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ROLE OF TRIPLE PHASE CT IN EVALUATION OF FOCAL LIVER LESIONS IN NON CIRRHOTICS

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ABSTRACT

Focal liver lesions are discrete abnormalities arising within liver and are increasingly being discovered with the widespread use of diagnostic imaging modalities. Triple phase CT has become the primary imaging modality for focal liver lesions. It is an effective aid in determining the number, location, and nature of such lesions and monitoring their size over time. This study was done to evaluate the usefulness of triple phase CT in detection and characterization of focal liver lesions. Patients are kept nil orally 4 hrs prior to the CT scan. Axial plain sections were taken from the level of lung bases to the level of ischial tuberosities. After contrast administration, Sections were taken in HAP, PVP and Delayed phases in craniocaudal direction from the superior margin to the inferior border of the liver. Dynamic viewing of all reconstructed images is done. Later the lesions are confirmed by biopsy/surgery/usg/follow-up as and when required. Appearance of each lesion in each phase was described on the basis of attenuation and homogeneity of the lesion in comparison to the liver parenchyma in that phase. Of the total 160 focal liver lesions seen in 50 patients, there were 114 hypo vascular lesions accounting for 71.2% of the total lesions and 46 hyper vascular lesions accounting for 29.8% of the total lesions. In our study we had 11 patterns of enhancement, four of the 11enhancement patterns were always due to benign lesions, another five of 11 enhancement patterns were always due to malignant lesions, and other two of the 11 enhancement patterns were due to both malignant and benign lesions. In our study hypo vascular lesions were best detected during PVP and hyper vascular lesions in HAP. The triple phase CT enhancement patterns were 100% sensitive and specific in diagnosing all cases of Abscess, Cysts and intrahepatic cholangiocarcinoma. The sensitivity of Triple phase CT enhancement patterns in diagnosing HCC is 84.3%, Hemangioma 93.0%, FNH 75% and Metastases 6%. There was 100% specificity in diagnosing all the cases only when the individual lesion had typical enhancement pattern. The PVP images are essential for detection of hypo vascular lesions. HAP images are helpful in detecting hyper vascular lesions. Characterization of focal liver lesions based on the enhancement patterns was satisfactory. Triple phase CT of liver is a standardized CT procedure, enables in detection and characterization of focal liver lesions.

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INTRODUCTION

Focal liver lesions are discrete abnormalities arising within liver and are increasingly being discovered with the widespread use of diagnostic imaging modalities [1]. Differentiation of various liver lesions is considered to be critical for determining the treatment options [2]. Consequently, the preferred liver imaging technique should comprise high sensitivity & specificity for lesion detection with good ability for lesion characterization and to differentiate lesions that do need further diagnostic tests / treatment from those lesions that do not. To meet these requirements, a Computed Tomography (CT) protocol was developed to image the entire liver in arterial, portal, and equilibrium phases.

Triple phase CT has become the primary imaging modality for detection and characterization of focal liver lesions. It is an effective aid in determining the number, location, and nature of such lesions and monitoring their size over time [3]. In patients with cancer, the accurate detection of metastatic disease at the time of diagnosis or during the course of treatment remains crucial to management of the disease [4]. CT has assumed primary role in evaluating hepatic masses. Despite increased competition from Magnetic Resonance Imaging over last decade, role of diagnosis of diseases of liver has not been significantly affected. Besides the general availability of the method, the dominance of CT is primarily due to its excellent visualization of anatomic relationship and of liver position relative to adjacent organs. This study is an effort to assess the role of Triple phases CT in detection and characterization of focal liver lesions and help in deciding further course of management.

MATERIALS AND METHODS

Data for the study was collected from 50 patients attending the department of Radio Diagnosis of NRI Medical College, Chinakakani, Guntur, with clinically suspected focal liver lesions, or in case where previous imaging depicted focal hepatic lesions with non specific appearance. A prospective correlation study was conducted over a period of two years (September 2013 to September 2015) on these fifty patients aged between 20-80yrs.They were evaluated with 16 slice MDCT (GE HEALTH CARE SYSTEMS) and findings were correlated with biopsy/surgical findings where ever applicable. The conspicuity and enhancement patterns of individual lesions after the CT examination was noted and these findings were correlated with histopathology/surgical findings USG/follow-up as applicable.

TRIPHASIC CT IMAGING OF LIVER:

Patients were kept nil orally 4 hrs prior to the CT scan to avoid complications while administrating contrast medium. Risks of contrast administration were explained to the patient and consent was obtained prior to the contrast study. Routine anteroposterior topogram of the abdomen was initially taken in all patients in the supine position with the breath held. Axial sections of 5 mm thickness were taken from the level of lung bases to the level of ischial tuberosities. In all cases plain (unenhanced) scan was followed by intravenous contrast scan in suspended inspiration. For contrast enhancement, 18G Vasofix (indwelling catheter) was placed in antecubital vein and dynamic injection at a rate of about 80-100cc of non ionic contrast material (Ultravist: Iopromide; 300mg iodine/ml) was given initially.

Sections were taken in hepatic arterial phase (HAP) (40s), portal venous phase (PVP) (60s) and delayed (3-5minutes) phases in craniocaudal direction from the superior margin to the inferior border of the liver after contrast administration. Post study reconstructions were done at 2.5 mm. Sagittal and coronal reconstructions were made wherever necessary. Newer techniques in Multislice CT like curved planar reformatting, volume rendering, Maximum and Minimum Intensity Projections were done as and when necessary. The magnification mode was commonly employed, and the scans were reviewed on a direct display console.

IMAGE INTERPRETATION

Dynamic viewing of all reconstructed images was done. In the present study, firstly the unenhanced, HAP, PVP and delayed images were reviewed for presence of focal liver lesions. Secondly the CT appearance of each lesion in each phases (unenhanced, HAP, PVP and delayed images) were characterized based on enhancement patterns and its attenuation compared with that of the liver parenchyma in that phase. Lesions were broadly grouped as hyper vascular or hypo vascular relative to the surrounding parenchyma. Later the lesions were confirmed by biopsy/surgery/USG/follow-up as and when required.
In some patients with multiple lesions biopsy was performed on only two lesions, rest with similar CT appearance was assumed to be the same lesion. If the lesion did not show any change in size after minimum of six months, then the lesion was presumed to be benign. If the number of lesions were >10, then analysis of 2 most representative lesions was performed using the combination of all the phases.

The size and consipiquity of lesions on each phase were noted. Lesion consipiquity was graded as, 0-Not Visualized, 1-Visualised, and if "Visualized" as 2-Good and 3-Excellent.

Appearance of each lesion in each phase was described on the basis of attenuation and homogeneity of the lesion in comparison to the liver parenchyma in that phase and was expressed as one of the five possible states

a) Area of water attenuation, homogenous: ***hypo*** **(cyst)**
b) Area of soft tissue attenuation, slightly in homogenous: ***hypo***
c) Area of mixed attenuation but hypoattenuation than

the arterial system: ***mixed***

d) Area of hyperattenuation but less than the arterial system: ***hyper***

e) Isoattenuating compared to the arterial system: ***arterial or A***

The pattern of enhancement is a three pattern name that includes appearance of lesion in each phase **(eg; *hypo/hypo/hypo*).** Additional patterns of subtype enhancement in arterial phase like peripheral puddles, variegated, continuous hyperattenuating rim, incomplete rim and cleft were also considered.

Statistical Methods:

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Repeated measures analyses of variance were conducted and analyzed by paired t test.

The conspicuity of lesions in each phase was compared by student t test. A *p* value less than 0.05 was considered statistically significant at the 95% confidence interval.

Chi-square test /Fisher Exact test has been used to find the significance of association of CT scan findings with Final diagnosis, Diagnostic statistics such as sensitivity, Specificity, PPV, NPV and Accuracy has been used to find the correlation of CT scan with final diagnosis.

RESULTS

Regarding age and gender distribution of individual focal liver lesions in our study: maximum percentage of patients was in the age of 50-59 years (28%), there was mild male preponderance (58%), when compared to females who accounted for (42%) of cases (Table 1 & 2).

Out of 160 focal liver lesions studied in 50 patients, 120 were found to be malignant (75%) focal liver lesions and 40 lesions were found to be benign (25%) focal liver lesions (Table 3). Overall most common malignant focal liver lesion was metastases accounting for 111 of the lesions. 50% of the total metastases were seen in age range of 60-80 years. 80% cases of hepatocellular carcinoma (HCC) were seen in range of 60-80 years. The youngest patient with HCC was 55 years old male patient and the oldest patient was 75 years old male patient. 2 patients with intrahepatic Cholangiocarcinoma (CCA) were in the range of 65-75 years. Of the patients with benign lesions, haemangiomas were the most common lesions accounting for 17 lesions, followed by cysts accounting for 12 lesions. Abscess was seen in 5 patients, FNH in 3 patients, adenoma in 1 patient.

Regarding gender distribution of focal liver lesions in our study: there was mild male preponderance (58%), when compared to females who accounted for (42%) of cases. Regarding gender distribution among individual abnormality in our study, there was male preponderance in HCC (80%) and metastases (63.3%) when compared to females. Two cases of Cholangiocarcinoma were reported, one in each gender. All cases of Adenoma, FNH, and most of the cases of Hemangiomas (60%) were seen in females. All cases of Abscess and most of the cases of Hydatid cyst (75%) were seen in males. Four cases of simple cysts were reported, two in each gender.

In our study, there were 114 hypo vascular lesions accounting for 71.2%, and 46 hyper vascular lesions accounting for 29.8% of total lesions (Table 4). Of the 114 hypo vascular lesions, 91 lesions were metastases accounting for 79.8%, of which gastrointestinal malignancies were the leading primary (Table 5). Cysts were most common benign hypo vascular lesions accounting for 12 lesions (10.5%).

Of the 46 hyper vascular lesions, 20 lesions were metastases (43.4%) and 13 lesions (28.2%) were haemangiomas (Table 6). Carcinoids and GIST were the primary malignancies contributing for hypervascular metastases. Few of hypovascular lesions are depicted in the figure 1. Few of hypervascular lesions are depicted in figure 2.

As far as size is concerned, in our study 66 lesions (41.2%) were in the range of 1-3 cms accounting for maximal lesions (Figure 3). Overall there were 11 enhancement patterns of focal liver lesions in Triphasic CT. Five were hypovascular patterns and six were hypervascular enhancing patterns. The five hypovascular enhancing patterns were hypo/hypo (cyst)/hypo, hypo (rim)/hypo (cyst)/hypo, hypo/hypo/hypo, hyper (rim)/hypo/hypo and hypo/hypo /hyper. The six hypervascular enhancing patterns were A(puddles)/A/A,A/A/A(cleft), A(variegated)/ A/A (capsule), hyper(incomplete)/A/A, hyper/A/A and mixed/mixed/mixed. These enhancement patterns and their importance in arriving at final diagnosis were depicted in tables 7 and 8.The Triphasic CT enhancement patterns of benign and malignant lesions were shown in the tables 9 and 10.

The Triphasic CT enhancement patterns were 100% sensitive and specific in diagnosing all cases of Abscess, Cysts and intrahepatic CCA. The sensitivity of Triphasic CT enhancement patterns in diagnosing most of the cases of focal liver lesions is mentioned in the brackets of the individual lesion concerned, in HCC (sensitivity-84.3%), Haemangioma (sensitivity-93.0%), FNH (sensitivity-75%), Metastases (sensitivity97.6%). There was 100% specificity in diagnosing all the cases only when the individual lesion had typical enhancement pattern. 100% sensitivity and specificity for intrahepatic CCA observed in our study was due to very small sample size and larger size (>3cm) of the lesion (Table 11).

Table 1. Age distribution of patients studied

Age	Frequency	Percentage
20-29	6	12
30-39	2	4
40-49	5	10
50-59	14	28
60-69	12	24
70-80	11	22
Total	50	100

Table 2. Gender distribution of patients studied

Gender	Number	Percentage
Male	29	58
Female	21	42
Total	50	100

Table 3. Distribution of Benign/Malignant focal liver lesions of the total lesions

Group	No of lesions	Percentage
Benign	40	33
Malignant	120	66
Total	160	100

Table 4. Distribution of the Hypo/Hyper vascular liver lesions of total lesions

Group	Number	Percentage
Hypo vascular lesions	114	71.2
Hyper vascular lesions	46	29.8
Total	160	100

Table 5. Distribution of Benign/Malignant Hypo vascular lesions

Group	Number	Percentage
Cyst	12	10.5
Abscess	7	6
Haemangioma	4	3.5
Metastases	91	79.8
Total	114	100

Table 6. Distribution of Benign/Malignant Hyper vascular lesions

Group	Number	Percentage
Haemangioma	13	28.2
FNH	3	6.5
Adenoma	1	2.1
HCC	7	15.2
Cholangiocarcinoma	2	4.2
Metastases	20	43.4
Total	46	100

Table 7. Clinical importance and correlation with final diagnosis in hypo vascular lesions

Enhancement patterns	Malignant lesions			Benign lesions		
	No	%	Diagnosis	No	%	Diagnosis
Hypo/Hypo(cyst)/Hypo (n=12)	-			12	100	Cysts
Hypo(rim)/Hypo(cyst)/Hypo (n=7)	-			7	100	Abscess
Hypo/Hypo/Hypo (n=83)	79	95.1	Metastases	4	4.9	Haemangioma
Hyper(rim)/Hypo/Hypo (n=12)	12	100	Metastases	-		
Hypo/Hypo/Hyper (n=10)	10	100	Metastases	-		

Table 8. Clinical importance and correlation with final diagnosis in hyper vascular lesions

Enhancement patterns	Malignant lesions			Benign lesions		
	No	%	Diagnosis	No	%	Diagnosis
A(puddles)/A/A	-			13	100	Haemangioma
A/A/A(cleft)	-			2	100	FNH
A(variegated)/A/A	6	100		-		
Hyper(incomplete)/A/A	2	100	Cholangio carcinoma	-		
Mixed/mixed/mixed	5	100	Mets	-		
Hyper/A/A	1	5.5	HCC	1	5.5	FNH
	15	83.3		1	5.5	Adenoma

Table 9. Observed enhancement patterns of benign lesions

Diagnosis	No	%	Enhancement Pattern
Cysts	12	100	Hypo/Hypo(cyst)/Hypo
Abscess	7	100	Hypo(rim)/Hypo(cyst)/Hypo
Haemangiomas	13	76.4	A(puddles)/A/A
	4	24.6	Hypo/Hypo/Hypo
FNH	2	66.6	A/A/A(cleft)
	1	33.3	Hyper/A/A
Adenoma	1	100	Hyper/A/A

Table 10. Observed enhancement patterns of malignant lesions

Diagnosis	No	%	Enhancement Pattern
Metastases	79	71.1	Hypo/Hypo/Hypo
	12	10.8	Hypo(rim)/Hypo/Hypo
	10	9	Hypo/Hypo/Hyper
	15	13.5	Hyper/A/A
	5	4.5	Mixed/Mixed/Mixed
HCC	6	85.7	A(variegated)/A/A(capsule)
	1	14.3	Hyper/A/A
Cholangio carcinoma	2	100	Hyper(incomplete)/A/A

Table 11. Correlation of CT enhancement patterns in diagnosis of focal liver lesions with final diagnosis – an Evaluation

	Sensitivity	Specificity	PPV	NPV	Accuracy	P Value
Abscesses	100	100	100	100	100	<0.001
Adenoma	-	100	-	99.6	99.6	<0.003
Cysts	100	100	100	100	100	<0.001
HCC	84.3	100	100	98.8	98.9	<0.001
Haemangioma	93	100	100	98.1	98.1	<0.001
FNH	75	100	100	99.6	99.6	<0.001
Intrahepatic Cholangiocarcinoma	100	100	100	100	100	<0.001
Metastases	97.6	100	100	97.9	98.9	<0.001

Figure 1. CT images of simple cyst, hydatid cyst, Metastases from gastric malignancy

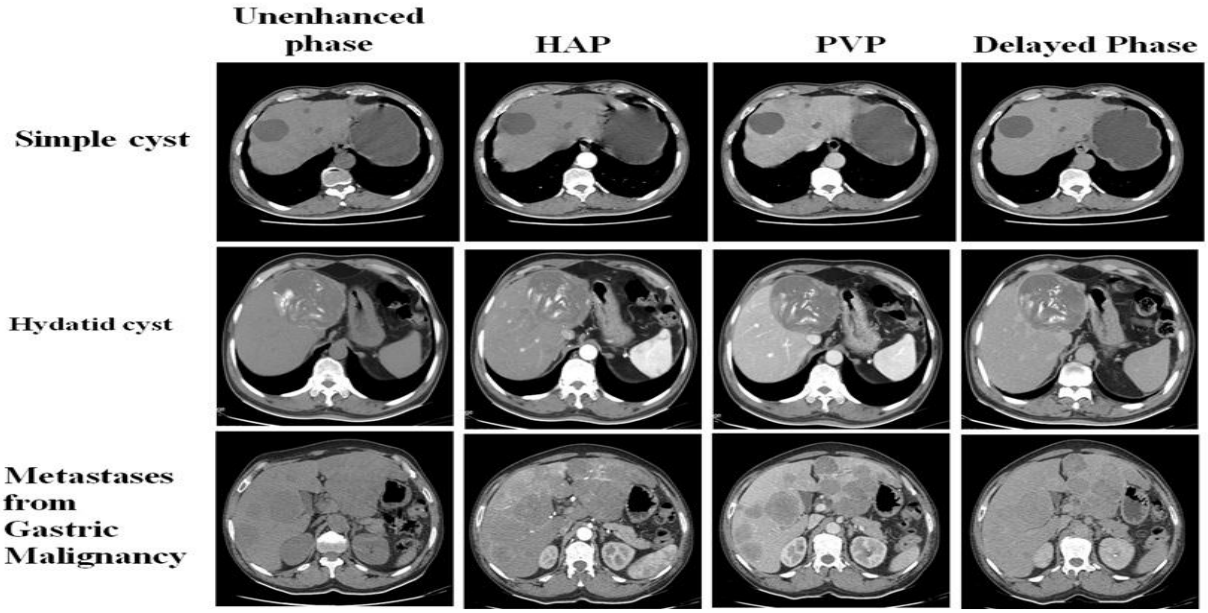


Figure 2. CT images of FNH, Haemangioma, Hepatocellular carcinoma, Intrahepatic cholangiocarcinoma, Metastases from carcinoid

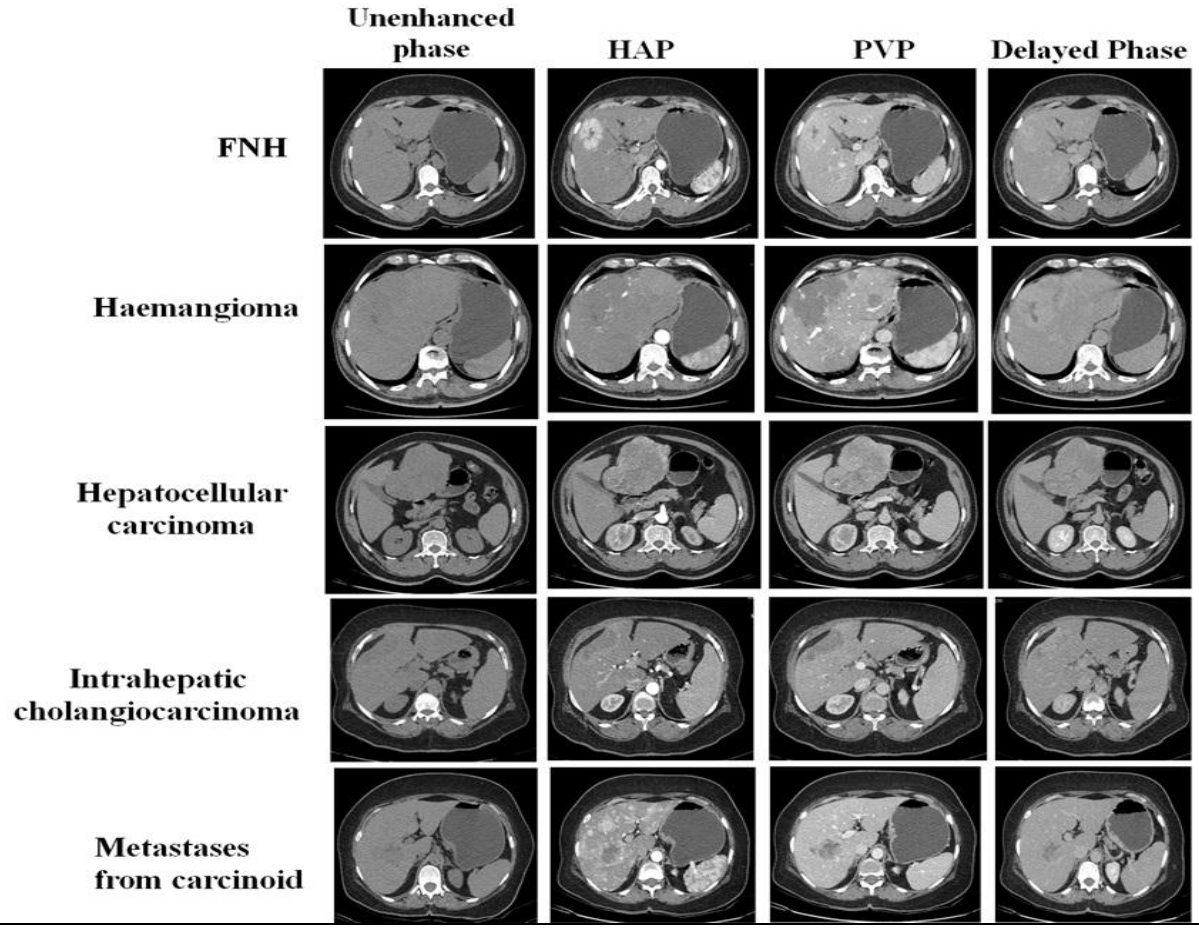
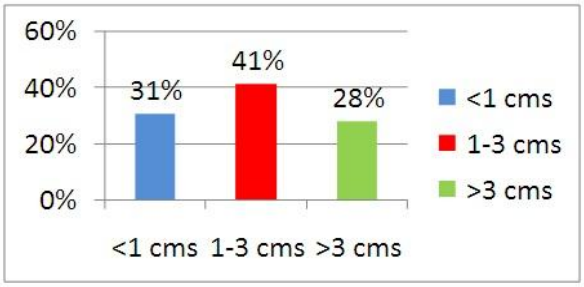


Figure 3. Size wise distribution of lesions



DISCUSSION

This prospective study was carried out in NRI Medical College, Chinakakani, Guntur district, over a period of two years (September 2013 to September 2015) on 50 patients with clinically suspected focal liver lesions, or previous images depicted focal hepatic lesions with non specific appearance. Patients were evaluated with 16 slice Multidetector Computed Tomography (GE HEALTH CARE SYSTEMS). The conspicuity and enhancement patterns of individual lesions after the CT examination was noted and these findings were correlated with histopathology /surgical findings /USG /follow-up as applicable.

In our study (160 focal liver lesions studied in 50 patients), the maximum cases was seen in the age of 50-59years. In our study, there was a male preponderance (52%) compared to females (48%). Even though liver has dual blood supply (nearly 80% from portal vein and 20% from hepatic artery), most of the primary and secondary neoplastic liver lesions receive most of the blood supply from hepatic artery [5].

During HAP hyper vascular lesions are easily identifiable against the background of minimally enhancing liver parenchyma. During PVP most of the hepatic lesions are perceived as hypo vascular lesions highlighted by strongly enhancing normal liver parenchyma [6]. Depending on the vascularity, a lesion will be more conspicuous during HAP or PVP. Most hypo vascular lesions were best detected during PVP and most hyper vascular lesions in HAP. In our study, a greater number of hypo vascular lesions were identified with greater lesion conspicuity on the PVP than on other phases especially when the size of the lesion was less than 3cm in size. Our present study findings are correlated with the study done by Philippe Soyer and co-workers concluded that the PVP images depicted significantly more hypo vascular metastases than in any other phases [7].

In our study the number of hyper vascular lesions seen was higher on HAP than on PVP and unenhanced phase when the lesion size was less than 3cm in size. When the lesions size were >3cm no statistically significant difference was seen between PVP and HAP because larger lesions were seen on all phases. No patient in our study had a lesion that was detected on unenhanced phase images that was not identified on with HAP or PVP images.

In detection of lesions, our findings were similar to the study done by Frank and co-workers, they detected that the conspicuity of the hypo vascular lesions was higher on the PVP than on other phases when the lesions were <3cm [8]. In patients with hyper vascular malignancies, the conspicuity of lesions were higher on HAP than other phases when the lesions size were <3cm. In our study we grouped the lesion size as <1cm, 1-3cm, and >3cm, our observation are in accordance with earlier findings [8].

In characterization of lesions with enhancement patterns, our study was similar and correlated with the earlier study done by Van Leeuwen and co-workers [9]. They found 11 patterns of enhancement in 94 patients. They demonstrated that six of the 11 enhancement patterns were always due to benign disease, three of the 11 patterns were always due to malignant disease, and the other two patterns were due to metastases and hemangiomas. In our study we had 11 patterns of enhancement of focal liver lesions, four of the 11enhancement were always due to benign lesions, another five of 11 enhancement patterns were always due to malignant lesions, and other two of the 11 enhancement patterns were due to both malignant and benign lesions. We found two different enhancement patterns one for the abscess and another for the intrahepatic cholangiocarcinoma which were not included in the study conducted by Van Leeuwen and co-workers [9].

In characterization of hypovascular lesions, first the distinction was made between cysts and hypovascular solid lesions. All the 12 (100%) lesions with hypo/hypo (cyst)/hypo enhancement pattern were confirmed to be cysts because of sharp margins and homogenous hypo vascular pattern. 4 of the 12 cystic lesions were hydatid cysts seen in 4 patients (in addition to the cystic enhancing patterns these lesions showed subtle areas of peripheral rim calcification with thin enhancing septae within). When enhancing rim was observed, with hyper (rim) /hypo(cyst)/hypo enhancing pattern, all the lesions (7 of 7) were abscesses. In non cystic hypo vascular lesions, when the lesions demonstrated hypo/hypo/hypo enhancing pattern, 79(95.1%) of 83 lesions were metastases and 4(4.9%) of 83 lesions were hemangiomas (atypical). when

an enhancing rim in arterial phase was observed with hyper(rim)/hypo/hypo pattern, all the lesions (12 of 12) were metastases. Hypo/hypo/hyper enhancing pattern, was seen in 10 lesions, and all were metastases.

In characterization of hyper vascular lesions, all the 13(100%) lesions with A (puddles)/A/A enhancement pattern were hemangiomas. The second group of hyper vascular lesions demonstrated non specific, hyper/A/A enhancement pattern found in both malignant and benign lesions. Most 15 (83.3 %) of the malignant hyper/A/A lesions were metastases and rest of the lesions 1(5.5%) were HCC. The benign lesions were FNH 1(5.5%) and Adenoma 1(5.5%). With mixed/mixed/mixed enhancement pattern, all the lesions (5 of 5) were metastases. 6 of 7 HCC presented as A(variegated)/A/A(delayed) and 1 Hyper/A/A enhancing pattern. 2 of 3 FNH showed A/A/A(cleft) enhancement pattern and 1 hyper/A/A enhancement pattern. Hyper (incomplete)/A/A was seen in 2 cases of intrahepatic CCA. Interpretation of hyper/A/A enhancing pattern, should be done in clinical context, biopsy is essential for differentiating these lesions.

Our study also correlated well with the study conducted by Gualdi and co-workers [10]**.** In their study to evaluate the role of Triphasic CT in characterization of noncystic focal lesions on sixty- six patients with suspected focal liver disease, they found 11 patterns of enhancement depending on the enhancement patterns of the lesions in different phases. Four of 11 enhancement patterns (were always referable to benign disease. (hemangioma, FNH-adenoma). Four of 11 enhancement patterns were always referable to malignant disease (hepatocellular carcinoma-HCC-metastases). The other three patterns were seen in both benign and malignant diseases.

Gualdi and co-workers also concluded that conspicuity of hypo vascular lesions was more in the PVP, and hyper vascular lesions in the HAP, and triple phase CT improved the characterization of HCC, FNH, adenoma and hemangioma. Patients with unclassified lesions at USG or conventional CT suspected HCC and metastases from pancreas neuroendocrine tumours should be submitted to triple phase CT of the liver [10]. The present study concludes that, triple phase CT of liver is a standardized CT procedure, enables in detection and characterization of vast majority of focal liver lesions. Despite increased competition from MRI over last decade, role of diagnosis of diseases of liver has not been significantly affected. Besides the general availability of the method, the dominance of CT is primarily due to its excellent visualization of anatomic relationship and of liver position relative to adjacent organs.

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STATEMENT OF HUMAN AND ANIMAL RIGHTS

All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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