

World Journal of *Hepatology*

World J Hepatol 2018 January 27; 10(1): 1-171



**MINIREVIEWS**

- 1 Role of inflammatory response in liver diseases: Therapeutic strategies
Del Campo JA, Gallego P, Grande L

ORIGINAL ARTICLE**Basic Study**

- 8 Preserved liver regeneration capacity after partial hepatectomy in rats with non-alcoholic steatohepatitis
Haldrup D, Heebøll S, Thomsen KL, Andersen KJ, Meier M, Mortensen FV, Nyengaard JR, Hamilton-Dutoit S, Grønbæk H
- 22 Bioengineered humanized livers as better three-dimensional drug testing model system
Vishwakarma SK, Bardia A, Lakkireddy C, Nagarapu R, Habeeb MA, Khan AA

Retrospective Cohort Study

- 34 Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease
Ayoub F, Trillo-Alvarez C, Morelli G, Lascano J
- 41 Fatty liver disease, an emerging etiology of hepatocellular carcinoma in Argentina
Piñero F, Pages J, Marciano S, Fernández N, Silva J, Anders M, Zerega A, Ridruejo E, Ameigeiras B, D'Amico C, Gaite L, Bermúdez C, Cobos M, Rosales C, Romero G, McCormack L, Reggiardo V, Colombato L, Gadano A, Silva M
- 51 Current state and clinical outcome in Turkish patients with hepatocellular carcinoma
Ekinci O, Baran B, Ormeci AC, Soyer OM, Gokturk S, Evirgen S, Poyanli A, Gulluoglu M, Akyuz F, Karaca C, Demir K, Besisik F, Kaymakoglu S

Retrospective Study

- 62 Predicting early outcomes of liver transplantation in young children: The EARLY study
Alobaidi R, Anton N, Cave D, Moez EK, Joffe AR
- 73 Collagen proportionate area correlates to hepatic venous pressure gradient in non-abstinent cirrhotic patients with alcoholic liver disease
Restellini S, Goossens N, Clément S, Lanthier N, Negro F, Rubbia-Brandt L, Spahr L
- 82 Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis
Iida H, Kaibori M, Matsui K, Ishizaki M, Kon M
- 88 Efficacy of direct-acting antiviral treatment for chronic hepatitis C: A single hospital experience
Kaneko R, Nakazaki N, Omori R, Yano Y, Ogawa M, Sato Y

- 95 Efficacy of intra-arterial contrast-enhanced ultrasonography during transarterial chemoembolization with drug-eluting beads for hepatocellular carcinoma

Shiozawa K, Watanabe M, Ikehara T, Yamamoto S, Matsui T, Saigusa Y, Igarashi Y, Maetani I

Clinical Practice Study

- 105 Proton nuclear magnetic resonance-based metabonomic models for non-invasive diagnosis of liver fibrosis in chronic hepatitis C: Optimizing the classification of intermediate fibrosis

Batista AD, Barros CJP, Costa TBBC, Godoy MMG, Silva RD, Santos JC, de Melo Lira MM, Jucá NT, Lopes EPA, Silva RO

Observational Study

- 116 High burden of hepatocellular carcinoma and viral hepatitis in Southern and Central Vietnam: Experience of a large tertiary referral center, 2010 to 2016

Nguyen-Dinh SH, Do A, Pham TND, Dao DY, Nguy TN, Chen Jr MS

- 124 Toll-like receptor 4 polymorphisms and bacterial infections in patients with cirrhosis and ascites

Alvarado-Tapias E, Guarner-Argente C, Oblitas E, Sánchez E, Vidal S, Román E, Concepción M, Poca M, Gely C, Pavel O, Nieto JC, Juárez C, Guarner C, Soriano G

Prospective Study

- 134 Effect of transplant center volume on post-transplant survival in patients listed for simultaneous liver and kidney transplantation

Modi RM, Tumin D, Kruger AJ, Beal EW, Hayes Jr D, Hanje J, Michaels AJ, Washburn K, Conteh LF, Black SM, Mumtaz K

META-ANALYSIS

- 142 Vitamin D levels do not predict the stage of hepatic fibrosis in patients with non-alcoholic fatty liver disease: A PRISMA compliant systematic review and meta-analysis of pooled data

Saberi B, Dadabhai AS, Nanavati J, Wang L, Shinohara RT, Mullin GE

- 155 Epigenetic basis of hepatocellular carcinoma: A network-based integrative meta-analysis

Bhat V, Srinathan S, Pasini E, Angeli M, Chen E, Baciu C, Bhat M

CASE REPORT

- 166 Contrast uptake in primary hepatic angiosarcoma on gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid-enhanced magnetic resonance imaging in the hepatobiliary phase

Hayashi M, Kawana S, Sekino H, Abe K, Matsuoka N, Kashiwagi M, Okai K, Kanno Y, Takahashi A, Ito H, Hashimoto Y, Ohira H

ABOUT COVER

Editorial Board Member of *World Journal of Hepatology*, Konstantinos Tziomalos, MD, MSc, PhD, Assistant Professor, First Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Thessaloniki 54636, Greece

AIM AND SCOPE

World Journal of Hepatology (*World J Hepatol*, *WJH*, online ISSN 1948-5182, DOI: 10.4254), is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJH covers topics concerning liver biology/pathology, cirrhosis and its complications, liver fibrosis, liver failure, portal hypertension, hepatitis B and C and inflammatory disorders, steatohepatitis and metabolic liver disease, hepatocellular carcinoma, biliary tract disease, autoimmune disease, cholestatic and biliary disease, transplantation, genetics, epidemiology, microbiology, molecular and cell biology, nutrition, geriatric and pediatric hepatology, diagnosis and screening, endoscopy, imaging, and advanced technology. Priority publication will be given to articles concerning diagnosis and treatment of hepatology diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJH*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Hepatology is now indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, and Scopus.

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Rui-Fang Li*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Li-Jun Cui*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Hepatology

ISSN
ISSN 1948-5182 (online)

LAUNCH DATE
October 31, 2009

FREQUENCY
Monthly

EDITOR-IN-CHIEF
Wan-Long Chuang, MD, PhD, Doctor, Professor,
Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung 807, Taiwan

EDITORIAL BOARD MEMBERS
All editorial board members resources online at <http://www.wjgnet.com/1948-5182/editorialboard.htm>

EDITORIAL OFFICE
Xiu-Xia Song, Director

World Journal of Hepatology
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

PUBLICATION DATE
January 27, 2018

COPYRIGHT

© 2018 Baishideng Publishing Group Inc. Articles published by this Open Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT

All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS

<http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION

<http://www.f6publishing.com>

Retrospective Study

Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis

Hiroya Iida, Masaki Kaibori, Kosuke Matsui, Morihiko Ishizaki, Masanori Kon

Hiroya Iida, Masaki Kaibori, Kosuke Matsui, Morihiko Ishizaki, Masanori Kon, Department of Surgery, Kansai Medical University, Osaka 573-1010, Japan

Author contributions: Iida H designed the research and performed the surgical interventions; Kaibori M performed the surgical interventions and contributed to the statistical assessment; Matsui K and Ishizaki M performed the surgical interventions; Kon M performed the surgical interventions and conferred on the final agreement for publication.

Institutional review board statement: The study was reviewed and approved by the Kansai Medical University Institutional Review Board.

Informed consent statement: Since this research was retrospective observation research using medical record information, the authors only gave the patient the opportunity to opt out. Therefore, there is no informed consent statement signed by the patients.

Conflict-of-interest statement: None of the authors have any conflicts of interest or financial disclosures.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Hiroya Iida, MD, Department of Surgery, Kansai Medical University, 2-5-1 Shinmachi Hirakata, Osaka 573-1010, Japan. hiroya0001@mac.com
Telephone: +81-72-8040101
Fax: +81-72-8042578

Received: March 26, 2017

Peer-review started: March 28, 2017

First decision: June 30, 2017

Revised: November 10, 2017

Accepted: December 4, 2017

Article in press: December 7, 2017

Published online: January 27, 2018

Abstract

AIM

To provide a simple surrogate marker predictive of liver cirrhosis (LC).

METHODS

Specimens from 302 patients who underwent resection for hepatocellular carcinoma between January 2006 and December 2012 were retrospectively analyzed. Based on pathologic findings, patients were divided into groups based on whether or not they had LC. Parameters associated with hepatic functional reserve were compared in these two groups using Mann-Whitney *U*-test for univariate analysis. Factors differing significantly in univariate analyses were entered into multivariate logistic regression analysis.

RESULTS

There were significant differences between the LC group ($n = 100$) and non-LC group ($n = 202$) in prothrombin activity, concentrations of alanine aminotransferase, aspartate aminotransferase, total bilirubin, albumin, cholinesterase, type IV collagen, hyaluronic acid, indocyanine green retention rate at 15 min, maximal removal rate of technetium-99m diethylene triamine penta-acetic acid-galactosyl human serum albumin and ratio of mean platelet volume to platelet count (MPV/PLT). Multivariate analysis showed that prothrombin activity, concentrations of alanine aminotransferase, aspartate aminotransferase, total bilirubin and hyaluronic acid, and MPV/PLT ratio were factors independently predictive of LC. The area under the curve value for MPV/PLT was 0.78,

with a 0.8 cutoff value having a sensitivity of 65% and a specificity of 78%.

CONCLUSION

The MPV/PLT ratio, which can be determined simply from the complete blood count, may be a simple surrogate marker predicting LC.

Key words: Mean platelet volume; Platelet count; Liver cirrhosis; Hepatic functional reserve; Liver fibrosis

© **The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Although liver biopsy is considered the gold standard in the diagnosis of liver fibrosis and cirrhosis, liver biopsy is an invasive procedure, with attendant morbidity. Less invasive procedures are needed in the diagnosis of liver cirrhosis. Multivariate analysis showed that the mean platelet volume to platelet count ratio was independently predictive of liver cirrhosis. This ratio, which can be determined from a routine complete blood count, may be a simple surrogate marker predicting liver cirrhosis.

Iida H, Kaibori M, Matsui K, Ishizaki M, Kon M. Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis. *World J Hepatol* 2018; 10(1): 82-87 Available from: URL: <http://www.wjgnet.com/1948-5182/full/v10/i1/82.htm> DOI: <http://dx.doi.org/10.4254/wjh.v10.i1.82>

INTRODUCTION

Mean platelet volume (MPV) is a machine-calculated measurement of average platelet size, usually included in complete blood count testing. Normal MPV ranges from 7.5 fL to 11.5 fL. Because average platelet size is directly proportional to the numbers of platelets produced, MPV is indicative of platelet production in bone marrow. Moreover, MPV is higher when there is destruction of platelets, as observed in patients with inflammatory bowel disease, immune thrombocytopenic purpura, myeloproliferative diseases and Bernard-Soulier syndrome^[1]. MPV may also be higher in patients with pre-eclampsia and those recovering from transient bone marrow hypoplasia^[2]. In contrast, abnormally low MPV values are indicative of thrombocytopenia because of impaired platelet production, as observed in patients with aplastic anemia.

Several studies have reported that liver cirrhosis (LC) and fibrosis are related to MPV^[3-6]. Increased MPV, as well as decreased platelet count (PLT), were found to reflect a greater degree of fibrosis. These findings suggested that the ratio of MPV to PLT may correlate strongly with the degree of liver fibrosis. This study was, therefore, designed to determine whether liver fibrosis and LC are associated with the MPV/PLT ratio or not.

MATERIALS AND METHODS

This retrospective study assessed samples obtained from 302 patients who underwent liver resection for hepatocellular carcinoma (HCC) between January 2006 and December 2012. All patients were assessed pathologically by stage of fibrosis in nontumor liver tissue using the new Inuyama classification^[7]. F0 was defined as no fibrosis ($n = 22$), F1 as chronic hepatitis with fibrous portal expansion ($n = 67$), F2 as chronic hepatitis with bridging fibrosis ($n = 62$), F3 as chronic hepatitis with bridging fibrosis and architectural distortion ($n = 51$), and F4 as LC with tendency toward nodular formation throughout the whole area. Patients classified as F0-F3 were assigned to the non-LC group ($n = 202$), and those classified as F4 to the LC group ($n = 100$).

Parameters associated with hepatic functional reserve were assessed in all patients; these included: MPV, PLT, and the MPV/PLT ratio; prothrombin activity (PT); concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, albumin, cholinesterase, type IV collagen, and hyaluronic acid; indocyanine green retention rate at 15 min (ICGR15); and, the maximal removal rate of technetium-99m diethylene triamine penta-acetic acid (99mTc-DTPA)-galactosyl human serum albumin (GSA-Rmax), a marker of hepatic functional reserve, as determined by scintigraphy^[8,9]. These factors were compared between the LC and non-LC groups. Multivariate regression analysis was performed to identify factors independently predictive of LC, and cutoff values were calculated. In addition, patients were divided by fibrosis stage (F0-F4), and these parameters were compared among the five subgroups.

Comorbidities that could be associated with an increase or decrease in the MPV/PLT ratio, such as inflammatory bowel disease, immune thrombocytopenic purpura, myeloproliferative disease or Bernard-Soulier syndrome, were not observed in any of the patients.

Statistical analysis

Parameters predictive of hepatic functional reserve in the LC and non-LC groups were compared using the Mann-Whitney *U*-test. Factors differing significantly in univariate analyses were entered into multivariate logistic regression analysis. Receiver operating characteristic (ROC) curves were used to calculate areas under the curve (AUC) and cutoff values. All analyses were performed using JMP 9 statistical analysis software (SAS Institute Inc., Cary, NC, United States), with a *P* value of < 0.05 defined as statistically significant.

RESULTS

There were 161 patients with hepatitis C and 53 patients with hepatitis B. The remaining 88 patients were negative for hepatitis B and C. The average age was 69.6 ± 9.7 years in the non-LC group and 68.2

Table 1 Univariate analysis of factors in non-liver cirrhosis and liver cirrhosis groups

	Non-LC group, <i>n</i> = 202	LC group, <i>n</i> = 100	<i>P</i> -value
Etiology			
HBV	43 (21.2%)	10 (10.0%)	< 0.001
HCV	89 (44.1%)	72 (72.0%)	
NBNC	70 (34.7%)	18 (18.0%)	
Edmonson-Steiner grade			
I	30 (30.0%)	36 (17.8%)	0.07
II	64 (64.0%)	151 (74.8%)	
III	4 (4.0%)	13 (6.4%)	
IV	2 (2.0%)	2 (1.0%)	
PLT, × 10 ⁴ /μL	18.9 ± 8.1	11.6 ± 4.6	< 0.0001
MPV, fL	10.2 ± 0.9	10.8 ± 0.9	< 0.0001
MPV/PLT ratio	0.64 ± 0.30	1.10 ± 0.51	< 0.0001
PT, %	92.9 ± 11.7	82.5 ± 11.1	< 0.0001
AST, IU/L	42 ± 26	51 ± 23	< 0.0001
ALT, IU/L	40 ± 30	47 ± 33	0.02
Total-bilirubin, mg/dL	0.67 ± 0.23	0.90 ± 0.34	< 0.0001
Albumin, g/dL	3.8 ± 0.5	3.6 ± 0.4	0.01
Cholinesterase, IU/L	235 ± 80	193 ± 60	< 0.0001
Type 4 collagen, ng/mL	6.3 ± 2.4	9.1 ± 4.4	0.04
Hyaluronic acid, ng/mL	147 ± 179	312 ± 318	< 0.0001
ICGR15, %	14.1 ± 8.3	22.1 ± 12.1	< 0.0001
GSA Rmax, mg/min	0.62 ± 0.21	0.44 ± 0.17	< 0.0001

All results reported as mean ± standard deviation. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GSA-Rmax: Maximal removal rate of 99mTc-DTPA-galactosyl human serum albumin; HBV: Positive for hepatitis B antigen; HCV: Positive for hepatitis C antibody; ICGR15: Indocyanine green retention rate at 15 min; LC: Liver cirrhosis; MPV: Mean platelet volume; PLT: Platelet count; PT: Prothrombin activity.

± 7.6 years in the LC group ($P = 0.21$). The ratio of males to females was larger in the non-LC group, with 164 (81.2%) male and 38 (18.8%) female patients; there were 69 (69.0%) male and 31 (31.0%) female patients in the LC group ($P = 0.02$).

Table 1 compares parameters (univariate analysis) between the LC and non-LC groups. The rate of hepatitis C was greater in the LC group than in the non-LC group ($P < 0.001$). The Edmondson-Steiner grade^[10] for HCC grade I was a little smaller and for grade II a little larger in the LC group; however, the difference was not significant ($P = 0.07$). The average PLT was $11.6 \pm 4.6 \times 10^4/\mu\text{L}$ and $18.9 \pm 8.1 \times 10^4/\mu\text{L}$, respectively, and the average MPV was 10.8 ± 0.9 fL and 10.2 ± 0.9 fL, respectively ($P < 0.05$ for each). The MPV/PLT ratio was significantly higher in the LC group than in the non-LC group (1.10 ± 0.51 vs 0.64 ± 0.30 , $P < 0.05$). Other factors associated with hepatic functional reserve also differed significantly between the two groups, including PT, the concentrations of AST, ALT, total bilirubin, albumin, cholinesterase, type IV collagen and hyaluronic acid, ICGR15 and GSA-Rmax ($P < 0.05$ for each).

Table 2 shows multivariate analysis of factors predictive of LC in these patients. MPV/PLT ratio, PT, and concentrations of AST, ALT, total bilirubin and hyaluronic acid were independent predictors of LC. The highest odds ratio was 3.71 for the MPV/PLT ratio. Although albumin, cholinesterase and type IV collagen concentrations, as well as ICGR15 and GSA-Rmax, were also predictors of LC on univariate analysis, they were not independently predictive on multivariate

analysis.

The ROC curves of all six independently predictive factors (MPV/PLT ratio, PT, and concentrations of AST, ALT, total bilirubin and hyaluronic acid) are shown in Figure 1. Calculation of AUC for all six factors showed that the MPV/PLT ratio had the highest AUC (0.78). A cutoff value of 0.8 had a sensitivity of 65% and a specificity of 78% in predicting LC. This ratio was a better predictor of LC than other parameters of hepatic functional reserve.

Patients were also divided by individual fibrosis stage and MPV/PLT ratio determined for each stage. The average MPV/PLT ratios for patients classified as F0-1, F2, F3 and F4 were 0.54 ± 0.24 , 0.65 ± 0.29 , 0.79 ± 0.35 and 1.10 ± 0.51 , respectively, with each pairwise difference being statistically significant (Figure 2).

Additionally, we examined the correlation between the MPV/PLT ratio and the pathological inflammation level according to the new Inuyama classification. The average MPV/PLT ratios for patients classified as A0, A1, A2 and A3 were 0.68 ± 0.21 , 0.70 ± 0.45 , 0.82 ± 0.39 and 0.73 ± 0.10 , respectively. There was no significant correlation between MPV/PLT and pathological inflammation level ($P = 0.214$).

DISCUSSION

LC is a result of advanced liver disease, in which normal liver tissue is replaced by fibrotic tissue. These changes lead to loss of liver function. LC is most frequently caused by alcoholism, infection with hepatitis B and hepatitis C viruses, and fatty liver

Table 2 Multivariate analysis of factors predicting liver cirrhosis

		Odds ratio	P-value	95%CI
MPV/PLT ratio	$\geq 0.71, n = 151$	3.71	< 0.0001	1.94-7.28
	$< 0.71, n = 151$			
PT, %	$\geq 89.0, n = 151$	2.68	0.0018	1.44-5.06
	$< 89.0, n = 151$			
AST, IU/L	$\geq 39, n = 155$	3.30	0.01	1.30-9.09
	$< 39, n = 147$			
ALT, IU/L	$\geq 34, n = 153$	2.57	0.04	1.02-7.09
	$< 34, n = 149$			
Total-bilirubin, mg/dL	$\geq 0.7, n = 177$	1.89	0.04	1.00-3.61
	$< 0.7, n = 125$			
Albumin, g/dL	$\geq 3.8, n = 168$	0.95	0.89	0.47-1.89
	$< 3.8, n = 134$			
Cholinesterase, IU/L	$\geq 211, n = 152$	0.98	0.96	0.48-1.98
	$< 211, n = 150$			
Type 4 collagen, ng/mL	$\geq 6.5, n = 166$	0.95	0.86	0.51-1.72
	$< 6.5, n = 136$			
Hyaluronic acid, ng/mL	$\geq 124, n = 153$	2.28	0.008	1.23-4.26
	$< 124, n = 149$			
ICGR15, %	$\geq 14.3, n = 151$	1.40	0.30	0.72-2.68
	$< 14.3, n = 151$			
GSA Rmax, mg/min	$\geq 0.555, n = 151$	1.51	0.24	0.75-3.04
	$< 0.555, n = 151$			

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CI: Confidence interval; GSA-Rmax: Maximal removal rate of ^{99m}Tc -DTPA-galactosyl human serum albumin; ICGR15: Indocyanine green retention rate at 15 min; MPV: Mean platelet volume; PLT: Platelet count; PT: Prothrombin activity.

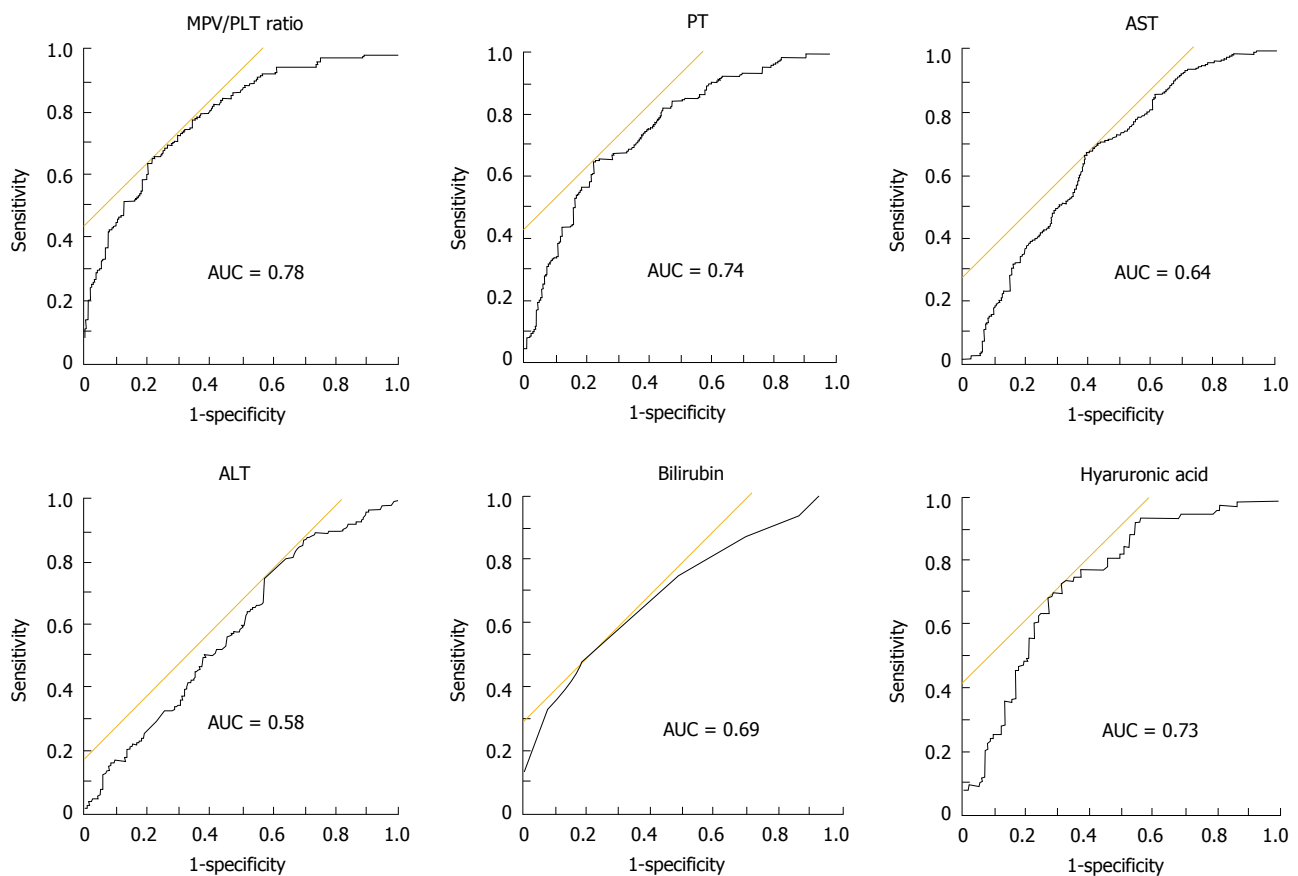


Figure 1 Receiver operating characteristic curve analysis of parameters differing significantly in the liver cirrhosis and non-liver cirrhosis groups on multivariate analysis. The area under the curve of MPV/PLT was the highest. A MPV/PLT ratio of 0.8 had a sensitivity of 65% and a specificity of 78%. MPV/PLT: Mean platelet volume to platelet count; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; PT: Prothrombin activity.

disease, but it may have many other causes. LC arising from nonalcoholic steatohepatitis (NASH) was recently

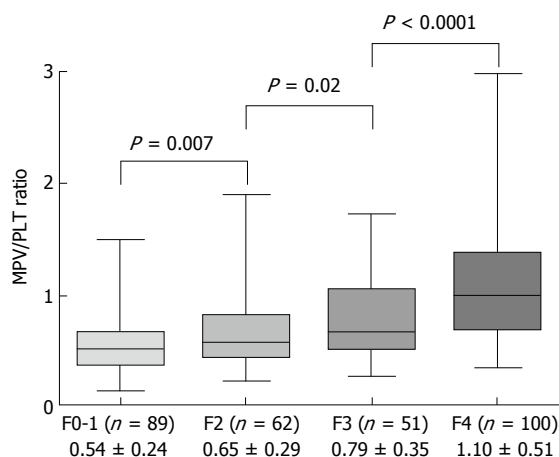


Figure 2 Relationship between MPV/PLT ratio and fibrosis stage. There were significant differences between each pair of stages. MPV/PLT: Mean platelet volume to platelet count.

shown to be a worldwide problem.

The standard method of diagnosing LC is liver biopsy. However, liver biopsy is an invasive procedure and cannot be performed on patients with severe ascites or severe coagulation disorders. Several studies have, therefore, assessed surrogate markers in blood predictive of LC; these include FibroTest (FibroSure) and the AST platelet ratio index^[11]. In addition, elastographic methods, such as FibroScan, have been reported to be noninvasive methods of predicting LC^[12,13]. We could not compare these methods with the MPV/PLT ratio because we do not have these examination devices.

MPV may be another predictor of LC. Higher MPV has been reported in patients with hepatitis B^[14], and LC, fibrosis level and MPV have been reported to correlate in patients with chronic hepatitis B^[3-5]. MPV may also be predictive of LC in patients with chronic hepatitis C^[6].

MPV has been associated not only with fibrosis stage but with degree of liver inflammation^[15]. For example, higher MPV has been observed in patients with NASH^[16], and MPV has been found to correlate with the presence of nonalcoholic fatty liver disease (NAFLD)^[17], although another study reported no correlation^[18]. In addition, MPV may or may not correlate with insulin resistance, which is closely related to NAFLD^[19,20]. To date, however, the relationship between NAFLD and MPV has not been determined.

MPV has been reported to strongly correlate with the prognosis of patients with non-small cell lung cancer^[21]. In addition, high MPV and MPV/PLT have been found to be associated with a high risk for HCC^[22,23]. An examination of the correlation between MPV/PLT ratio and postoperative prognosis of patients undergoing hepatic resection for HCC found that the MPV/PLT ratio was unrelated to overall or recurrence-free survival rate after resection.

This study had several limitations, including its retro-

spective design, performance at a single center and small sample size. Moreover, all patients included had undergone resection for HCC. Therefore, the results should not be generalized to patients without HCC before verification. Prospective, multicenter studies with large numbers of patients are needed to confirm these findings.

In conclusion, we found that the MPV/PLT ratio was predictive of LC, suggesting that this ratio may be a simple surrogate marker predictive of LC.

ARTICLE HIGHLIGHTS

Background

Several noninvasive methods for predicting cirrhosis have been reported, but liver biopsy is the only method for obtaining a definitive diagnosis. However, liver biopsy is invasive, and a noninvasive diagnostic method is desirable. Mean platelet volume (MPV), the size of platelets, can be determined from routine complete blood count data of blood samples. Generally, if bone marrow hematopoietic function decreases, MPV decreases. In contrast, if spleen function increases, new platelets are made rapidly and MPV increases. In recent years, the relationship between MPV and liver disease has attracted attention.

Research frontiers

There are reports that MPV correlates with liver function, and there are reports that MPV is related to the incidence of HCC. However, there is no report to evaluate the correlation between MPV/platelet count (PLT) and liver function, so we undertook this study.

Innovations and breakthroughs

The authors studied only patients who were diagnosed with cirrhosis histopathologically after liver resection. The MVP/PLT ratio could predict cirrhosis more sensitively than other general liver function tests.

Applications

The MPV/PLT ratio also correlated with the degree of hepatic fibrosis according to the Inuyama classification. The authors examined the relationship between prognosis after hepatic resection of hepatocellular carcinoma and the value of the MPV/PLT ratio, but unfortunately no correlation was found.

Terminology

MPV is the size of platelets and can be determined from routine complete blood count data of blood samples. Liver cirrhosis and fibrosis are related to MPV.

REFERENCES

- 1 Liu S, Ren J, Han G, Wang G, Gu G, Xia Q, Li J. Mean platelet volume: a controversial marker of disease activity in Crohn's disease. *Eur J Med Res* 2012; **17**: 27 [PMID: 23058104 DOI: 10.1186/2047-783X-17-27]
- 2 Lippi G, Filippozzi L, Salvagno GL, Montagnana M, Franchini M, Guidi GC, Targher G. Increased mean platelet volume in patients with acute coronary syndromes. *Arch Pathol Lab Med* 2009; **133**: 1441-1443 [PMID: 19722752 DOI: 10.1043/1543-2165-133.9.1441]
- 3 Karagoz E, Ulcay A, Tanoglu A, Kara M, Turhan V, Erdem H, Oncul O, Gorenek L. Clinical usefulness of mean platelet volume and red blood cell distribution width to platelet ratio for predicting the severity of hepatic fibrosis in chronic hepatitis B virus patients. *Eur J Gastroenterol Hepatol* 2014; **26**: 1320-1324 [PMID: 25210777 DOI: 10.1097/MEG.0000000000000203]
- 4 Qi XT, Wan F, Lou Y, Ye B, Wu D. The mean platelet volume is a potential biomarker for cirrhosis in chronic hepatitis B virus infected patients. *Hepatogastroenterology* 2014; **61**: 456-459 [PMID: 24901161]

- 5 **Ekiz F**, Yüksel O, Koçak E, Yılmaz B, Altınbaş A, Çoban S, Yüksel I, Üsküdar O, Köklü S. Mean platelet volume as a fibrosis marker in patients with chronic hepatitis B. *J Clin Lab Anal* 2011; **25**: 162-165 [PMID: 21567462 DOI: 10.1002/jcla.20450]
- 6 **Purnak T**, Olmez S, Torun S, Efe C, Sayilir A, Ozaslan E, Tenlik I, Kalkan IH, Beyazit Y, Yuksek O. Mean platelet volume is increased in chronic hepatitis C patients with advanced fibrosis. *Clin Res Hepatol Gastroenterol* 2013; **37**: 41-46 [PMID: 22572524 DOI: 10.1016/j.clinre.2012.03.035]
- 7 **Ichida F**, Tsuji T, Omata M, Ichida T, Inoue K, Kamimura T, Yamada G, Hino K, Yokosuka O, Suzuki H. New Inuyama classification: new criteria for histological assessment of chronic hepatitis. *Int Hepatol Commun*. 1996: 112
- 8 **Ha-Kawa SK**, Tanaka Y. A quantitative model of technetium-99m-DTPA-galactosyl-HSA for the assessment of hepatic blood flow and hepatic binding receptor. *J Nucl Med* 1991; **32**: 2233-2240 [PMID: 1744708]
- 9 **Kwon AH**, Matsui Y, Ha-Kawa SK, Kamiyama Y. Functional hepatic volume measured by technetium-99m-galactosyl-human serum albumin liver scintigraphy: comparison between hepatocyte volume and liver volume by computed tomography. *Am J Gastroenterol* 2001; **96**: 541-546 [PMID: 11232703 DOI: 10.1111/j.1572-0241.2001.03556.x]
- 10 **Edmondson HA**, Steiner PE. Primary carcinoma of the liver: a study of 100 cases among 48,900 necropsies. *Cancer* 1954; **7**: 462-503 [PMID: 13160935]
- 11 **Castéra L**, Vergniol J, Foucher J, Le Bail B, Chanteloup E, Haaser M, Darriet M, Couzigou P, De Lédinghen V. Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. *Gastroenterology* 2005; **128**: 343-350 [PMID: 15685546]
- 12 **Sandrin L**, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, Christidis C, Ziol M, Poulet B, Kazemi F, Beaugrand M, Palau R. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. *Ultrasound Med Biol* 2003; **29**: 1705-1713 [PMID: 14698338]
- 13 **Foucher J**, Chanteloup E, Vergniol J, Castéra L, Le Bail B, Adhoute X, Bertet J, Couzigou P, de Lédinghen V. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut* 2006; **55**: 403-408 [PMID: 16020491 DOI: 10.1136/gut.2005.069153]
- 14 **Turhan O**, Coban E, Inan D, Yalcin AN. Increased mean platelet volume in chronic hepatitis B patients with inactive disease. *Med Sci Monit* 2010; **16**: CR202-CR205 [PMID: 20357720]
- 15 **Ceylan B**, Fincanci M, Yardimci C, Eren G, Tözalgan Ü, Müderrisoğlu C, Paşaoğlu E. Can mean platelet volume determine the severity of liver fibrosis or inflammation in patients with chronic hepatitis B? *Eur J Gastroenterol Hepatol* 2013; **25**: 606-612 [PMID: 23325286 DOI: 10.1097/MEG.0b013e32835d08da]
- 16 **Shin WY**, Jung DH, Shim JY, Lee HR. The association between non-alcoholic hepatic steatosis and mean platelet volume in an obese Korean population. *Platelets* 2011; **22**: 442-446 [PMID: 21751850 DOI: 10.3109/09537104.2010.540049]
- 17 **Ozhan H**, Aydin M, Yazici M, Yazgan O, Basar C, Gungor A, Onder E. Mean platelet volume in patients with non-alcoholic fatty liver disease. *Platelets* 2010; **21**: 29-32 [PMID: 19947902 DOI: 10.3109/09537100903391023]
- 18 **Kilciler G**, Genc H, Tapan S, Ors F, Kara M, Karadurmus N, Ercin CN, Karslioglu Y, Kilic S, Bagci S, Erbil MK, Dogru T. Mean platelet volume and its relationship with carotid atherosclerosis in subjects with non-alcoholic fatty liver disease. *Ups J Med Sci* 2010; **115**: 253-259 [PMID: 20731535 DOI: 10.3109/03009734.2010.500062]
- 19 **Arsilan N**, Makay B. Mean platelet volume in obese adolescents with nonalcoholic fatty liver disease. *J Pediatr Endocrinol Metab* 2010; **23**: 807-813 [PMID: 21073123]
- 20 **Celikbilek M**, Gürsoy S, Deniz K, Karaman A, Zararsiz G, Yurci A. Mean platelet volume in biopsy-proven non-alcoholic fatty liver disease. *Platelets* 2013; **24**: 194-199 [PMID: 22646469 DOI: 10.3109/09537104.2012.688898]
- 21 **Inagaki N**, Kibata K, Tamaki T, Shimizu T, Nomura S. Prognostic impact of the mean platelet volume/platelet count ratio in terms of survival in advanced non-small cell lung cancer. *Lung Cancer* 2014; **83**: 97-101 [PMID: 24189108 DOI: 10.1016/j.lungcan.2013.08.020]
- 22 **Cho SY**, Yang JJ, You E, Kim BH, Shim J, Lee HJ, Lee WI, Suh JT, Park TS. Mean platelet volume/platelet count ratio in hepatocellular carcinoma. *Platelets* 2013; **24**: 375-377 [PMID: 22835043 DOI: 10.3109/09537104.2012.701028]
- 23 **Kurt M**, Onal IK, Sayilir AY, Beyazit Y, Oztas E, Kekilli M, Turhan N, Karaman K, Akdogan M. The role of mean platelet volume in the diagnosis of hepatocellular carcinoma in patients with chronic liver disease. *Hepatogastroenterology* 2012; **59**: 1580-1582 [PMID: 22683976 DOI: 10.5754/hge10444]

P- Reviewer: Atta H, Ji F, Preda CM S- Editor: Kong JX

L- Editor: Filipodia E- Editor: Li D





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

