ORIGINAL ARTICLE

Validity of colour doppler sonography for evaluation of portal venous system in hepatocellular carcinoma

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Abstract

Objective: To assess the validity of colour doppler sonography in the evaluation of portal venous system in hepatocellular carcinoma.

Methods: The study was conducted at the Department of Diagnostic and Interventional Radiology at Shifa International Hospital, Islamabad, from March to November 2009, and comprised 100 patients who were already diagnosed cases of hepatocellular carcinoma or those having high suspicion based on clinical criteria (e.g chronic hepatitis B or C, liver cirrhosis, increased alpha fetoprotein level [>400ng/dl]) and/or Imaging findings (e.g sonography, magnetic resonance imaging, computed tomography). Data was collected on pre-designed proforma and analysed on SPSS 10.

Results: Portal vein thrombosis was found in 28 (28%) patients having hepatocellular carcinoma. Colour doppler sonography had 89.3% sensitivity and 95.8% specificity in the detection of portal vein thrombosis in comparison with biphasic computed tomography, which was taken as the gold standard.

Conclusion: Colour doppler sonognaphy is an effective, non-invasive method for evaluating the presence of portal vein thrombosis associated with hepatocellular carcinoma.

Keywords: Spiral computed tomography, Doppler sonography, Portal venous thrombosis, Hepatocellular carcinoma. (JPMA 63: 365; 2013)

Introduction

Hepatocellular carcinoma (HCC), also called hepatoma, is a malignant tumour of hepatocytes. It is the most common primary hepatic tumour and also the fifth most common tumour in the world.[1] Among cancer-related deaths, HCC is the third most common cause after lung and stomach cancer.[2]

Compared to the other hepatic tumours, HCC invades adjacent vasculature much more easily. Incidence of portal vein thrombosis (PVT) in HCC varies. It is about 20-30% in small HCC (<3cm) and up to 50-75% in HCC>5cm.[3] This has important implications for therapy. Patients with invasion of major branches of portal vein (PV) are graded as stage IV by the TNM classification dealing with the site of the tumour, the regional lymph node involved, and the presence or otherwise of distant metastatic spread. Stage IV patients have poor prognosis as they are not candidates for surgical resection and transplantation.[4] Although some reports indicate a tendency towards aggressive management of advanced HCC, such as extending partial hepatic resection and liver transplantation to patients with documented PV tumour thrombus, but macroscopic tumour thrombus is still the most significant predictor of tumour recurrence in patients undergoing orthotopic liver transplantation.[5]

Ultrasound is generally the first imaging technique used to detect PVT. Thrombi appear on sonography as solid intraluminal material that may have a hypo-, iso-, or hyper-echoic pattern. Recent developments and continuing refinement in colour doppler imaging techniques have made possible high-quality colour doppler sonography for showing blood flow and local haemodynamics in various organs. The overall sensitivity and specificity of colour doppler sonography for PV involvement is 86.5% and 97.4%.[6]

Hepatitis B and C is almost endemic in Pakistan with rising incidence of HCC. PVT directly affects the management of patients with HCC. Ultrasound is a readily available modality and the current study was carried out to assess the validity of colour doppler sonography in the evaluation of portal venous system.

Patients and methods

The cross-sectional (validation) study was conducted at the Radiology Department of Shifa International Hospital (SIH), Islamabad. The study, which included both out-patients and in-patients, was conducted from

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March to November 2009. Purposive sampling technique was used. Written informed consent was obtained from all the patients.

Initially, examination was done with a preliminary gray-scale sonography of the upper abdomen. Portal vein and its branches were examined with colour doppler sonography. A number of flow settings were used depending on the underlying flow velocity and colour gains were adjusted during each examination to select the highest value allowing artifact-free images.

CT imaging of each patient was then performed on a 64-slice CT scanner (Aquilion 64, Toshiba). An upper extremity 18- or 20-gauge intravenous (IV) cannula was used for venous access. Non-ionic contrast (Iopamidol) was administered with the dose of 1ml/kg at the rate of 4-5ml/s. The following parameters were used: Collimation, 0.5mm; tube voltage, 120mV; and rotation time, 0.5 seconds. The tube current was adjusted according to patient characteristics (mean, 235 mA; range, 100-440mA). Scanning during both arterial and venous phases were performed in the cranio-caudal direction during a single breath-hold at deep inspiration. Arterial phase was done by placing Sure Start at abdominal aorta (150HU) in automatic mode. Portal venous phase imaging was initiated 65 seconds after the start of contrast material injection. Reconstructions were performed on an offline workstation (Vitrea, Vital Images) for multiplanner reformations (MPRs) and maximum intensity projections (MIPs).

Data was collected using proformas of patients after taking informed consent. To remove bias, the findings were reviewed by a senior radiologist. Data was analysed using SPSS version 10.0. For continuous data (i.e age), mean standard deviation (SD) was calculated. For categorical data (i.e visualisation of main PV) frequency and (percentage) were calculated for both doppler sonography and spiral CT. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of colour doppler sonography in comparison with spiral CT were reported as shown by 2x2 table below:

		Biphasicspiral CT (gold standard)	
		+	-
Colour doppler	+	**a**	**b**
Sonography	-	**c**	**d**

Sensitivity= a / a + c x 100

Specificity= d / d + b x 100

Positive predictive value= a / a + b x 100

Negative predictive value= d / d + c x 100

Results

The mean age of the 100 patients in the study was 53±16.9 years with a range of 12-87 years. Maximum number of patients (n=38; 38%) were in the age group of 51-60 years, followed by the 61-70 age group (n=29; 29%).

PVT was visualised on CT in 28 (28%) patients. The

Table-1: Sensitivity and Specificity of the Doppler Ultrasonography in depicting Portal vein thrombosis compared to the CT Scan (Gold Standard).

		CT of the Portal Vein		
		Portal Vein Thrombosis (n)	**No Portal Vein Thrombosis (n)**	**Total**
Doppler Ultrasonography of Portal Vein	Portal Vein Thrombosis (Sensitivity%=a/a+c)	25 (25%)	3 (3%)	28 (28%)
	No Portal Vein Thrombosis (Specificity%=d/b+d)	3 (3%)	69 (69%)	72 (72%)
Total		28 (28%)	72 (72%)	100

CT: Computed tomography.

Table-2: PPV and NPV of the Doppler Ultrasonography in depicting Portal vein thrombosis compared to the CT Scan (Gold Standard).

		CT of the Portal Vein		
		Portal Vein Thrombosis (n)	**No Portal Vein Thrombosis (n)**	**Total**
Doppler Ultrasonography of Portal Vein	Portal Vein Thrombosis (PPV%= a/a+b)	25	3	28
	No Portal Vein Thrombosis (NPV%=d/c+d)	3	69	72
Total		28	72	100

*PPV= Positive predictive value = 89.3%.
NPV= Negative predictive value = 95.8%.
CT: Computed tomography.

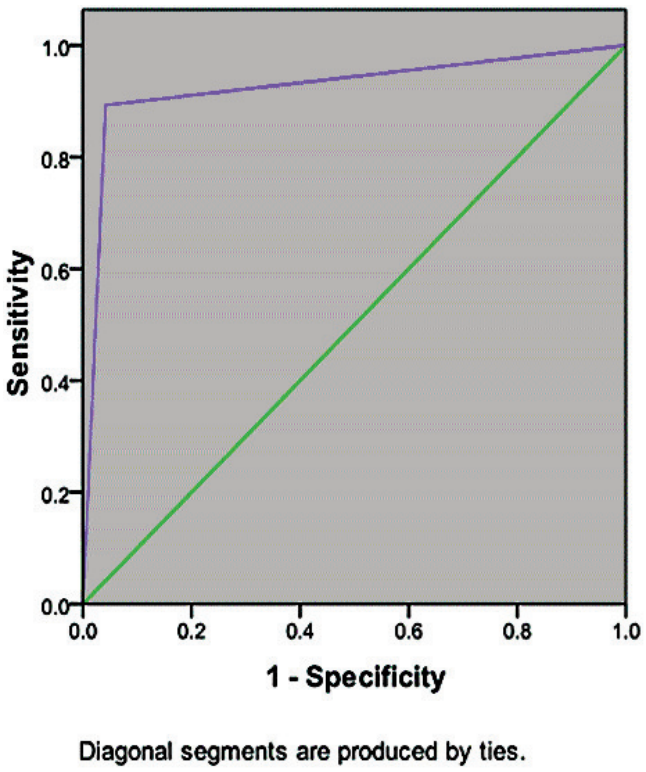

Figure: Receiver operating characteristic (ROC) curve.

Area Under the Curve

Test Result Variable(s): Doppler Ultrasonography in depicting Portal vein thrombosis

Area	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
		Lower Bound	Upper Bound
0.93	0.001	0.85	0.98

doppler ultrasonography (USG) also detected the PVT in the same number of patients. However, out of the 28 patients actually having the PVT (on CT), 25 were correctly diagnosed as having PVT on doppler sonography (89.3% sensitivity) (Table-1), and the USG could not detect PVT in 3 (3%) patients i.e false negative. Of the remaining 72 (72%) patients who were normal on CT (i.e normal PV visualisation), 69 were also depicted normal on doppler sonography (95.8%, specificity). Three (3%) cases were diagnosed as false positive by USG while they were normal on CT. Hence the sensitivity and specificity of the doppler ultrasonography in depicting PVT compared to CT scan, the gold standard, were 89.3% and 95.8% respectively. The PPV and NPV of the doppler USG were also calculated (Table-2).

The area under receiver operator curves (AUROC) of doppler sonography was calculated for diagnosing PVT in patients compared to the CT scan (Figure). Receiver operator characteristic curves were used to evaluate the diagnostic values. The area under receiver curve (AURC) at admission for doppler USG was 0.93 (95 % CI= 0.85-0.98).

Discussion

Hepatocellular carcinoma is currently one of the most common worldwide causes of deaths due to cancer. Since the mid-1980s the incidence of hepatocellular carcinoma has been rising at an alarming rate. Much of this increase is likely due to hepatitis C infection, a known risk factor for HCC. Areas such as Asia and sub-Saharan Africa with high rates of infectious hepatitis have increased incidence of HCC. Length of survival depends largely on the extent of cirrhosis in the liver; cirrhotic patients have shorter survival times with limited therapeutic options; portal vein occlusion, which occurs commonly, portends an even shorter survival.

HCC has greater propensity for portal venous invasion compared to metastatic or other primary liver neoplasms. Portal vein invasion in HCC has important implications in the management of the patient. Firstly, it is a bad prognostic factor and in its presence mean survival time of patient decreases even more. Secondly, it is associated with increased risks of complications e.g it can lead to tumour spread throughout the liver, increase portal venous pressure, variceal formation and increased risk of their rupture, ascites, hepatic encephalopathy and liver failure. Thirdly, the presence of portal vein thrombus is an important staging criterion in systems such as TNM and Cancer of the Liver Italian Programme. These patients are not good candidates for surgical resection and transplantation, having a poor prognosis.

Sonographic features of PVT include echogenic area within the vein lumen, evidence of portal vein collateral circulation, enlargement of the thrombosed segment of the vein, and cavernous transformation of the portal vein.

The reported incidence of PVT in association with HCC ranges from 5% to 44%.[7,8] In the current study, there was PVT incidence of 28%. Also, sensitivity and specificity of doppler sonography in depicting PVT in comparison with CT were 89.3% and 95.8% respectively. A study found 100% sensitivity of colour doppler sonography for non-visualisation of portal vein flow i.e thrombosis.[9] Another study determined 80.75% sensitivity and 100% specificity of doppler sonography in detecting PVT.[10] The detection sensitivity of doppler sonography reported here may well

be underestimated. For the three thrombi undetected on ultrasound, it is possible that some of these were actually new/small thrombi which are sometimes difficult to detect on ultrasound, which also depends upon operator's expertise.

In this preliminary clinical experience, colour doppler sonography appeared to be a reliable technique for evaluating the patency of the portal venous system. Sonography has the advantages of convenience, availability, cost-effectiveness and absence of radiation and contrast material risks. However, it can be affected by several factors, such as operator's experience, the patient's body habitus and patient's condition like breathlessness and poor response to command. In such cases, confirmation by other modalities like CT/MRI of portal vein patency or thrombus may be required.

Conclusion

Considering reasonable sensitivity, specificity and cost effectiveness, the colour doppler sonognaphy is a reliable investigation for evaluating the presence of PVT associated with HCC.

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