



## Diagnostic Accuracy of Color Doppler Ultrasound in Detecting Portal Vein Thrombosis in Patients Having Hepatocellular Carcinoma Due to Chronic Hepatitis C Keep Triphasic CT as Gold Standard

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### Declaration

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### ABSTRACT

**Objective:** With triphasic CT as the gold standard, the purpose of this study is to ascertain the diagnostic accuracy of color doppler ultrasonography in identifying portal vein thrombosis in patients with hepatocellular carcinoma caused by chronic hepatitis C. **Study design:** Cross-sectional (validation) study. **Settings:** Department of Radiology, Fouji Foundation Hospital, Rawalpindi. **Duration of study:** September 2024 to February 2025. **Methodology:** The study comprised 334 patients, aged 18 to 60 years presenting with hepatocellular carcinoma due to chronic hepatitis C infection. Prothrombotic disorders such as protein C, S, or factor V deficiency were excluded. 3.5 MHz matched imaging and Doppler frequency transducer was used for Color Doppler US. GE and Philips Health Care's MDCT scanner 16 detectors were used to perform triphasic CT scans of the abdomen and pelvis. Consultant radiologists performed the color doppler and CT reports. **Results:** 92.12% color doppler sensitivity, 91.60% specificity, 94.44% PPV, 88.24% NPV, and 91.92% diagnostic accuracy were used to diagnose PVT. **Conclusion:** Doppler ultrasonography has been shown to have a good diagnostic accuracy in identifying portal vein thrombosis (PVT) in individuals with hepatocellular cancer.

### INTRODUCTION

The primary cause of hepatocellular carcinoma (HCC) is liver cirrhosis.<sup>1</sup> Hepatitis-C infection is the primary cause of cirrhosis in Pakistan, causing 52–61% of cases. Five to twenty out of every 100 HCV-infected individuals go on to develop cirrhosis.<sup>2</sup> HCC is the fifth most prevalent type of cancer overall and the third most common cause of cancer-related deaths. Its incidence is 35 percent in poorer nations. Compared to wealthy nations, this is two to three times higher. Patients with non-alcoholic fatty liver disease are also experiencing an increase in HCC cases in Western nations.<sup>1</sup> In poor nations, cirrhosis resulting from hepatitis C virus infection is linked to the majority of hepatocellular carcinoma (HCC) cases.<sup>3</sup> Portal vein thrombosis complicates HCC in as many as 44% of patients.<sup>4</sup> A thrombus that partially or totally blocks the portal vein or its branches within its lumen is known as portal vein thrombosis (PVT).<sup>5</sup> It happens in conjunction with either hepatic cancer or liver cirrhosis. It is essential to distinguish between tumoral and bland PVT in order to decide on tumor staging and the best course of treatment. In clinical practice, thrombus discrimination is frequently

based on a combination of clinical and laboratory data, as well as diagnostic imaging techniques like as Doppler US and Triphasic CT, even though histological analysis is the reference standard for characterizing PVT.<sup>6</sup> The initial line of radiological investigation for PVT detection is ultrasound. On ultrasonography, thrombus manifests as solid intraluminal material that is hypo-, iso-, or hyperechoic. Color Doppler Sonography displays local hemodynamics and blood flow in different organs.<sup>7</sup> Visualizing the pattern of artery waveforms in a thrombus on Doppler spectral ultrasonography is thought to be a very specific diagnostic of neoplastic thrombus. By identifying an intraluminal substance and thrombus enhancement, CT can identify PVT. Forty-four percent of hepatocellular cancer patients had portal vein thrombosis.<sup>8,9</sup> Color Doppler sonography was the gold standard for diagnosing portal vein thrombosis in one study, with 89.3% sensitivity, 95.8% specificity, 89% PPV, 95.7% NPV, and 93.7% overall diagnostic accuracy.<sup>10</sup>

My study intends to assess the diagnostic accuracy of color doppler sonography in assessing the portal venous system in HCC caused by hepatitis C, using triphasic computed tomography data as the gold standard. Data on

this research issue in our local population was previously unavailable. Using such evidence will aid in the development of more effective medical plans to address such instances and assist them in managing more effectively to achieve the desired outcomes. The alarming rise in hepatitis C cases in Pakistan is causing an increase in the prevalence of HCC. PVT has a direct impact on HCC management. A conveniently available, reasonably priced, and commonly used modality is the color doppler.

## METHODOLOGY

334 patients, ages 18 to 60, who presented to the Radiology Department of Fouji Foundation Hospital in Rawalpindi with hepatocellular carcinoma (abdominal distention and ultrasound showing shrunken liver along with ascites plus increased alpha fetoprotein 3level [ $>400\text{ng/dl}$ ]) as a result of a chronic hepatitis C infection (hepatitis C qualitative PCR positive for more than 12 months) were the subjects of this descriptive, cross-sectional study. Based on the 44% prevalence of PVT in HCC,<sup>3</sup> 89.3% sensitivity (10% absolute precision), and 95.7% specificity (5% absolute precision) of color doppler, the sample size was determined using a sensitivity and specificity calculator with a 95% confidence level. There will be 334 patients in the sample.<sup>10</sup> Patients were selected using a non-random consecutive sampling technique. Excluded were patients with prothrombotic disorders such as protein C, S, or factor V deficiency.

Patients who met the inclusion criteria were recruited from the radiology department of Fouji Foundation Hospital following permission by the hospital ethics board. After outlining the goal of the study, a formal informed consent was obtained. Age, gender, and symptom duration demographic information were recorded. For symptoms, a full medical history was obtained. 3.5 MHz matched imaging and Doppler frequency transducer was used for Color Doppler US. After obtaining a grayscale image of the PV thrombus, the neighboring hepatic artery and thrombus extension are determined by performing color, power, and duplex Doppler US on the PV thrombus, PV tributaries, and branches. Anterior sub-xiphoid technique was used to assess thrombi in the left portal vein, while intercostal or subcostal techniques were used to assess thrombi in the right portal vein between the mid-clavicular line and the posterior axillary line. The flow was classified as either continuous or pulsatile based on its spectral structure. A subjective definition of pulsatile flow was a waveform in which the end diastolic and peak systolic velocities differed significantly.

Triphasic CT scans of the abdomen and pelvis were performed using the MDCT scanner 16 detectors from GE and Philips Health Care. Double arterial phase scanning was performed using a power injector to deliver 150 ml of Omnipaque 300 mg/ml at a rate of 4 ml/s. With scanning delays of 20 and 35 seconds, respectively, from the beginning of the contrast material injection, we used a single breathing hold for both early and late arterial phase imaging capture to lessen the effect of variance on lesion detection and conspicuity. Six to ten minutes after bolus tracking, the delayed phase was recorded, and the portal venous phase was conducted with a 60 s scanning delay and a 5 mm image thickness. A craniocaudal scan was performed on the whole liver. After being moved to the

post-processing workstation, the scan data was measured. Consultant radiologists with at least five years of post-fellowship experience performed the color doppler and CT reports. Data was entered into a proforma that was specially created.

Data entry and analysis were done using SPSS version 22.0. The mean  $\pm$  SD were calculated for age and the duration of HCC. Frequency and percentage were calculated for gender and portal vein thrombosis detected by color doppler and triphasic CT scan. Using a triphasic CT scan as the gold standard, sensitivity, specificity, PPV, NPV, and diagnostic accuracy were computed by building a 2x2 table. Data stratification was used to address effect modifiers such as age, gender, and length of HCC. By creating a 2x2 table, the post-stratification diagnostic accuracy was determined.

Diagnosis of PVT by color doppler	Diagnosis of PVT by triphasic CT scan	
	Yes	No
Yes	TP	FP
No	FN	TN

## RESULTS

Participants in the study were between the ages of 18 and 60, with a mean age of  $43.19 \pm 7.49$  years. 219 (65.57%) of the patients were between the ages of 41 and 60, according to Table I. Of these 334 individuals, 182 (54.49%) were male and 152 (45.51%) were female, resulting in a male to female ratio of 1.2:1. HCC lasted  $5.75 \pm 2.78$  weeks on average. Table I displays the distribution of patients with different factors.

Eleven patients (False Positive) had no PVT based on a triphasic CT scan, while 187 patients (True Positive) had PVT among those who tested positive for them on color doppler. Twelve (True Negative) and sixteen (False Negative) of the 136 patients with negative color doppler exhibited PVT on triphasic CT scans, respectively ( $p=0.0001$ ), as indicated in Table II. 92.12% color doppler sensitivity, 91.60% specificity, 94.44% PPV, 88.24% NPV, and 91.92% diagnostic accuracy were used to diagnose PVT. Table III displays the diagnosis accuracy stratification by age, gender, and HCC duration.

**Table I**

*Distribution of patients with other confounding variables (n=334)*

	Frequency	%age	
Age (years)	18-40	115	34.43
	41-60	219	65.57
Gender	Male	182	54.49
	Female	152	45.51
Duration (weeks)	$\leq 8$	292	87.43
	$> 8$	42	12.57

**Table II**

*Diagnostic accuracy of color doppler ultrasound in detecting portal vein thrombosis in patients having hepatocellular carcinoma due to chronic hepatitis C.*

	PVT on triphasic CT scan (+ive)	PVT on triphasic CT scan (-ive)	P-value
PVT on color doppler (+ive)	187 (True positive)	11 (False Positive)	0.0001
PVT on color doppler (-ive)	16 (False negative)	120 (True Negative)	

**Sensitivity:** 92.12%

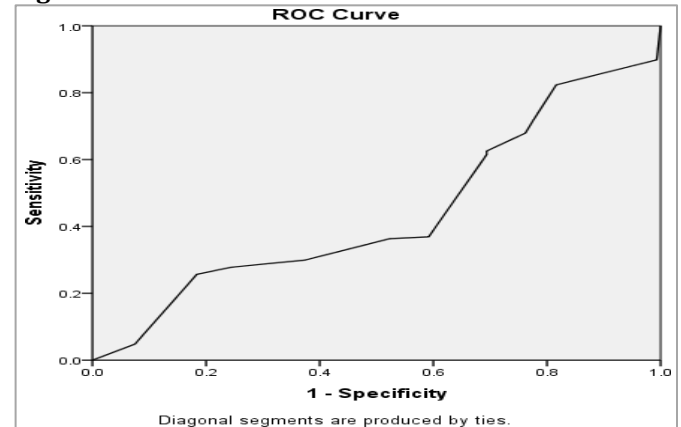
**Specificity:** 91.60%

**Positive Predictive Value (PPV):** 94.44%

**Negative Predictive Value (NPV):** 88.24%

**Diagnostic Accuracy:** 91.92%

**Figure 1**



**Area under the curve = 0.441**

**Table III**

*Stratification of diagnostic accuracy with respect to age, gender and duration of HCC.*

		Sensitivity	Specificity	PPV	NPV	DA	
Age (years)	18-40	91.11%	86.67%	91.11%	86.67%	89.33%	<b>0.001</b>
	41-60	100.0%	72.73%	78.57%	100.0%	86.36%	<b>0.001</b>
Gender	Male	96.55%	81.48%	84.85%	95.65%	89.29%	<b>0.001</b>
	Female	88.89%	85.71%	92.31%	80.0%	87.80%	<b>0.001</b>
Duration (weeks)	≤8	91.43%	85.71%	88.89%	88.89%	88.89%	<b>0.001</b>
	>8	95.24%	76.92%	86.96%	90.91%	88.24%	<b>0.001</b>

## DISCUSSION

The study's authors looked at how successfully Doppler ultrasounds detect PVT in patients with HCC in comparison to CT, which is the industry standard. In situations where scheduling complete CT exams is challenging, doctors can rely on Doppler ultrasound's excellent reliability. CT confirmed that PVT was present in 60.78% of the 334 cases. Doppler ultrasonography had a sensitivity of 92.12% and a specificity of 91.60%, properly detecting 187 out of all the cases. These results are comparable to those shown in earlier studies.<sup>11</sup>

Doppler is 83% sensitive and 93% specific in identifying PVT in cirrhotic patients with HCC, according to research by Tarantino's group.<sup>12</sup> According to Evangelos C, et al.<sup>13</sup>, the accuracy of Doppler can range from 80 to 90%, contingent on the type of thrombus and the operator's level of skill. This demonstrates the efficacy of Doppler ultrasonography in non-invasive diagnoses. Our findings indicate that Doppler ultrasound can accurately rule in and rule out the majority of venous thrombosis patients due to its significant PPV and NPV. The 91.92% accuracy rate supports the use of this diagnostic tool in standard clinical care for patients with HCC.

Doppler can detect big vessel invasion in HCC with an accuracy of over 90%<sup>14</sup>, according to Sofia C et al. Doppler ultrasonography was somewhat more likely to identify bland thrombus (87.8%) than tumor thrombus (82.8%) when looking for either type of thrombus. The likelihood of finding tumor thrombi is enhanced since they may exhibit waveforms similar to those found in pulsatile arteries. They could be overlooked, though, if they're in a challenging location.

According to research by Khan AR et al.<sup>15</sup>, it is more difficult to identify tumor thrombi using Doppler because signals from blood arteries are identical and the lumen contains several elements. According to our research, individuals with the best liver function (Child-Pugh Class

A) had the highest Doppler accuracy, whereas patients with worsening liver function (Class C) had the lowest accuracy. One possible explanation is that the portal vein cannot be clearly seen due to changes in the liver, fluid buildup, and organ placements.

Numerous studies show that the usefulness of the Doppler instrument in decompensated liver disease is largely dependent on the patient's health and how well it is used.<sup>16-18</sup> This indicates that Doppler ultrasonography reported the presence of PVT in five cases while missing roughly ten cases. Therefore, when a precise diagnosis is required for medical treatment planning, CT should always be utilized, even when Doppler is useful for first diagnosis.

A cross-sectional analytical investigation<sup>19</sup> involving 185 patients with a hepatocellular cancer diagnosis was carried out. Every subject received both contrast-enhanced CT and Doppler ultrasound. For PVT confirmation, CT was regarded as the gold standard. Seventy of the 185 individuals had PVT verified by CT. Of the 65 patients who had PVT identified by Doppler ultrasound, 60 had true positive results and 5 had false positive results. Ten patients had false negative results, meaning that PVT was not detected. There were 110 true negatives. Doppler ultrasound had a 91.9% overall diagnostic accuracy, a 92.3% PPV, a 91.7% NPV, a 95.6% specificity, and an 85.7% sensitivity.<sup>19</sup>

According to this study, color Doppler sonography can accurately depict the structure of the portal venous system as well as pathological alterations like thrombus. Doppler sonography is a helpful tool in our setting due to its high sensitivity and specificity, ease of availability, lack of radiation or contrast problems, and reduced financial load on low-income patients. Therefore, it is advantageous since it eliminates unnecessary treatment procedures and unnecessary diagnostic measures, particularly invasive ones like liver biopsies. However, it is important to

remember that the primary drawbacks of sonography are: structural alterations, pneumobilia, operator dependence, difficulties resulting from significant hepatic lesions or lobar hypertrophy, inadequate visibility of splanchnic arteries, and patient cooperation.<sup>20,21</sup>

## CONCLUSION

In patients with hepatocellular carcinoma, Doppler ultrasound is found to have a high diagnostic accuracy in

detecting portal vein thrombosis (PVT). The modality is especially effective in detecting both bland and tumor thrombus, especially in patients with preserved liver function. Due to its broad availability, non-invasive nature, and strong predictive values, Doppler ultrasound can be a dependable screening tool in situations where CT is not easily accessible.

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