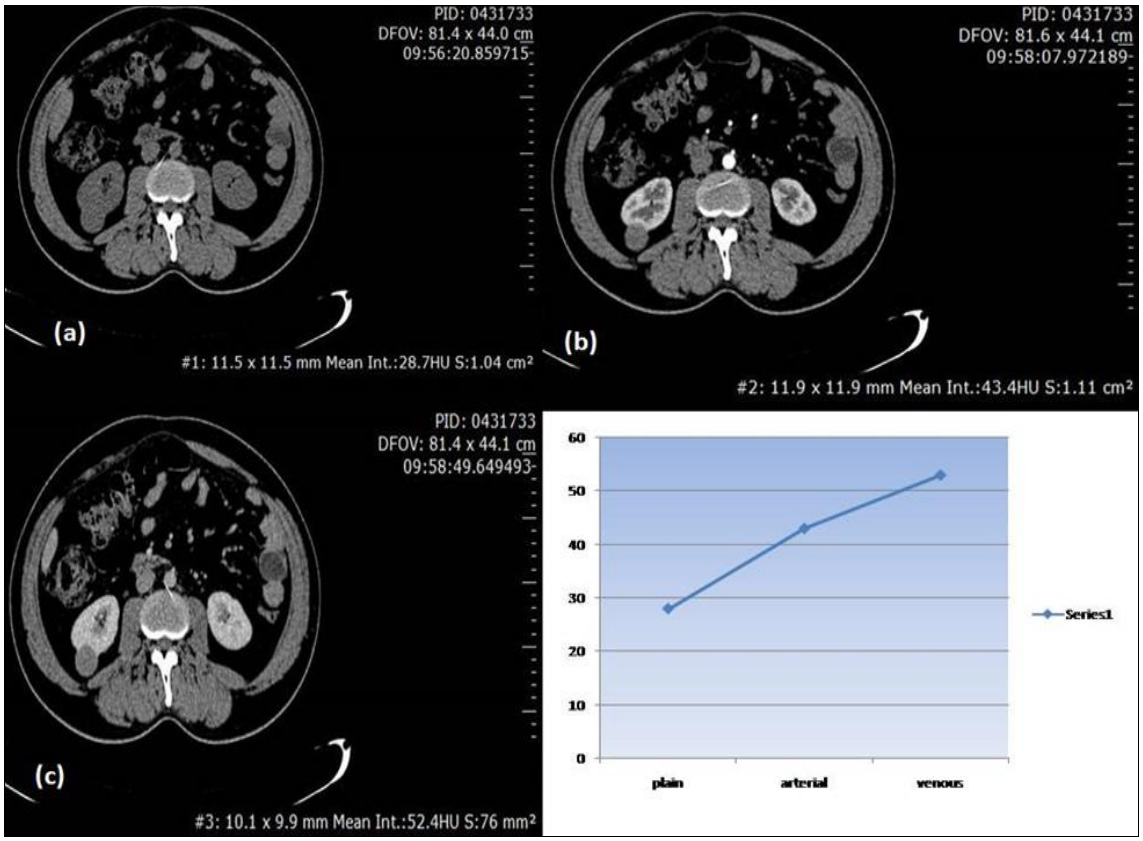

Fig 2: MDCT scan showing exophytic small mass lesion at lower pole of right kidney in pre contrast (a), arterial (b) and venous (c) phases with a graph depicting enhancement in HU density in all phases. The mass lesion shows homogeneous mild enhancement with Enhancement (in Hounsefield units) gradually increasing in later phase. Histological diagnosis was papillary renal cell carcinoma.

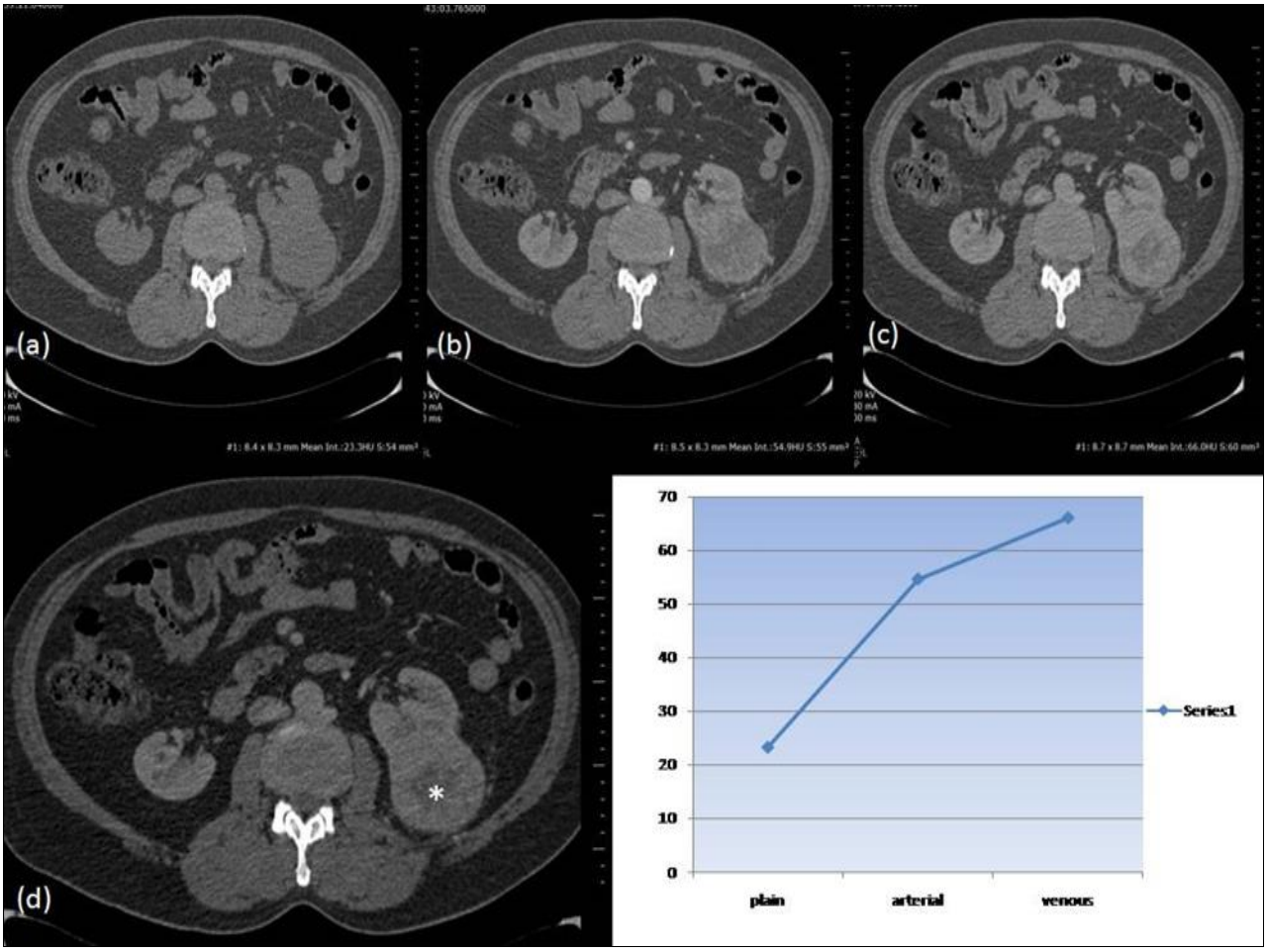

Fig 3: MDCT scan showing exophytic mass lesion in left kidney in pre contrast (a), arterial (b) and venous (c) phases with a graph depicting enhancement in HU density in all phases. The mass lesion shows homogeneous mild enhancement with Enhancement (in Hounsefield units) gradually increasing in later phase. Central non enhancing hypodense scar is seen (*). Histological diagnosis was oncocytoma

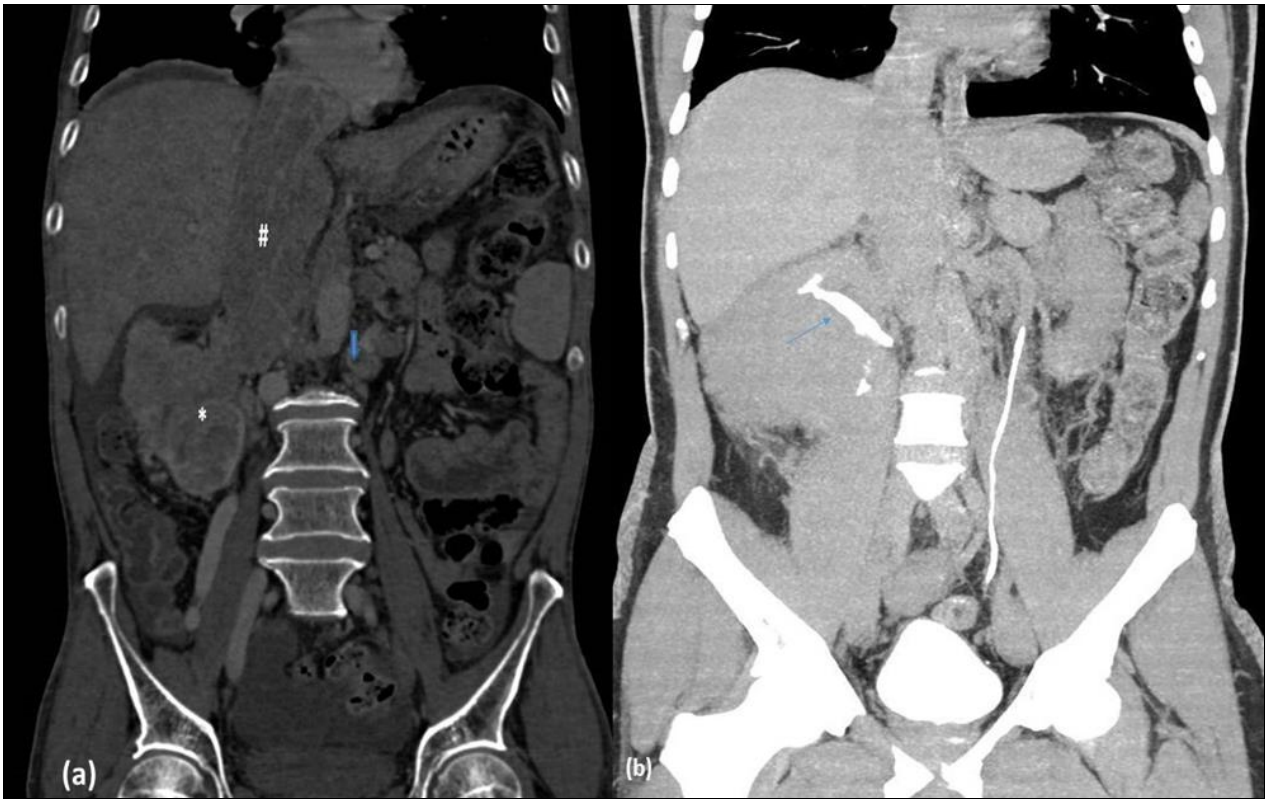

Fig 4: (a) large right renal mass lesion (*) with tumour thrombus in right renal vein, IVC (#) and left lumbar vein (thick arrow). (b) MPR reformation of another mass lesion in right kidney showing involvement of PC system (thin arrow).

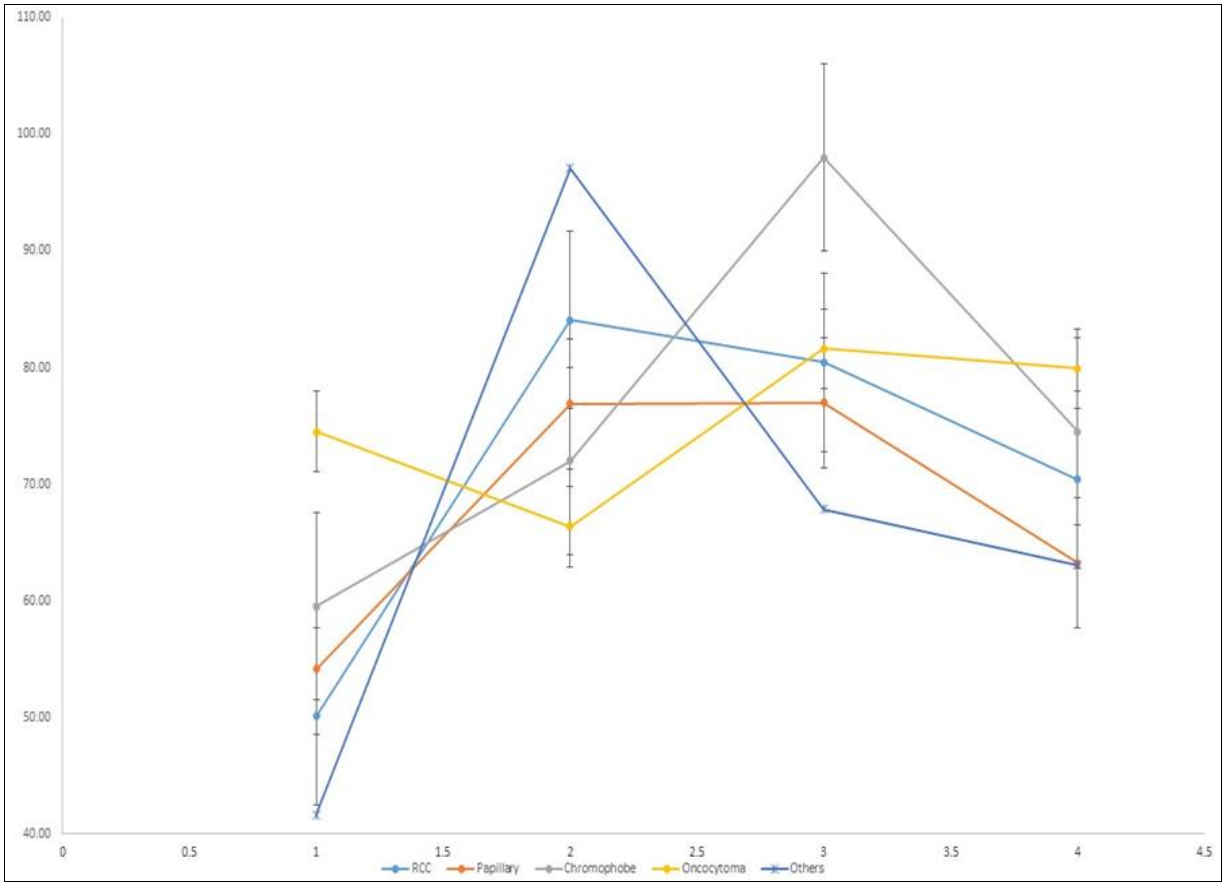

Fig 5: Chart shows multiphasic absolute attenuation of renal subtypes. Data represents mean absolute attenuation values in Hounse field units. Error bars represents standard error of mean. RCC = Renal Cell Carcinoma

Discussion

The aim of any pre-operative radio-imaging modality is to differentiate benign from malignant lesions, to adequately assess tumor size, localization of the lesion and organ confinement, to identify lymph node involvement, visceral metastases, and to reliably predict the presence and extent of any thrombus of the renal vein and IVC. Ultrasound is readily available, fast and easy, easily repeatable and cost effective means for primary detection of lesions. It has no involvement of radiation. And due to widespread use of ultrasound, asymptomatic renal mass lesions are more frequently found incidentally while imaging for some other causes. However presence of smaller lesions, operator dependency and limited visibility due to obese patients or bowel gas shadow are some of the limitations of ultrasound. CT scan is the gold standard technique for imaging lesions diagnosed or suspicious on ultrasound. It offers high resolution, reproducibility, reasonable preparation and acquisition time and acceptable cost. However risk of radiation and iodinated contrast media are some of its demerits. MRI helps in evaluation of patients where CT scan is contraindicated (pregnant patients and patients allergic to CT iodinated contrast medium) and helps in serial monitoring of patients post operatively. Lesions which are indeterminate on CT scan can undergo MRI for characterization. FDG PET scanning helps to diagnose metastatic lesions and can also diagnose post-operative recurrence of lesions. The primary step in the *work-up of renal masses* is to differentiate benign cysts from more complex cysts or solid masses. Simple cysts are easily and confidently diagnosed by Ultrasound. However CT scan may be needed to diagnose more complex cysts or enhancing solid mass lesions. Simple cysts show HU density as of water i.e <10 Hu on CT scan. Complex cystic lesions show high density or calcification foci on non-enhanced images and internal septations or mural nodules which enhance on administration of contrast media. Solid renal mass contains minimal or no fluid and show vascularized tissue prominently which shows enhancement on CT scan post administration of contrast media. Many of such lesions show internal non enhancing necrotic regions or presence of hemorrhage which can aid in diagnosing the lesion and may help to predict the type of mass lesion. As the mass is diagnosed to be a solid renal mass; many of the *differentials* are to be kept in mind. Renal cell carcinoma (RCC), oncocytoma and transitional cell carcinoma (TCC) are the differentials which need surgery. Angiomyolipoma (AML), lymphoma, metastasis and other pseudo tumours do not always need surgery and can be differentiated from the rest of them through imaging findings and meticulous clinical history. Infiltrating lesions include lymphoma, invasive transitional cell carcinoma, RCC and metastasis. All these lesions imitate each other on imaging but are quite different clinically and histologically. Infiltrating lesions including transitional cell carcinoma, metastasis and sarcomatoid type RCC cause reduced nephrographic regions with ill-defined margins; here the kidney enlarges but contains its normal shape. Hence, careful clinical history and imaging techniques combination is important for diagnosis. Some feasible cases may also be offered biopsy to confirm the diagnosis. Lymphoma can show varied appearances and most frequently it appears as bilateral renal

masses. In presence of associated systemic lymphoma; the diagnosis is easily done. Lymphoma invades the kidney through renal sinus or surrounds the kidney. Rarely may it show up as solitary renal mass. Presence of systemic lymphoma should be sought of in such cases. Transitional cell carcinoma (TCC) is usually detected as filling defect in collecting system. However some of them infiltrate in to renal sinus and parenchyma; which are very aggressive and show poor prognosis. The differentiation of Infiltrating Lymphoma and TCC is very crucial as the treatment option differs in both of them. Metastasis to kidney presents as multiple bilateral renal masses with known primary lesion. Moreover, renal pseudo tumours, inflammatory masses and vascular lesions are other causes which are confused with renal masses. Proper clinical history and imaging techniques can aid to differentiate them. Vascular anomalies like aneurysm or arteriovenous fistula may be seen as enhancing renal mass on enhanced scans. Enhancement same as adjacent vasculature and location can be a clue for their diagnosis. Moreover enlarged draining vein or feeding artery can also be seen [2]. CT scan offers valuable *additional information* about multi-focality, lymph node involvement, adrenal gland involvement, visceral metastasis and presence and extension of tumour thrombus. The incidence of multi-focality ranges between 4.5 to 25% and it is major source of local recurrence after excision of the lesion. Kopka *et al* reported that evaluation of unenhanced CT scan together with enhanced corticomedullary and nephrogenic phases results in 100% sensitivity for the detection of multifocal lesions [3]. The overall 5 year survival rate for Robson stage II RCC is 43-100% however it is as low as 8-35% once lymph nodes are involved. Catalona *et al* reported that using MDCT, all patients with synchronous lymphadenopathy at the time of nephrectomy were identified; the false positive rate due to reactive hyperplasia was reduced to 6.3% [4]. Metastatic spread to ipsilateral adrenal gland occurs in 1.2-8.5% of patients with RCC. Presence of metastatic disease, vascular invasion and multi-focality are some of independent risk factors which may arise suspicion of adrenal gland metastases. About 15-25% of patients show some degree of venous invasion. The cranial extent of tumour thrombus is important to report which helps to plan the surgical approach. Unenhanced scans show presence of calcification within the lesion which is thin and peripheral in benign lesions and chunky and dense in malignant lesions. Cysts which show high density (in the range of ≥ 40 HU) can cause suspicion for RCC and those lesions have to be scanned for enhancement in further phases. Hypo vascular hemorrhagic cysts can also cause confusion as papillary carcinoma if unenhanced scans were not taken. In plain unenhanced CT scan images, presence of fat containing regions can be effectively excluded. Such regions show density in the range of -30 to -70. And they are mostly benign angiomyolipoma; and those were excluded from our study. Pooler *et al* reported that Attenuation values on unenhanced CT in pathologically proven RCCs showed 100%(193/193) of RCCs had regions measuring 20 to 70 HU density and 72.5% (140/193) of pathologically proven tumors were completely within the 20 to 70 HU range [5]. First post contrast phase is arterial phase which shows maximum cortical enhancement as the contrast remains mostly within the renal cortical capillaries. In arterial phase maximum cortical enhancement ranges from 147 ± 41 HU and medullary enhancement ranges from 56 ± 25 HU. In this phase corticomedullary lesions are seen more accurately and arterial structures are seen which can aid in pre-operative planning. Very small cortical lesions can be missed if only this phase is taken. Papillary renal carcinoma shows lesser enhancement in this phase as compared to other subtypes of renal carcinoma. In arterial phase, kidney enhances homogeneously so, heterogeneously enhancing lesions are more easily depicted on this phase. Excretory or delayed phases do not have any primary advantage but they help to comment upon the status of involvement of PC system. Involvement or splaying of calyces, obstruction or displacement of ureters and bladder can be commented upon in those scans. Pre-operative knowledge of PC system involvement can minimize the post-operative complications such as urinary fistula or urinoma. *Determination of enhancement* is the most criteria used to differentiate renal masses. It depends on various factors like amount and rate of the contrast material injection, imaging delay and nature of the tissue within the mass lesion. The tumours which are hyper vascular will enhance considerably and hypo vascular lesions will enhance to a lesser extent. Enhancement is measured in Hounsefield units measured on unenhanced and contrast enhanced images. A difference of 10 HU in enhancement of two phases was earlier considered significant. However this limit has been changed to 15-20 HU these days [6, 7, 8, 9, 10]. While measuring enhancement Region of interest (ROI) on same areas of mass should be taken in all phases if possible. Masses with cystic or necrotic areas require multiple small ROI measurements. The degree of enhancement is quite useful for differentiating various mass lesions however possibility of pseudo enhancement should also be kept in mind. Sometimes simple renal cysts may exhibit enhancement more than 10 HU on enhanced scans which can be misdiagnosed as neoplasm. This pseudo enhancement is due to image reconstruction algorithm used to adjust beam hardening effects [6, 9, 10]. Pseudo enhancement is mostly seen when the cyst is surrounded by renal tissue and it is seen during peak renal parenchymal enhancement. Such lesions are mostly < 2 cm in diameter and are completely intra renal in location. When such a mass in question measures ≤ 10 HU on unenhanced images; pseudo enhancement should be considered. When the mass shows ≥ 10 HU on unenhanced images and shows approximately 10-15 HU enhancement on post contrast images; differentiation of pseudo enhancement of benign cyst and true neoplastic lesion cannot be done and further investigations are required. When a mass measures ≤ 20 HU on unenhanced images; Simple cyst may be the possibility which can be diagnosed on ultrasound but if it measures ≥ 20 HU, high attenuating cyst or solid renal neoplasm may be considered. High attenuating cyst with no blood or debris within it may be easily diagnosed on ultrasound. Otherwise further imaging with MRI must be done. Knowledge of histologic type of renal cell carcinoma influences the preoperative and operative strategies. As renal papillary carcinoma shows better prognosis; patients with higher surgical risks can be observed and choose a minimally invasive strategy such as radiofrequency or cryotherapy [11]. Also better operation planning can be done in such cases. The operating surgeon also gets help if he knows the type of tumour as he must expect more bleeding in hypervascular renal clear cell carcinoma rather than hypovascular renal papillary carcinoma. Palliative procedures like radiofrequency

ablation or cryotherapy also demands prior knowledge of renal mass type. Moreover renal clear cell carcinoma might be safer to undergo embolization before planned curative treatment to reduce the risk of bleeding. Radiofrequency ablation and cryotherapy do not provide any histopathological material to work on; so prior information through CT scan helps a lot for classification [11]. Multiple phases of MDCT will help to differentiate enhancement patterns of various subtypes of renal cell carcinoma before and after contrast injection. Instead of evaluating single phase, multiple phasic evaluation should be done for characterization of mass lesion [12].

Conclusion

Imaging plays a key role in diagnosis, staging and follow up of renal cancers. Each available modality has its own merits and demerits. Ultrasound is the basic investigation which can primarily exclude benign cystic lesion and diagnose more complicated or solid lesions. CT scan further can help in characterization and helps in staging the lesions pre-operatively and for follow up of lesions post operatively. Pattern of enhancement of the lesion can give a clue about the subtype of the lesion and can help in further management.

Limitation of the study was smaller sample size of different subtypes of renal cell carcinoma. So that we could not get significant *p* value for enhancement (in HU density) in various phases between each subtype.

Main points

- Various phases must be taken during contrast enhanced CT scan for evaluation of renal carcinoma
- Enhancement pattern in terms of hounse field units within the lesion is useful in differentiating various subtypes
- Clear cell renal cell carcinoma shows enhancement in arterial phase with de-enhancement in venous phase, whereas papillary renal cell carcinoma shows more enhancement in venous phase.

Summary

In this study we want to highlight the importance of various phases of CT scan in correlation to enhancement patterns of various sub types with emphasis on Hounse field density within the lesion and to correlate it with histopathological findings.

Abbreviations

MDCT- multi detector computed tomography
RCC– Renal cell carcinoma
MRI– Magnetic Resonance Imaging
HU- Hounsefield Unit
AML- Angiomyolipoma
IVC- Inferior Venacava
PC system- Pelvi calyceal system
FDG-PET– Fluorodeoxyglucose - positron emission tomography
TCC- Transitional cell carcinoma
ROI- Region of interest

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