BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

Predictive Value of Serum Lactate Levels for Mortality in Patients with Hepatitis B-Related Decompensated Cirrhosis: A Retrospective Analysis

Hong Yang[1], Bin Zhang[1], Chunxian Peng[1], Chun Yu[2], Xiaolin Mou[3,*]

[1]Department of Infectious Diseases, The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital, Quzhou, Zhejiang, China
[2]Department of Gastrointestinal Surgery, The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital, Quzhou, Zhejiang, China
[3]Department of Gastroenterology, The Second People's Hospital of Quzhou, Quzhou, Zhejiang, China
*Correspondence: 18057052571@163.com (Xiaolin Mou)

Abstract

Aims/Background Decompensated cirrhosis is characterized by the progression of cirrhosis from an asymptomatic state to elevated portal pressure and marked deterioration of liver function. This pathological condition progresses rapidly following onset, significantly raising the risk for mortality. The aim of this study is to explore the association between serum lactate concentrations and mortality rates in individuals with hepatitis B-induced decompensated cirrhosis and to evaluate its potential as a clinical prognostic indicator.

Methods This retrospective analysis involved 200 individuals (134 men and 66 women) diagnosed with decompensated cirrhosis related to hepatitis B and hospitalized between March 2017 and May 2023. Out of these patients, 162 survived while 38 did not. Clinical information and laboratory results, including the Model for End-Stage Liver Disease (MELD) score, Child-Pugh score, and serum lactate levels, were collected. Logistic regression was applied to identify mortality risk factors from the patient sample and groups categorized according to gender. The predictive value of serum lactate levels for mortality was assessed using the area under the curve (AUC), i.e., receiver operating characteristic (ROC) curve.

Results The surviving patient group showed significantly lowered MELD scores, Child-Pugh scores, and serum lactate levels compared to those who were deceased ($p < 0.05$). Multivariate analysis revealed that the MELD score, Child-Pugh score, and serum lactate levels were independent predictors of mortality in patients with decompensated hepatitis B cirrhosis, with odds ratios (OR) of 1.321, 1.432, and 49.082, respectively ($p = 0.012$, 0.028, and <0.001, respectively). Additionally, the OR for serum lactate levels was notably higher in female patients compared to male patients (46.824 vs. 30.451). Thus, the MELD score, Child-Pugh score, and serum lactate levels are effective predictors for mortality in cirrhosis patients (AUCs = 0.628, 0.675, and 0.809; $p = 0.014$, 0.001, and <0.001, respectively), with serum lactate levels showing the most excellent predictive efficacy profile (sensitivity 65.8% and specificity 97.5%). Additionally, the AUC value for serum lactate levels was lower in male patients (0.785) compared to female patients (0.875), indicating that changes in serum lactate levels were more sensitive in female patients. In summary, serum lactate concentration is a prognostic indicator of mortality in individuals with decompensated cirrhosis due to hepatitis B, exhibiting higher predictive significance in female patients.

Conclusion Deceased patients with decompensated cirrhosis linked to hepatitis B exhibit markedly increased serum lactate levels. Thus, monitoring serum lactate levels offers an effective tool for predicting patient prognosis, exhibiting higher sensitivity for disease detection in female patients.

Key words: hepatitis B; cirrhosis; serum lactate

Submitted: 14 August 2024 Revised: 24 September 2024 Accepted: 26 September 2024

How to cite this article:
Yang H, Zhang B, Peng C, Yu C, Mou X. Predictive Value of Serum Lactate Levels for Mortality in Patients with Hepatitis B-Related Decompensated Cirrhosis: A Retrospective Analysis. Br J Hosp Med. 2024. https://doi.org/10.12968/hmed.2024.0531

Introduction

Hepatitis B poses a major health challenge in China, affecting around 70 million individuals (Cui et al, 2023). The chronic form of this infection is a critical public health concern due to the prevalence of fibrosis triggered by the infection, which deteriorates to liver fibrosis and subsequently liver cirrhosis (LC). The World Health Organization (WHO) reports that approximately 30% of the global cirrhosis cases are attributed to hepatitis B virus (HBV) infection, with approximately 15% of the world's cirrhosis-related deaths reported in China alone. Ultimately, 16% of hepatitis B-infected individuals may develop decompensated cirrhosis, with a five-year mortality rate of 70% to 86% (Alberts et al, 2022; Shan et al, 2021). Therefore, it is imperative to identify potent predictors for mortality in decompensated hepatitis B cirrhosis in order to strengthen clinical treatment and prevention strategies.

At present, the severity of cirrhosis is primarily assessed by measuring Model for End-Stage Liver Disease (MELD) scores and Child-Pugh scores, as well as conducting liver biopsies. However, these methods may introduce significant biases, affecting diagnosis and prognosis (Bedreli et al, 2016). A variety of novel serum markers with preliminarily verified prognostic value have been reported, but their detection specificity and feasibility in clinical settings remain unsatisfactory (Gao et al, 2024; Shan et al, 2021; Tong et al, 2021). Serum lactate concentration is an indicator of metabolic alterations resulting from tissue hypoxia or stress responses triggered by adrenaline. On the basis of cirrhosis being commonly accompanied by metabolic dysfunction, numerous clinical investigations have further confirmed that serum lactate levels can reliably predict the prognosis for patients with severe cirrhosis (Haas et al, 2016; Zhang et al, 2023). Nonetheless, the predictive value of serum lactate levels for mortality risk in cases of decompensated hepatitis B cirrhosis has not been documented. Additionally, as lactate production is closely related to human metabolism, hormone levels, and body composition, there may be significant differences in lactate production capacity and response to lactate between males and females (Viña et al, 2018). This research seeks to investigate potential gender-specific variations in the prognostic significance of serum lactate concentrations for decompensated hepatitis B cirrhosis, aiming to offer new perspectives.

Methods

Clinical Data

This study utilized a retrospective design, collecting clinical data from 200 patients with hepatitis B virus-induced decompensated cirrhosis treated at the Quzhou Affiliated Hospital of Wenzhou Medical University between 2017 and 2023. The cohort consisted of 134 males and 66 females, with 162 survivors and 38 deceased cases. The follow-up end point was death by May 31, 2023. Diagnoses were made in adherence to the "Guidelines for the Prevention and Treatment of Chronic Hepatitis B (2022 Edition)" (Chinese Society of Hepatology and Chinese Society of Infectious Diseases, 2023). Subject inclusion was conducted by following the criteria defined in the following: (1) patients age $\geq$18 years; (2) patients diagnosed with hepatitis B-related decompensated cirrhosis; and (3) patients and family mem-

bers who have given their informed consent to join the study. The exclusion criteria applied to this study are as follows: (1) individuals with liver cancer, other malignancies, or concurrent diseases like hepatitis C virus (HCV), non-alcoholic fatty liver (NAFL), or human immunodeficiency virus (HIV) infection; (2) pregnant women, minors, or individuals with mental disorders; (3) individuals with severe comorbidities in other systems; (4) individuals with incomplete clinical data, insufficient follow-up information, or who had been followed up for less than 6 months; and (5) individuals who died from non-disease causes. This study was approved by the Ethics Committee of the Quzhou Affiliated Hospital of Wenzhou Medical University (2024-025) and was conducted in compliance with all relevant human research guidelines. The research was conducted in accordance with the Declaration of Helsinki, with the ethical principles followed throughout the study. Informed consent was obtained from all participants or their guardians prior to their inclusion in the study.

Data Collection

During the study period, patient clinical records were examined to collect the following data: demographic information (age and gender), results from laboratory tests (including white blood cell count, platelets, hemoglobin, sodium, potassium, urea nitrogen, creatinine, bilirubin, albumin, alkaline phosphatase, aspartate aminotransferase [AST], alanine aminotransferase [ALT], and lactate), as well as MELD and Child-Pugh scores (when the patient was admitted), and outcomes (whether the patient survived or died). Laboratory tests were performed using the Architect c16000 (Abbott, Chicago, IL, USA) for biochemical analysis, the ACL Top 800 and ACL Top 500 (Werfen, Barcelona, Spain) for coagulation analysis, and the ABL800 (Radiometer, Copenhagen, Denmark) and GEM Premier 5000 (Werfen, Barcelona, Spain) for serum lactate measurement. The collected data were systematically organized into an Excel spreadsheet prior to further analysis.

Statistical Analysis

Statistical analysis was conducted using SPSS 23.0 software (SPSS Inc., Chicago, IL, USA). For quantitative data, the *t*-test was employed for data that conformed to normal distribution, verified using the Shapiro-Wilk test, and the Mann-Whitney *U* test was employed for data not conforming to normal distribution. Categorical data were assessed using the χ^2 test or Fisher's exact test. A *p*-value of less than 0.05 was considered statistically significant. To assess the influence of multiple variables (both quantitative and categorical) on the binary outcome (survival or death), a binary multivariate logistic regression model was utilized. Additionally, receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic accuracy of serum lactate levels.

Table 1. Comparison of clinical indicators between the surviving and deceased patient groups.

Indicator	Survival group (n = 162)	Death group (n = 38)	t/χ^2 value	p
Male	110 (67.9%)	24 (63.2%)	0.313	0.576
Age	50.3 ± 12.7	51.4 ± 15.9	0.457	0.648
ALT (U/L)	78.9 ± 16.1	80.4 ± 13.3	0.533	0.595
AST (U/L)	103.6 ± 15.8	100.0 ± 15.7	1.266	0.207
Creatinine (μmol/L)	69.8 ± 8.3	71.0 ± 9.9	0.773	0.440
Urea nitrogen (mmol/L)	7.7 ± 1.0	7.8 ± 1.4	0.514	0.610
Albumin (g/L)	25.0 ± 3.0	25.0 ± 3.6	0.093	0.926
MELD score	13.8 ± 2.3	14.8 ± 2.0	2.469	0.014
Child-Pugh score	9.0 ± 1.6	10.1 ± 1.5	3.858	<0.001
Serum lactate (mmol/L)	2.9 ± 0.3	3.8 ± 0.8	11.372	<0.001

Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase; MELD score, Model for End-Stage Liver Disease score.

Results

Analysis of Clinical Indicators between Surviving and Deceased Patient Groups

The analysis revealed no significant differences between the surviving and deceased patient groups in gender ratio, age, ALT, AST, creatinine, urea nitrogen, or albumin levels ($p > 0.05$). In contrast, the deceased patient group exhibited significantly higher MELD scores (14.8 ± 2.0) and Child-Pugh scores (10.1 ± 1.5) compared to the surviving group (MELD score: 13.8 ± 2.3; Child-Pugh score: 9.0 ± 1.6) ($p < 0.05$). Furthermore, the serum lactate levels were significantly higher in the deceased group (3.8 ± 0.8) than in the surviving group (2.9 ± 0.3) (Table 1) ($p < 0.001$). These results suggest that patients in the deceased group might had experienced more severe metabolic disorders.

Predictive Value of Serum Lactate Levels for Mortality in Patients with Decompensated Hepatitis B Cirrhosis

Previous part of this studie have shown that the MELD and Child-Pugh scores are effective in predicting mortality risk in patients with decompensated hepatitis B cirrhosis. However, the predictive potential of serum lactate levels in this regard remains largely unexplored. Thus, this study was designed to determine the predictive values of MELD score, Child-Pugh score, and serum lactate levels. Our findings indicated that all these three variables are independent risk factors for mortality in decompensated hepatitis B cirrhosis (Table 2).

Additionally, considering that serum lactate production is closely linked to hormonal levels, body composition, and metabolic status influenced by gender, we posited that the relationship between serum lactate levels and mortality risk might vary between male and female patients. Logistic regression analyses were separately conducted for MELD score, Child-Pugh score, and serum lactate levels in male and female groups. The findings revealed that while serum lactate levels are a

Table 2. Logistic regression analysis of predictors of mortality in patients with decompensated hepatitis B cirrhosis.

Indicator	β	Standard error	Wald χ^2	p value	OR (95% CI)
MELD score	0.279	0.111	6.318	0.012	1.321 (1.062–1.643)
Child-Pugh score	0.359	0.163	4.850	0.028	1.432 (1.039–1.972)
Serum lactate	3.893	0.722	29.048	<0.001	49.082 (11.913–202.223)
MELD score (male group)	0.265	0.124	4.567	0.033	1.303 (1.021–1.662)
Child-Pugh score (male group)	0.496	0.207	5.741	0.016	1.643 (1.095–2.464)
Serum lactate (male group)	3.416	0.867	15.539	<0.001	30.451 (5.571–166.441)
MELD score (female group)	1.246	0.505	6.104	0.031	3.478 (1.294–9.349)
Child-Pugh score (female group)	1.367	0.619	4.873	0.027	3.925 (1.166–13.217)
Serum lactate (female group)	3.846	1.425	7.289	0.007	46.824 (2.869–764.027)

Note: MELD score, Model for End-Stage Liver Disease score; OR, odds ratio.

risk factor for both genders, the odds ratio (OR) was significantly higher in females (46.824) compared to males (30.451) (Table 2). This indicates a stronger association between serum lactate levels and mortality risk in female patients, suggesting that female patients with decompensated hepatitis B cirrhosis are more sensitive to changes in serum lactate levels.

Effectiveness of Serum Lactate Levels in Predicting Mortality among Patients with Decompensated Hepatitis B Cirrhosis

To further assess the effectiveness of serum lactate levels in predicting mortality among patients with decompensated hepatitis B cirrhosis, we plotted ROC curves for the MELD score, Child-Pugh score, and serum lactate levels, and calculated the area under the ROC curve (AUC). Analysis of the ROC curves confirmed that these three variables boast predictive value (Fig. 1). Notably, the AUC for serum lactate levels was 0.809, surpassing those of the MELD and Child-Pugh scores. The sensitivity and specificity of serum lactate levels were 65.8% and 97.5%, respectively, also outperforming the scores of the other two variables (Table 3).

When examining the male and female groups separately, the AUCs for the MELD score, Child-Pugh score, and serum lactate levels in males were 0.687, 0.748, and 0.785, respectively, while in females, they were 0.790, 0.827, and 0.875, respectively (Table 3 and Fig. 1). These findings suggested that serum lactate levels are a superior predictor of mortality in decompensated hepatitis B cirrhosis compared to the MELD and Child-Pugh scores, with higher sensitivity in female patients.

Discussion

Chronically affecting around 250 million individuals globally, HBV presents a serious threat to human health. Notably, approximately 28% of these cases are reported in China, constituting a significant public health challenge for the nation (Alberts et al, 2022; Chinese Society of Hepatology and Chinese Society of Infec-

Table 3. Effectiveness of serum lactate levels in predicting mortality in patients with decompensated hepatitis B cirrhosis.

Indicator	AUC (95% CI)	Standard error	*p*	Cut-off value	Sensitivity (%)	Specificity (%)
MELD score	0.628 (0.538–0.718)	0.046	0.014	12.5	89.5	67.3
Child-Pugh score	0.675 (0.581–0.770)	0.048	0.001	10.5	50.0	77.8
Serum lactate	0.809 (0.706–0.912)	0.053	<0.001	3.4	65.8	97.5
MELD score (male Group)	0.687 (0.582–0.791)	0.053	0.004	12.5	95.8	35.5
Child-Pugh score (male group)	0.748 (0.635–0.860)	0.058	<0.001	11.5	45.8	92.7
Serum lactate (male group)	0.785 (0.649–0.921)	0.069	<0.001	3.35	62.5	96.4
MELD score (female group)	0.790 (0.654–0.926)	0.069	0.001	14.5	78.6	61.5
Child-Pugh score (female group)	0.827 (0.705–0.949)	0.062	<0.001	11.5	71.4	90.4
Serum lactate (female group)	0.875 (0.781–0.969)	0.048	<0.001	3.6	78.6	78.8

Note: MELD score, Model for End-Stage Liver Disease score; AUC, area under the curve.

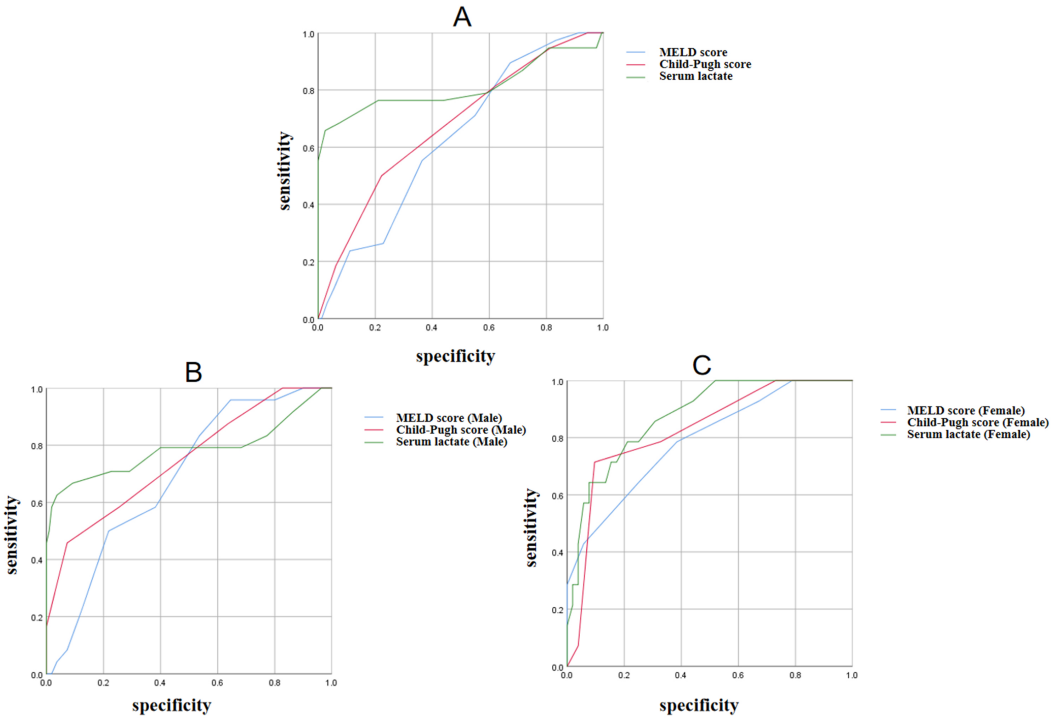

Fig. 1. Receiver operating characteristic (ROC) curves depicting the predictive accuracy of the MELD score, Child-Pugh score, and serum lactate levels for the overall patient cohort, as well as for male and female subgroups. (A) ROC curve for the overall patient cohort. (B) ROC curve for the male subgroup. (C) ROC curve for female subgroup. Note: MELD score, Model for End-Stage Liver Disease score.

tious Diseases, 2023). Chronic HBV infection often leads to cirrhosis, a severe liver condition marked by extensive cell degeneration and necrosis, widespread fibrous tissue proliferation, and the formation of regenerative nodules (Wu and Chen, 2017). In China, chronic HBV infection accounts for over 60% of cirrhosis cases. Pathological deterioration of the condition can bring hepatitis B cirrhosis to a decompensated phase, characterized by portal hypertension and compromised liver

function. Patients in this stage frequently experience multi-organ failure due to complications such as ascites, gastrointestinal bleeding, sepsis, hepatic encephalopathy, hepatorenal syndrome, and cancer. While these complications add to the current healthcare burdens, alarmingly, the prevalence of decompensated cirrhosis caused by hepatitis B is rising annually, largely due to the aging population living with chronic HBV infection (Chinese Society of Hepatology, 2020).

At present, the primary methods used for evaluating decompensated cirrhosis are the MELD score, Child-Pugh score, and liver biopsy. However, the MELD and Child-Pugh scores are measured using the International Normalized Ratio (INR), whose computation is considerably variable across different laboratories, thus potentially providing inaccurate measure of liver function. Additionally, the assessment of ascites and hepatic encephalopathy in the Child-Pugh score can be affected by subjective judgments and medication use, leading to possible biases. Finally, the invasive nature, error margin, and high cost of liver biopsies also limit their clinical application (Bedreli et al, 2016). Therefore, it is crucial to find simple and efficient serum markers with better predictive performance to help evaluate decompensated cirrhosis due to HBV. Lactate is a byproduct of anaerobic glycolysis, and up to 70% of it is metabolized by the liver. However, severe systemic inflammation and oxidative stress can impair mitochondrial function and reduce adenosine triphosphate (ATP) production, leading to lactate accumulation due to anaerobic glycolysis (Drolz et al, 2019). Previous research has shown that elevated lactate levels and reduced clearance rates are valuable indicators for predicting the prognosis of critically ill patients in the intensive care unit (ICU) (Drolz et al, 2019). Thus, it is plausible to assume that lactate levels would be markedly elevated in individuals with advanced cirrhosis and acute-on-chronic liver disease.

This research employed a retrospective approach to gather clinical data from 200 patients diagnosed with decompensated cirrhosis caused by HBV. Analysis revealed that serum lactate levels were markedly elevated in patients who did not survive. Further correlation analysis identified serum lactate levels as an independent risk factor for mortality in HBV-related decompensated cirrhosis. These findings align with previous studies that have associated high lactate levels with increased short-term mortality in individuals with severe alcoholic cirrhosis, suggesting that serum lactate level is a potential marker for prognosticating patients with cirrhosis (Zhang and Xu, 2014). Moreover, the results from ROC curve analysis and AUC calculations indicated that serum lactate levels are a reliable predictor of mortality in patients with HBV-related decompensated cirrhosis. Consistent with these findings, a recent study has shown a correlation between serum lactate levels and mortality rates in cirrhosis patients admitted to ICU (Krispin et al, 2023). Finally, we explored whether the predictive performance of serum lactate levels varies with gender. The results showed that serum lactate levels have better predictive performance in female patients than in male patients, suggesting that female patients are more sensitive to changes in lactate levels. This phenomenon may be related to physiological characteristics of females, including lower maximal oxygen uptake and higher fat percentage. Lower maximal oxygen uptake means that the lactate

threshold is easier to achieved in women, while a higher proportion of fat means higher rate of lipid metabolism, which may lead to a slower rate of lactate clearance.

This study has several limitations, including a relatively small sample size and potential variations in serum lactate levels over the course of the disease, which were not taken into account. The present study demonstrates that serum lactate levels can be a fairly reliable indicator of mortality in patients with decompensated cirrhosis caused by HBV, with higher sensitivity observed in female patients. These findings highlight the significance of serum lactate levels as a prognostic marker, which can help strengthen clinical decision-making and patient management by identifying high-risk individuals who may require more intensive monitoring and treatment. Future research should focus on larger, more diverse populations to validate these findings and explore dynamic changes in lactate levels throughout the course of disease progression. Additionally, understanding the mechanisms behind the elevation of lactate levels could help with the discovery effort for new therapeutic targets. Through this study, we learned that the clinical value of serum lactate levels extends beyond prognostication, offering potential improvements in patient outcomes through early identification and timely interventions. Despite its limitations, this study supports the use of serum lactate levels as a meaningful prognostic tool in decompensated hepatitis B cirrhosis, with promising implications for advancing understanding and treatment of this condition.

Conclusion

Serum lactate levels represent a potential prognostic indicator of mortality in decompensated hepatitis B cirrhosis and features a better predictive ability in female than in male patients.

Key Points

- High serum lactate level is a risk factor for poor prognosis of HBV-related decompensated cirrhosis.
- Compared with MELD and Child-Pugh scores, serum lactate level stands out as a more superior predictor for mortality.
- Serum lactate levels have a better predictive performance in female patients than in male patients affected by hepatitis B-associated decompensated cirrhosis.
- Serum lactate level is a reliable indicator of mortality risk in patients with HBV-related decompensated cirrhosis.

Availability of Data and Materials

The data analyzed was available on the request for the corresponding author.

Author Contributions

HY and XLM designed the research study and wrote the first draft. BZ and CXP performed the research. HY, BZ and CY analyzed the data. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study received approval from the Ethics Committee of the Quzhou Affiliated Hospital of Wenzhou Medical University (2024-025) and complied with all relevant human subjects research guidelines. The research was conducted in accordance with the Declaration of Helsinki, ensuring that ethical principles were maintained throughout the study. Informed consent was obtained from all participants or their guardians prior to their inclusion in the study.

Acknowledgement

Not applicable.

Funding

This work was supported by Traditional Chinese Medicine Science and Technology Project of Zhejiang Province (2022ZA180) and Medical and health 258 key discipline personnel training project of QuZhou City (RC258-2021-23).

Conflict of Interest

The authors declare no conflict of interest.

References

Alberts CJ, Clifford GM, Georges D, Negro F, Lesi OA, Hutin YJF, et al. Worldwide prevalence of hepatitis B virus and hepatitis C virus among patients with cirrhosis at country, region, and global levels: a systematic review. The Lancet. Gastroenterology & Hepatology. 2022; 7: 724–735. https://doi.org/10.1016/S2468-1253(22)00050-4

Bedreli S, Sowa JP, Gerken G, Saner FH, Canbay A. Management of acute-on-chronic liver failure: rotational thromboelastometry may reduce substitution of coagulation factors in liver cirrhosis. Gut. 2016; 65: 357–358. https://doi.org/10.1136/gutjnl-2015-309922

Chinese Society of Hepatology, Chinese Society of Infectious Diseases. Guidelines for the prevention and treatment of chronic hepatitis B (2022 Edition). Chinese Journal of Infectious Diseases. 2023; 41: 3–28.

Chinese Society of Hepatology. Guidelines for the diagnosis and treatment of cirrhosis. Journal of Modern Medicine & Health. 2020; 36: 320, Insert 1–Insert 18.

Cui F, Blach S, Manzengo Mingiedi C, Gonzalez MA, Sabry Alaama A, Mozalevskis A, et al. Global reporting of progress towards elimination of hepatitis B and hepatitis C. The Lancet. Gastroenterology & Hepatology. 2023; 8: 332–342. https://doi.org/10.1016/S2468-1253(22)00386-7

Drolz A, Horvatits T, Rutter K, Landahl F, Roedl K, Meersseman P, et al. Lactate Improves Prediction of Short-Term Mortality in Critically Ill Patients With Cirrhosis: A Multinational Study. Hepatology. 2019; 69: 258–269. https://doi.org/10.1002/hep.30151

Gao N, Yuan P, Tang ZM, Lei JG, Yang ZR, Ahmed M, et al. Monomeric C-reactive protein is associated with severity and prognosis of decompensated hepatitis B cirrhosis. Frontiers in Immunology. 2024; 15: 1407768. https://doi.org/10.3389/fimmu.2024.1407768

Haas SA, Lange T, Saugel B, Petzoldt M, Fuhrmann V, Metschke M, et al. Severe hyperlactatemia, lactate clearance and mortality in unselected critically ill patients. Intensive Care Medicine. 2016; 42: 202–210. https://doi.org/10.1007/s00134-015-4127-0

Krispin I, Mahamid M, Goldin E, Fteiha B. Elevated lactate/albumin ratio as a novel predictor of in-hospital mortality in hospitalized cirrhotics. Annals of Hepatology. 2023; 28: 100897. https://doi.org/10.1016/j.aohep.2023.100897

Shan S, Zhao LH, Ma H, Ou X, You H, Jia J. Definition, etiology, and epidemiology of cirrhosis. Journal of Clinical Hepatology. 2021; 37: 14–16.

Tong L, Yan C, Wang M, Yang J, Wang H, Wang Y. Prognostic Value of Serum Exosomal AHCY Expression in Hepatitis B-Induced Liver Cirrhosis. Frontiers in Medicine. 2021; 8: 777452. https://doi.org/10.3389/fmed.2021.777452

Viña J, Borras C, Gomez-Cabrera MC. A free radical theory of frailty. Free Radical Biology & Medicine. 2018; 124: 358–363. https://doi.org/10.1016/j.freeradbiomed.2018.06.028

Wu XQ, Chen YJ. Research progress on liver regeneration in cirrhosis. Chinese Journal of Digestive Surgery. 2017; 16: 210–214.

Zhang MM, Zhou GH, Wang ZH. Clinical significance of dynamic monitoring of Lac, cTnI, FBG, and D-D levels in patients with sepsis. Journal of Molecular Diagnosis and Therapy. 2023; 15: 472–476.

Zhang Z, Xu X. Lactate clearance is a useful biomarker for the prediction of all-cause mortality in critically ill patients: a systematic review and meta-analysis*. Critical Care Medicine. 2014; 42: 2118–2125. https://doi.org/10.1097/CCM.0000000000000405