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Prognostic role of mean platelet volume in patients with cirrhosis

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ABSTRACT

Background: Studies carried out in patients with chronic hepatitis have shown that mean platelet volume (MPV) is associated with worse disease stage, although the role of MPV in patients with cirrhosis is less clear.
Aim: To evaluate the association between MPV values and clinical characteristics and stage of cirrhosis, and to assess its prognostic role.
Methods: We studied 75 patients with cirrhosis and assessed the association between MPV values and cirrhosis characteristics, prognostic scores, and survival. The prognostic role of longitudinal variations of MPV was also assessed in 50 patients who had at least 12 months follow-up and who had MPV determination at 3-monhtly intervals.
Results: Median MPV values were not statistically different according to aetiology of liver disease ($P = 0.485$) and disease severity both taking into consideration the Child–Pugh classification ($P = 0.438$) and the Model for End-stage Liver Disease score ($P = 0.978$). Median MPV values were not significantly different in 23 Child–Pugh class C patients who died or survived (9.15 fL *versus* 9.10 fL, $P = 0.794$) during a 12-month follow-up. Lastly, there was no significant modification of MPV over time at the various study time-points (3-month, 6-month, 9-month, 12-month) between patients who died and those who survived.
Conclusions: In patients with cirrhosis, MPV has no association with severity of disease and prognosis.

1. Introduction

Both quantitative and qualitative platelet defects can frequently be observed in patients with chronic liver disease, and thrombocytopenia is the most common haematological abnormality in patients with liver cirrhosis [1–3]. In these patients, decreased platelet count can be used as a diagnostic tool for non-invasively assessing the presence of features of portal hypertension, and as a prognostic parameter in patients with end-stage liver disease [4–6]. However, besides alteration of platelet number, patients affected by chronic liver disease may display alteration in platelet morphology, and also this characteristic has demonstrated to be of clinical utility in the diagnostic assessment of these patients [7].

Mean platelet volume (MPV) is considered a marker of platelet activation and function, and the relevance of MPV has been clearly underlined in studies carried out in patients with chronic inflammatory conditions [8]. Some studies evaluated the role of MPV in patients with chronic viral hepatitis, and found that MPV was associated with both greater fibrosis histological scores and necro-inflammatory activity, especially in patients with chronic hepatitis B virus (HBV) infection [9–11]. Moreover, in patients with chronic HBV infection, higher MPV has been identified as a marker associated with cirrhosis, and as an independent, very short-term (*i.e.*, 4 weeks) prognostic indicator in patients with HBV-related acute-on-chronic liver failure [12,13]. Lastly, in cirrhotic patients, an increase in MPV values was noted in patients with ascitic fluid infection, thus emphasizing the role of MPV as a possible marker of inflammation [14,15]. However, there are no data on the possible association between either clinical features or prognosis of cirrhotic patients and MPV.

In this study we aimed at assessing the association between MPV and both severity of cirrhosis and its clinical features. Moreover, we assessed the possible role of MPV in the short- and long-term prognostic assessment in cirrhotic patients. Lastly, we evaluated whether longitudinal, iterative evaluation of MPV may have any prognostic meaning.

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2. Patients and methods

The study population was made up of 75 patients with cirrhosis of various aetiologies who were followed-up at our Institution. Liver cirrhosis was diagnosed on the basis of histology results, clinical findings (presence of ascites, hepatic encephalopathy), or instrumental findings (ultrasonographic, endoscopic). Well-compensated cirrhosis was defined as absence of jaundice, ascites (and no use of diuretics), hepatic encephalopathy, and previous portal hypertension-related bleeding episodes. At the time of enrollment none of the patients had spontaneous bacterial peritonitis or hepatorenal syndrome.

In all patients both the Child–Pugh and the Model for End-stage Liver Disease (MELD) scores, measures of severity of cirrhosis and prognostic indexes, were calculated on parameters obtained at inclusion [16,17]. We evaluated the association of MPV values with disease characteristics as well as its prognostic role at baseline in the whole cohort of 75 patients. Moreover, we assessed the prognostic role of baseline MPV values in patients with Child–Pugh class C patient. Lastly, we assessed both the baseline and longitudinal, iterative (every 3 months) prognostic value of MPV in 50 patients with cirrhosis who had been regularly followed-up and who had a survival of at least 12 months.

Platelet counts and MPV were measured using EDTA blood in Advia 2120 (Siemens Healthcare Diagnostics Inc., Tarrytown, NY, USA) within 2 hours of blood withdrawal. Normal values for MPV were 7.2–11.1 fL. This study was carried out according to the 1975 Declaration of Helsinki as revised in 1983, and informed consent was obtained from each patient.

Data are shown as median values and interquartile range or absolute value and percentage. Continuous variables were compared using the Mann–Whitney *U*-test and categorical variables were compared using the χ^2 or Fisher's exact test as appropriate. Correlation between MPV values and both platelet counts and MELD scores was assessed by Spearman's rank correlation test. A multivariate Cox regression analysis was carried out in the whole cohort on baseline data in order to identify independent prognostic predictors. In all analyses, a *P*-value <0.05 was considered statistically significant.

3. Results

3.1. Mean platelet volume and cirrhosis characteristics at baseline

The main clinical, biochemical, and haematological characteristics of the 75 cirrhotic patients included in this study are shown in Table 1. The majority of patients were males ($n = 54$, 72%) and aetiology of liver disease was mainly viral ($n = 53$, 71%), either with ($n = 12$, 16%) or without ($n = 41$, 55%) concomitant alcohol abuse. Four patients (5%) had well-compensated cirrhosis, and 50 patients (67%) had a MELD score <15. Thrombocytopenia (*i.e.*, platelet count $<150 \times 10^9$/L) and severe thrombocytopenia (*i.e.*, platelet count $<50 \times 10^9$/L) were observed in 64 (85%) and 23 (31%) of patients, respectively. An MPV value above the upper limit of normal (*i.e.*, >11.1 fL) was observed in 5 patients (7%).

Table 2 shows MPV values according to clinical parameters at baseline. Median MPV values were not statistically different according to the aetiology of liver disease ($P = 0.485$), and showed no statistically significant difference in patients with more severe liver disease both taking into consideration the Child–Pugh classification ($P = 0.438$) and the MELD score ($P = 0.978$). Moreover, MPV values were similar in patients with compensated and decompensated cirrhosis (9.00 fL *versus* 9.10 fL, $P = 0.884$), and there were no significant differences according to type of decompensation (ascites, $P = 0.758$; hepatic encephalopathy, $P = 0.992$). MPV values were not associated with the presence of both thrombocytopenia ($P = 0.127$) and severe thrombocytopenia ($P = 0.524$), and were not correlated with platelet counts ($r_s = -0.077$, $P = 0.509$). Lastly, there was no correlation between MPV values and MELD scores ($r_s = -0.052$; $P = 0.654$, Fig. 1).

Table 1
Main demographic, clinical, and haematological characteristics of the study population.

Parameter	Unit	Value
Gender	Male-to-female ratio	54:21
Age	Years	56 (48–67)
Liver disease aetiology	Hepatitis viruses	41 (55)
	Alcohol	17 (23)
	Hepatitis viruses and alcohol	12 (16)
	Nonalcoholic steatohepatitis	4 (5)
	Cholestatic	1 (1)
Serum creatinine	mg/dL	0.9 (0.7–1.0)
Serum bilirubin	mg/dL	1.90 (1.10–2.97)
International normalized ratio		1.43 (1.28–1.66)
Ascites	Present	62 (83)
Hepatic encephalopathy	Present	33 (34)
Child–Pugh class		
	A	10 (13)
	B	42 (56)
	C	23 (31)
MELD score		13 (10–16)
Platelet count	$n \times 10^9$/L	68.0 (44.3–112.0)
Mean platelet volume	fL	9.10 (8.40–9.68)

MELD, Model for End-stage Liver Disease.
Data are shown as median values and interquartile range or absolute value and percentage.

3.2. Prognostic value of mean platelet volume in patients with cirrhosis

Twenty-three patients (31%) had Child–Pugh class C cirrhosis. After a median follow-up of 12 months (9–14 months), 11 patients (48%) died. At baseline, only 1 patient (4%) had an MPV above the upper limit of normal. There was no difference in median MPV values between patients who died (9.10 fL, 9.00–9.70 fL) and those who survived (9.05, 8.40–9.05 fL, $P = 0.356$). Furthermore, 5 patients died within 12 months of follow-up, and baseline median MPV values were not significantly different between these patients and those with longer survival (9.15 fL *versus* 9.10 fL, $P = 0.794$).

Fifty patients had at least one year of follow-up (median, 15 months, 12–19 months), and during this observation period 15 patients (30%) died. Median MPV values were not significantly different in patients who survived (9.10 fL, 8.30–9.68 fL) compared to those who died (9.0 fL, 8.13–9.60 fL, $P = 0.649$), while MELD score was significantly higher in patients who died [13 (11–17) *versus* 11 (8–13), $P = 0.03$]. In these patients longitudinal evaluation of MPV showed that there was no significant modification of MPV over time at the various study time-points (3-month, 6-month, 9-month, 12-month) between patients who died and those who survived (Fig. 2). Lastly, taking into consideration the whole cohort ($n = 75$), a multivariate Cox regression analysis that included demographic (age, gender) and clinical (aetiology of disease, Child–Pugh class, MELD score, MPV values, platelet counts) characteristics at baseline showed that the MELD score (odds ratio, 1.279; 95% confidence interval: 1.136 to 1.439, $P = 0.0001$) was the only independent prognostic predictor.

4. Discussion

In this study, we assessed the possible association between MPV and clinical characteristics of patients with liver cirrhosis, and