Thrombosis Research 161 (2018) 7–11

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

The disseminated intravascular coagulation score is a novel predictor for portal vein thrombosis in cirrhotic patients with hepatitis B

ShaoBo Cui[a,b], Zhenmei Fu[a], YueMin Feng[a], XiaoYu Xie[a], XiaoWen Ma[a], TianTian Liu[a], Le Wang[a], Hao Wu[a], Qiang Zhu[a,*]

[a] Department of Gastroenterology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, Shandong, China
[b] Department of Gastroenterology, General Hospital of Jincheng Anthracite Coal Mining Group Co. Ltd, Jincheng, Shanxi Province, China

ARTICLE INFO

Keywords:
Disseminated intravascular coagulation score
Predictor
Cirrhosis
Portal vein thrombosis
Hepatitis B

ABSTRACT

Background: The development of portal vein thrombosis (PVT) in cirrhotic patients has not been fully elucidated. The disseminated intravascular coagulation (DIC) score, which is based on readily available and relatively inexpensive coagulation parameters, including platelet count, fibrin-related markers, prothrombin time and fibrinogen, has not been reported regarding PVT development in cirrhotic patients to date. We aimed to evaluate the prognostic value of the DIC score in predicting PVT development in cirrhotic patients with hepatitis B.

Material and methods: A total of 109 cirrhotic patients with hepatitis B were included. Clinical data, laboratory tests and imaging were collected from the patients at baseline and every three months after enrollment. All patients were followed until the study endpoint (either occurrence of PVT or 12 months after baseline). We measured routine laboratory parameters and conducted imaging examinations in cirrhotic patients and evaluated the prognostic value of the DIC score as a novel predictor for PVT in patients with cirrhosis. We also compared the effectiveness of the DIC score with other common coagulation and hemodynamic parameters.

Results: Among the 109 patients, 14 (12.8%) developed PVT. At the study endpoint, significant increases in D-dimer, Child-Pugh score and DIC score (all $P < 0.001$) and significantly reduced portal flow velocity ($P < 0.001$) were noted in the PVT group. Among the selected factors, the DIC score had the largest area under the curve (AUC) (0.845), followed by the Child-Pugh score (0.778), D-dimer (0.732), and portal vein velocity (0.709).

Conclusion: Among the selected factors, the DIC score showed non-significantly higher diagnostic performance in predicting the PVT development in cirrhotic patients compared with other factors. A validation cohort of the study is needed in the near future.

1. Introduction

Portal vein thrombosis (PVT) is commonly observed in cirrhotic patients [1]. Severe PVT may lead to intestinal infarction, life-threatening variceal bleed or even death [2–5]. Currently, there are no optimal modalities for monitoring PVT. Studies have shown that a hypercoagulable state, decrease in the blood flow velocity, endothelial cell injury, and cirrhosis-related complications can predict the development of PVT in cirrhotic patients, but the conclusions are inconsistent [6–11].

Some single routine coagulation parameters are associated with PVT development in cirrhotic patients [6,9,12]. However, it is difficult for a single coagulation parameter to reflect the entire coagulation state in cirrhotic patients. The DIC score, which integrates routine coagulation parameters, including platelet count, fibrin-related markers (D-dimer), prothrombin time (PT) and fibrinogen (FIB) [13,14], is a useful tool in assessing cirrhotic patients in intensive care units (ICU) [15]. In addition, the DIC score significantly predicted arterial and venous thrombosis of myeloid leukemia in a prospective study [16]. However, no date exist on the relationship between DIC score and PVT of cirrhosis to date.

In the study, we measured routine coagulation parameters and conducted imaging examinations in cirrhotic patients and evaluated the prognostic value of the DIC score as a novel predictor for PVT in patients with cirrhosis. We also compared the prognostic value of the DIC score with other common coagulation and hemodynamic parameters.

* Corresponding author at: Department of Gastroenterology, Shandong Provincial Hospital Affiliated to Shandong University, 324, Jing 5 Rd, Ji'nan 250021, Shandong Province, China.
E-mail address: zhuqiang@medmail.com.cn (Q. Zhu).

https://doi.org/10.1016/j.thromres.2017.11.010
Received 3 July 2017; Received in revised form 13 November 2017; Accepted 14 November 2017
Available online 15 November 2017

2. Material and methods

2.1. Patients

A total of 109 consecutive patients with hepatitis B-related cirrhosis (68 men, 41 women) with a median age of 54.3 years (range 38–70 yrs) were enrolled in this study. The inclusion criteria were as follows: clinical confirmation of hepatitis B-related cirrhosis and available laboratory tests and imaging based on the American Association for the Study of Liver Diseases (AASLD) practice guidelines [17]. The exclusion criteria were as follows: liver cirrhosis resulting from autoimmune liver disease, metabolic liver disease, alcohol consumption, drug-induced liver disease or other liver diseases; pre-existing PVT; Budd-Chiari syndrome; splenectomy; malignant disease; ongoing antiaggregation treatment; pregnancy or breastfeeding; or concomitant systemic disease. Patients were ineligible if they underwent endoscopic sclerotherapy or presented either active bleeding or hematologic disease. All patients signed informed consent, and the study procedures were approved by the medical ethics committee at Provincial Hospital Affiliated with Shandong University.

2.2. Study design

Patient demographics and associated clinical data, routine coagulation tests and imaging examinations were collected at the beginning of the study, and the DIC score for each patient was also calculated. All patients were followed until the study endpoint (either 12 months after baseline measurements or the occurrence of PVT within 12 months). Patients were monitored and evaluated every 3 months with biochemical tests and Doppler ultrasound (US) examination. To explore predictors for PVT, cirrhotic patients were classified into the PVT group (i.e., occurrence of PVT by the study endpoint) and the non-PVT group (no PVT by the study endpoint).

The data of the two groups at baseline were analyzed to determine any predictive variables for PVT. The receiver operating characteristic (ROC) curve was used to identify the best predictor for PVT development in patients with cirrhosis.

2.3. Blood collection and laboratory analysis

Venous blood samples of all the participants were collected after 8 h of fasting. The primary coagulation parameters included platelet count, PT, FIB, D-dimer, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL) and serum albumin (ALB). The levels of these parameters were calculated according to published formulas.

2.4. Doppler ultrasonography examination

All patients were examined in the supine position after overnight fasting. SSA-390A (Toshiba, Tokyo, Japan) Doppler ultrasound was used to examine the patients. The portal flow velocity was measured thrice in the portal vessel, and the average of the results was used for data analysis. All patients underwent follow-up Doppler ultrasound at 3-month intervals. In cases with worsening of ascites or variceal bleeding, additional Doppler ultrasound imaging was performed to detect the presence of PVT.

2.5. Diagnosis of PVT

Acute PVT is defined as the sudden formation of a thrombus in the portal system, including the portal vein, splenic vein and mesenteric vein. The absence of flow within the portal system lumen can be observed by Doppler imaging [17].

Table 1
DIC scoring system.

	DIC score
Platelet count ($\times 10^9$/L)	> 100 = 0; 50–100 = 1; < 50 = 2
D-dimer (ng/L)	< 400 = 0; 400–4000 = 2; > 4000 = 3
Prolonged PT (s)	< 3 = 0; 3–6 = 1; > 6 = 2
FIB (g/L)	≥ 1 = 0; < 1 = 1

Data are expressed as the mean ± SD or median (IQR).
PT, prothrombin time; FIB, fibrinogen.

2.6. DIC score

The DIC score of the patients was determined using the International Society of Thrombosis and Haemostasis (ISTH) scoring system [13], which incorporates platelet count, fibrin-related markers (D-dimer level), PT and FIB. The D-dimer level was assayed as presented in Table 1 [18]. The DIC score was calculated by adding the values of these four parameters.

2.7. Statistical analysis

Statistical analysis was conducted using the SPSS 16.0 package (SPSS Inc., Chicago, Illinois, USA). Quantitative variables are reported as either the mean ± standard deviation or median (IQR), and qualitative variables are presented as relative and absolute frequencies. Comparisons between groups were performed using the appropriate parametric/non-parametric test. ROC curves were calculated to determine the ability of the factors to predict PVT in patients with cirrhosis, and the area under the curve (AUC) was calculated for each parameter. All P-values were two-sided, and P-values < 0.05 were considered statistically significant.

3. Results

3.1. Patient characteristics

Initially, 133 patients were prospectively considered for this study. Twelve patients were lost after the first visit. In addition, 3 patients developed hepatic carcinoma during the follow-up period and were excluded from the analysis. Four patients died (1 of hepatic failure, 2 of hepatorenal syndrome, and 1 of severe infection) without PVT development and were subsequently excluded. A total of 109 patients were finally enrolled in the study. The study flowchart of patient enrollment at baseline is presented in Table 2.

Table 2
Baseline characteristics of the patients.

	Patients (n = 109)
Age (year) ± SD	54.3 ± 5.7
Sex (M: F)	68/41
Bilirubin (μmol/L)	34.5 ± 10.2
albumin (g/L)	31.3 ± 3.1
PT (s)	15.9 (14.7–16.9)
D-dimer (ng/L)	353.0 (302.5–442.5)
FIB (g/L)	2.5 (2.4–2.7)
Platelet count ($\times 10^9$/L)	79.6 ± 17.6
Ascites (none/mild/ severe)	34/55/20
Encephalopathy (none/I–II/III–IV)	66/43/0
portal vein flow velocity (cm/s)	14.2 (13.2–15.7)
Child-Pugh score	8.0 (7.0–8.0)
DIC score	2.0 (1.0–3.0)

Data are expressed as the mean ± SD or median (IQR).
M, male; F, female; PT, prothrombin time; FIB, fibrinogen.