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Amira M. Gerges
Radiodiagnosis department, National Hepatology and Tropical Medicine Research Institute, amira.mounir.092@gmail.com

Mohamed A. Abo El Maaty
Radiodiagnosis Department, Faculty of Medicine, Ain Shams University

Mohamed M. Fawzi
Radiodiagnosis department, National Hepatology and Tropical Medicine Research Institute

Ayman H. Hassan
Radiodiagnosis department, National Hepatology and Tropical Medicine Research Institute

Ahmed Said Badr
Radiodiagnosis department, National Hepatology and Tropical Medicine Research Institute

See next page for additional authors

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Authors

Amira M. Gerges, Mohamed A. Abo El Maaty, Mohamed M. Fawzi, Ayman H. Hassan, Ahmed Said Badr, and Sherihan S. Madkour

ORIGINAL STUDY

Role of Doppler ultrasound and triphasic computed tomography in differentiation between benign and malignant portal vein thrombosis

Amira M. Gerges [a,*], Mohamed A. Abo El Maaty [b], Mohamed M. Fawzi [a], Ayman H. Hassan [a], Ahmed S. Badr [a], Sherihan S. Madkour [b]

[a] Department of Radiodiagnosis, National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt
[b] Department of Radiodiagnosis, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Abstract

Background: **Portal vein thrombosis (PVT) is typically a consequence of cirrhosis that already exists, abdominal malignancy, hypercoagulable conditions, or abdominal inflammation. Imaging techniques are used to identify PVT. Once a thrombus has been identified using ultrasound (US), Doppler US can be used to exclude malignancy activity. If more information is needed, the following step is computed tomography or magnetic resonance angiograms. If these tests are insufficient, digital subtraction angiography should be carried out.**

Methods: **The study included 40 patients diagnosed by B-mode US to have PVT. It referred to the radiology department of the National Hepatology and Tropical Medicine Research Institute to differentiate between benign and malignant PVT using color Doppler and Triphasic computed tomography (CT).**

Results: **A total of 40 patients were included in the final analysis report. The CT categorized 17 patients as benign PVT and 23 patients as malignant PVT. However, all of them had neovascularity and showed early arterial enhancement and delayed washout.**

Intra-thrombus pulsatile flow by color Doppler was detected in 19 patients with a percentage of agreement of 80%, sensitivity of 73.9%, and specificity of 88.2%.

Conclusion: **Color Doppler US is considered an effective noninvasive tool to differentiate between benign and malignant PVT, but it is operator-dependent which need the expertise to detect the vascularity within the thrombus. But is an easy, low-cost, available, with no contraindications to be done and no exposure to radiation. Although the absence of intra-thrombus vasculature does not exclude the intra-vascular malignancy invasion, here comes the role of Triphasic CT.**

Keywords: Benign, Doppler ultrasound, Malignant portal vein thrombosis, Triphasic computed tomography

1. Background

Portal vein thrombosis (PVT) is a condition commonly observed in liver cirrhosis, abdominal cancer, or abdominal inflammation conditions [1]. The prevalence of PVT among patients with cirrhosis ranges from 5% to 26% [1]. In individuals with liver cirrhosis or hepatocellular carcinoma (HCC), thrombosis can occur in both benign and malignant forms [2].

Malignant PVT, resulting from tumor invasion into the portal venous system, is a well-known complication of hepatocellular carcinoma [2]. Benign PVT can also manifest in HCC patients, particularly in the early stages of the disease [3]. However, differentiating between benign and malignant thrombi usually requires an invasive procedure, such as ultrasound (US)-guided small needle biopsy [3].

To facilitate the diagnosis of PVT, US is typically the initial imaging modality employed [3]. Doppler

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* Corresponding author.
E-mail address: amira.mounir.092@gmail.com (A.M. Gerges).

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US and triphasic computed tomography (CT) scans are additional imaging techniques that can aid in distinguishing between benign and malignant PVT [3]. In this study, our objective was to assess the US-based conclusion of the nature of PVT in comparison to triphasic CT. By evaluating the diagnostic accuracy of these imaging modalities, we aim to provide valuable insights into their roles in the management and prognosis of patients with PV.

2. Methods

2.1. Study design and participants

This comparative study was conducted at the Radiodiagnosis Department of the National Hepatology and Tropical Medicine Research Institute over 1 year. A total of 40 patients diagnosed with PVT were included in the study, without any age or sex limitations. Pregnant female patients and those with contraindications to intravenous contrast agents (such as severe allergic reactions, terminal liver or renal failure with serum creatinine levels >2 mg/dl), and hemodynamically unstable patients were excluded from the study.

2.2. Ethical considerations

Written informed consent was obtained from all participants, explaining the details of the procedure. The study was conducted by the ethical guidelines and regulations set by the ASU Ethical and Scientific Committee. The privacy and confidentiality of the participant's data were ensured throughout the study.

2.3. Study tools and procedures

All patients underwent a thorough history-taking and clinical examination, including a general and abdominal examination. Laboratory investigations were conducted, including serum creatinine, alpha-fetoprotein, anti-hepatitis C virus, and anti-hepatitis B virus tests.

Real-time US was performed using LOGIQ P9 US machines equipped with a 3.5 MHz transducer to assess liver pattern, presence of disease, and the presence or absence of focal lesions. Color Doppler was implemented to assess the portal vein using the same high-resolution prob. The protocol involved obtaining gray-scale images of the portal vein thrombus and conducting color duplex imaging. The diagnostic criteria for PVT involves the absent of flow during color implementation, and event partial flow is detected denting partial thrombosis. The rest of the venous tree is scanned to track the extent of the thrombosis including hepatic veins, and intrahepatic branches of the portal vein and superior mesenteric vein. Upon focusing the color box on the intravascular thrombosis, the malignant thrombosis exhibits internal vascularity (pulsatile flow pattern). However, benign thrombosis has no vascularity within.

Triphasic CT examination of the liver with splenic-portography was performed using a Toshiba Aquilion 64-slice CT system. A power injector was used to inject 100 ml of Omnipaque 300 mg/ml contrast agent at a rate of 4 ml/s. Arterial phase scanning, portal venous phase imaging, and delayed phase imaging of the entire abdomen were performed using specific scanning delays and image thicknesses.

Using a Toshiba Aquilion 64-slice CT scanner, a triphasic CT was carried out for a dedicated examination of the liver and splenic vascularity. The contrast agent Omnipaque 300 mg/ml was injected into 100 ml at a rate of 4 ml/s using a power injector. Utilizing certain scanning delays and image thicknesses, the whole abdomen was imaged utilizing delayed phase imaging, portal venous phase imaging, and arterial phase scanning. Detection of the PVT is easily noticed through opacification (partially or totally) of the portal phase. Enhancement of the PVT raises the possibility of malignancy. The benign thrombosis has no enhancement through all vascular phases.

2.4. Risks and complications

The potential risks associated with contrast-enhanced CT included radiation exposure and rare side effects of the iodinated contrast agent, such as allergic reactions, contrast-induced acute kidney injury, arrhythmia, and other minor side effects. In case of an allergic reaction, appropriate management was provided, including administration of antihistamines and adrenaline. For patients with contrast-induced nephropathy, immediate dialysis was initiated.

2.5. Data analysis

Descriptive statistics, such as mean, standard deviation, range, median, interquartile range, frequency, and percentage, were calculated based on the type of data obtained. The difference between CT and Doppler studies regarding PV diameter, extent of the thrombosis, presence of focal lesion, and presence of collaterals, and diagnosis of both benign and malignant thrombosis was tested using the χ^2 test or Fisher's exact test when applicable. The

two investigation methodologies' agreement was assessed using Kappa statistics, where values below 0.40 indicate poor agreement, values between 0.40 and 0.75 indicate fair to good agreement, and values over 0.75 indicate excellent agreement. At *P* less than 0.05, statistical significance was established. Statistical Package of the Social Sciences (SPSS), version 23 (SPSS Inc. Released by 2015. IBM SPSS Statistics for Windows, version 23.0, Armonk, NY: IBM Corp.) was used for the final data analysis.

3. Results

3.1. Demographic data

In 40 patients, there were 26 male patients and 14 female patients with mean age 59.18 and SD 10.93. As shown in Table 1.

3.2. U/S findings and diagnosis

Regarding the PV diameter, there were 77.5% had Dilated PV. Regarding to the extent of the thrombus, it may be partial or completely occluded the PV, there were 67.5% had a complete thrombus. The extension of the thrombus may include the main PV, main PV and one or both of its branches, right or left branches or both, main PV and its main branches extending up to its tributaries or involving the extension of the thrombus to right PV, main PV, and its tributaries. With 40% involving only one or both PV branches. Regarding the echogenicity of the thrombus, 47.5% showed an echogenic thrombus. Regarding the vascularity within the thrombus, 47.5% does not have vascularity. Regarding the presence of focal lesions, 62.5% have focal lesion. Regarding the presence of Porto-systemic collaterals, 55% have collaterals. Final diagnosis by U/S: 52.5% had a benign thrombus and 47.5 had a malignant thrombus. As shown in Table 2.

3.3. Triphasic CT findings and diagnosis

Regarding the PV diameter, there were 77.5% had Dilated PV. Regarding to the extent of the thrombus, it may be partial or completely occluded the PV, there were 67.5% had a complete thrombus. The extension of the thrombus may include the main PV,

Table 1. Demographic data for the studied group.

	Mean/N	SD/%	Median (IQR)	Range
Age	59.18	10.93	60 (53–65.5)	(21–85)
Sex				
Male	26	65.0		
Female	14	35.0		

Table 2. Ultrasound findings and diagnosis for the studied group.

	N (%)
Portal vein diameter	
Not dilated	9 (22.5)
Dilated	31 (77.5)
Extent	
Partial	13 (32.5)
Complete	27 (67.5)
Extension	
Main portal	2 (5.0)
Main and right or left PV or both	15 (37.5)
Right or left PV or both	16 (40.0)
Main PV, branches and tributries	4 (10.0)
Main PV, right and tributries	3 (7.5)
Echochenicity	
Hypoechoic	5 (12.5)
Echogenic	19 (47.5)
Isoechoic	16 (40.0)
Vascularity	
No	21 (52.5)
Yes	19 (47.5)
Focal lesion	
No	15 (37.5)
Yes	25 (62.5)
Collaterals	
No	18 (45.0)
Yes	22 (55.0)
Diagnosis	
Benign thrombus	21 (52.5)
Malignant thrombus	19 (47.5)

Table 3. Triphasic computed tomography findings and diagnosis for the studied group.

	N (%)
Portal vein diameter	
Not dilated	9 (22.5)
Dilated	31 (77.5)
Extent	
Partial	13 (32.5)
Complete	27 (67.5)
Extension	
Main portal	2 (5.0)
Main and right or left PV or both	15 (37.5)
Right or left PV or both	16 (40.0)
Main PV, branches and tributries	4 (10.0)
Main PV, right and tributries	3 (7.5)
Arterial enhancement	
No	17 (42.5)
Yes	23 (57.5)
Wash out	
No	17 (42.5)
Yes	23 (57.5)
Focal lesion	
No	15 (37.5)
Yes	25 (62.5)
Collaterals	
No	19 (47.5)
Yes	21 (52.5)
Diagnosis	
Benign thrombus	17 (42.5)
Malignant thrombus	23 (57.5)

main PV and one or both of its branches, right or left branches or both, main PV and its main branches extending up to its tributaries or involving the extension of the thrombus to right PV, main PV, and its tributaries. With 40% involving only one or both PV branches. Regarding the enhancement in the arterial phase and washout in the delayed phase, there were 57.5% showed enhancement in the arterial phase and washout in the delayed phase. Regarding the presence of focal lesions, 62.5% have focal lesions. Regarding the presence of Porto-systemic collaterals, 52.5% have collaterals. Final diagnosis by CT: 42.5% had a benign thrombus and 57.5% had a malignant thrombus. As shown in Table 3.

Comparison between CT and U/S findings revealed no significant difference regarding PV diameter (P value = 1.0), extent of the thrombosis (P value = 1.0), presence of focal lesion (P value = 1.0), and presence of collaterals (P value = 0.823), and diagnosis of both benign and malignant thrombosis (P value = 0.37). As shown in Table 4.

As shown in Table 5 and Figs. 1–10.

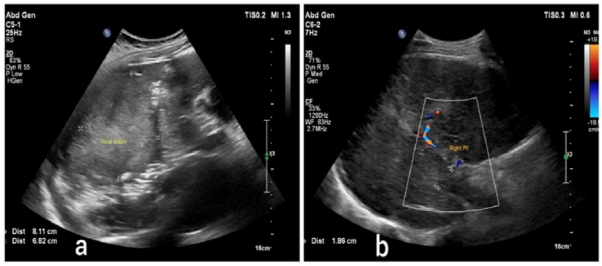

Fig. 1. (a) Showing cirrhotic liver with a focal lesion occupying the right lobe. (b) Showing dilated portal vein with thrombus isoechoic to the focal lesion totally occluding the right portal vein and extending of to the main portal vein with no detected vascularity within the thrombus.

Table 4. Comparison between computed tomography and U/S findings.

	Grouping		Test of significance	
	U/S *N* (%)	CT *N* (%)	*P* value	Significance
Portal vein diameter				
Not dilated	9 (22.5)	9 (22.5)	1.00[a]	NS
Dilated	31 (77.5)	31 (77.5)		
Extent				
Partial	13 (32.5)	13 (32.5)	1.00[a]	NS
Complete	27 (67.5)	27 (67.5)		
Extension				
Main portal	2 (5)	2 (5)	1.00[b]	NS
Main and right or left PV or both	15 (37.5)	15 (37.5)		
Right or left PV or both	16 (40)	16 (40)		
Main PV, branches and tributries	4 (10)	4 (10)		
Main PV, right and tributries	3 (7.5)	3 (7.5)		
Focal lesion				
No	15 (37.5)	15 (37.5)	1.00[a]	NS
Yes	25 (62.5)	25 (62.5)		
Collaterals				
No	18 (45)	19 (47.5%)	0.823[a]	NS
Yes	22 (55)	21 (52.5		
Diagnosis				
Benign thrombus	21 (52.5)	17 (42.5)	0.37[a]	NS
Malignant thrombus	19 (47.5)	23 (57.5)		

[a] Chi-Square test of significance.
[b] Fisher's Exact test of significance.

Table 5. Agreement test between diagnosis by computed tomography as a gold standard test and diagnosis by ultrasound.

	Diagnosis by CT		%	Sensitivity	Agreement			
	Malignant thrombus *N* (%)	Benign thrombus *N* (%)			Specificity	Kappa	*P* value	Significance
Diagnosis by U/S								
Malignant thrombus	17 (73.9)	2 (11.8)	80.0	73.9	88.2	0.603	<0.001	S
Benign thrombus	6 (26.1)	15 (88.2)						

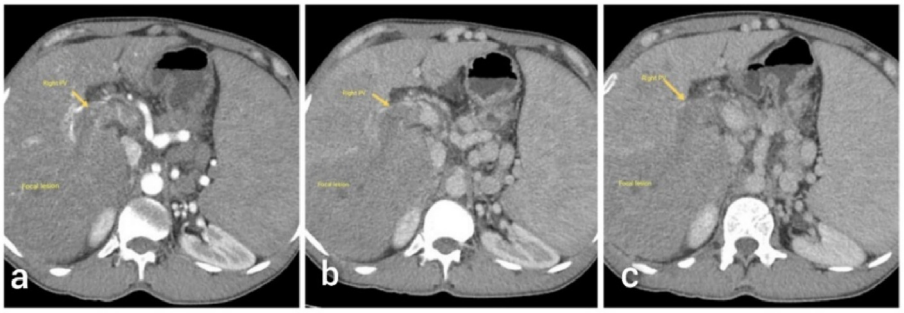

Fig. 2. (a) Arterial phase: showing contrast enhancement of right hepatic focal lesion with contrast-enhancing right portal vein. (b) Portal phase: showing right portal vein thrombosis extending to the main portal vein and multiple dilated porto-systemic collaterals at the splenic hilum. (c) Delayed phase: showing wash out of the contrast from the focal lesion as well as the right portal vein thrombus.

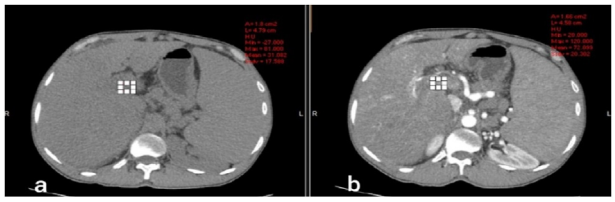

Fig. 3. (a) Noncontrast phase showing HU in the right portal vein thrombus = 31. (b) Arterial phase showing HU in the thrombus = 72.

4. Discussion

PVT is a serious condition observed in individuals with complicated liver cirrhosis, abdominal cancer, or abdominal inflammation [1]. Since liver transplantation is not recommended for malignant thrombus, it is imperative to accurately distinguish between benign and malignant PVT [4]. In this study, we compared the diagnostic capabilities of

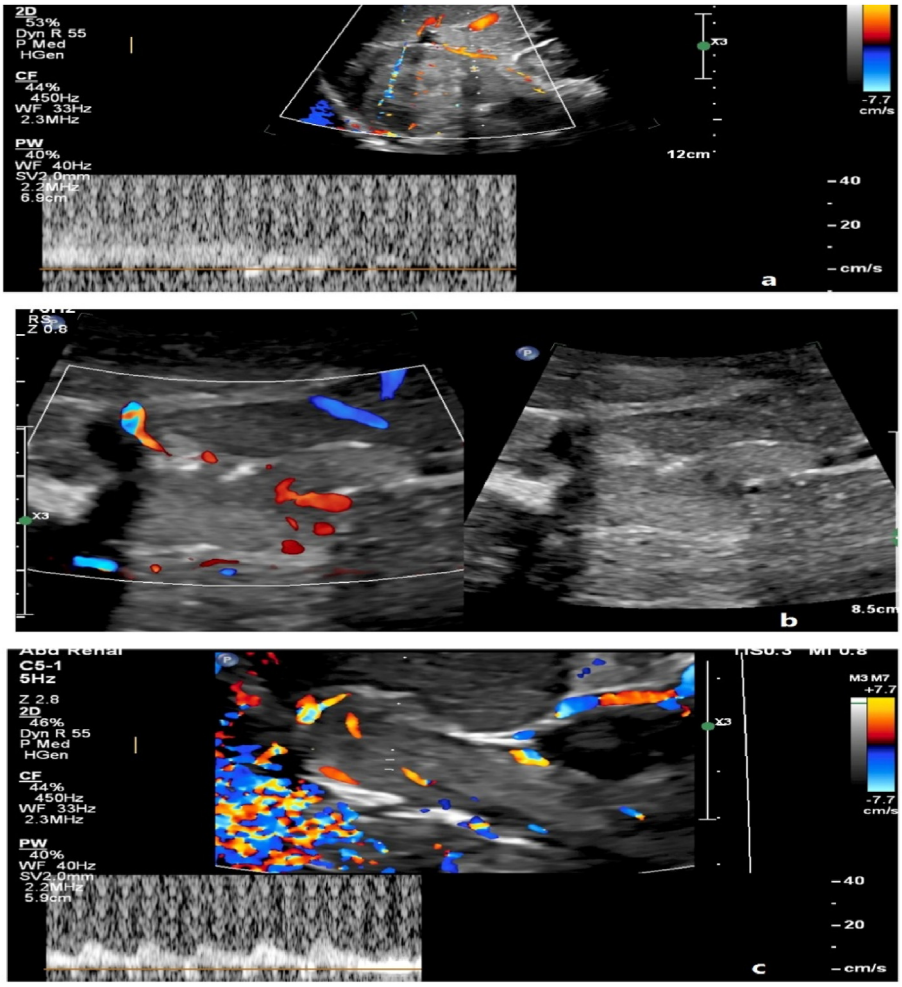

Fig. 4. (a) Showing cirrhotic liver with right lobe hepatic focal lesion. (b) An echogenic right portal vein thrombus. (c) Detected vascularity within the thrombus.

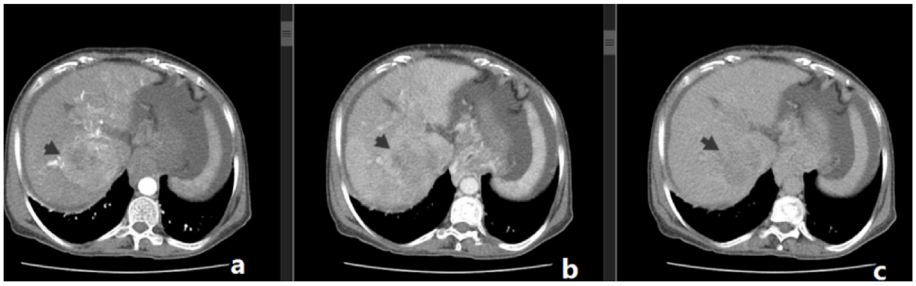

Fig. 5. (a) Arterial phase: showing contrast-enhancing right hepatic lobe focal lesion (arrow). (b) and (c) Portal and delayed phases showing wash out of the contrast from the focal lesion.

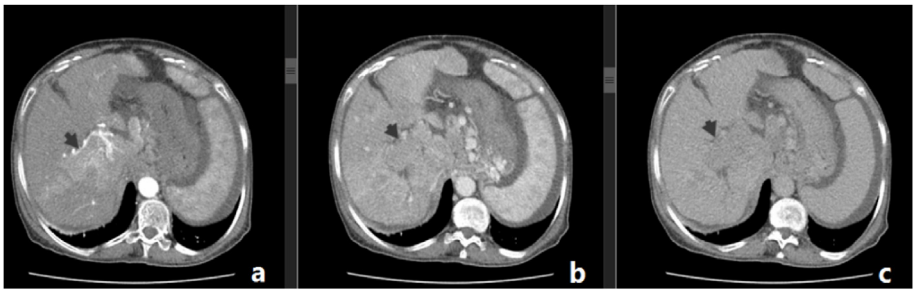

Fig. 6. (a) Arterial phase: right portal vein (arrow) showing contrast enhanced. (b) and (c) Portal and Delayed phases: showing wash out of the contrast from the thrombus.

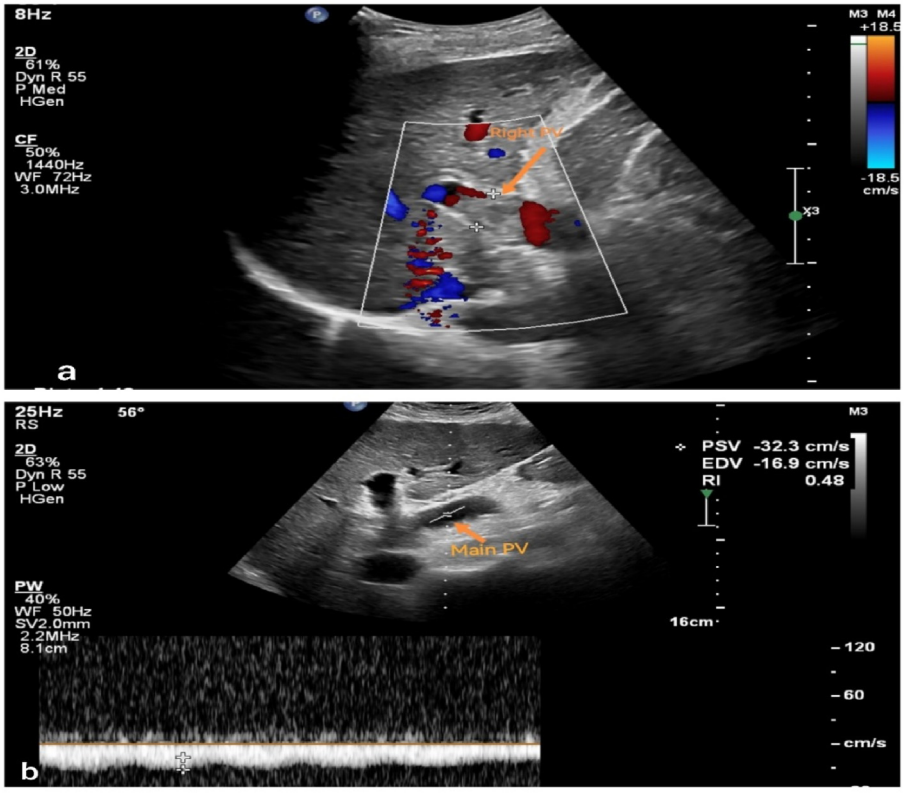

Fig. 7. (a) Shows a cirrhotic liver with a partially thrombosed right portal vein with no vascularity within the thrombus. (b) Showing extension of the thrombus to the main PV.

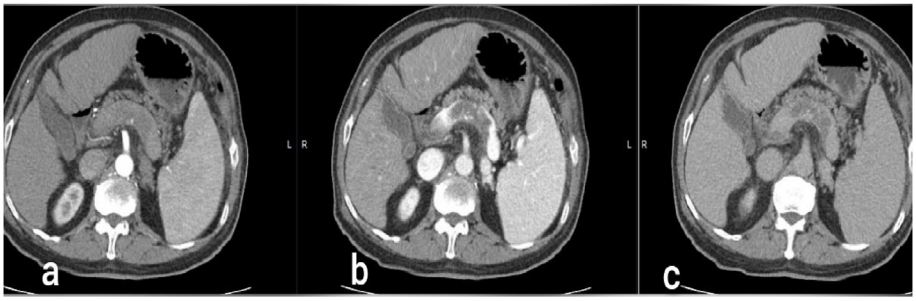

Fig. 8. (a) Arterial phase, (b) Portal phase and (c) Delayed phase: showing hypodensity partial thrombus within the main PV with no contrast enhancement.

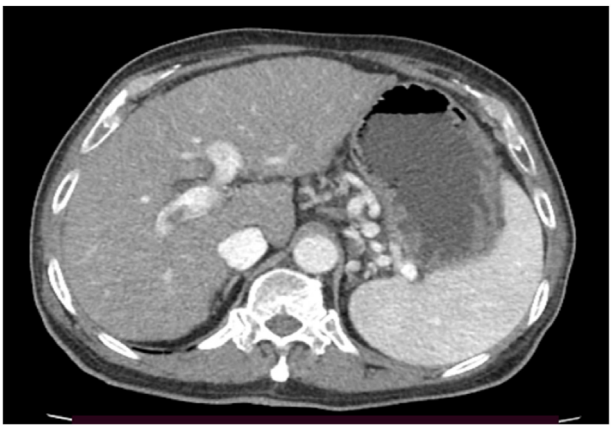

Fig. 9. Portal phase of the triphasic computed tomography showing partial right portal vein thrombus.

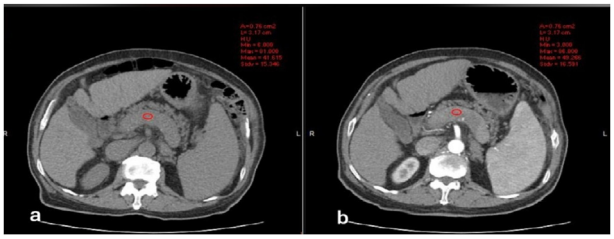

Fig. 10. (a) Noncontrast phase showing HU of the main portal vein thrombus = 41. (b) Arterial phase showing HU of the thrombus = 49.

Doppler US and triphasic CT in distinguishing between benign and malignant PVT.

Our findings are consistent with previous studies that have reported the prevalence of PVT in cirrhotic patients to range from 5 to 26% [2]. Furthermore, malignant PVT is a well-known consequence of hepatocellular carcinoma (HCC), resulting from tumor invasion into the portal venous system [2]. Differentiating between benign and malignant PVT is essential for appropriate management, and our study aimed to evaluate the diagnostic accuracy of Doppler US and triphasic CT in achieving this objective.

Doppler US is a noninvasive modality that can provide valuable information about blood flow characteristics within the thrombus. According to previous research, the presence of pulsatile flow within the portal vein thrombus, along with a clear distinction from the hepatic artery and a patent segment of the portal vein, indicates a high specificity for malignant thrombus [5]. Our study supports these findings, as we observed pulsatile flow in the thrombus using color Doppler imaging in a subset of patients with malignant PVT.

However, it is important to note that the sensitivity of color Doppler US in detecting pulsatile flow within malignant thrombi has been reported to be low, ranging from 21 to 80.7% [3,6,7]. This suggests that relying solely on color Doppler imaging may lead to false-negative results and subsequent misclassification of malignant PVT as benign. Therefore, additional imaging modalities are necessary to improve diagnostic accuracy.

When evaluating PVT, triphasic CT with contrast enhancement provides several benefits, such as the capacity to locate the PVT's origin and identify any related issues. Based on certain imaging criteria, the dynamic nature of contrast enhancement makes it possible to distinguish between benign and malignant thrombi. Previous research has shown that the presence of malignant PVT is indicated by arterial phase increase, fast washout in the portal phase, neovascularity within the thrombus, and direct tumor invasion of the thrombus [6–11].

These results are corroborated by our investigation, which used triphasic CT to detect arterial phase augmentation and delayed phase washout in most patients with malignant PVT. Furthermore, benign PVT was linked to the lack of thrombus neovascularity, arterial augmentation, or tumor invasion in the thrombus. In several cases, the specificity of these CT results for the diagnosis of malignant PVT was over 100%.

It is important to remember that triphasic CT has various drawbacks, such as ionizing radiation

exposure and the possibility of contrast agent nephrotoxicity. When choosing the right imaging modality, these variables should be taken into account, particularly in individuals who are not a good fit for CT or who are worried about radiation exposure.

To confirm our results in larger cohorts and investigate the possibility of additional imaging modalities, including MRI, in the assessment of PVT, more study is necessary. Furthermore, it would be extremely beneficial for clinical practice to create noninvasive, highly sensitive biomarkers for the distinction between benign and malignant PVT.

4.1. Conclusion

Although color Doppler US is thought to be a useful non-invasive technique for distinguishing between benign and malignant PVT, its ability to identify vascularity inside a thrombus depends on the operator. However, it is simple, affordable, accessible, requires no special preparation, and does not involve radiation exposure. While the lack of intrathrombus vasculature does not rule out the thrombus's malignant origin, triphasic CT plays a crucial role in this situation.

Ethics information

Ethical approval was taken from the Institutional review board (IRB) at the National Hepatology and Tropical Medicine Research Institute with approval number: FWA 000017585.

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Nil.

Authors contribution

All authors contributed equally to this work regarding putting the study design. Dr Amira collected the data and followed up with the patients. All the authors participated in writing of the manuscript and approved the final version of the manuscript.

Institutional review board (IRB) approval number

FWA 000017585.

Conflicts of interest

There are no conflicts of interest.

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