The value of dynamic (triphasic) computed tomography in differentiating malignant and benign portal vein thrombi using thrombus density

[1]Samuel M Danjem, [1]Abdul S Jimoh, [1]Gabkwet A Epga, [1]Emmanuel O Igoh, [1]Yetunde F Taiwo, [2]Hadijat O Kolade-Yunusa.

Abstract

Background: Portal vein thrombosis (PVT) is the development of thrombus in the main trunk of a portal vein and its intrahepatic right and left branches. Malignant PVT typically arises from invasion of hepatocellular carcinoma into the portal vein of patients with liver cirrhosis. In contrast, bland PVT is attributed to sluggish portal venous flow in cirrhotic patients with portal hypertension. The study was to determine the diagnostic performance of Triphasic CT imaging using thrombus density in differentiating malignant from benign portal vein thrombi.

Methods: In this retrospective study, 46 patients with PVT who had contrast-enhanced Triphasic CT of the abdomen were evaluated for PVT. The assessment was performed by measuring the CT attenuation values of the thrombi in Hounsfield Units (HU). ROC (Receiver Operating Characteristic) curves were used to identify accuracy and optimal cutoff values.

Results: Out of the 46 CT studies, 32 neoplastic thrombi and 14 bland thrombi were identified on the images. All patients with malignant thrombosis showed contrast enhancement while all patients with bland thrombi demonstrated no contrast enhancement. Contrast enhanced CT showed thrombi density sensitivity of 93.8%, specificity of 100% and accuracy of 95.7%. The AUCs was 0.539 in precontrast and 0.996 in portovenous phase for thrombus density. The optimal cut off in precontrast was 28.5 and in porto-venous phase was 59.0.

Conclusion: Estimating thrombi density with triphasic dynamic CT may represent a vital tool for reliable differentiation of neoplastic from bland thrombi in patients with PVT.

Key Words: Dynamic CT, Differentiating Benign, Malignant, PVT.

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Introduction

Portal vein thrombosis (PVT) is the development of thrombus in the main trunk of a portal vein and its intrahepatic right and left branches. PVT can occur due to local inflammation and infection, blunt trauma as well as from surgical procedures that cause injury to the portal venous system.[1,2]

PVT is a common complication of liver cirrhosis and hepatocellular carcinoma (HCC). It has been reported to occur in 0.6% to 15.8% of patients with chronic liver disease and in 38 to 44% of patients with HCC[3]. Malignant or neoplastic PVT is reported to occur in 6.5 to 44% of patients with HCC.[4]

Even though PVT can be asymptomatic in some patients with liver cirrhosis, in more than half of patients it can manifest with life threatening complications such as gastrointestinal bleeding and intestinal infarction.[3]

Malignant PVT typically arises from invasion of HCC into the portal vein of patients with liver cirrhosis.[5] The presence of malignant PVT greatly determines tumor staging, the selection of treatment plan and it also has serious influence on the prognosis. Unfortunately, the presence of malignant PVT is an absolute contraindication in surgical resection, orthotopic liver transplantation and percutaneous ablation therapy and a relative contraindication in Trans-arterial chemo-embolization (TACE) due to the unusual high incidence of tumor recurrence and dismal survival that is associated with malignant PVT.[6,7] In contrast, bland PVT, which is attributed to sluggish portal venous flow in cirrhotic patients with portal hypertension,[6] is considered to be treatable using anticoagulation and/or thrombolytic treatment,[8] and patients with bland PVT can undergo liver transplantation.[9] Hence, in determining the therapeutic strategy and in predicting patient survival, the detection of non-bland Portal Vein Tumor Thrombosis (PVTT) is of paramount clinical importance, particularly for HCC patients meeting the Milan criteria for liver transplantation.[10]

It is therefore pivotal to differentiate Benign or bland PVT from Malignant PVT. The reference standard for characterizing portal vein thrombus is histopathological examination which is achieved by ultrasound (US)-guided fine needle biopsy of the thrombus. However, this procedure is invasive. Furthermore, in many patients with advanced cirrhosis, biopsy of the thrombus may be contraindicated by the presence of impaired blood coagulation and/or ascites. Accordingly, it is desirable to

[1]Radiology Department, Faculty of Clinical Sciences, College of Health Sciences, University of Jos PMB 2084, Plateau State, Nigeria.[2]Radiology Department, University of Abuja, Gwagwalada, Abuja FCT

All correspondences to:
Danjem S.M
E-mail: samueljiblik@gmail.com; danjems@unijos.edu.ng

evaluate the reliability of noninvasive techniques such as dynamic CT scan (Triphasic CT imaging) in determining the benign or malignant nature of PVT. Other imaging modalities such as contrast enhanced ultrasonography and Gadoxetic Acid-enhanced Magnetic Resonant Imaging (MRI) have also been used to differentiate benign from malignant PVT.[11] However, these imaging modalities are not available in our environment but CT machines are relatively available and can be used as a non-invasive method of assessing thrombus in the porto-venous system.

Malignant and benign thrombi can often be differentiated by radiologists on the basis of CT imaging characteristics.[12] CT imaging findings of tumor thrombus suggesting malignancy are: Dilatation of portal vein, intra thrombus neovascularity (thread and streak sign seen as multiple enhancing intraluminal smaller vessels that can be seen at arterial phase), contiguity of the thrombus to tumor often with direct invasion.[13]

Mean thrombus density values (CT density) can distinguish neoplastic and bland thrombi by measuring thrombus density (in Hounsfield Unit) in arterial and portal venous phase.[14] Therefore the aim of this study was to determine the diagnostic performance of Triphasic CT imaging using thrombus density in differentiating malignant from benign portal vein thrombi.

Materials and Methods

This retrospective study was approved by our institutional review board and the requirement for informed consent was waived. In this study, we reviewed the CT images of all patients who had contrast enhanced triphasic CT examination of the abdomen between the period of January 2019 to April 2020 and for whom PVT was noted on the images.

CT Imaging Technique: All examinations were performed using a 16 slice CT machine (Brivo, General Electric (GE), USA). For all three phases, section thickness, collimation, and reconstruction interval were adjusted as 5 mm (120Kvp, 180 mAs). A volume of 100mls to 110mls of nonionic contrast material containing 300 mg/ml of iodine was intravenously administered to each patient at the rate of 3.5 ml/s. Images were acquired in triphasic sequences; arterial at 28–35s, portovenous phase at 60–70s, and delayed phase at 5–10 min all in axial planes. The obtained images were reformatted in coronal and sagittal planes.

Inclusion criteria were: patients over 18 years of age who had triphasic CT scan and those with PVT. Exclusion criteria were patients without PVT on triphasic CT images, those patients who had non enhanced CT abdomen.

Image Analysis:

All the triphasic CT images retrieved were retrospectively reviewed on a GE Advantage Windows 4.4 CT Workstation by a Radiologist with more than 5 years' experience. The information recorded from the CT images include the presence of hepatic mass; the presence of cirrhosis; the presence of thrombus along the portal vein; the mean thrombi density value; portal vein size and the presence of ascites. One hundred and twenty-one (121) patients were noninvasively diagnosed with liver cirrhosis and HCC according to the American Association for the Study of Liver Diseases guidelines.[15] Among the 121 patients, we only included 46 patients who had PVT on their CT images. Thrombi were evaluated in the post contrast (arterial and portovenous phases) images. Where thrombi were noted in the post contrast images, the mean density of the thrombi in porto-venous phase were recorded, then we searched for the thrombi in the pre contrast images and recorded the mean thrombi density values.

The findings of PVT of the dynamic CT are filling defect partially or totally occluding the vessel lumen and rim enhancement of the vessel wall (Fig. 1), sometimes with extension into splenic or superior mesenteric veins. Unenhanced scans have been shown to be of minimal benefit in the identification of thrombus.[6] Indirect signs of PVT are the presence of portosystemic collateral vessels, cavernous transformation of the portal vein, and arterioportal shunts.[16]

The mean thrombus density values of all the 46 patients were taken by measuring the thrombi density (in Hounsfield Unit) in pre contrast and porto-venous phases. ROC (Receiver Operating Characteristic) curves were used to identify accuracy and optimal cutoff values (Figures 2 and 3).

Results

Forty-six patients were diagnosed to have portal vein thrombosis by triphasic CT scan. Out of the 46 patients with PVT, 14 of them had features of benign PVT while 32 of the remaining patients had malignant PVT. Twenty (20) patients with PVT had cavernous transformation (Table 1).

All patients (100%) with malignant PVT and 75.0% of patients with cavernous transformation showed enhancement of the thrombus, while all patients with benign PVT showed no enhancement. This finding was statistically significant (p-value=0.013) (Table 1).

In patients with benign PVT, 85.7% of them had dilated portal vein, while 75.0% of patients with malignant PVT had dilated portal vein and 90.0% of patients with cavernous transformation were found to have dilated portal vein (Table 1).

Table 2 shows 92.9% sensitivity of thrombus density in

the pre-contrast phase, specificity 28.1% and accuracy 68%. The sensitivity of thrombus density in porto-venous phase is 93.8%, with specificity of 100% and accuracy of 95.7%. The best cut off CT density value in pre-contrast phase was 28.5 and 59.0 in porto-venous phase.

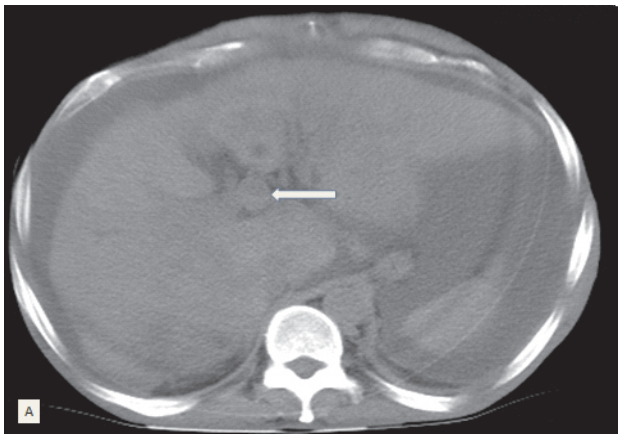
Table 1: Comparison between benign, malignant PVT & cavernous transformation

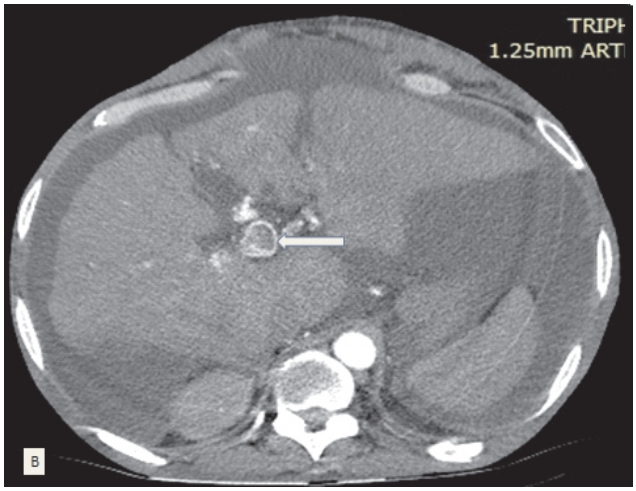
	Benign (14)		Malignant PVT (32)		Carvenous transformation(20)		p-value
	No.	%	No.	%	No.	%	
Cirrhosis							
Yes	0	0.0	1	3.1	0	0.0	0.667
No	14	100.0	31	96.9	0	0.0	
HCC							
Yes	14	100.0	31	96.9	20	100.0	0.583
No	0	0.0	1	3.1	0		
Portal vein size							
Yes (abnormal)	12	85.7	24	75.0	18	90.0	0.360
No (normal)	2	14.3	8	25.0	2	10.0	
Enhancement	0	0.0	32	100.0	15	75.0	0.013
Ascites							
Yes	12	85.7	22	68.8	17	85.0	0.276
No	2	14.8	10	31.3	3	15.0	

Table 2: Sensitivity and specificity of HU in detection of nature of thrombus

	AUC*	Best cut off (HU)	Sensitivity	Specificity	PPV	NPV	Accuracy
Thrombus pre-contrast	0.539	28.5	92.9%	28.1%	36.1%	90%	68%
Thrombus porto-venous	0.996	59.0	93.8%	100.0%	87.5%	100.0%	95.7%

**: AUC (Area Under Curve) is significant if more than 0.7.*





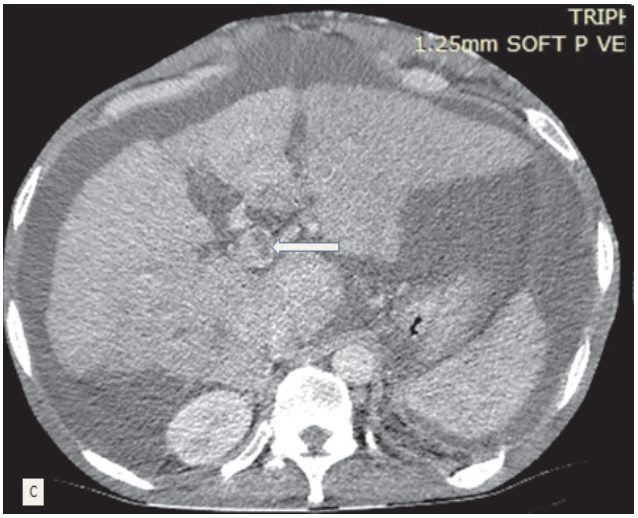


Figure 1: Triphasic computed tomography images showing a filling defect (arrows) in the right main portal vein as a hypodense (Hounsfield unit =17) in (a) precontrast phase; (b) In arterial phase (HU=47) and (c) portovenous phases (HU=62). There is moderate to massive ascites.

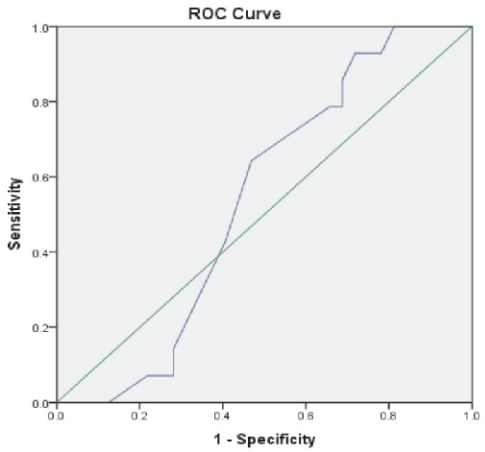


Figure 2: Receiver operating characteristic (ROC) curve for thrombus pre-contrast

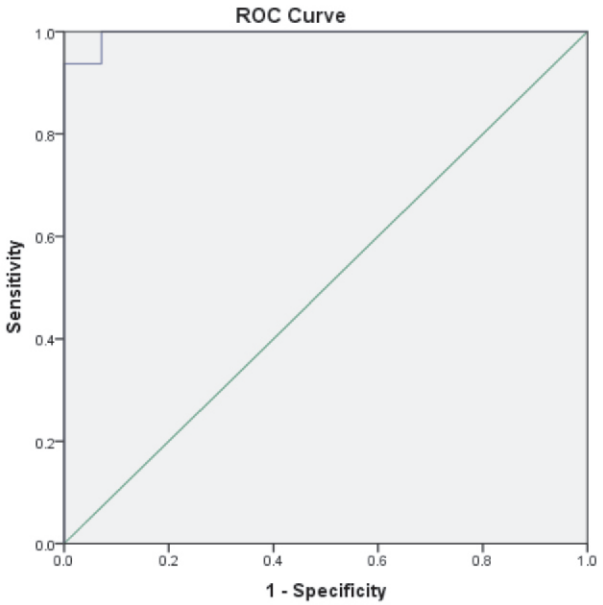


Figure 3: Receiver operating characteristic (ROC) curve for thrombi in porto-venous phase.

Discussion

Dynamic contrast enhanced CT has shown significant improvement in the detection of PVT and in fact it is said to be the best means of diagnosis of PVT and evaluation of various causative diseases.[17] This is quite important to poor resource countries where high earn equipment such as MRI, contrast enhanced ultrasound and angiography machines are not readily available and patients pay out of pocket to get all investigations done. CT machines are relatively available.

Our study shows that all patients with malignant PVT (100%) demonstrated enhancement of thrombi in the porto-venous phase, while all patients with benign PVT showed no enhancement, our finding is consistent with the study by Mona et al,[18] who also reported contrast enhancement in all patients with malignant PVT in the arterial phase with wash out in the porto-venous phase, while no contrast enhancement was noted in all patients with benign PVT. Similarly Osman et al[19] reported that 84.8% of patients with malignant PVT showed neo-vascularity of PVT, with 87.8% of early arterial enhancement and rapid washout of the thrombus and none of the patients with benign PVT showed intra-thrombus neovascularity or enhancement.

In this study, we found out that dynamic CT is highly sensitive in the diagnosis of malignant PVT with a sensitivity of 93.8%, specificity of 100% and 95.7% accuracy. Our study is in agreement with the study of Osman et al who found that MDCT assessment has a significant value in diagnosis of malignant PVT, with a sensitivity of 91.7%, 100% specificity and 94% accuracy. Lee at al[20] and Piscaglia et al[6] also considered neovascularity sign 100% in malignant PVT. Mano et al[18] however reported a sensitivity of 100%, specificity of 93.0% and 100% accuracy of contrast enhanced CT in evaluation of malignant PVT.

Osman et al[19] conducted a study in Egypt using multi modalities imaging evaluation of benign and malignant porto-venous thrombosis, they revealed that dynamic CT has a specificity of 100% while Apparent Diffusion Coefficient (ADC) MRI showed a specificity of 82.5%, ADC MR showed the same accuracy with dynamic CT (94.0%). However, MRI was shown to have a higher sensitivity (100%) when compared to CT (91.7%). A recent study by Jae et al[21] concluded that Gadoxetic Acid-enhanced MRI (GA-MRI) was demonstrated to be superior to CECT in terms of sensitivity in the detection of PVTT without significant loss of specificity in patients with HCC meeting the Milan criteria.

Our study indicates that the best cut off value to diagnose malignant thrombus in porto-venous phase is 59HU. The Area Under the Curve (AUC) is 0.996 in porto-venous phase which is more than 0.7 (significant), but in pre-contrast phase the AUC is 0.539 which is less than 0.7, this implies that the precontrast phase is not significant in differentiating between benign and malignant PVT. Our finding is in agreement with Mona et al[18] who reported the best cut off values of 50 in the porto-venous phase with AUC of 0.981 for the portovenous phase and 0.552 for the precontrast phase. This finding also corresponds with the study of Canellas et al[22] who reported that the mean thrombus density values could also reliably distinguish neoplastic (81 .39HU) and bland (32.88HU) thrombi. They also documented the optimal cutoff value of 54HU for thrombus density in porto-venous phase.

Conclusion

Dynamic CT imaging is essential in providing accurate evaluation and differentiation of benign from malignant PVT. Triphasic CT has indicated that attenuation values allow for reliable differentiation between neoplastic and bland thrombi in the post contrast phases with high sensitivity, specificity and accuracy. Dynamic CT imaging may be an adjunct to other imaging modalities such as Ultrasound and Magnetic Resonance Imaging and possibly limits the needs for more invasive procedures like liver biopsy for histology for clinical decision making.

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