ORIGINAL ARTICLE

UDC: 616.14-005.6:616.36-004
DOI: https://doi.org/10.2298/VSP240116029S

Portal vein thrombosis in patients with liver cirrhosis

Tromboza vene porte kod bolesnika sa cirozom jetre

Željka Savić*†, Dimitrije Damjanov*†, Olgica Latinović Bošnjak†, Nebojša Janjić*†, Božidar Dejanović*†, Žarko Krnetić†, Vladimir Vračarić†

***University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia; †University Clinical Center of Vojvodina, Clinic for Gastroenterology and Hepatology, Novi Sad, Serbia**

Abstract

Background/Aim. Portal vein thrombosis (PVT) in patients with liver cirrhosis (LC) has a prevalence of 0.6–26%. It is most commonly discovered incidentally as part of the evaluation of LC or in the context of acute decompensation of LC due to portal hypertension. The aim of the study was to determine the prevalence of PVT in patients with LC in relation to the severity of the disease and individual elements of portal hypertension. **Methods.** A total of 326 patients treated for LC decompensation were included in a retrospective study. Standard laboratory analyses, abdominal ultrasonography and/or computed tomography, and esophagogastroduodenoscopy were performed. **Results.** The diameter of the portal vein (PV) differed between patients without esophageal varices (12.2 mm) and those with large varices (13.6 mm), $p = 0.026$. PVT was identified in 6.1% of patients with LC. The patients were classified according to the Child-Pugh scoring system, which has the A, B, and C categories used to assess the severity of liver disease. PVT was present in 3.0% of patients in class C and 12.0% in class B, while none of the patients in class A had PVT ($p = 0.005$). PVT was present in 4.4% of patients with small varices and 16.7% with large varices ($p < 0.001$). There was no difference in the presence of PVT between the groups of patients with and without variceal bleeding nor between groups with different degrees of ascites. A fatal outcome occurred in 29.4% of patients, but there was no difference between patients with and without PVT. **Conclusion.** PVT is present in more advanced stages of LC and predominantly in patients with large esophageal varices. There was no higher prevalence of PVT observed with the occurrence of variceal bleeding or with the death outcome in patients with LC.

Key words:
esophageal and gastric varices; hypertension, portal; liver cirrhosis; portal vein; thrombosis.

Apstrakt

Uvod/Cilj. Tromboza vene porte (TVP) kod bolesnika sa cirozom jetre (CJ) ima prevalenciju od 0,6–26%. Najčešće se TVP otkriva slučajno, u sklopu evaluacije CJ, ili u sklopu akutne dekompenzacije CJ zbog portne hipertenzije. Cilj rada bio je da se ustanovi zastupljenost TVP kod bolesnika sa CJ u odnosu na težinu bolesti i pojedine elemente portne hipertenzije. **Metode.** Retrospektivnim istraživanjem obuhvaćeno je 326 bolesnika lečenih zbog dekompenzacije CJ. Bolesnicima su rađene standardne laboratorijske analize, ultrasonografija abdomena i/ili kompjuterizovana tomografija abdomena i ezofagogastroduodenoskopija. **Rezultati.** Dijametar vene porte (VP) razlikovao se kod bolesnika bez variksa jednjaka (12,2 mm) i onih koji su imali velike varikse (13,6 mm), $p = 0,026$. TVP je ustanovljena kod 6,1% bolesnika sa CJ. Bolesnici su klasifikovani u skladu sa *Child-Pugh* sistemom bodovanja, kojim se težina oboljenja jetre izražava kategorijama A, B i C. TVP je bila prisutna kod 3.0% bolesnika iz kategorije C, kod 12,0% bolesnika iz kategorije B, a nije bila prisutna ni kod jednog bolesnika iz kategorije A ($p = 0,005$). TVP je bila prisutna kod 4,4% bolesnika sa malim variksima i kod 16,7% bolesnika sa velikim variksima ($p < 0,001$). Nije bilo razlike u prisustvu TVP između grupa bolesnika sa i bez variksnog krvarenja, kao ni između grupa sa različitim stepenom ascita. Kod 29,4% bolesnika nastupio je smrtni ishod, ali nije bilo razlike između bolesnika sa i bez TVP. **Zaključak.** TVP je prisutna kod težih stadijuma CJ i pretežno kod bolesnika sa velikim variksima jednjaka. Nije ustanovljena veća prevalencija TVP povezana sa pojavom variksnog krvarenja ili smrtnim ishodom bolesnika sa CJ.

Ključne reči:
jednjak, variksi; hipertenzija, portalna; jetra, ciroza; v.portae; tromboza.

Correspondence to: Dimitrije Damjanov, University of Novi Sad, Faculty of Medicine, Hajduk Veljkova 3, 21 137 Novi Sad, Serbia.
E-mail: dimitrije.damjanov@mf.uns.ac.rs

Introduction

Liver cirrhosis (LC) is a disease characterized by two stages – the compensated and decompensated stage. Clinical characteristics of decompensation include ascites, variceal bleeding (VB), and overt hepatic encephalopathy [1]. Portal hypertension (PH) is a clinical syndrome characterized by increased pressure in the portal vein (PV). The values of the hepatic venous pressure gradient > 10 mm indicate clinically significant PH. Esophageal varices (EVs) are present in 50–60% of patients with compensated and 85% with decompensated LC [2, 3].

Portal vein thrombosis (PVT) refers to thrombus formation within the PV or its intrahepatic branches, with or without extension to the superior mesenteric and splenic veins. The condition is commonly incidentally diagnosed during the evaluation of LC or, in the case of acute LC decompensation associated with PH. It is necessary to identify the initial site, number of affected blood vessels, and obstruction rate and determine whether the disease is acute or chronic [4–6]. PVT prevalence in patients with LC ranges between 0.6% and 26%, with a yearly incidence rate of 4.6–26% [7, 8]. Chronic PVT is associated with complications of PH, such as esophagogastric varices, with an increased risk of VB, splenomegaly, and hypersplenism [7, 9, 10].

Although the first description of PVT dates back to 1868 [11], there are still questions related to predisposing factors, primarily whether PVT in patients with LC is clinically significant or merely an epiphenomenon of advanced liver disease (LD) [12].

The pathogenesis of PVT is multifactorial and pathophysiologically related to the vertices of Virchow's triad (venous stasis, hypercoagulability, and endothelial dysfunction) [13]. In LC, reduced portal flow velocity (FV) occurs as a consequence of changes in porto-collateral circulation combined with increased PV diameter, which is commonly seen in patients with clinically significant PH. A decrease in portal FV to less than 15 cm/s measured by Doppler ultrasonography (US) is a significant predictive factor for the development of PVT [6, 14]. Endothelial dysfunction is commonly present in LC patients and is associated with procedures such as sclerotherapy, portosystemic shunt surgery, and splenectomy [15]. A rebalanced coagulation concept, a delicate balance between procoagulant and anticoagulant factors, characterizes LC. The existence of relative hypercoagulability in the PV and splanchnic circulation compared to systemic circulation has been established [16–18]. Hyperfunction and increased platelet aggregation potential, especially in portal circulation, can be explained by increased stimulation by the lipopolysaccharide derived from the leaky gut [19].

PVT can be regarded as the underlying cause and consequence of decompensated LC. The prognosis and therapy depend on the localization, extension and progression rate, the presence of relevant risk factors, and the stage of chronic LD [6]. US is the method of choice in the initial evaluation of the portal venous system because it has an accuracy of 88–98% in detecting PVT (sensitivity and specificity range from 80–100% in most studies). Various techniques are employed, including 2D grey-scale US, which displays thrombosis as isoechoic or hypoechoic material filling the vessel either involving a part of the lumen (partial thrombosis) or the entire lumen (complete thrombosis). Color Doppler US, spectral Doppler (pulsed wave US), and contrast-enhanced US improve the characterization of thrombosis, enabling confirmation of the absence of flow in complete PVT. Portal hemodynamics depends on whether the thrombosis is partial or complete [20]. In the evaluation of PVT, contrast-enhanced computed tomography (CT) or magnetic resonance imaging is also applied, especially their venous phase, to determine the extent of thrombus spread in the branches of the PV and to detect potential complications such as intestinal infarction [21].

Classification of PVT should be treatment-oriented and, *inter alia*, include extension of thrombus and grade of occlusion [22].

PVT is currently treated similarly to any other thrombosis with anticoagulant therapy, but the response to this treatment is poor. Thirty to sixty percent of patients with PVT do not achieve thrombus resolution, suggesting that the composition of the thrombus in the PV likely differs from that in the systemic circulation [4, 14, 23].

The objective of this study was to establish the occurrence of PVT in patients with LC related to cirrhosis severity and individual elements of PH.

Methods

A retrospective study encompassed 326 patients treated at the Clinic for Gastroenterology and Hepatology of the University Clinical Center of Vojvodina, Serbia for decompensated LC from January 1, 2020, to December 31, 2022. The research was approved by the Ethics Committee of the Clinical Center of Vojvodina (from July 28, 2023; No. 00-136).

Although PVT is common in patients with hepatocellular carcinoma, they were not included in the study because they represent a heterogeneous population with different disease behaviors [24]. Likewise, the study did not include patients with inflammation of abdominal organs (gallbladder and biliary tree, pancreas, intestine) and those with hematological disorders.

All patients underwent clinical examination and laboratory analysis. The analysis of blood parameters was performed using the hematology analyzer Sysmex XN 1000. Biochemical analysis – urea, creatinine, electrolytes, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, bilirubin, and albumin – were performed using an automated biochemical analyzer Abbott Alinity c, and with the original reagents supplied by Abbott. Hemostatic parameters were determined by the automated coagulation analyzer Sysmex CS – 5100 and original reagents. Patients were classified according to the Child-Pugh (C-P) scoring system, a modification of the original Child-Turcotte score. This scoring system is generally used to assess the severity of LD.

Based on the degree of expression of ascites and encephalopathy, as well as on the basis of serum values of bilirubin, albumin, and prothrombin time (1–3 points are assigned for each parameter), the C-P score of the patients was calculated. The patients were classified into classes A, B, or C. Patients in classes B and C, with higher C-P scores, have advanced LD with an increased risk of one-year mortality [25, 26]. The Model for End-Stage LD (MELD) score (range from 6–40), which has the ability to stratify patients with end-stage LD according to their three-month mortality, was calculated as well. The formula for calculating the MELD score includes serum values of bilirubin, creatinine, and international normalized ratio (INR):

MELD = 3.8 × $\log_e$ serum bilirubin (mg/dL) + 11.2 × $\log_e$INR + 9.6 × $\log_e$ serum creatinine (mg/dL) + 6.4 [27–29].

Samsung RS 85 US system was used for the evaluation of liver parenchyma homogeneity, liver margins, dimensions of the hepatic lobes (right, left, and caudate), bipolar spleen diameter, and the AP diameter of the main trunk of the PV. Doppler US was applied to assess PV FV (main PV and the left and right portal branches). The diameter of PV of 7–13 mm and PV FV of 20–40 cm/s were considered normal values. Multilayer CT on the GE Revolution Evo CT scanner enabled insight into the thrombus extension into the lienal and superior mesenteric vein. Esophagogastroduodenoscopy was performed by applying Fujinon EPH 4400. The presence and size of EVs were classified into three grades – no EVs, small EVs (less than 5 mm), and large EVs (over 5 mm).

The data obtained were analyzed using descriptive statistics, absolute numbers and percentages, and central tendency and dispersion measures. The χ^2 test was used to analyze the differences between category parameters. The differences between numerical values for parametric and non-parametric data were analyzed using one-way Analysis of Variance and the Kruskal-Wallis test, respectively, following up with a *post hoc* evaluation of the obtained results. In all applied tests, statistical hypotheses were tested at the level of statistical significance 95% ($p < 0.05$). All data were entered into the specifically created database of the Microsoft Excel package. Statistical analysis was performed using the SPSS v23 software program.

Results

Patient characteristics

The majority of patients (80%) had alcoholic LC, while one-fifth of patients had LC of other etiologies. The LC of other etiologies included the following: autoimmune, cholestatic, metabolic, cardiogenic, and cryptogenic. The average C-P score was 9.9, and the MELD score was 19.3. The average age of the patients was 59.0 years. The majority of the patients were male. The characteristics of patients are presented in Table 1.

Portal hypertension

Esophagogastroduodenoscopy was performed in 276/326 (84.7%) patients. EVs were not detected in 48/276 (17.4%) patients, whereas small and large EVs were identified in 163/276 (59.1%) and 65/276 (23.6%) patients, respectively.

Of 228 patients with EVs, VB was endoscopically confirmed in 59 (25.9%) patients. In the group with established varicosity, there were no differences in bleeding incidence associated with the LC etiology [27% vs. 20.9%, $\chi^2 = 0.676$, degree of freedom (df) = 1, $p = 0.411$].

The average PV diameter was 12.8 ± 2.5 mm (range 9–25 mm). Portal venous FV was measured in 24/296 (8.1%) patients, and it was 14.7 ± 6.3 cm/s (range 2–28 cm/s). PV

Table 1

Demographic and laboratory characteristics of patients

Characteristics	Values
Males	233 (71.5)
Age, years	59.0 ± 10.8
Liver cirrhosis etiology	
alcohol	260 (79.8)
autoimmune	14 (4.3)
cholestatic	19 (5.8)
metabolic	4 (1.2)
cardiogenic	7 (2.1)
cryptogenic	22 (6.7)
Child-Pugh score	9.9 ± 2.2
MELD score	19.3 ± 7.7
Albumin (g/L) (RR 34–52)	27.3 ± 5.3
Prothrombin time (INR) (RR 0.83–1.30)	1.5 ± 0.5
Bilirubin total (μmol/L) (RR 3.0–21.0)	54.2 (92.2) †
Creatinine (μmol/L) (RR 49–115)	90.0 (67.0) †
Sodium (mmol/L) (RR 135–150)	136.5 ± 5.8
Platelets (×10^9/L) (RR 140–400)	127.5 (104.8) †

MELD – Model for End-Stage Liver Disease; RR – reference range; INR – international normalized ratio. Categorical variables are presented as numbers (percentage) and continuous variables as mean ± standard deviation or median with interquartile range where indicated with †.

diameter in patients without EVs was 12.2 ± 1.9 mm, with small EVs, the diameter was 12.9 ± 2.4 mm, and in those with large EVs, it was 13.6 ± 3.5 mm, $p = 0.035$. *Post hoc* analysis revealed significant differences in the PV diameter between patients without EVs and those with large EVs ($p = 0.026$). The results are presented in Figure 1.

We established the differences in the spleen diameter between patients with large EVs (15.0 ± 3.3 cm) and those without EVs (13.2 ± 3.1 cm) or with small EVs (13.6 ± 2.3 cm); $p = 0.003$ and $p = 0.004$, respectively. The results are displayed in Figure 2.

The average platelet count in patients without EVs was 168.5 ± 107.4 $\times 10^9$/L, compared to 144.9 ± 83.5 $\times 10^9$/L in patients with small EVs and 136.0 ± 83.7 $\times 10^9$/L in those with large EVs. The difference was not statistically significant ($p = 0.216$).

Of the 296/326 patients who underwent abdominal inspection by visualization methods as a part of the standard evaluation of LC, 198 (66.9%) manifested with large ascites volume, and 40 (13.5%) had moderate-volume ascites. In contrast, ascites was not detected in 58 (19.6%) patients.

Portal vein thrombosis

The standard evaluation included abdominal US, CT, and, in some cases, magnetic resonance imaging examination in 90.8% of patients. Abdominal examination revealed PVT in 18/298 (6.1%) patients, by using the abdominal Doppler US in 7/18 (38.9%) by using Doppler US and in 11/18 (61.1%) patients by using CT. Occlusive PVT was diagnosed in 6/18 (33.3%) and non-occlusive in 12/18 (66.7%) patients. Of the 18 patients with PVT, single-branch and main-trunk thrombosis were established in three and four patients, respectively. Three patients had a main trunk and single-branch thrombosis, while eight manifested with the main trunk TVP and both right and left hepatic branches (Figure 3). Thrombus extension into the superior mesenteric and splenic vein was observed in 1/18 (5.6%) patient.

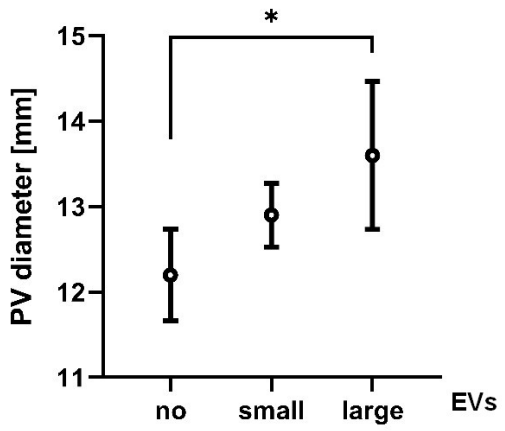

Fig. 1 – The average portal vein (PV) diameter related to the presence and grade of esophageal varices (EVs). Results are presented as the mean value with 95% confidence interval. *$p < 0.05$.

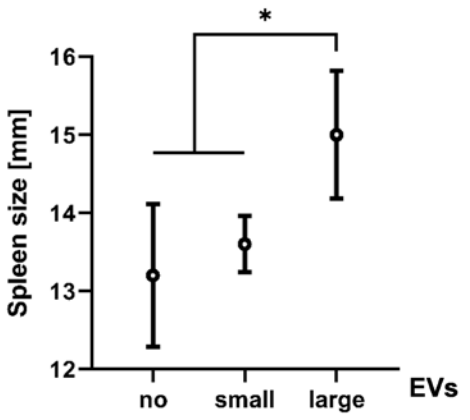

Fig. 2 – The average spleen size related to the presence and grade of esophageal varices (EVs). Results are presented as the mean value with 95% confidence interval. *$p < 0.05$.

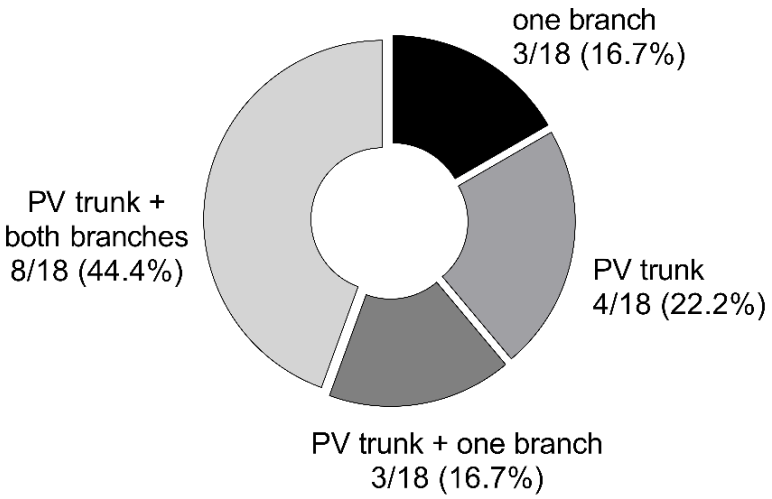

Fig. 3 – The distribution of thrombus extension into the portal vein (PV) and its hepatic branches.

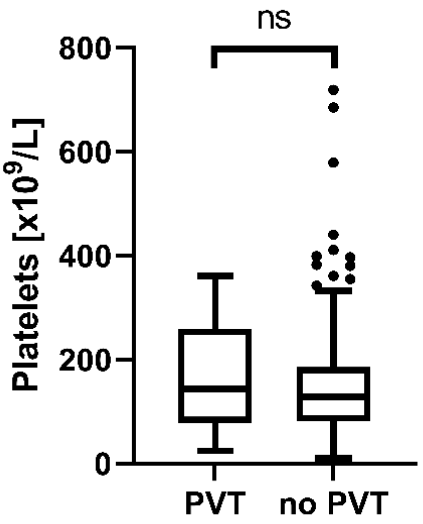

Fig. 4 – Median platelet values related to the presence of portal vein thrombosis (PVT).
Results are presented as the mean value with 95% confidence interval; ns – non-significant.

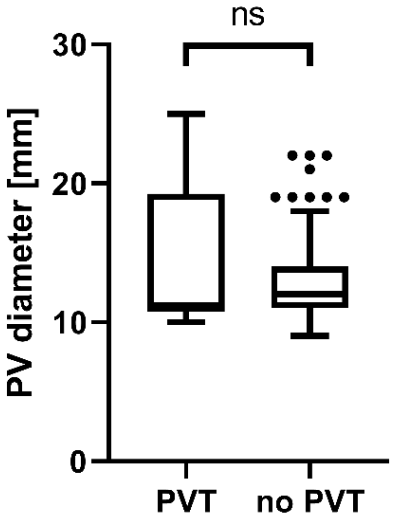

Fig. 5 – The average portal vein (PV) diameter related to the presence and grade of PV thrombosis (PVT).
Results are presented as the mean value with 95% confidence interval; ns – non-significant.

PVT was diagnosed in 12/236 (5.1%) patients with alcoholic LC and 6/60 (10.0%) of those with other LC types. The difference was not statistically significant (χ^2 = 2.02, df = 1, p = 0.155).

In 296 patients who underwent abdominal inspection by visualization methods, thrombosis was established in 5/168 (3.0%) patients with C-P class C and 13/108 (12.0%) patients with C-P class B, whereas none (0/20) of the C-P class A patients had thrombosis (χ^2 = 10.7, df = 2, p = 0.005).

Mann-Whitney *U* test revealed statistically significantly lower PT INR (1.3 vs. 1.56, p = 0.007) and total bilirubin (50.5 μmol/L vs. 104.1 μmol/L, p = 0.009) values in the group with PVT vs. group without PVT, respectively, whereas albumin values did not differ (p = 0.619).

Median platelet values did not differ between the PVT and no PVT group (143.5 ×10^9/L vs. 128.0 ×10^9/L, respectively; p = 0.45) (Figure 4).

PV diameter did not differ significantly between PVT and no PVT group (median 11 mm vs. 12 mm, respectively; p = 0.77) (Figure 5).

We established the differences in PVT prevalence among our patient population depending on the EV grade (χ^2 = 14.0, df = 2, p < 0.001). PVT was established in 2/45 (4.4%) patients without EVs, 4/150 (2.7%) patients with small EVs, and 9/54 (16.7%) patients with large EVs.

There were no differences in PVT prevalence between the groups with or without VB (χ^2 = 0.151, df = 1, p = 0.698) or groups with different ascites grades (χ^2 = 3.19, df = 2, p = 0.203).

Lethal outcomes during the hospitalization period occurred in 96/326 (29.4%) patients, and there were no differences in the mortality rate of patients with or without PVT (16.7% vs. 29.2%, χ^2 = 1.31, df = 1, p = 0.252).

Discussion

Patient characteristics and portal vein thrombosis

This investigation included a retrospective analysis of 326 patients treated for LC to establish the incidence of PVT and its potential association with LD characteristics and individual elements of PH. The majority of patients were males and had LC of alcoholic etiology. PVT was confirmed in 6.1% of patients. PVT was present in 3.0% of patients with C-P class C and 12.0% with C-P class B. However, none of the patients with C-P class A had PVT. There were no differences between PVT prevalence in patients with alcoholic LC and those with LC of other etiologies. The investigation did not include the analysis of beta-blocker administration or previous endoscopic treatment of EVs. Yerdel et al. [30] established that male gender, treatment for PH, C-P class C, and alcoholic LD were associated with PVT. According to the PVT etiology, some studies reported alcoholic and post-viral cirrhosis as the most common causes of PVT; however, other investigations did not establish any association between LC etiology and PVT [31].

According to the data from the literature, the PVT prevalence in LC and PH ranges from 0.6% to 15.8% and increases with cirrhosis grade. It is most commonly classified as C-P class B or C. In compensated LC, the incidence rate is below 1%, corresponding with our investigation [30, 32]. The results of an Italian multicenter prospective study involving 753 patients with chronic LD found a prevalence of PVT in 17% of patients. Cirrhotic patients with PVT were older, but no difference in the etiology of LC was observed. Cirrhotic patients with PVT exhibited a more advanced and decompensated disease, and the presence of ascites and encephalopathy was more frequently observed [33]. Dong et al. [34] did not confirm the

importance of the C-P score for developing PVT. That can be due to the fact that most of the participants were C-P class A, with average C-P scores of 6.6 and 5.8 in the PVT and non-PVT groups, respectively. Conversely, most patients in our study were C-P class B or C.

In our study, the survival rate was 70.6%. The mortality rate was not associated with the presence or absence of PVT. Likewise, Dong et al. [34] did not establish any influence of PVT on the survival rate in patients with LC. Luca et al. [35] reported spontaneous improvement of partial PVT in 45% of patients with LC, as well as the lack of association between partial PVT progression and clinical outcome of the disease, consistent with the severity of the LC. A prospective study by Nery et al. [36] established an association between PVT development and severity of LD at baseline; however, it does not follow a recent progression of LD. There is no evidence that the development of PVT is responsible for the further progression of LD. Borjas-Almaguer et al. [37] reported that the presence of PVT itself does not lead to a worse prognosis of LC. It could be just an epiphenomenon and not a marker of advanced cirrhosis. The authors indicated the MELD score as the most reliable predictor for clinical outcome. Stine et al. [38] conducted a meta-analysis, establishing an increased risk for ascites and mortality in PVT patients; however, the authors emphasized that the data were insufficient to determine the effects of other decompensation markers, such as VB or hepatic encephalopathy. After conducting a systematic review of the literature, Qi et al. [39] concluded that heterogeneity in data reporting did not allow conclusions to be drawn about PVT consequences on LC outcomes. Our study did not reveal any differences in the prevalence of PVT between the patients with or without VB or groups with different ascites grades.

Most authors agree that PVT in LC patients has a minor influence on the course of LD, except in those with PVT after liver transplantation, which is associated with increased graft failure, morbidity, and mortality rates [40–43]. Our study revealed the presence of occlusive and non-occlusive PVT in 33.3% and 66.7% of patients, respectively. Non-occlusive PVT most commonly has an asymptomatic course with a spontaneous recanalization in about 70% of cases, which may be attributed to the improvement of liver function [31, 44].

Portal vein characteristics and EVs, spleen diameter, and platelet count

EVs are a characteristic of PH. EVs can be classified as small or large, with or without red color signs [45]. In our study, EVs were diagnosed in 82.6% of patients. Singh et al. [46] investigated the correlation between EVs and PV diameter, reporting an EV prevalence of 78%. Endoscopic examination confirmed the VB in 25.9% of our patients with LC, which corresponds with the data from the literature, reporting prevalence rates ranging from 25 to 40% [47]. PVT was more common in patients with large EVs compared to those with small EVs and those without EVs. Our investigation did not reveal any association between the presence of PVT and VB, which is contrary to the results of D'Amico et al. [48]. Our study established the differences in the PV diameter between patients without EVs and those with large EVs. Rani et al. [49] have compared the PV diameter with the occurrence of EVs in patients with LC and PH. The authors reported a PV diameter of 11.1 ± 0.8 mm in patients without EVs and 13.1 ± 2.1 mm in those with EVs ($p < 0.001$), which corresponds with the results of our investigation. We established the differences in spleen diameters between patients without EVs or small EVs and those with large EVs. This result is consistent with the report of Rani et al. [49], who reported spleen diameters of 14.0 ± 1.1 cm and 15.2 ± 1.4 cm ($p < 0.01$) in patients without and with EVs, respectively.

Similar results were reported by Gyawali and Acharya [50], who concluded that US measurement of the PV and spleen diameter is recommendable as a non-invasive predictor of esophagogastric varices in LC patients.

In our study, there was no statistically significant difference in the number of platelets among patients in relation to the presence of EVs. Conversely, Rani et al. [49] reported the platelet counts in patients without EVs and those with EVs of 158.6 ± 31.9 $\times 10^9$/L and 114.6 ± 54.0 $\times 10^9$/L, respectively, $p < 0.001$. Bhattarai et al. [51] detected sensitivities of 92.7% and 94.5%, while specificities for the presence of EVs were 90% and 75%, and the cut-off values for PV diameter and spleen size were 12.3 mm and 13.9 cm, respectively. The platelet count cut-off point < 144 $\times 10^9$/L had 87.9% sensitivity. High specificity has also been established for serum albumin at a cut-off point of 25.5 g/L. The authors concluded that these parameters can be recommended as non-invasive predictors for gastro-esophageal varices in LC patients. The study of Mandal et al. [52] established a direct correlation between EV rate and PV diameter and spleen size ($r = 0.707$ and $r = 0.467$, respectively). In higher-grade EVs, the average PV diameter was 14.4 ± 0.9 mm, and the spleen diameter was 15.4 ± 2.1 cm. Schepis et al. [53] reported an association between PV diameter of 13 mm and higher-grade EVs, which corresponds with our investigation. Our results correspond with the study of Uppalapati and Lokesh [54] who reported that a PV diameter at a cut-off value above 13 mm had a strong significant relationship ($p < 0.01$) with the presence of EVs (sensitivity of 100%, specificity of 90%, and positive predictive value of 95.2%). Singh et al. [55] reported an association between the grade of EVs and increased spleen diameter (the mean spleen size of the patients with grade I EVs was 12.1 ± 0.7 cm, grade II EVs was 14.3 ± 0.9 cm, grade III EVs was 16.4 ± 1.1 cm, and with grade IV EVs was 19.1 ± 1.2 cm), as well as the increased PV diameter (grade I, II, III, and IV where the corresponding EVs were 13.2 ± 0.6 mm, 14.6 ± 0.6 mm, 16.4 ± 0.7 mm, and 19.0 ± 1.0 mm, respectively). These results are consistent with the findings in our study. Dong et al. [34] published a study confirming a positive association between PV diameter and PVT in patients with LC. The

average PV diameter in patients with PVT was 14.0 ± 3.0 mm and 10.8 ± 1.1 mm in non-PVT patients. The authors reported that the PV diameter cut-off value with predictive capacity for PVT development was > 12.5 mm and suggested that B-type US should be considered a potential initial diagnostic method. The authors also identified the portal flow, platelet count, and D-dimer as potential risk factors for PVT development. PV diameter proved to be the most predictive factor for developing PVT (odds ratio: 3.96; area under the receiver operating characteristic curve = 0.88, $p < 0.01$).

Unlike Dong et al. [34], other authors found a lower platelet count in patients with PVT compared to patients without PVT [56, 57]. In our study, no statistically significant difference was found in platelet count between patients who had and those who did not have PVT. Such a result was also obtained by Maruyama et al. [58]. Platelet count and function are altered *in vivo* in patients with chronic LD. A complex approach is essential to quantify the real-time platelet function to monitor the unstable counterbalancing between hyperaggregable and hypoaggregable states [59]. In the conducted research, no significant difference was found in the diameter of the PV between patients who had and those who did not have PVT. However, an established difference in the diameter of the PV between patients with large varices and patients without varices could have prognostic significance in assessing the course and degree of severity of LC. Bhattarai et al. [51] found a significantly larger PV diameter in the group of patients with varices compared to patients without varices, as well as a significant association between the Child-Pugh class and the presence of varices. They also reported that the risk for VB in patients of C-P class C was 1.43 times higher than in class B.

Limitations of our study

This study has some limitations. First of all, the data are retrospective. Secondly, PVT was not categorized into acute or chronic forms. Chronic PVT is characterized by the development of venous collaterals known as portal cavernoma. However, PH and potential pre-existing collaterals associated with LC often cause difficulties differentiating between acute and chronic PVT. Moreover, the analysis of therapeutic modalities before and after establishing the diagnosis of PVT was not performed. Finally, the investigation did not include the analysis of beta-blocker administration or previous endoscopic treatment of EVs (this was not the objective of this investigation). Therefore, further prospective studies, including the abovementioned data, are necessary.

Conclusion

Among patients with LC, PVT was diagnosed in the severe stages of the disease (C-P classes B and C). However, there were no differences in the mortality rates in patients with and without PVT. There is a significant difference in the PV diameter between patients without EVs and those with large EVs. PVT is more frequent in patients with large EVs than in those with small EVs and no EVs, even though the existing PVT was not associated with the presence or absence of VB. Esophagogastroduodenoscopy is required in patients with PVT. On the other hand, Doppler US and/or abdominal CT are indicated in patients with large EVs and those of C-P classes B and C. In patients with LC, it is always necessary to consider thrombosis, not only hemorrhagic conditions.

REFERENCES

1. *De Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C; Baveno VII Faculty*. Baveno VII – Renewing consensus in portal hypertension. J Hepatol 2022; 76(4): 959–74. Erratum in: J Hepatol 2022.
2. *Garcia-Tsao G, Bosch J*. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med 2010; 362(9): 823–32. Erratum in: N Engl J Med 2011; 364(5): 490.
3. *Diaz-Soto MP, Garcia-Tsao G*. Management of varices and variceal hemorrhage in liver cirrhosis: a recent update. Therap Adv Gastroenterol 2022; 15: 17562848221101712.
4. *Caiano LM, Riva N, Carrier M, Gatt A, Ageno W*. Treatment of portal vein thrombosis: an updated narrative review. Minerva Med 2022; 112(6): 713–25.
5. *Ma J, Yan Z, Luo J, Liu Q, Wang J, Qiu S*. Rational classification of portal vein thrombosis and its clinical significance. PLoS One 2014; 9(11): e112501.
6. *Von Köckritz L, De Gottardi A, Trebicka J, Praktiknjo M*. Portal vein thrombosis in patients with cirrhosis. Gastroenterol Rep (Oxf) 2017; 5(2): 148–56.
7. *Tsochatzis EA, Senzolo M, Germani G, Gatt A, Burroughs AK*. Systematic review: portal vein thrombosis in cirrhosis. Aliment Pharmacol Ther 2010; 31(3): 366–74.
8. *Turon F, Driever EG, Baiges A, Cerda E, García-Criado Á, Gilabert R*, et al. Predicting portal thrombosis in cirrhosis: A prospective study of clinical, ultrasonographic and hemostatic factors. J Hepatol 2021; 75(6): 1367–76.
9. *European Association for the Study of the Liver*. EASL Clinical Practice Guidelines: Vascular diseases of the liver. J Hepatol 2016; 64(1): 179–202.
10. *De Franchis R; Baveno VI Faculty*. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. J Hepatol 2015; 63(3): 743–52.
11. *Balfour GW, Stewart TG*. Case of enlarged spleen complicated with ascites, both depending upon varicose dilatation and thrombosis of the portal vein. Edinb Med J 1869; 14(7): 589–98.
12. *Faccia M, Ainora ME, Ponziani FR, Riccardi L, Garcovich M, Gasbarrini A*, et al. Portal vein thrombosis in cirrhosis: Why a well-known complication is still matter of debate. World J Gastroenterol 2019; 25(31): 4437–51.
13. *Anton A, Campreciós G, Pérez-Campuzano V, Orts L, García-Pagán JC, Hernández-Gea V*. The pathophysiology of portal vein thrombosis in cirrhosis: getting deeper into Virchow's triad. J Clin Med 2022; 11(3): 800.
14. *Turon F, Hernández-Gea V, García-Pagán JC*. Portal vein thrombosis: yes or no on anticoagulation therapy. Curr Opin Organ Transplant 2018; 23(2): 250–6.

15. *Odriozola A, Puente Á, Cuadrado A, Rivas C, Anton Á, González FJ,* et al. Portal vein thrombosis in the setting of cirrhosis: a comprehensive review. J Clin Med 2022; 11(21): 6435.
16. *Lisman T, Porte RJ*. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. Blood 2010; 116(6): 878–85.
17. *Delahousse B, Labat-Debelleix V, Decalonne L, d'Alteroche L, Perarnau JM, Gruel Y*. Comparative study of coagulation and thrombin generation in the portal and jugular plasma of patients with cirrhosis. Thromb Haemost 2010; 104(4): 741–9.
18. *Praktiknjo M, Trebicka J, Carnevale R, Pastori D, Queck A, Ettorre E,* et al. Von Willebrand and factor VIII portosystemic circulation gradient in cirrhosis: implications for portal vein thrombosis. Clin Transl Gastroenterol 2020; 11(2): e00123.
19. *Zanetto A, Campello E, Senzolo M, Simioni P.* Assessment of whole blood platelet aggregation in patients with cirrhosis: challenges and opportunities. Platelets 2023; 34(1): 2178823.
20. *Berzigotti A, García-Criado A, Darnell A, García-Pagán JC*. Imaging in clinical decision-making for portal vein thrombosis. Nat Rev Gastroenterol Hepatol 2014; 11(5): 308–16.
21. *DeLeve LD, Valla DC, Garcia-Tsao G; American Association for the Study Liver Diseases*. Vascular disorders of the liver. Hepatology 2009; 49(5): 1729–64.
22. *Senzolo M, Garcia-Tsao G, García-Pagán JC*. Current knowledge and management of portal vein thrombosis in cirrhosis. J Hepatol 2021; 75(2): 442–53.
23. D*elgado MG, Seijo S, Yepes I, Achécar L, Catalina MV, García-Criado Á,* et al. Efficacy and safety of anticoagulation on patients with cirrhosis and portal vein thrombosis. Clin Gastroenterol Hepatol 2012; 10(7): 776–83.
24. *Khan AR, Wei X, Xu X*. Portal vein tumor thrombosis and hepatocellular carcinoma – the changing tides. J Hepatocell Carcinoma 2021; 8: 1089–115.
25. *Child CG, Turcotte JG*. Surgery and portal hypertension. Major Probl Clin Surg 1964; 1: 1–85.
26. *Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R*. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 1973; 60(8): 646–9.
27. *Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL,* et al. A model to predict survival in patients with end-stage liver disease. Hepatology 2001; 33(2): 464–70.
28. *Ruf A, Dirchwolf M, Freeman RB*. From Child-Pugh to MELD score and beyond: Taking a walk down memory lane. Ann Hepatol 2022; 27(1): 100535.
29. *Gülcicegi DE, Goeser T, Kasper P*. Prognostic assessment of liver cirrhosis and its complications: current concepts and future perspectives. Front Med (Lausanne) 2023; 10: 1268102.
30. *Yerdel MA, Gunson B, Mirza D, Karayalçin K, Olliff S, Buckels J,* et al. Portal vein thrombosis in adults undergoing liver transplantation. Transplantation 2000; 69(9): 1873–81.
31. *Mantaka A, Augoustaki A, Kouroumalis EA, Samonakis DN*. Portal vein thrombosis in cirrhosis: diagnosis, natural history, and therapeutic challenges. Ann Gastroenterol 2018; 31(3): 315–29.
32. *Amitrano L, Guardascione MA, Brancaccio V, Margaglione M, Manguso F, Iannaccone L,* et al. Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. J Hepatol 2004; 40(5): 736–41.
33. *Violi F, Corazza GR, Caldwell SH, Perticone F, Gatta A, Angelico M,* et al. Portal vein thrombosis relevance on liver cirrhosis: Italian Venous Thrombotic Events Registry. Intern Emerg Med 2016; 11(8): 1059–66.
34. *Dong G, Huang XQ, Zhu YL, Ding H, Li F, Chen SY*. Increased portal vein diameter is predictive of portal vein thrombosis development in patients with liver cirrhosis. Ann Transl Med 2021; 9(4): 289.
35. *Luca A, Caruso S, Milazzo M, Marrone G, Mamone G, Crinò F,* et al. Natural course of extrahepatic nonmalignant partial portal vein thrombosis in patients with cirrhosis. Radiology 2012; 265(1): 124–32.
36. *Nery F, Chevret S, Condat B, de Raucourt E, Boudaoud L, Rautou PE,* et al. Causes and consequences of portal vein thrombosis in 1,243 patients with cirrhosis: Results of a longitudinal study. Hepatology 2015; 61(2): 660–7.
37. *Borjas-Almaguer OD, Cortez-Hernández CA, González-Moreno EI, Bosques-Padilla FJ, González-González JA, Garza AA,* et al. Portal vein thrombosis in patients with cirrhosis: just a common finding or a predictor of poor outcome? Ann Hepatol 2017; 15(6): 902–6.
38. *Stine JG, Shah PM, Cornella SL, Rudnick SR, Ghabril MS, Stukenborg GJ,* et al. Portal vein thrombosis, mortality and hepatic decompensation in patients with cirrhosis: A meta-analysis. World J Hepatol 2015; 7(27): 2774–8.
39. *Qi X, Dai J, Yang M, Ren W, Jia J, Guo X*. Association between portal vein thrombosis and survival in non-liver-transplant patients with liver cirrhosis: a systematic review of the literature. Gastroenterol Res Pract 2015; 2015: 480842.
40. *Ghabril M, Agarwal S, Lacerda M, Chalasani N, Kwo P, Tector AJ*. Portal vein thrombosis is a risk factor for poor early outcomes after liver transplantation: Analysis of risk factors and outcomes for portal vein thrombosis in waitlisted patients. Transplantation 2016; 100(1): 126–33.
41. *Englesbe MJ, Schaubel DE, Cai S, Guidinger MK, Merion RM*. Portal vein thrombosis and liver transplant survival benefit. Liver Transpl 2010; 16(8): 999–1005.
42. *Zanetto A, Rodriguez-Kastro KI, Germani G, Ferrarese A, Cillo U, Burra P,* et al. Mortality in liver transplant recipients with portal vein thrombosis - an updated meta-analysis. Transpl Int 2018; 31(12): 1318–29.
43. *Xian J, Tang Y, Shao H, Wang X, Zhang M, Xing T*. Effect of portal vein thrombosis on the prognosis of patients with cirrhosis without a liver transplant: A systematic review and meta-analysis. Medicine (Baltimore) 2021; 100(16): e25439.
44. *Qi X, Yang Z, Fan D*. Spontaneous resolution of portal vein thrombosis in cirrhosis: Where do we stand, and where will we go? Saudi J Gastroenterol 2014; 20(5): 265-6.
45. *Abby Philips C, Sahney A*. Oesophageal and gastric varices: historical aspects, classification and grading: everything in one place. Gastroenterol Rep (Oxf) 2016; 4(3): 186–95.
46. *Singh H, Sharma S, Singh G, Kaur D*. Study of the correlation of oesophageal varices with portal vein diameter and ratio of platelet count to splenic diameter and their comparative evaluation in liver cirrhosis. Int J Adv Med 2021; 8(9): 1405–11.
47. *Lisman T, Hernandez-Gea V, Magnusson M, Roberts L, Stanworth S, Thachil J,* et al. The concept of rebalanced hemostasis in patients with liver disease: Communication from the ISTH SSC working group on hemostatic management of patients with liver disease. J Thromb Haemost 2021; 19(4): 1116–22.
48. *D'Amico G, De Franchis R; Cooperative Study Group*. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology 2003; 38(3): 599–612.
49. *Rani S, Sudarsi B, Siddeswari R, Manohar S*. Correlation of portal vein size with esophageal varices severity in patients with cirrhosis of liver with portal hypertension. Int J Sci Res Publ 2015; 5(1): 1–5.
50. *Gyawali M, Acharya RR*. Role of ultrasonography in predicting gastro-oesophageal varices in patients with liver cirrhosis. J Coll Med Sci-Nepal 2021; 17(1): 10–5.
51. *Bhattarai S, Dewan KR, Shrestha G, Patowary BS*. Non-invasive predictors of gastro-oesophageal varices. J Nepal Med Assoc 2017; 56(207): 298–303.
52. *Mandal L, Mandal SK, Bandyopadhyay D, Datta S*. Correlation of portal vein diameter and splenic size with gastro-oesophageal

varices in cirrhosis of liver. J Indian Acad Clin Med 2011; 12(4): 266–70.
53. *Schepis F, Cammà C, Niceforo D, Magnano A, Pallio S, Cinquegrani M,* et al. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection? Hepatology 2001; 33(2): 333–8.
54. *Uppalapati S, Lokesh S*. Correlation of portal vein diameter with the presence of oesophageal varices in chronic liver disease: a prospective study. Int J Adv Med 2018; 5(4): 859–64.
55. *Singh I, Sehgal R, Singh H, Chuchra P, Neki NS*. Correlation of portal vein diameter, splenomegaly and thrombocytopenia with gastro-espohageal varices in cirrhotic patients. Int J Curr Res Biol Med 2017; 4(12): 38–44.
56. *Abdel-Razik A, Mousa N, Elhelaly R, Tawfik A*. De-novo portal vein thrombosis in liver cirrhosis: risk factors and correlation with the Model for End-stage Liver Disease scoring system. Eur J Gastroenterol Hepatol 2015; 27(5): 585–92.
57. *Quan X, Ye X, Qian S, Wei B, Tong H, Wang Z,* et al. Portal vein thrombosis associates with high platelet-fibrin clot strength and platelet activation in decompensated cirrhosis: A retrospective study. Dig Liver Dis 2023; 55(5): 629–36.
58. *Maruyama H, Okugawa H, Takahashi M, Yokosuka O*. De novo portal vein thrombosis in virus-related cirrhosis: predictive factors and long-term outcomes. Am J Gastroenterol 2013; 108(4): 568–74.
59. *Chen SH, Tsai SC, Lu HC*. Platelets as a gauge of liver disease kinetics? Int J Mol Sci 2022; 23(19): 11460.

Received on January 16, 2024
Revised on March 10, 2024
Revised on March 20, 2024
Accepted on April 9, 2024
Online First April 2024