

# IJMA



## INTERNATIONAL JOURNAL OF MEDICAL ARTS

Volume 7, Issue 8 (August 2025)



<http://ijma.journals.ekb.eg/>

P-ISSN: 2636-4174

E-ISSN: 2682-3780





Available online at Journal Website  
<https://ijma.journals.ekb.eg/>  
 Main Subject [Radiology]



## Original Article

# The Role of CT scan In Differentiating between Neoplastic and Benign Portal Vein Thrombosis Using Thrombus Density

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## Abstract

### Article information

Received: 14-04-2025

Professionally accepted: 29-05-2025

DOI: [10.21608/ijma.2025.375241.2166](https://doi.org/10.21608/ijma.2025.375241.2166)

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**Citation:** Gomaa MI, Alwarraky MS, El Sayed MR, Ellaban HS. The Role of CT scan In Differentiating between Neoplastic and Benign Portal Vein Thrombosis Using Thrombus Density. IJMA 2025 August; 7[8]: 5923-5928. doi: [10.21608/ijma.2025.375241.2166](https://doi.org/10.21608/ijma.2025.375241.2166)

**Background:** Portal vein thrombosis (PVT) is described as the presence of a clot in the portal vein lumen. It's considered as common complication of chronic liver disease and hepatocellular carcinoma (HCC). The aim of this study was to assess the diagnostic value of CT density measurements in differentiating between neoplastic and benign PVT on Triphasic CT studies .

**Methods:** This retrospective study was carried out on thirty patients who presented with ultrasound diagnosis of portal vein thrombosis to the radiology department at National Liver Institute, Menoufia University, Egypt.

**Results:** Our study showed excellent sensitivity, specificity and accuracy of thrombus density measurements in determining the nature of the portal vein thrombosis at the arterial and portovenous phases on Triphasic CT studies. At the arterial phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%. At the portovenous phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%. The best cut off value of thrombus density at the arterial phase was (45) and at the portovenous phase was (52).

**Conclusion:** Differentiation between benign and neoplastic PVT is very important to determine the strategy of treatment especially for liver transplantation. Triphasic CT is considered a reliable tool for the detection of PVT. CT density measurements can differentiate between neoplastic and benign PVT at the arterial and portovenous phases.

**Keywords:** Triphasic; Differentiating Benign; Neoplastic; Portal vein thrombosis; Thrombus density.



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## INTRODUCTION

Portal vein thrombosis is described as the presence of a clot in the portal vein lumen, [1] it's considered as common complication of chronic liver disease and hepatocellular carcinoma. 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 [2]. Neoplastic PVT renders a patient unsuitable for some treatment approaches, such as surgical resection of the tumor or chemoembolization of HCC, due to the high incidence of tumor recurrence. In contrast, benign PVT that occurs in patients with chronic liver disease and patients with HCC can be resolved after anticoagulant and thrombolytic therapy [3].

The discrimination between neoplastic and benign PVT has a great clinical significance for determination of the therapeutic approach, assessment for liver transplantation, and survival prediction [4]. In the cases of benign PVT without HCC, thrombi noted on the follow up studies to be resolved, decreased in size, or had no change without any treatment. The cases of mixed neoplastic and benign thrombus within the same vessel lumen were considered as neoplastic PVT [5].

Ultrasonography is generally the first technique used to detect PVT in patients with liver disease. However, it has a limited ability to discriminate between neoplastic and benign PVT. So, CT and MRI are considered the next effective diagnostic steps of PVT. However, there is an overlap between the imaging criteria of benign and neoplastic PVT but thrombus-tumor continuity is widely considered as a reliable indicator of neoplastic PVT. So, the discrimination between benign and neoplastic PVT is challenging especially in the absence of a primary liver tumor [6].

Contrast enhanced computed tomography imaging remains the main investigation for characterization of PVT and its underlying cause. There are specific CT features to differentiate between neoplastic and benign PVT. The presence of main PV dilation ( $\geq 23$  mm) and intra-thrombus enhancement at the arterial phase is highly suggestive of neoplastic PVT [7]. The measured mean density values of PVT (CT density) can differentiate between neoplastic and benign PVT by measuring the PVT mean density (in Hounsfield Units) at the arterial and portovenous phases on Triphasic CT studies [8].

The aim of this study was to assess the diagnostic value of CT density measurements in differentiating between neoplastic and benign PVT on Triphasic CT studies.

## PATIENTS AND METHODS

This retrospective study was carried out on thirty patients who presented with ultrasound diagnosis of portal vein thrombosis to the radiology department at National Liver Institute, Menoufiya University, Egypt.

### The patients were included according to the following criteria:

**Inclusion criteria:** 1] Patients with HCC associated with PVT; 2] Patients over 18 years old who had Triphasic CT scan of the abdomen showing PVT; 3] Patients with chronic parenchymatous liver disease associated with PVT; 4] Patients with no chronic parenchymatous liver disease presented with PVT.

**Exclusion criteria:** 1] Patients without PVT at the Triphasic CT images; 2] Patients who had no contrast enhanced CT abdomen; 3]

Patients with severe allergic reaction or end stage renal failure; 4] Hemodynamically unstable patients; 5] Patients with hepatic failure; 6] Hepatic patients with encephalopathy.

### In our study, all patients were subjected to the following:

**Clinical history:** Personal data focusing on the age, sex, occupation, residence and special habits e.g. alcoholism; Complaints of the patients including upper abdominal pain, abdominal distension, hematemesis and/or melena; Past history of jaundice, schistosomiasis or previous blood transfusion; History of previous trans-arterial embolization or local ablative therapy for HCC.

**Clinical examination:** General examination: stressing on jaundice and encephalopathy; Local abdominal examination: stressing on liver, spleen, ascites and abdominal wall collaterals.

**Laboratory investigations:** Tumor markers especially serum alpha fetoprotein; Serum creatinine, serum albumin, serum bilirubin (total and direct) and INR.; Detection of hepatitis C antibodies and hepatitis B surface antigen.

**Ultrasonography:** Real time ultrasound was performed using LOGIQ P9 or LOGIQ F8 Expert ultrasound machines with 3.5 MHz transducer for examination of: The liver size, echogenicity and the presence of hepatic focal lesions (site, size and echogenicity); Portal vein diameter, presence of echogenic thrombus or not, color flow & waveform by Doppler studies; Presence or absence of enlarged portahepatis lymph nodes; Spleen, pancreas, abdominal lymph nodes and ascites if present.

**Triphasic CT study of the liver:** Triphasic CT abdomen and pelvis was performed to all cases using MDCT scanner Somatom definition AS 128 slices from SIEMENS

**Imaging Technique (CT parameters):** In all patients, Non contrast CT of the abdomen and pelvis was taken prior to contrast medium injection. Then via a power injector, 150 mL of contrast medium; Omnipaque 300 mg/mL (iohexol 300 mg/mL; Nycomed, Princeton, NJ) was injected intravenously at a rate of 4 mL/sec. Arterial phase of the abdomen was taken during a breath-hold after 15-20 seconds post contrast medium injection. Liver was scanned with a table speed of 15 mm/0.8 sec and an image thickness of 5 mm in a cephalad-to-caudal direction using a detector collimation of 5 mm, pitch of 3 (HQ mode). Portovenous phase of the abdomen was taken during a breath-hold after 70-80 seconds post contrast medium injection. Liver was scanned with a table speed of 15 mm/0.8 sec and an image thickness of 5 mm in a cephalad-to-caudal direction using a detector collimation of 5 mm, pitch of 3 (HQ mode). Delayed phase of the abdomen was taken after 3-6 minutes post contrast medium injection with the same parameters. The used CT scanning parameters were 150–250 mAs and 120 kVp [9].

The density of the thrombus was measured using ROI (mean area,  $99.8 \pm 32.0 \text{ mm}^2$ ) placement over the site of PVT, and mean Hounsfield unit values were recorded. And these data were acquired to be compared with the diagnosis.

**In this retrospective study,** we included thirty patients suspected to have PVT with ultrasound examination and confirmed by Triphasic CT examination of the abdomen and pelvis. The thirty patients were divided into two groups according to one or more of the following criteria:

**By Triphasic CT: Group A: Neoplastic PVT (16 cases):** Continuity with tumor; Enhancement in arterial phase; High levels of AFP. **Group B: Benign PVT (14 cases):** Apart from tumor; No enhancement; Normal levels of AFP

**By Ultrasound: In both benign and neoplastic PVT:** Portal vein lumen showed an echogenic filling material; Absence of color flow within the portal vein lumen (complete or partial).

**Criteria specific for neoplastic PVT:** Direct continuity between the tumor and the PVT; intrathrombus color flow signals with arterial waveforms. The two studied groups (A & B) were processed at the work station of CT to measure Hounsfield unit of the PVT. The density of the thrombus was measured using ROI (mean area,  $99.8 \pm 32.0 \text{ mm}^2$ ) placement, and mean Hounsfield unit values were recorded. And these data were acquired to be compared with the diagnosis.

**Statistical analysis:** Data were collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis, (version 20; Inc., Chicago. IL); Data were entered as numerical or categorical, as appropriate.

#### Two types of statistics were done:

**Descriptive statistics:** Quantitative data were shown as mean, SD, and range; Qualitative data were expressed as frequency and percent.

**Analytical statistics:** Chi-square test was used to measure association between qualitative variables; Student t-test was used to compare mean and SD of 2 sets of quantitative normally distributed data, while Mann Whitney test was used when this data was not normally distributed; The ROC (Receiver Operating Characteristic) curve was done to detect the cutoff value with highest sensitivity and specificity; Sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy were calculated; Fisher exact test was used for 2x2 qualitative variables when more than 25% of the cells have expected count less than 5; P-value was considered statistically significant when it was less than 0.05.

## RESULTS

This study was carried out on thirty patients presented with ultrasound diagnosis of PVT to the radiology department at National Liver Institute, Menoufia University (Egypt).

As regard patients' age, they ranged from 53 to 76 years old with the mean of 63 years old. The study showed prevalence of PVT in Males (80%) in comparison to females (20%)

As regard associations with PVT, (96 %) of the patients with portal vein thrombosis complained of cirrhosis. HCC was seen in about (70%) of patient complained of PVT

Concerning the types of managements were applied to patients complained of HCC with subsequent development of PVT, Embolization was done for 9 patients, tumor ablation for 6 patients and only one patient underwent liver transplantation.

According to the nature of the thrombus [Table 1], PVT was divided into neoplastic thrombus (16 cases) and benign thrombus (14 cases).

As regarding to the correlation between laboratory data and the nature of thrombus [Table 2], there is no significant association between the abnormal laboratory data with determining the nature of the thrombus as they are abnormal in some patients with benign PVT and normal in the other patients.

According to the thrombus site [Table 3], Most of patients (10 cases) had PVT at the main, left and right branches, (5 cases) at the main PV, (5 cases) at the left PV, (5 cases) at the right PV, (2 cases) at the main and left PVs, (2 cases) in main and right PVs, (1 case) in right and left PVs.

As regards the comparison between neoplastic and benign PVT [Table 4], all patients with neoplastic PVT showed thrombus enhancement at the arterial phase, while all patients with benign PVT showed no enhancement. Venous collaterals were found in 21.4 % of patients with benign PVT, in 37.5 % of patients with neoplastic PVT. Arterio-portal shunts were found in 50 % of patients with neoplastic PVT. None of patients with benign PVT had arterio-portal shunts.

Concerning the Sensitivity & specificity of CT density in the detection of thrombus nature [Table 5], Out of thirty patients (14 cases with benign PVT and 16 cases with neoplastic PVT), the following study was detected: At the pre-contrast phase, the sensitivity of thrombus density measurements was 51%, the specificity was 48% and the accuracy was 48%. At the arterial phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%. At the portovenous phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%. At the delayed phase, the sensitivity of thrombus density measurements was 52%, the specificity was 50% and the accuracy was 50%. The best cut off value of thrombus density at the precontract phase was (27), at the arterial phase was (45), at the portovenous phase was (52) and at the delayed phase was (29) [Figure 1].

**Table [1]:** Nature of the thrombus of the studied group

| Variable   | N = 30      |
|------------|-------------|
| Neoplastic | 16 [53.3 %] |
| Benign     | 14 [46.6 %] |

**Table (2):** Correlation between laboratory data and nature of thrombus

| Variable           | Total      | Neoplastic PVT | Benign PVT |
|--------------------|------------|----------------|------------|
| High AFP           | 20 [66.6%] | 14 [70%]       | 6 [30%]    |
| High INR           | 14 [46.7%] | 13 [92.9%]     | 1 [7.1%]   |
| hypoalbuminemia    | 12 [40%]   | 10 [83.3%]     | 2 [16.7%]  |
| hyperbilirubinemia | 13 [43.3%] | 10 [76.9%]     | 3 [23.1%]  |

**Table (3):** Site of the thrombus

| Variable           | N           |
|--------------------|-------------|
| Left               | 5 [16.7 %]  |
| Right              | 5 [16.7 %]  |
| Main               | 5 [16.7 %]  |
| Right & left       | 1 [3.3 %]   |
| Main & left        | 2 [6.6 %]   |
| Main & right       | 2 [6.6 %]   |
| Main, left & right | 10 [33.3 %] |



Table 4: Comparison between neoplastic and benign PVT:

| Variable                  | Neoplastic PVT<br>(16 cases) | Benign PVT<br>(14 cases) | P- value |
|---------------------------|------------------------------|--------------------------|----------|
| Liver cirrhosis           | 16 [100%]                    | 13 [90.9%]               | 0.09     |
| HCC                       | 16 [100%]                    | 8 [57.1%]                | 0.42     |
| HCC embolization          | 5 [31.2%]                    | 5 [35.7%]                | 0.13     |
| HCC ablation              | 3 [18.8%]                    | 3 [21.4%]                | 0.07     |
| High AFP levels           | 14 [87.5%]                   | 6 [42.9%]                | 0.61     |
| High INR                  | 13 [81.3%]                   | 1 [7.1%]                 | 0.94     |
| Hypoalbuminemia           | 10 [62.5%]                   | 2 [14.3%]                | 0.74     |
| Hyperbilirubinemia        | 10 [62.5%]                   | 3 [21.4%]                | 0.79     |
| Dilated PV caliber        | 7 [43.8%]                    | 4 [28.6%]                | 0.29     |
| PVT enhancement           | 16 [100%]                    | 0 [0%]                   |          |
| Venous collaterals        | 6 [37.5%]                    | 3 [21.4%]                | 0.2      |
| Arterio-portal shunts     | 8 [50%]                      | 0 [0%]                   | 0.5      |
| Ascites                   | 6 [37.5%]                    | 3 [21.4%]                | 0.2      |
| Tumor-thrombus continuity | 16 [100%]                    | 0 [0%]                   |          |

Table (5): Sensitivity &amp; specificity of CT density in the detection of thrombus nature

| Variable                           | AUC   | Best cut<br>Off value<br>(HU) | Sensitivity | Specificity | Positive predictive<br>value | Negative predictive<br>value | Accuracy |
|------------------------------------|-------|-------------------------------|-------------|-------------|------------------------------|------------------------------|----------|
| Precontrast phase thrombus density | 0.572 | 27                            | 51%         | 48%         | 62%                          | 56%                          | 48%      |
| Arterial phase thrombus density    | 0.981 | 45                            | 100%        | 93%         | 100%                         | 100%                         | 100%     |
| Portovenous phase thrombus density | 0.981 | 52                            | 100%        | 93%         | 100%                         | 100%                         | 100%     |
| Delayed phase thrombus density     | 0.612 | 29                            | 52%         | 50%         | 64%                          | 54%                          | 50%      |

\*The Area under Curve (AUC) was considered significant if it was more than 0.7

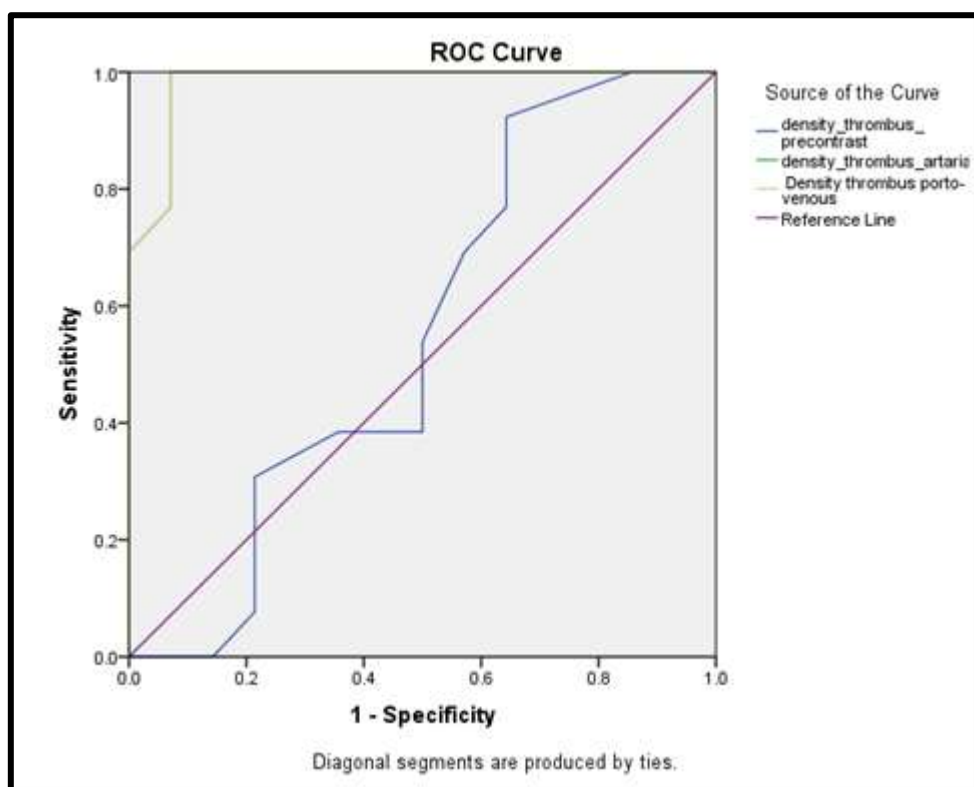


Figure (1): Sensitivity and specificity of HU in the detection of the nature of thrombus

## CASE PRESENTATION (Figures 2 and 3).



Figure (2): Male patient, 57 years old, presented with abdominal pain and distension, Triphasic CT showed distended main and right portal vein branch with isodense thrombus showing no enhancement at the arterial phase [22 HU] (Fig. 2A) and portovenous phase [17 HU] (Fig. 2B).

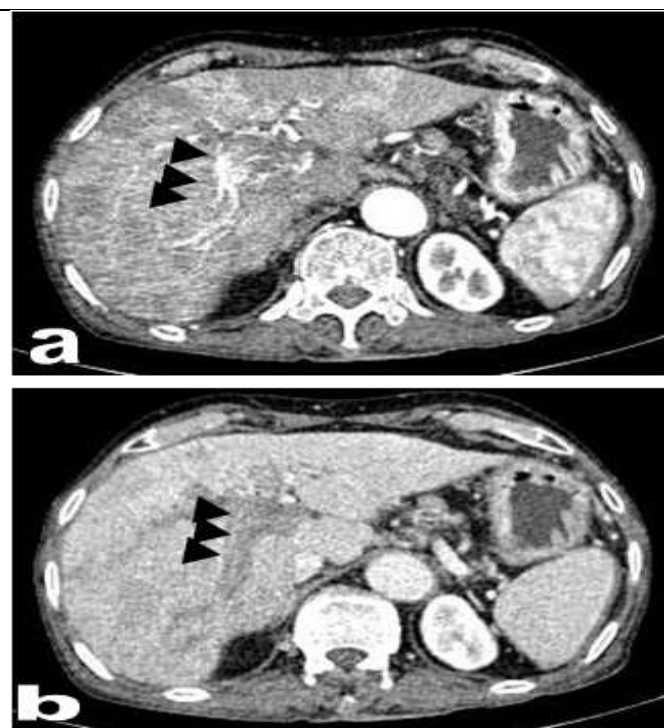


Figure (3): Male patient 76 years old, presented by jaundice and abdominal pain and had a history of HCC, Triphasic CT showed Heterogeneously enhancing hepatic parenchyma with right portal vein thrombus showing enhancement at the arterial phase [75 HU], complicated by right arterio-portal fistula (fig. 3A) and washout in portovenous phase [80 HU] (fig. 3B).

## DISCUSSION

PVT can be a complication of coagulation disorders, inflammatory, and neoplastic diseases, and splenectomy. Its clinical presentation, management and prognosis vary according to its cause. It can be classified into acute or chronic, occlusive or non-occlusive, extra- or intrahepatic and progressive or self-resolving [10]. Clinical presentation of PVT varies from asymptomatic to a life-threatening condition at its first presentation [11]. The detection and characterization of PVT is very important in HCC patients because neoplastic PVT renders the patient contraindicated for liver transplantation, surgical resection and local ablative therapy, and also, it is considered a relative contraindication for TACE [12]. Triphasic CT is the best diagnostic mean for PVT and also evaluation of its underlying causative diseases [13]. Our study was done on thirty patients with suspected PVT by ultrasound and confirmed by Triphasic CT, according to our results, PVT was divided into the following categories: neoplastic thrombus (16 cases), benign thrombus (14 cases). In our study, the patients' age ranged from 53 to 76 years old with the mean of 63 years old. The study showed prevalence of PVT in Males (80%) in comparison to females (20%). The study of **Burroughs et al.** [14] and study of **Adel et al.** [15] matched with our study in prevalence of PVT in males. Males were (80%) and females were (20%) with PVT.

In our study, liver cirrhosis was present in 96.7% of patients with PVT, in 90.9% of patients with benign PVT, and in 100% of patients with neoplastic PVT. The study of **Osman et al.** [16] matched with our study as the liver cirrhosis was present in 15 patients with benign PVT (15/17) (88.23%), and in 33 patients with neoplastic PVT (33/33) (100%).

In our study, HCC was seen in 76.6% of patients with PVT. 57.1% of patients with benign PVT, 100% of patients with neoplastic PVT. The study of **Osman et al.** [16] and study of **Adel et al.** [15] matched with the

present study as they found that HCC was present in all patients with neoplastic PVT (100%).

In the current work, High levels of AFP were found in 63.3% of patients with PVT. 87.5% of patients with neoplastic PVT, 42.9% of patients with benign PVT. And normal levels of AFP were found in 57.1% of patients with benign PVT. It matched with the study of **Catalano et al.** [17] as they found that high levels of AFP were present in 66.5% of patients with neoplastic PVT. And normal levels of AFP were present in 33.5% of patients with benign PVT.

In our study, 10 cases (33.3%) of patients had PVT at the main, left and right branches, 5 cases (16.7%) at the main portal vein, 5 cases (16.7%) at the left portal vein branch, 5 cases (16.7%) at the right portal vein branch, 2 cases (6.6%) at the main and left portal vein branch, 2 cases (6.6%) at the main and right portal vein branch, 1 case (3.3%) at the right and left portal vein branches. Based on the study of **McNamara C, et al.**, [18] in 26% of patients with PVT (13/50) thrombi were present at the main portal vein, while the remainder 37/50 (74%) showed involvement of the other portal vein segmental branches. which matched with our study in prevalence of the site of PVT at the main portal vein, but with lesser different percentages in the branches.

Results of the current work showed that, 100% of patients with neoplastic PVT showed enhancement of the thrombus at the arterial phase and washout at the delayed phase. But 100% of patients with benign PVT showed no enhancement. Our results are in agreement with the following studies. The study of **Adel et al.** [15] 100% of patients with neoplastic PVT (14/14) showed arterial enhancement and delayed washout in the thrombus. And none of the 13 patients with benign PVT showed thrombus enhancement. In addition, **Osman et al.**, [16] study revealed that, 84.8% of patients with neoplastic PVT (28/33) showed intrathrombus neovascularity, arterial enhancement and delayed

washout in the thrombus. And none of the 17 patients with benign PVT showed thrombus enhancement. The study of **Teama et al.** [19] used triphasic CT scans and showed neovascularity in 87.5% (14/16) of patients with neoplastic PVT and in 0% of patients with benign PVT. This matches with the present study.

In our study, 50 % of patients with neoplastic PVT were found to have an arteriportal shunts. None of patients with benign PVT had arteriportal shunts. This matched with the study of **Adel et al.** [14]

The current work showed that, at the pre-contrast phase, the sensitivity of thrombus density measurements was 51%, the specificity was 48% and the accuracy was 48%. At the arterial phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%. At the portovenous phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%. At the delayed phase, the sensitivity of thrombus density measurements was 52%, the specificity was 50% and the accuracy was 50%. The best cut off value of thrombus density at the precontrast phase was (27), at the arterial phase was (45), at the portovenous phase was (52) and at the delayed phase was (29). AUC was more than 0.7 at the arterial and portovenous phases (significant). But in pre-contrast and delayed phases, they were less than 0.7, so these phases were not significant in differentiating between neoplastic and benign PVT. This matched with the study of **Canellas et al.** [20] who showed that, the optimal cut off value was 54 HU for thrombus density at the portovenous phase. And matched with the study of **Adel et al.** [15] the optimal cut off value was 45 HU for thrombus density at the arterial phase and 52 HU at the portovenous phase. These matched with our study to diagnose neoplastic PVT as the optimal cut off value at the arterial and portovenous phases were almost the same.

**Conclusion:** Differentiation between benign and neoplastic PVT is very important to determine the strategy of treatment especially for liver transplantation; Triphasic CT is considered a reliable tool for the detection of PVT. It is widely used for assessment of the portal vein; CT density measurements can differentiate between neoplastic and benign PVT at the arterial and portovenous phases; At the arterial phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%. At the portovenous phase, the sensitivity of thrombus density measurements was 100%, the specificity was 93% and the accuracy was 100%.

**Financial and non-financial activities and relationships of interest:** None

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# IJMA



## INTERNATIONAL JOURNAL OF MEDICAL ARTS

Volume 7, Issue 8 (August 2025)



<http://ijma.journals.ekb.eg/>

P-ISSN: 2636-4174

E-ISSN: 2682-3780