June 2011

Triphasic computed tomography (CT) scan in focal tumoral liver lesions

Saima Hafeez
Aga Khan University

Muhammad Shahbaz Alam
Aga Khan University

Zafar Sajjad
Aga Khan University

Zahid Anwar Khan
Aga Khan University

Waseem Akhter
Aga Khan University

See next page for additional authors

Authors
Saima Hafeez, Muhammad Shahbaz Alam, Zafar Sajjad, Zahid Anwar Khan, Waseem Akhter, and Fatima Mubarak

Original Article

Triphasic computed tomography (CT) scan in focal tumoral liver lesions

Saima Hafeez, Muhammad Shahbaz Alam, Zafar Sajjad, Zahid Anwar Khan, Waseem Akhter, Fatima Mubarak
Department of Diagnostic Radiology, Aga Khan University Hospital, Karachi, Pakistan.

Abstract

Objective: To assess the diagnostic accuracy of triphasic spiral CT in differentiating benign from malignant focal tumoral liver lesions.

Methods: The study was conducted in Department of Radiology of Aga Khan University Hospital and Sind Institute of Urology and Transplantation, Karachi from Feb 2006 to Feb 2007. By convenient sampling, 45 patients found to have focal tumoral liver lesions were recruited for one year period and their triphasic CT scans findings were evaluated and later correlated with histopathology. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of triphasic CT scan were calculated.

Results: Among 45 patients, 136 liver lesions (11 benign and 125 malignant) were detected with the help of different enhancement patterns. Out of these, 37(82.2%) patients had malignant while 8 (17.8%) had benign lesions. On later histopathological examination, 35 (77.8%) of the total 45 cases had malignant lesions while 10 (22.2%) were diagnosed as benign lesions. Based on these results, it could be assessed that triphasic CT Scan has a sensitivity of 100 %, specificity of 80%, positive predictive value of 94.5%, negative predictive value of 100% and diagnostic accuracy of 95.5 % in differentiating benign from malignant liver lesions.

Conclusion: Triphasic CT Scan is a good non-invasive tool in characterizing and differentiating benign from malignant liver lesions.

Keywords: Liver lesions, Triphasic-CT scan, Radiology (JPMA 61:571; 2011).

Introduction

Focal liver lesions can be defined as any lesion in the liver other than the normal parenchyma with or without causing structural and functional abnormality of hepatobiliary system and can be of variable size. These lesions can be benign or malignant. Prevalence of various liver lesions has marked differences across geographic regions and ethnic groups.[1] Focal liver lesion is more likely to represent a metastatic deposit than primary malignancy in Europe and United States; however, hepatocellular carcinoma is the fourth most common hepatic disorder in Pakistan with prevalence of 8-10%. This prevalence rate is high when compared to western data.[2,3]

In a patient without known cancer or history of chronic liver disease, these lesions usually can be evaluated with serial follow-up imaging tests because nearly all will be benign. In patients with cancer, however, prompt determination of the cause of such lesions may be pivotal for defining prognosis and therapy. Small hepatic lesions were deemed benign in 51% of the 82% of patients with a known underlying malignancy.[4] Benign hepatic tumours have been reported in up to 52% of the general population.[5] It is therefore important to differentiate between benign and malignant focal liver lesions for further management of the patient.

It is often difficult to characterize hepatic lesions with various imaging studies. Although histopathology is the gold standard, biopsy is always not possible as it is an invasive technique. Computed tomography (CT) is the imaging modality most often used to evaluate focal liver lesions, however, the complex blood supply of the liver frustrates the search for an optimal contrast-enhanced CT protocol for the detection and characterization of focal hepatic lesions. Although the liver receives approximately 30% of its blood supply from the hepatic artery and 70% from the portal vein, most primary and secondary liver neoplasms receive 80-95% of their blood supply from the hepatic artery. Because of the high frequency of benign focal liver lesions such as cysts, haemangiomas and focal nodular hyperplasia, characterization of these lesions is essential. Consequently, the preferred liver CT technique should combine a high sensitivity for lesion detection with a good ability for lesion

characterization, to differentiate lesions that do need further diagnostic tests or treatment for lesions that do not. To meet these requirements, a triphasic spiral CT technique was developed to image the entire liver in arterial, portal, and equilibrium phases.[6,7] Although current literature search shows that MRI has a comparable rate in detection and classification of focal liver lesions, however, rapid availability and short scanning time made CT an ideal imaging technique.[8-10] Recent studies have also reported an improvement in lesion detection if arterial phase imaging is performed in addition to portal venous imaging especially in the presence of hypervascular neoplasms, such as hepatocellular carcinoma.[11-13]

In the current study, we evaluated a triphasic spiral computed tomogram technique that allowed imaging of the entire liver in arterial, portal and equilibrium phases.[6-9] The rationale behind the protocol is that the portal phase is the most sensitive phase for lesion detection, whereas the arterial and equilibrium phases can supply additional information on the vascularity of the lesion which may help to identify the nature of lesion.[10-14] The vascular haemodynamics is the key to detect characterization of hypervascular lesions.

Several studies have been done worldwide on the role of triphasic CT scan in characterizing and differentiating benign and malignant lesions. However, to the best of our knowledge, no data has been published locally, so purpose of this study was to describe the role of triphasic CT scan in focal liver lesions and to determine its diagnostic accuracy.

Patients and Methods

The study was simultaneously conducted in Department of Diagnostic Radiology of Sind Institute of Urology and Transplantation (SIUT) and Aga Khan University Hospital. Data was collected from 15th February 2006 to 18 Feb 2007. All the patients of age over 18 years with suspected focal hepatic lesion were included in the study. There were 60 patients: 41 (68.3%) males and 19 (31.6%) females. Forty cases were taken from SIUT and 20 from AKU. Permission was sought from institutional ethical review committees of both institutes. Informed consent was taken from all the patients to enroll them in the study. Patients who were pregnant at the time of the study or who had a history of chronic renal failure were excluded. Focal fatty and inflammatory lesions were also excluded along with 15 cases in which histopathology was not available.

All the relevant features like age, sex, characterization of lesion by CT and final histopathological characterization and follow-up were recorded on a Performa.

Triphasic CT scanning of the liver was performed with CTi/Pro GE Medical system and Toshiba X-Vision single slicer CT scanner at 120 kvp and 200-250 mAs in AKU and SIUT respectively. Patients were given I/V contrast of 1.5 ml/Kg with overall dose ranging from 80-100 ml according to departmental protocol. Patient preparation also included administration of 2000 ml of water/gastrografin 30-60 minutes prior to the examination used as oral contrast.

After oral and injection of intravenous contrast material, liver was scanned in arterial (scanning delay, 20-40 seconds), portal (scanning delay, 60-90 seconds), and equilibrium (scanning delay, 2-5 minutes) phases. Enhancement of each lesion in each phase was evaluated, and the lesions were tabulated according to hyper enhancement, hypo enhancement, iso-dense to liver parenchyma and mixed enhancement pattern.

On the basis of triphasic CT scan findings, lesions were categorized as benign and malignant lesions. Benign lesions like hepatic cysts appear hypodense and have no enhancement in arterial, portovenous phase and equilibrium phases. Haemangioma showed peripheral enhancement in arterial phase and centripetal filling of contrast in portovenous and equilibrium phase. Focal nodular hyperplasia and hepatic adenoma have pattern of hyper enhancement, mixed and mixed on arterial, portovenous and equilibrium phases respectively. Hepatomas also have hyper enhancement, iso/mixed enhancement and iso/mixed enhancing pattern in arterial, portovenous and equilibrium phases respectively. Hypervascular metastasis appears hyper enhancing on arterial phase with mixed pattern on portovenous and equilibrium phase. However, hypovascular metastasis appears hypoenhancing on arterial phase and shows maximum enhancement on portovenous phase. History and clinical presentation were also considered for diagnosis.

All the images were interpreted by the consultant radiologist having experience in CT reporting. Reporting was done on console as well as hard copies. Histopathology was performed in all 45 patients. In cases of multifocal lesion, biopsy of the largest and most approachable lesion was performed.

False Positive cases in this study were defined as lesions deemed malignant on triphasic CT scan but turned out to be benign on histopathology. Similarly, False Negative can be defined as lesions reported benign on triphasic CT scan but were malignant on histopathology.

Data was entered and analyzed using Statistical Package of Social Sciences (SPSS) programme version 10.0. The diagnostic accuracy of spiral CT to identify focal liver lesions as malignant or benign was calculated using SPSS programme using histopathological findings and follow-up as gold standard.

Results

Overall 136 liver lesions, 11 benign and 125

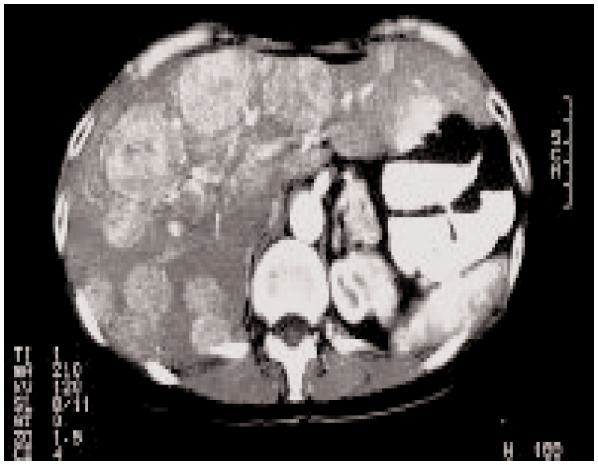

Figure-1: Liver, metastases. Characteristic appearance of carcinoid liver metastases on contrast-enhanced axial CT scan through the upper abdomen, which shows early arterial enhancement of the liver metastases.

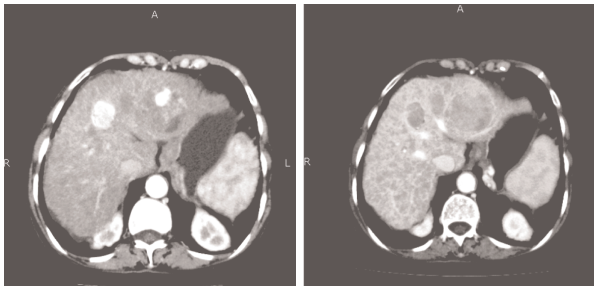

Figure-2: Hepatoma: Enhancing lesions in arterial phase with washout in portovenous phase.

malignant were identified with the help of different enhancement patterns and categorized into benign and malignant lesion. Nineteen patients had unifocal and 26 patients had multifocal lesions in the liver. Patients having mixed pattern i.e. both benign and malignant lesions were categorized as having malignant lesions.

Most common clinical presentation was jaundice (32%) followed by pain (23%) and fever (15%). The mean and standard deviation for age were 46.5 ± 13.4 years. Mean lesion size was 3.4± 2.6 cm ranging from 0.9 to 13 cm.

Out of 45 patients, 8 (17.8%) had benign while 37 (82.2%) had malignant lesions on CT Scan. Benign lesions included haemangioma (n =3); adenoma (n =4) and FNH (n =4). Malignant lesions were hepatoma (n =74) and metastasis (n =51) (Table-2). Hepatomas were seen in 26 patients out of whom 23 patients had a history of chronic liver disease from infective etiology like Hepatitis B, D and C. Two patients gave a history of alcoholic liver disease while in one patient cause was not known. All the hepatomas were enhancing on arterial phase, out of which

Table-1: Total No. of Lesions reported on Triphasic CT Scan.

Benign lesions	Malignant lesions
Hemangioma = 3	Hepatoma = 74
Adenoma = 4	Metastasis = 51
FNH = 4	

Table-2: Diagnostic Yield of Triphasic CT Scan.

CT Diagnosis	Biopsy Report	
	Malignant	Benign
Neoplastic	35 (True Positive)	2 (False Positive)
Non-neoplastic	0 (False Negative)	8 (True Negative)

54 were detected in arterial phase only. Nine lesions were better seen in portovenous phase and 11 lesions were hypoattenuating in portovenous phase. There were 30 hypervascular and 21 hypovascular metastatic lesions in 11 patients. Hypervascular metastasis were from renal cell carcinoma (n =6), carcinoid (n =8), gastric tumours (n =6), pancreatic tumours (n =6), sarcoma (n =3) and melanoma (n =1). Hypovascular metastatic lesion were from lung (n =6), breast (n =7), gastrointestinal tumours (n =3), lymphoma (n =4) and endometrial cancer (n =1).

On later histopathological examination, 35 (77.8%) of the total 60 cases had malignant lesions while 10 (22.2%) were diagnosed as benign lesions.

Thus there were 35 true positive, 2 false positive, 8 true negative and 0 false negative results reported on CT based assessment of liver lesions (Table-2). Based on these findings, triphasic CT Scan was found to have a sensitivity of 100 %, specificity of 80%, positive predictive value of 94.5%, negative predictive value of 100% and diagnostic accuracy of 95.5 % in differentiating benign from malignant liver lesions.

Discussion

Triphasic spiral liver Computed Tomography (CT) is a standardized procedure for the detection and characterization of a large variety of benign and malignant liver lesions. This helps in the decline of mortality and morbidity rates among patients with liver disease. Spiral computed tomography has gained acceptance as the preferred computed tomography technique for routine liver evaluation because it provides image acquisition at peak enhancement of liver parenchyma during a single breath hold.[15,16] In addition fast data acquisition allows successive scanning of the entire liver at different intervals after injection of the iodinated contrast material, thus creating the possibility of multiphase liver computed tomography.[17,18]

Most metastases to the liver are hypovascular and

consequently are best detected during the portal venous phase. Hypervascular primary malignancies (e.g., hepatocellular carcinomas) and certain metastases (e.g., pancreatic islet cell carcinomas, carcinoids, melanomas, pheochromocytomas, choriocarcinomas, and sarcomas) have a proportionately greater hepatic arterial blood supply and, as a result, may be visible only on hepatic arterial phase images.[19] In our study, 30 metastatic lesions were hypervascular and 21 lesions were hypovascular. Most of the hypervascular metastatic lesions (n =24) were best visualized on arterial phase images rather than on portovenous phase. Most of them become iso or hypodense on portovenous and equilibrium phases making it difficult to diagnose on single phase thus signifying the importance of additional arterial phase images.

Advanced or poorly differentiated hepatocellular carcinomas are usually hypervascular lesions that derive most of their blood supply from the hepatic artery with the portal venous contribution decreasing as the grade of malignancy increases. Similarly, cirrhosis and its associated altered portal venous blood flow may help reveal more lesions on the hepatic arterial phase than on the portal venous phase. In our study, all the 74 hepatomas presented as hyper/mixed/mixed; 54 detected only in the arterial phase; 11 were hypoattenuating in the portal phase and 9 were better seen in portal phase. These findings are in keeping with the well-known hypervascularity of HCC. All hyper/mixed/mixed lesions occurring in patients with chronic liver disease truly represent HCC lesions.[14,16,20] Therefore; lesions seen during only the hepatic arterial phase may require biopsy. In patients with hypervascular malignancies such as hepatoma, detection of small lesions especially if solitary is important because these lesions are more likely to be resectable or respond to therapy than the larger lesions.[4,21]

Focal nodular hyperplasia and adenomas may appear hyperdense during the hepatic arterial phase and may rapidly become isodense to the liver or invisible during the portal venous phase and equilibrium phase, simulating hepatomas or hypervascular metastases.[19,22] We had very few cases of focal nodular hyperplasia (FNH) and adenomas diagnosed in our study and all of them were hyperenhancing on arterial phase. Three lesions labeled as adenomas became isodense on portovenous and equilibrium phase. Similarly, one case of FNH was more conspicuous on portovenous images. These lesions could have been easily overlooked if only single phase imaging was acquired.

The triphasic helical CT examination can create certain diagnostic dilemmas, including the inability to specifically characterize some lesions seen only on the hepatic arterial phase and not on the equilibrium or portal venous phase. Although high accuracy (95%) was noted in our results, we had 2 false positive results. These lesions were labeled as malignant because of hypervascularity and patient's history of renal cell carcinoma and gastrointestinal malignancy. These lesions proved to be focal nodular hyperplasia and haemangioma and not metastases. Hepatomas, hypervascular metastases, focal nodular hyperplasia and adenomas may all appear similar on triphasic helical CT examination. In spite of this, our study showed sensitivity of triphasic helical CT scan to be hundred percent for differentiation of benign and malignant liver lesions. There was no false negative case in our study. Possible causes of false negative cases would be faulty imaging technique, scans not done in true arterial, portovenous and delayed phases, observer (Radiologist) interpretation error, lesions less than 2 cm in size or lesions isodense to liver parenchyma on all phases.

Our study has some limitations like small sample size especially for benign lesions. Interobserver agreement for interpretation of CT images was not calculated. In cases of multifocal lesion, only biopsy of largest and most approachable lesion was performed. Other potential limitation is that scans were performed on two different CT Scanners of different make.

Conclusion

Triphasic CT scan is a good non-invasive tool and can be used as first line imaging modality for differentiating benign and malignant focal liver lesions. Benign lesions like haemangioma can be reliably differentiated from malignant liver lesion; therefore unnecessary biopsies can be avoided. It is also particularly useful for hypervascular lesions which can be easily missed on routine CT scanning.

References

1. Méndez-Sánchez N, Villa AR, Chávez-Tapia NC, Ponciano-Rodriguez G, Almeda-Valdés P, González D, et al. Trends in liver disease prevalence in Mexico from 2005 to 2050 through mortality data. Annals of Hepatology 2005; 4: 52-5.
2. Javed IF, Rukhsana JF. Prevalence of hepatocellular carcinoma in Pakistan in liver cirrhosis: An experience in NWFP. J Coll Physicians Surg Pak 2000; 2:54-5.
3. Yaqoob J, Bari V, Usman M U, Munir K, Mosharaf F, Akhtar W. The evaluation of hepatocellular carcinoma with biphasic contrast enhanced helical computed tomography scan J Pak Med Assoc 2004; 54: 123-7.
4. Schwartz LH, Gandras EJ, Colangelo SM, Ercolani MC, Panicek DM. Prevalence and importance of small hepatic Lesions Found at CT in Patients with cancer. Radiology 1999; 210:71-4.
5. Karhunen PJ. Benign hepatic tumours and tumour-like conditions in men. J Clin Pathol 1986; 39: 183-8.
6. Bonaldi VM, Bret PM, Reinhold C, Atri M. Helical computed tomogram of liver, value of an early hepatic arterial phase Radiology 1995; 197: 357-63.
7. Francis IR, Cohan RH, McNulty NJ, Platt JF, Korobkin M, Gebremariam A, et al. Multidetector CT of the liver and hepatic neoplasms: Effect of multiphasic imaging on tumor conspicuity and vascular enhancement. AJR Am J Roentgenol 2003; 180: 1217-24.
8. Ichikawa T, Saito K, Yoshioka N, Tanimoto A, Gokan T, Takehara Y et al. Detection and characterization of focal liver lesions: a Japanese phase III,

multicenter comparison between gadoxetic acid disodium enhanced magnetic resonance imaging and contrast enhanced computed tomography predominantly in patients with hepatocellular carcinoma and chronic liver disease. Invest Radiol 2010; 45: 133-41.

9. Hammerstingl R, Huppertz A, Breuer J, Balzer T, Blakeborough A, Carter R et al. Diagnostic efficacy of gadoxetic acid (Primovist)-enhanced MRI and spiral CT for a therapeutic strategy: comparison with Intraoperative and histopathologic findings in focal liver lesions. Eur Radiol 2008; 18: 457-67.
10. Soyer P, Sirol M, Fargeaudou Y, Duchat F, Hamzi L, Boudiaf M, et al. Differentiation between true focal liver lesions and psudolesions in patients with fatty liver: evaluation of helical CT criteria. Eur Radiol 2010; 20: 1726-37.
11. Van Leeuven MS, Noordzij J, Feldberg MA, Hennipman AH, Doorneewaard H. Focal Liver lesions; characterization with triphasic computed tomography Radiology 1996; 201: 327-36.
12. Szklaruk J, Silverman PM, Chamsangavej C. Imaging in the diagnosis, staging, treatment and surveillance of hepatocellular carcinoma. AJR Am J Roentgenol 2003; 180: 441-54.
13. Iannaccone R, Piacentini F, Murakami T, Paradis V, Belghiti J, Hori M, et al. Hepatocellular carcinoma in patients with non-alcoholic fatty liver disease: helical CT and MR imaging findings with clinical-pathologic comparison. Radiology 2007; 243: 422-30.
14. Iannaccone R, Laghi A, Catalano C, Rossi P, Mangiapane F, Murakami T, et al. Hepatocellular carcinoma, role of unenhanced and delayed phase multi detector row helical computed tomography in patients with cirrhosis. Radiology 2005; 234: 460-7.
15. Foley WD, Mallisee TA, Hohenwalter MD, Wilson CR, Quiroz FA, Taylor AJ. Multiphase hepatic computed tomography with a multirow detector computed tomography scanner. AJR Am J Roentgenol 2000; 175: 679-85.
16. Oliver JH 3rd, Baron RL, Federle MP, Rockette HE Jr. Detecting hepatocellular carcinoma, value of unenhanced or arterial phase computed tomography imaging or both used in conjunction with conventional portal venous phase contrast enhanced computed tomography imaging. AJR Am J Roentgenol 1996; 167: 71- 7.
17. Miller FH, Butler RS, Hoff FL, Fitzgerald SW, Nemcek AA Jr, Gore RM. Using triphasic helical computed tomography to detect focal hepatic lesions in patients with neoplasms. AJR Am J Roentgenol 1998; 171: 643-9.
18. Vallls C, Andia E, Rocca Y, Cos M, Figueras J. Computed tomography in hepatic cirrhosis and chronic hepatitis. Semin Ultrasound, CT MRI 2002; 23: 37-61.
19. Sheafor DH, Frederick MG, Paulson EK, Keogan MT, DeLong DM, Nelson RC. Comparison of unenhanced, hepatic arterial-dominant and portal venous-dominant phase helical CT for the detection of liver metastases in women with breast carcinoma. AJR Am J Roentgenol 1999; 172: 961-8.
20. Johnson PT, Fishman EK. IV Contrast selection for MDCT: Current thoughts and practice. AJR Am J Roentgenol 2006; 186: 406-15.
21. Takayasu K, Moriyama N, Muramatsu Y, Makuuchi M, Hasegawa H, Okazaki N et al. The diagnosis of small hepatocellular carcinomas efficacy of various imaging procedures in 100 patients. AJR Am J Roentgenol 1990; 155:49-54.
22. Carlson SK, Johnson CD, Bender CE, Welch TJ: CT of focal nodular hyperplasia of the liver. AJR Am J Roentgenol 2000; 174: 705-12.