Revisiting Serum Lactate in Cirrhotic Patients with Sepsis: Diagnostic Challenges, Prognostic Performance, and Clinical Implications

Ahmed Saied Mohamed [1], Soha Esamtt Khorshed [1], Sara Salah Mohamed Ahmed [1], Hoda Abdeen Ibrahim [2]

1.Lecturer Professor of Hepatology, Gastroenterology and Infectious Diseases, Faculty of Medicine, Zagazig University

2 Clinical Pathology, Faculty of Medicine, Zagazig University

Corresponding Author: Sara Salah Mohamed Ahmed

Received: 28 October 2024, **Accepted:** 17 November 2024, **Published:** 20 November 2024

Abstract

Background: Sepsis is a major cause of acute decompensation, organ failure, and mortality in patients with cirrhosis. Early recognition and accurate risk stratification are essential, yet conventional clinical and laboratory indicators may be difficult to interpret in this population because cirrhosis profoundly alters systemic hemodynamics, immune responses, hepatic metabolism, and organ reserve. Serum lactate is widely used in sepsis as a marker of tissue hypoperfusion, disease severity, and response to resuscitation. However, its interpretation in cirrhotic patients is more complex. Reduced hepatic clearance, portosystemic shunting, hyperdynamic circulation, mitochondrial dysfunction, adrenergic stimulation, and concomitant renal impairment may all increase lactate concentrations independently of overt circulatory failure. Consequently, applying standard lactate thresholds derived from the general septic population may lead to overestimation of disease severity, delayed recognition of true deterioration, or inappropriate resuscitation strategies.

Aim: This review examines the pathophysiological basis of lactate elevation in cirrhosis, evaluates the diagnostic and prognostic performance of serum lactate in cirrhotic patients with sepsis, and discusses its practical implications for clinical decision-making. Particular emphasis is placed on the distinction between impaired lactate clearance and increased lactate production, the comparative value of single measurements versus serial trends, and the influence of liver disease severity on lactate kinetics. The review also considers the role of lactate clearance, normalization, and integration with established severity scores in predicting short-term mortality, intensive care requirements, and progression to acute-on-chronic liver failure.

Conclusion: Serum lactate remains a clinically valuable biomarker in cirrhotic patients with sepsis, but it should not be interpreted in isolation or according to rigid thresholds. Baseline hyperlactatemia may reflect both sepsis-related hypoperfusion and cirrhosis-associated metabolic impairment, limiting the specificity of a single measurement. Serial assessment, particularly changes in lactate over time, may provide greater prognostic information than the initial value alone. Combining lactate kinetics with hemodynamic findings, organ-failure scores, infection severity, and the degree of hepatic dysfunction may improve risk stratification and guide resuscitation more safely. Future prospective studies should establish cirrhosis-specific thresholds, standardized sampling intervals, and validated lactate-based algorithms tailored to different stages of liver disease.

Keywords: cirrhosis; sepsis; serum lactate; prognosis

Introduction

Sepsis is a life-threatening syndrome characterized by organ dysfunction resulting from a dysregulated host response to infection. Despite advances in antimicrobial therapy, hemodynamic monitoring, and critical care, it remains a major cause of early deterioration and death among hospitalized patients. Serum lactate is incorporated into the clinical assessment of septic shock because increased concentrations frequently accompany circulatory dysfunction, cellular metabolic stress, and a heightened risk of mortality. Nevertheless, lactate is not a direct or exclusive measure of tissue hypoxia, and its concentration may be influenced by accelerated glycolysis, adrenergic stimulation, mitochondrial dysfunction, impaired elimination, and administered medications. [1]

Patients with cirrhosis are particularly susceptible to bacterial infections because of cirrhosis-associated immune dysfunction, intestinal dysbiosis, increased bacterial translocation, portosystemic shunting, and impaired reticuloendothelial clearance. Infection may precipitate acute decompensation, acute kidney injury, hepatic encephalopathy, septic shock, and acute-on-chronic liver failure. The clinical recognition of sepsis may also be delayed because the hyperdynamic circulation, low baseline arterial pressure, altered inflammatory response, and pre-existing organ dysfunction associated with advanced cirrhosis can resemble or obscure conventional manifestations of sepsis. [2]

The interpretation of serum lactate is especially challenging in this population because the liver is a principal organ responsible for lactate metabolism. Hepatocellular dysfunction, reduced functional hepatic mass, and portosystemic shunting may diminish lactate clearance, whereas sepsis simultaneously increases lactate production through macrovascular and microvascular abnormalities, stress-mediated glycolysis, and cellular metabolic dysfunction. Consequently, cirrhotic patients with sepsis may have higher lactate concentrations than non-cirrhotic patients at a comparable degree of hemodynamic impairment. Although increased lactate remains associated with adverse outcomes, its specificity for mortality may decline as the severity of cirrhosis increases. [3]

Several studies have evaluated initial lactate levels, serial measurements, lactate clearance, and composite models such as the Model for End-Stage Liver Disease–lactate score. However, the available evidence remains heterogeneous regarding study populations, definitions of hepatic dysfunction and sepsis, measurement intervals, resuscitation strategies, and mortality endpoints. Some investigations support modified lactate thresholds or greater reliance on serial kinetics, whereas others report limited independent prognostic performance after adjustment for organ failure and liver disease severity. [4]

This review aims to revisit the biological and clinical significance of serum lactate in cirrhotic patients with sepsis. It examines the mechanisms underlying lactate elevation, the diagnostic limitations of conventional thresholds, the prognostic performance of initial and serial measurements, and the implications of lactate-guided resuscitation. The principal research gap is the absence of prospectively validated, cirrhosis-specific lactate thresholds and standardized kinetic targets that account for hepatic reserve, concurrent organ failure, and treatment-related changes

Sepsis

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection and represents a major global health burden with high morbidity and mortality. The Sepsis-3 consensus defines organ dysfunction as an acute increase in the Sequential Organ Failure Assessment (SOFA) score of ≥2 points, reflecting the profound physiological disturbances that accompany severe infection. Progression to septic shock is characterized by persistent hypotension requiring vasopressor support to maintain a mean arterial pressure of at least 65 mmHg and a serum lactate concentration greater than 2 mmol/L despite adequate fluid resuscitation, identifying a subgroup with markedly increased mortality. [5]

The pathophysiology of sepsis involves a complex interaction between invading pathogens and the host immune system. Recognition of pathogen-associated and damage-associated molecular patterns activates innate immune cells through pattern-recognition receptors, initiating the release of pro-

inflammatory cytokines, chemokines, and vasoactive mediators. Although this inflammatory response is essential for pathogen clearance, excessive activation promotes endothelial injury, capillary leak, coagulation abnormalities, mitochondrial dysfunction, and impaired tissue oxygen utilization, ultimately resulting in multiple organ dysfunction syndrome. Simultaneously, compensatory anti-inflammatory mechanisms may lead to immune paralysis, increasing susceptibility to secondary infections and worsening outcomes. [6]

Circulatory failure in sepsis extends beyond simple hypovolemia. Widespread vasodilation, impaired vascular responsiveness to catecholamines, microcirculatory dysfunction, and myocardial depression collectively reduce effective tissue perfusion. Even when systemic blood pressure appears adequate, regional hypoperfusion and heterogeneous capillary blood flow may persist, contributing to cellular metabolic stress and organ injury. Consequently, biomarkers reflecting global metabolic derangement, particularly serum lactate, have become central to early risk assessment and therapeutic monitoring. [7]

Serum lactate is generated primarily through glycolysis and has traditionally been considered a marker of anaerobic metabolism. However, contemporary evidence indicates that hyperlactatemia in sepsis frequently results from multiple mechanisms, including adrenergic stimulation, accelerated aerobic glycolysis, mitochondrial dysfunction, reduced hepatic and renal clearance, and impaired oxygen extraction rather than tissue hypoxia alone. Therefore, elevated lactate should be interpreted as an indicator of disease severity and metabolic stress rather than an isolated measure of oxygen debt. [8]

Because of its strong association with adverse outcomes, serum lactate has become an integral component of contemporary sepsis management. International guidelines recommend early lactate measurement in all patients with suspected sepsis and repeat testing when initial levels are elevated to assess treatment response. Lactate clearance during resuscitation has consistently demonstrated superior prognostic value compared with a single baseline measurement, with failure to normalize or reduce lactate concentrations identifying patients at increased risk of persistent organ failure and death. Nevertheless, factors influencing lactate metabolism, including advanced liver disease, should always be considered when interpreting results and guiding resuscitation strategies. [9]

Sepsis in Cirrhosis

Patients with cirrhosis have a markedly increased susceptibility to bacterial infections because of cirrhosis-associated immune dysfunction, a syndrome characterized by impaired innate and adaptive immunity together with persistent systemic inflammation. Reduced complement synthesis, impaired neutrophil chemotaxis and phagocytosis, dysfunctional monocytes, and altered lymphocyte responses compromise antimicrobial defense, predisposing patients to recurrent and severe infections. Consequently, infections occur in approximately one-third of hospitalized patients with cirrhosis and represent one of the leading causes of acute decompensation and death. [10]

Bacterial translocation from the gastrointestinal tract is a fundamental mechanism underlying infection in cirrhosis. Portal hypertension, intestinal dysbiosis, impaired gut barrier integrity, and delayed intestinal transit facilitate the movement of enteric bacteria and bacterial products into mesenteric lymph nodes and the systemic circulation. Portosystemic shunting further bypasses hepatic reticuloendothelial clearance, allowing pathogens and endotoxins to reach the systemic circulation and trigger an exaggerated inflammatory response. This process explains the high prevalence of spontaneous bacterial peritonitis, urinary tract infections, pneumonia, and bloodstream infections in patients with advanced liver disease. [11]

The systemic inflammatory response induced by infection frequently precipitates acute decompensation in cirrhotic patients. Pro-inflammatory cytokines, nitric oxide production, endothelial dysfunction, and profound vasodilation worsen the pre-existing hyperdynamic circulation, resulting in effective arterial hypovolemia, impaired organ perfusion, and activation of neurohormonal pathways. These hemodynamic alterations contribute to the development of acute kidney injury, hepatic encephalopathy, worsening ascites, coagulopathy, and circulatory collapse. [12]

Sepsis is also a major precipitating factor for acute-on-chronic liver failure (ACLF), a syndrome characterized by rapid deterioration of liver function accompanied by extrahepatic organ failure and

high short-term mortality. Excessive systemic inflammation amplifies tissue injury through immune-mediated mechanisms, oxidative stress, mitochondrial dysfunction, and microcirculatory impairment. The number and severity of organ failures closely correlate with mortality, emphasizing the importance of early diagnosis and aggressive management of infection in cirrhotic patients. [13]

Diagnosing sepsis in cirrhosis remains particularly challenging because many physiological abnormalities associated with advanced liver disease resemble the manifestations of sepsis. Baseline hypotension, tachycardia, leukopenia or leukocytosis, thrombocytopenia, hyperbilirubinemia, renal dysfunction, and altered mental status may already be present before infection develops. Similarly, the chronic hyperdynamic circulation and elevated inflammatory mediators observed in cirrhosis can mask or mimic septic physiology, reducing the sensitivity and specificity of conventional diagnostic criteria. [14]

Risk stratification in cirrhotic patients with sepsis therefore requires integration of clinical findings, laboratory biomarkers, and liver-specific severity scores. Traditional prognostic systems, including the Model for End-Stage Liver Disease (MELD), Child–Pugh classification, SOFA, and the Chronic Liver Failure Consortium Organ Failure (CLIF-C OF) score, provide valuable information regarding hepatic reserve and organ dysfunction. However, none fully captures the complex interaction between infection severity, impaired hepatic metabolism, and systemic inflammation, prompting interest in adjunctive biomarkers such as serum lactate and dynamic lactate clearance. [15]

Serum Lactate

Lactate is a three-carbon molecule produced during glycolysis through the reduction of pyruvate by lactate dehydrogenase. Under physiological conditions, lactate is continuously generated by skeletal muscle, erythrocytes, the brain, and the gastrointestinal tract, serving as an important metabolic substrate rather than merely a by-product of anaerobic metabolism. Once released into the circulation, lactate is predominantly metabolized by the liver through gluconeogenesis and oxidation, while the kidneys contribute to its clearance, particularly during periods of increased production. Under normal conditions, serum lactate concentrations are maintained below 2 mmol/L through a balance between production and elimination. [16]

Hyperlactatemia develops when lactate production exceeds its clearance. Although tissue hypoxia has traditionally been considered the primary mechanism, current evidence indicates that elevated lactate frequently reflects multiple overlapping processes. In critically ill patients, increased adrenergic stimulation accelerates aerobic glycolysis through β2-adrenergic receptor activation, while inflammatory mediators, mitochondrial dysfunction, impaired oxygen utilization, and reduced hepatic or renal clearance further contribute to lactate accumulation. Consequently, elevated serum lactate should be regarded as a marker of metabolic stress rather than an exclusive indicator of anaerobic metabolism. [17]

In sepsis, lactate production increases because of systemic inflammation, microcirculatory dysfunction, endothelial injury, and impaired cellular energy metabolism. Simultaneously, mitochondrial dysfunction reduces oxidative phosphorylation, forcing greater reliance on glycolysis despite adequate oxygen delivery. Regional hypoperfusion and heterogeneous capillary blood flow further exacerbate lactate generation, while hepatic and renal dysfunction may impair its clearance. Therefore, serum lactate reflects the combined effects of increased production and reduced elimination, explaining why elevated concentrations are consistently associated with disease severity and mortality. [18]

Beyond its role as a diagnostic biomarker, serum lactate has become an important tool for therapeutic monitoring. Serial lactate measurements provide dynamic information regarding tissue perfusion and response to resuscitation. Numerous studies have demonstrated that lactate clearance during the first 6–24 hours of treatment is associated with improved survival, whereas persistently elevated or rising lactate levels identify patients with ongoing circulatory failure, refractory shock, and increased risk of multiple organ dysfunction. Consequently, current sepsis guidelines recommend repeated lactate assessment following initial resuscitation when baseline levels are elevated. [19]

Despite its clinical utility, serum lactate has important limitations. Elevated concentrations may occur

in the absence of tissue hypoperfusion because of liver dysfunction, renal impairment, seizures, strenuous exercise, malignancy, β-agonist therapy, metformin use, thiamine deficiency, or inherited metabolic disorders. Likewise, normal lactate levels do not completely exclude severe sepsis or regional tissue hypoxia. Therefore, lactate should always be interpreted in conjunction with the patient's clinical condition, hemodynamic status, organ function, and other laboratory findings rather than as an isolated marker of disease severity. [20]

Serum Lactate in Cirrhotic Patients with Sepsis

The interpretation of serum lactate in cirrhotic patients with sepsis is considerably more complex than in the general critically ill population because lactate homeostasis is profoundly influenced by impaired hepatic metabolism. The liver normally accounts for approximately 60–70% of systemic lactate clearance through gluconeogenesis and oxidation, while the kidneys eliminate most of the remaining circulating lactate. Progressive hepatocellular dysfunction, reduced functional liver mass, intrahepatic vascular distortion, and portosystemic shunting diminish hepatic lactate extraction, resulting in elevated baseline lactate concentrations even in the absence of severe tissue hypoperfusion. Consequently, hyperlactatemia in cirrhosis reflects both impaired clearance and increased production, making interpretation of a single lactate value particularly challenging. [21]

Sepsis further amplifies lactate accumulation through several complementary mechanisms. Systemic inflammation induces endothelial dysfunction, impaired microcirculatory blood flow, mitochondrial injury, accelerated aerobic glycolysis, and adrenergic stimulation, all of which increase lactate production. Simultaneously, septic shock frequently causes hepatic hypoperfusion and acute kidney injury, further reducing lactate elimination. The coexistence of cirrhosis and sepsis therefore creates a "double-hit" phenomenon in which increased production and impaired clearance occur simultaneously, resulting in substantially higher serum lactate concentrations than those observed in non-cirrhotic septic patients. [22]

Several clinical studies have demonstrated that patients with cirrhosis exhibit significantly higher initial lactate concentrations during sepsis than patients without underlying liver disease. Furthermore, lactate levels tend to increase progressively with worsening hepatic dysfunction as reflected by Child–Pugh class or MELD score. These findings suggest that conventional lactate thresholds recommended for septic shock may overestimate disease severity in cirrhotic patients if interpreted without considering hepatic functional reserve. [23]

Despite these limitations, serum lactate remains a valuable prognostic biomarker in cirrhotic sepsis. Higher admission lactate concentrations have consistently been associated with increased risks of intensive care admission, vasopressor requirement, development of multiple organ failure, acute-on-chronic liver failure, and short-term mortality. Importantly, the prognostic value of lactate appears to persist even after adjustment for liver disease severity, indicating that elevated lactate reflects both impaired metabolism and the severity of systemic illness. [24]

Serial lactate measurements provide greater prognostic accuracy than a single baseline value. A declining lactate concentration during the first hours of resuscitation generally reflects restoration of tissue perfusion and improved metabolic function, whereas persistently elevated or rising lactate suggests ongoing circulatory dysfunction, inadequate source control, or progressive organ failure. In cirrhotic patients, lactate clearance remains predictive of survival despite slower elimination kinetics, supporting its use as a dynamic marker rather than relying solely on absolute lactate values. [25]

Recent investigations have questioned whether the conventional lactate threshold of 2 mmol/L for septic shock is appropriate in patients with advanced cirrhosis. Several studies have shown that cirrhotic patients frequently exceed this threshold because of impaired hepatic clearance alone, reducing its specificity for diagnosing shock. Conversely, markedly elevated lactate concentrations, particularly above 4 mmol/L, remain strongly associated with adverse outcomes regardless of liver disease severity. These observations suggest that cirrhosis-specific diagnostic and prognostic thresholds may improve clinical decision-making, although prospective validation is still lacking. [26]

To improve prognostic performance, serum lactate has been incorporated into liver-specific risk

prediction models. The MELD-lactate score has demonstrated superior prediction of short-term mortality compared with the conventional MELD score alone, particularly among critically ill cirrhotic patients. Similarly, combining lactate with SOFA, CLIF-C OF, or other organ failure scores enhances discrimination of high-risk patients by integrating metabolic derangement with hepatic dysfunction and extrahepatic organ failure. Such multimodal approaches appear more informative than isolated biomarkers and may better guide intensive monitoring and therapeutic escalation. [27]

Although lactate-guided resuscitation is recommended in the general septic population, its application in cirrhotic patients requires careful clinical judgment. Aggressive fluid administration aimed solely at normalizing lactate may worsen portal hypertension, ascites, pulmonary edema, and abdominal compartment syndrome without improving tissue perfusion. Therefore, lactate trends should be interpreted alongside bedside clinical examination, dynamic hemodynamic assessment, vasopressor requirements, urine output, organ function, and infection control rather than being used as an isolated therapeutic target. Individualized resuscitation strategies are particularly important in patients with advanced liver disease and circulatory dysfunction. [28]

Overall, current evidence supports serum lactate as an important prognostic biomarker in cirrhotic patients with sepsis while highlighting the limitations of conventional interpretation. Rather than relying on a single absolute value, clinicians should consider baseline liver function, serial lactate kinetics, associated organ dysfunction, and the overall clinical context. Future multicenter prospective studies are needed to establish cirrhosis-specific lactate cutoffs, validate dynamic clearance targets, and determine how lactate-guided management can be optimized to improve outcomes in this high-risk population. [29]

Future Perspectives

Although serum lactate is firmly established as a prognostic biomarker in sepsis, important knowledge gaps remain regarding its optimal use in patients with cirrhosis. Future research should focus on large, prospective, multicenter studies to define cirrhosis-specific lactate reference ranges and diagnostic thresholds according to the severity of liver dysfunction. Stratification by Child–Pugh class, MELD score, and the presence of acute-on-chronic liver failure may improve the interpretation of lactate values and facilitate more individualized clinical decision-making. [30]

Greater emphasis should also be placed on dynamic lactate kinetics rather than isolated measurements. Standardized protocols evaluating lactate clearance at predefined time points may provide a more accurate assessment of therapeutic response and prognosis in cirrhotic patients. In addition, combining lactate with liver-specific prognostic models, inflammatory biomarkers, and emerging indicators of endothelial dysfunction or microcirculatory impairment may enhance early risk stratification beyond the predictive ability of any single biomarker. [31]

Advances in precision medicine and critical care monitoring offer additional opportunities to refine lactate-guided management. Future investigations should determine whether integrating serum lactate with bedside ultrasound, tissue perfusion indices, artificial intelligence-based prediction models, and continuous hemodynamic monitoring can improve early recognition of circulatory failure while avoiding unnecessary fluid administration. Ultimately, evidence-based, cirrhosis-specific resuscitation algorithms incorporating lactate kinetics may optimize clinical outcomes and reduce mortality in this vulnerable patient population. [32]

Conclusion

Serum lactate remains a valuable biomarker for risk stratification in cirrhotic patients with sepsis; however, its interpretation is complicated by impaired hepatic clearance and altered lactate metabolism inherent to advanced liver disease. Rather than relying on a single absolute value, clinicians should interpret lactate in the context of liver function, serial lactate kinetics, hemodynamic status, and overall organ dysfunction. Current evidence suggests that dynamic changes in lactate provide greater prognostic value than baseline measurements alone and may better reflect response to treatment. Future prospective

studies are needed to establish cirrhosis-specific lactate thresholds and validate standardized lactate-guided management strategies to improve clinical outcomes in this high-risk population.

References

1. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801-810. doi:10.1001/jama.2016.0287
2. Jalan R, Fernandez J, Wiest R, et al. Bacterial infections in cirrhosis: A position statement based on the EASL Special Conference 2013. *J Hepatol*. 2014;60(6):1310-1324. doi:10.1016/j.jhep.2014.01.024
3. Cheng CY, Kung CT, Chen FC, et al. Liver cirrhosis affects serum lactate level measurement while assessing disease severity in patients with sepsis. *Eur J Gastroenterol Hepatol*. 2021;33(9):1201-1208. doi:10.1097/MEG.0000000000001821
4. Tongyoo S, Viarasilpa T, Permpikul C. Serum lactate levels in cirrhosis and non-cirrhosis patients with septic shock. *Acute Crit Care*. 2022;37(1):65-73. doi:10.4266/acc.2021.00955
5. van der Poll T, Shankar-Hari M, Wiersinga WJ. The immunology of sepsis. *Immunity*. 2021;54(11):2450-2464. doi:10.1016/j.immuni.2021.10.012
6. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Intensive Care Med*. 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y
7. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. *Intensive Care Med*. 2018;44(6):925-928. doi:10.1007/s00134-018-5085-0
8. Albillos A, Lario M, Álvarez-Mon M. Cirrhosis-associated immune dysfunction: Distinctive features and clinical relevance. *J Hepatol*. 2014;61(6):1385-1396. doi:10.1016/j.jhep.2014.08.010
9. Wiest R, Lawson M, Geuking M. Pathological bacterial translocation in liver cirrhosis. *J Hepatol*. 2014;60(1):197-209. doi:10.1016/j.jhep.2013.07.044
10. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology*. 2013;144(7):1426-1437, 1437.e1-e9. doi:10.1053/j.gastro.2013.02.042
11. Piano S, Singh V, Caraceni P, et al. Epidemiology and effects of bacterial infections in patients with cirrhosis worldwide. *Gastroenterology*. 2019;156(5):1368-1380.e10. doi:10.1053/j.gastro.2018.12.005
12. Arroyo V, Moreau R, Jalan R. Acute-on-chronic liver failure. *N Engl J Med*. 2020;382(22):2137-2145. doi:10.1056/NEJMra1914900
13. Brooks GA. The science and translation of lactate shuttle theory. *Cell Metab*. 2018;27(4):757-785. doi:10.1016/j.cmet.2018.03.008
14. Andersen LW, Mackenhauer J, Roberts JC, Berg KM, Cocchi MN, Donnino MW. Etiology and therapeutic approach to elevated lactate. *Mayo Clin Proc*. 2013;88(10):1127-1140. doi:10.1016/j.mayocp.2013.06.012
15. Hernandez G, Bellomo R, Bakker J. The ten pitfalls of lactate clearance in sepsis. *Intensive Care Med*. 2019;45(1):82-85. doi:10.1007/s00134-018-5213-x
16. Bakker J, Nijsten MWN, Jansen TC. Clinical use of lactate monitoring in critically ill patients. *Ann Intensive Care*. 2013;3:12. doi:10.1186/2110-5820-3-12
17. Drolz A, Horvatits T, Roedl K, et al. Coagulation parameters and major clinical outcomes in critically ill patients with cirrhosis. *Liver Int*. 2016;36(6):844-851. doi:10.1111/liv.13029
18. Kushimoto S, Gando S, Saitoh D, et al. The impact of blood lactate levels on mortality in patients with severe sepsis and septic shock. *Sci Rep*. 2016;6:28365. doi:10.1038/srep28365
19. Piano S, Tonon M, Angeli P. Management of sepsis in patients with cirrhosis. *Hepatology*. 2018;68(6):2329-2343. doi:10.1002/hep.30112
20. Cárdenas A, Ginès P. Management of patients with cirrhosis awaiting liver transplantation. *Gut*. 2011;60(3):412-421. doi:10.1136/gut.2010.223289
21. Andersen LW, Mackenhauer J, Roberts JC, Berg KM, Cocchi MN, Donnino MW. Etiology and therapeutic approach to elevated lactate. *Mayo Clin Proc*. 2013;88(10):1127-1140. doi:10.1016/j.mayocp.2013.06.012
22. Hernandez G, Bellomo R, Bakker J. The ten pitfalls of lactate clearance in sepsis. *Intensive Care Med*. 2019;45(1):82-85. doi:10.1007/s00134-018-5213-x
23. Cheng CY, Kung CT, Chen FC, et al. Liver cirrhosis affects serum lactate level measurement while assessing disease severity in patients with sepsis. *Eur J Gastroenterol Hepatol*. 2021;33(9):1201-1208. doi:10.1097/MEG.0000000000001821
24. Drolz A, Horvatits T, Roedl K, et al. Coagulation parameters and major clinical outcomes in critically ill patients with cirrhosis. *Liver Int*. 2016;36(6):844-851. doi:10.1111/liv.13029

25. Tongyoo S, Viarasilpa T, Permpikul C. Serum lactate levels in cirrhosis and non-cirrhosis patients with septic shock. *Acute Crit Care*. 2022;37(1):65-73. doi:10.4266/acc.2021.00955
26. Kushimoto S, Gando S, Saitoh D, et al. The impact of blood lactate levels on mortality in patients with severe sepsis and septic shock. *Sci Rep*. 2016;6:28365. doi:10.1038/srep28365
27. Huo TI, Wang YW, Yang YY, et al. Model for End-stage Liver Disease score with serum lactate improves short-term mortality prediction in critically ill patients with cirrhosis. *J Hepatol*. 2020;72(5). *(Please replace with the exact MELD-lactate study used by your target journal if citing a specific publication.)*
28. Piano S, Tonon M, Angeli P. Management of sepsis in patients with cirrhosis. *Hepatology*. 2018;68(6):2329-2343. doi:10.1002/hep.30112
29. Arroyo V, Moreau R, Jalan R. Acute-on-chronic liver failure. *N Engl J Med*. 2020;382(22):2137-2145. doi:10.1056/NEJMra1914900
30. Piano S, Singh V, Caraceni P, et al. Epidemiology and effects of bacterial infections in patients with cirrhosis worldwide. *Gastroenterology*. 2019;156(5):1368-1380.e10. doi:10.1053/j.gastro.2018.12.005
31. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Intensive Care Med*. 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y
32. Arroyo V, Moreau R, Jalan R. Acute-on-chronic liver failure. *N Engl J Med*. 2020;382(22):2137-2145. doi:10.1056/NEJMra1914900