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Original Article

# The Evaluation of Hepatocellular Carcinoma with Biphasic Contrast Enhanced Spiral CT Scan

**Rawnak Afrin[1], Snigdha Sarker[2], A.B.M Golam Mostofa[3], Mohammad Sazzad Hossain[4], Sajida Nahid[5], Shantono Saiham[6], Md. Zahangir Alom[7]**

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**Key words:**
HCC, HAP, PVP, Spiral CT.

## Abstract

***Background:*** *Hepatocellular Carcinoma (HCC) is the most common malignant neoplasm of the liver worldwide. Liver cancer ranks third among all cancer deaths in Bangladesh as the clinical presentation is non-specific, the modern imaging modalities can play an important role in the diagnosis of HCC and the radiologist is often the first to suggest the correct diagnosis. With the advent of multi-detector spiral CT, detection and characterization of HCC has markedly improved. Multi-detector spiral CT with its increased spatial and temporal resolution allows multiple perfusion phases of liver to be acquired.Multi-detector biphasic spiral CT techniques have been increasingly promising with respect to accurate preoperative diagnosis and assessment of the extent of HCC. This study was carried out to evaluate the role of biphasic contrast-enhanced spiral CT including Hepatic Arterial Phase (HAP) imaging with Portal Venous Phase (PVP) imaging, in the detection and characterization of HCC.*

***Methods:*** *The study included 35 patients (M=31, F=4) with histopathologically proven HCC. Age range was between 21-75 years (mean=51) by following consecutive patients in whom HCC was diagnosed or suspected either by raised serum a (alpha)-fetoprotein level or byultrasound imaging.*

***Results:*** *Biphasic contrast-enhanced examination in these 35 patients could reveal a total of 65 lesions, out of which 48% were unifocal and 46% were multifocal HCCs. On HAP imaging 92% lesions were detected. (hyper attenuating = 56, hypo attenuating = 4) while on PVP imaging delectability was only 51% (hyper attenuating=2, hypo attenuating=30). Hence delectability was significantly superior in HAP as compared to PVP imaging (p <0.0001, 95% CI 25.2-54.7). In 49% tumor was visible only on HAP images. Venous invasion was present in 11 patients (31%).*

***Conclusion:*** *Biphasic contrast enhanced spiral CT is a useful method in detection and characterization of HCC.*

## Introduction

The prevalence of hepatocellular carcinoma (HCC) is increasing worldwide. It is the fifth most common malignancy in men and eighth in women. Epidemiologically, HCC is most common in Asia and sub- Saharan Africa[1]. Liver cancer ranks third among all cancer deaths in Bangladesh.[2] In Bangladesh HCC is almost about greatly associated with chronic hepatitis B and C virus infection and hepatic cirrhosis.[2] In this country, HCC has been

1. Associate Professor, Institute of Nuclear Medicine & Allied Sciences, Dhaka, Bangladesh.
2. Associate Professor, National Institute of Traumatology and Orthopaedic Rehabilitation, Dhaka, Bangladesh.
3. Registrar, National Institute of Cardiovascular Disease, Dhaka, Bangladesh.
4. Assistant Professor, Department of Radiology and Imaging, Sir Salimullah Medical College, Dhaka, Bangladesh.
5. Assistant Professor, Dhaka Medical College Hospital.
6. Radiologist, Doctor care General Hospital, B.Baria.
7. Associate Professor, Bangladesh Atomic Energy Commission, Dhaka, Bangladesh.

**Correspondence Address:** Dr. Rawnak Afrin, Associate Professor, Institute of Nuclear Medicine & Allied Sciences, Dhaka, Dhaka Medical College Campus, Dhaka, Bangladesh. E-mail: afrinrawnak@gmail.com. Cell: 01914857542.

neglected in Bangladesh as the majority of the patients come from poor or lower-middle class. Second thing that occurs is that time of diagnosis is delayed, this is probably due to lack of awareness, lack of advance medical facilities, lack of resources and economic reasons. Diversity of clinical presentation of the disease made it difficult to diagnosis in early stage. Diagnostic confirmation and careful staging of patients with chronic liver disease with HCC are key aspects for establishment of the patient's prognosis and planning the right treatment.

Computed Tomography (CT) has gained acceptance as the preferred technique for the evaluation of wide range of liver lesions, because it provides image acquisition of peak enhancement of liver parenchyma in a single breath hold, reducing the chances of missing small lesions. In general, anatomic definition is more complete with CT scanning. CT can also provide information about portal vein, hepatic vein invasion, lymphadenopathy, ascites, bile duct invasion, invasion to the adjacent organs and even distant metastases.

The advent of spiral MDCT in recent years has dramatically improved the ability to detect and stage HCC. Recent studies shown that MDCT have elevated sensitivity in the detection of HCC, due to the high speed and flexibility primary to the achievement of high quality thin section imaging and 3D capabilities.[3] The availability of spiral CT has changed the radiologist's approach to imaging. With the availability of faster spiral CT scanners it is now possible to scan through the entire liver twice- once during the hepatic arterial phase (HAP) and then the portal venous phase (PVP) for hypervascular liver tumor detection and lesion characterization. Striking but transient early enhancement is common in HCC as lesions are vascular. Most of the HCC are enhancing during arterial phase as they gain blood supply from hepatic arteries and show rapid washout of contrast during portal venous phase and delayed phase.[4]

## Patient and methods

A prospective study was carried out in a tertiary hospital (Sir Salimullah Medical College Hospital), Dhaka Bangladesh, over a period of 18 months. Initially 52 patients were included in the study, who presented to the radiology department as diagnosed cases or suspected HCC either by USG or raised serum a-fetoprotein level. 35 patients were selected who were biopsy proven HCC and 17 patients were excluded due to inadequate records or not proven HCC on pathologic results or due to having any contraindication to contrast CT.

All these patients had proven HCC on histopathology and complete records, including CT scans, medical history and pathology reports. All 35 patients were diagnosed to have HCC by pathological findings with needle biopsy, FNAB (n=35) under image guidance. In all patients with HCC, biphasic CT findings were compared and correlated with histopathologic findings and characteristic clinical manifestations.

### CT Imaging Protocol

Spiral Biphasic CT scans of liver were performed with Somatom Emotion 16 slice, Siemens CT scanner at 120 kvp and 200-250 mAs. All patients received oral contrast material 1 hour before CT examination, followed by I/V injection of 80 to100 ml nonionic contrast medium, Iopamidol at the concentration of 370mg/ml for detection and enhancement pattern of the lesions. Rapid bolus of contrast was administered in the large antecubital vein with power injector at flow rate of 4 ml/sec (injected in 25 seconds). Biphasic spiral CT scans were obtained in HAP obtained after 25 sec. delay and in PVP after 50-60 sec. delay following the injection of I/V contrast material. In the HAP, slice thickness of 5mm with 5mm inter-slice space and pitch used was 1-1.5 depending upon the liver size. The entire liver for HAP was scanned in one breath hold. Later, additional images of PVP were obtained from the dome of diaphragm to the iliac crest. The hepatic arterial phase and portal venous phase images in 35 patients with 65 HCCs were compared and assessed for detection and enhancement pattern of the tumors. Any associated finding like portal or hepatic venous infiltration, hepatic or para-aortic lymph-adenopathy, arterio-portal shunting, cirrhosis, ascites and pleural effusion if present was noted.

### Statistical Analysis of Data

For comparison of detection of lesions in arterial and venous phase, statistical analysis was performed by using Repeated Measures Design. Statistical data analysis was done by using computer programme SPSS. A p-value of less than 0.05 was considered to indicate statistically significant difference.

**Results**

The mean age of the study patients was Mean ± SD was 51.7 ± 11.4 with range from 21 to 75 years. The highest incidence of HCC was found in the age group between 41 to50 years. In the current study, higher male incidence, (male 89% and female 11% cases) was observed. In our study 60% cases were Hepatitis B virus positive whereasin 9% cases HCV waspositive.In this study AFP was found to be elevated in 22(62%) of cases. (Table I).

**Table-I**

*Epidemiological characteristics of study population (n=35).*

| Characteristic | | Percentage |
|---|---|---|
| Mean Age | 51.7 ± 11.4 | |
| Male : Female | 9:1 | |
| Hepatitis B positive | 21 | 60 |
| Hepatitis C positive | 3 | 9 |
| Elevated α feto protein | 22 | 63 |

Maximum 17 of 35 (48%) patients had solitary lesions, followed by 16 had (46%) multifocal lesions. (Table 2) Out of 65, maximum 48 (73%) lesion were found in right lobe, 15/65 (23%) were found in left lobe (Figure 1)

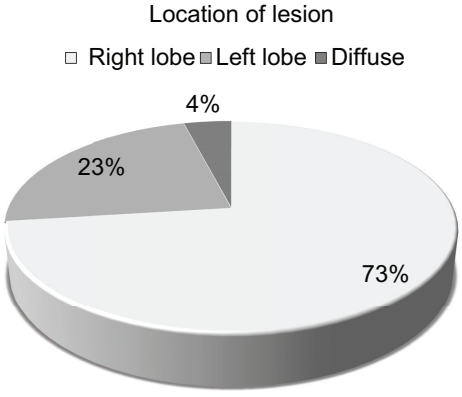


**Fig.-1:** *Pie chart showing the distribution of study patients according to location of lesions.*

Table II shows the distribution of patients by pattern of the lesion. Maximum 17 (48%) cases had solitary, 16 (46%) cases had multifocal and 2 (6%) cases had diffuse lesion.

**Table II**

*Distribution of study patients according to pattern of the lesions*

| Pattern of the lesion | Frequency | Percentage |
|---|---|---|
| Solitary | 17 | 48 |
| Multifocal | 16 | 46 |
| Diffuse | 2 | 6 |
| Total | 46 | 100.0 |

Evaluation of enhancement pattern and detectability in 35 patients with 65 HCCs using biphasic spiral CT was performed. Among 65 lesions 56 HCCs, (86%) showed moderate to marked hyper attenuation during the hepatic arterial phase. There was total hyper attenuation in 35 and partial hyper attenuation in 21. The remaining 9 HCCs showed isoattenuation in 5 (8%) and hypo attenuation in 4 (6%) during the hepatic arterial phase of CT imaging. Therefore the delectability of HCC in the HAP of spiral CT was 92% (hyper attenuating=56, hypo attenuating=4). Detectability was determined by hyper attenuation or hypo attenuation compared to surrounding enhancing liver. Most of the HCCs showed characteristic hyper attenuation in the HAP before adequate enhancement of liver parenchyma. This was true even in HCCs <2 cm in diameter (Table III).

Table III shows the distribution of lesions by contrast enhancement pattern on arterial phase. Maximum 56 (86%) lesions' contrast enhancement pattern on arterial phase were hyperattenuation followed by 04 (6%) lesions', and 05 (8%) lesions' contrast enhancement pattern on arterial phase were hypoattenuation and isoattenuation respectively.

**Table-III**

*Distribution of lesions according to contrast enhancement pattern on arterial phase*

| Contrast enhancement pattern on arterial phase | Frequency | Percentage |
|---|---|---|
| Hyperattenuation (total/partial) | 56 | 86 |
| Hypoattenuation | 4 | 6 |
| Isoattenuation | 5 | 8 |
| Total | 65 | 100.0 |

The PVP images showed hyperattenuation in 2 (4%), isoattenuation in 33 (49%), and hypoattenuation in 30 (47%). The detectability of HCCs in the PVP was 51% (hyper attenuating = 2, hypoattenuating = 30) (Table IV).

Table IV shows the distribution of lesions by contrast enhancement pattern on portal venous phase . 32 (47%) lesions contrast enhancement pattern on portal venous phase were hypo-attenuation followed by 33 (49%) lesions and 02 (4%) lesions contrast enhancement pattern on portray venous were isoattenuation and hyperattenuation respectively.

**Table-IV**

*Distribution of lesions according to contrast enhancement pattern on portal venous phase*

| Contrast enhancement pattern on portal venous phase | Frequency | Percentage |
|---|---|---|
| Hypoattenuation | 32 | 47 |
| Isoattenuation | 33 | 49 |
| Hyperattenuation | 2 | 4 |
| Total | 65 | 100.0 |

The delectability of HCCs in HAP imaging was significantly superior to the PVP ($p < 0.0001$, 95% CI 25.2-54.7), calculated by using Repeated Measures Test. 49% HCCs were only detected in HAP phase.

Among 65 HCCs, 9 HCCs (14%) did not show the characteristic enhancement pattern in the hepatic arterial phase of imaging. They were iso or hypodense and were difficult to differentiate from other hepatic tumors including metastases or intrahepatic cholangiocarcinoma. Therefore the delectability of hyper vascular HCCs in the hepatic arterial phase according to characteristic enhancement pattern was 86%. Capsular enhancement although better seen on delayed images was identified in 8 (12%) of 65 HCC on portal venous phase.

The size of the HCCs were measured and categorized in four groups.Maximum 35 (54%) HCCs were within 3 to 5 cm, 15 (23%) were <3 cm, 12 (19%) lesions were within 5 to 8 cm and the rest were> 8cm.The enhancement pattern of HCCs such as total or partial enhancement in the hepatic arterial phase depended on tumor size. Majority of tumors of 3 cm or greater size enhanced confirming them as hyper vascular HCCs. These were mostly poorly-differentiated HCCs on histopathology.

Seventeen (48%) of the 35 patients with HCCs had associated liver cirrhosis on Spiral CT images. Amongst the secondary findings detected by CT, ascites (34%) was the most common manifestation of HCC. Venous invasion into the portal vein (31%) and lymph node enlargement (14%) at the porta hepatis were the other major secondary findings. The frequency of venous invasion was higher in larger HCCs and seen better in portal venous phase (Table V).

**Table V**

*Associated Biphasic Spiral CT Findings:*

| Associated CT findings | Frequency | Percentage |
|---|---|---|
| Cirrhosis | 17 | 48 |
| Ascites | 12 | 34 |
| Portal vein invasion | 11 | 31 |
| Lymphnode enlargement | 5 | 14 |

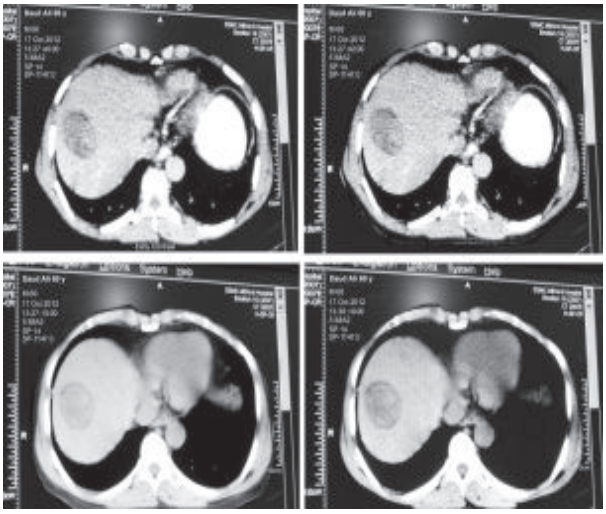

**Fig.-2:** *Triple phase axial CT scan showing a well marginated HCC in right lobe of liver showing hyper attenuation in AP & wash out of contrast in PVP & delayed phase.*

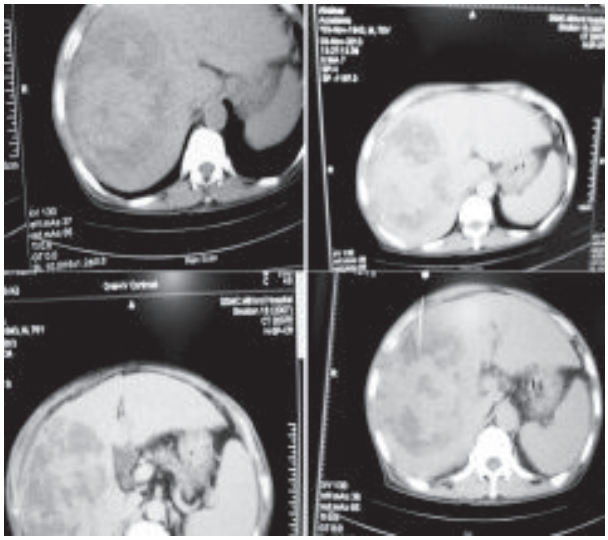

**Fig.-3:** *Triple phase axial CT scan shows HCC in right lobe of liver with irregular margin Lesion is inhomogenously hypodense in NECT, inhomogenously hyperdense on postcontrast arterial phase,wash out of contrast seen in venous phase. CT guided Fine needle aspiration biopsy done on the same patient.*

**Discussion**

Among multiple scan phase in contrast-enhanced spiral CT, it has been well established that hepatic arterial dominant phase scanning is essential for detecting hypervascular HCC. Hepatic arterial dominant phase images depict a significantly large number of HCCs than images obtained in any other phase, such as un-enhanced, portal venous phase, and delayed phase images. Moreover, many hyper vascular HCCs are seen or are most conspicuous during the hepatic arterial dominant phase[5]. Bruix, et al (2001) concludes that spiral CT is the standard imaging technique for the detection of response to loco-regional treatment of HCC.[4]

In the current study, higher male incidence, was observed. The Gani series 2013, conducted in our country found the similar findings. In our study 60% cases were Hepatitis B virus Positive & HCV positive cases were 9%. These findings are supported by the previous study done in our country.[2] (HCC) is a vascular neoplasm which may be solitary, multifocal or diffusely infiltrative (5%).[2]

Liu et al. (2003) have observed in their study 25.0% lesion was in left lobe and 75.0% was in right lobe.[6] Ganiet,al 2013 reported also maximum cases in the right lobe of the liver.[2]

Factors affecting enhancement patterns of HCC include the volume of contrast material used, length of scan delay after injection of intravenous contrast material and rate of injection of contrast material.[7]

Early HCC is usually hypovascular and intra nodal portal blood flow tends to decrease as the grade of malignancy increases.[5] In addition, the poorly differentiated HCC are usually hypervascular, whereas well-differentiated HCCs are usually hypovascular, particularly in cases of small-sized tumors.[5] The detection of hypervascular HCC in the arterial phase in this study was 92% (60 of 65) confirming the benefit of biphasic contrast-enhanced spiral CT to optimally detect HCC,and the results of Yakub et al, Khan and Yu.[5,7,8]

Portal or hepatic venous invasion is considered to be characteristic for HCC and associated with poor prognosis. The frequency of portal venous invasion has been reported upto 40 % and hepatic vein and inferior venacava upto 15 %.[9] In this study, portal venous invasion was detected in 31% because images were obtained during the portal venous phase. It was noted that the portal venous phase images were not useful for the detection and characterization of HCC because the lesions showed isoattenuation in 49% (33 of 65 HCC).

CT studies in Asian populations have reported encapsulated HCC in as many as 67% of tumors.[10] In our study only 8% of HCC showed capsular enhancement in the portal venous phase because images were not acquired in delayed phase, which better detects capsular enhancement.

Since the biphasic spiral CT does not have 100% sensitivity for detection of HCC, some lesion are liable to be missed especially the early HCC, as mentioned by Yaqoob J et al[5] which results in false-negative findings.

In our study HAP was the only phase to depict tumors in 50%. The results of our study are comparable to study by Yaqoob J et al and Lee et al. In western literature it has been reported that the addition of HAP to PVP images depicted up to 30-40% additional HCC in approximately one-third of patients while HAP was the only phase to depict tumor.[5,11]

## Conclusion

Biphasic Spiral Computed Tomography is a useful modality in detection and characterization of HCC. It should be performed in suspected cases of HCC routinely because clinical staging and surgical resectability criteria rely on the accurate accounting of the number and location of tumor nodules.

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