tailed information on critical care books, visit our website www.ejaypee.com, for detailed information on critical care books, visit our website www.ejaypee.com,

YEARBOOK

Yearbook of CRITICAL CARE 2025

HICS Initiative

Editors
Srinivas Samavedam
Ganshyam Jagathkar

JAYPEE

Contents

SECTION 1 **Cardiac/Hemodynamics/Fluids 1**
Section Editor: *Supradip Ghosh*
Associate Editors: *Ripenmeet Salhotra, Saurabh Kumar Rai, Aditya Lyall, Amandeep Singh, Atul Phillips*

SECTION 2 **Respiratory/Ventilation/Acute Respiratory Distress Syndrome..... 29**
Section Editor: *Jaicob Varghese*
Associate Editors: *Biji Thomas Philip, Melwin George, Nilanjan Umesh*

SECTION 3 **Neurocritical Care..... 47**
Section Editor: *Sivakumar MN*
Associate Editor: *Lakshmikanth Charan S*

SECTION 4 **Gastroenterology/Hepatobiliary 62**
Section Editor: *Lalita Gouri Mitra*
Associate Editors: *Jagdeep Sharma, Harsimran Singh Walia*

SECTION 5 **Nephrocritical Care 88**
Section Editor: *Kanwalpreet Sodhi*
Associate Editors: *Atul Phillips, Manu Gupta, Alaukik Goyal*

SECTION 6 **Antimicrobials/Infections..... 133**
Section Editor: *Sumesh Arora*

SECTION 7 **Hematology 148**
Section Editor: *Saswati Sinha*

SECTION 8 **Ethics/Organization/Outcomes in Intensive Care Unit 189**
Section Editors: *Prashant Nasa, Deven Juneja*

SECTION 9 **Intensive Care Unit Sonography/Imaging..... 205**
Section Editor: *Shrikanth Srinivasan*
Associate Editors: *NVSN Prasant, Velmurugan Selvam*

SECTION 10 **Nutrition/Metabolic 210**
Section Editor: *Ketan Kargirwar*
Associate Editors: *Vivek Arvindkumar Jain, Utkarsh Shah, Sanket Hansora*

SECTION 11 **Guidelines..... 234**
Section Editor: *Deven Juneja*
Associate Editor: *Sahil Kataria*

Index 249

4 SECTION Gastroenterology/Hepatobiliary

Section Editor: *Lalita Gouri Mitra*

Associate Editors: *Jagdeep Sharma, Harsimran Singh Walia*

ARTICLE 1

Exploring the Impact of Therapeutic Plasma Exchange on Organ Function in Patients with ACLF: A Retrospective, Single-center Propensity Score-matched Cohort Study[1]

Schumacher J, Henschler R, Buhmann R, Petros S, Weidhase L, Veelken R, et al. Exploring the Impact of Therapeutic Plasma Exchange on Organ Function in Patients with ACLF: A Retrospective, Single-center Propensity Score-matched Cohort Study.

J Clin Exp Hepatol. 2025;15(5):102550.

INTRODUCTION

The EASL-CLIF consortium defines acute-on-chronic liver failure (ACLF) as a life-threatening syndrome in patients with an underlying chronic liver disease, usually cirrhosis, which is characterized by acute decompensation and multiorgan failures and carries a high short-term mortality. Based on the number, type, and severity of associated organ failures, ACLF is classified into grade 1, grade 2, and grade 3.[2]

The pathophysiology of ACLF is associated with severe systemic inflammation, combined with tissue hypoperfusion, direct-immune-mediated damage, and mitochondrial dysfunction, causing organ failures. The presenting clinical features include jaundice, deranged international normalized ratio (INR), hepatic encephalopathy, ascites, and other signs of severe inflammation. Infections are the most common precipitating factor, and renal failure is the most frequent organ involved and is a key predictor of poor patient outcomes.[3]

Acute-on-chronic liver failure can manifest its impact on various organ systems as hepatic encephalopathy, deranged oxygenation requiring high FiO_2, hyperbilirubinemia (serum bilirubin levels >12 mg/dL), vasopressors to support circulation, coagulopathy (INR >2.5), and increased creatinine levels and might even require renal replacement therapy, cirrhotic cardiomyopathy, severe systemic inflammation associated with immune deficiencies, adrenal insufficiency, barrier dysfunction in the gut leading to bacterial translocation, and increased frailty with sarcopenia.[4]

JAYPEE BROTHERS

The management of these patients includes admission to the intensive care unit for close monitoring, risk stratification, and focusing on the underlying cause, the severity of organ failures requiring support, and the availability of liver transplantation. Identification of the precipitants, such as proven bacterial infection, gastrointestinal hemorrhage with shock, severe alcohol-related hepatitis, and toxic encephalopathy, is the core element of the treatment process.

PAST RESEARCH AND CLINICAL PROBLEM

There are significant advances in the management of ACLF, but considerable morbidity and mortality still exist. Liver transplant remains the treatment of choice in patients with a high risk of mortality; however, there is limited access to transplant. Expanding the scope of treatment, other options are required to bridge critically ill patients to liver transplant or to preserve liver function when it is either contraindicated or unavailable. Therapeutic plasma exchange (TPE) has been advocated to benefit patients with ACLF. It acts by multiple mechanisms by removing circulating toxins and inflammatory mediators, replenishing essential proteins, stabilizing hemodynamics, improving hepatic encephalopathy, correcting coagulopathy, and thus reducing organ dysfunction, bridging patients on the road to recovery or transplant.[5]

Stahl et al. conducted a retrospective analysis to investigate whether TPE might have comparable beneficial effects in patients with ACLF. They enrolled 31 patients with ACLF who were treated with TPE and 1:1 matched to an ACLF cohort treated with standard medical therapy (SMT) only. 21 out of 31 patients treated with TPE were considered as bridge to recovery, which showed no significant difference in mortality as compared to the SMT group. However, mortality occurred significantly earlier in the SMT group (mortality at 5 days: 33.3% for TPE and 66.7% for SMT; $p = 0.048$). 10 patients in the TPE group were treated as a bridge to transplant; 60% cases survived and showed better organ dysfunction stabilization than patients in the SMT group. They concluded that TPE in ACLF patients is feasible but unsuitable as a bridge to recovery strategy; however, it might assist as a bridge to transplant in selected patients.[6]

Tan did a systematic review on plasma exchange (PLEX) in patients with acute liver failure (ALF) and ACLF. Nine studies included patients treated for ACLF and six studies included patients treated for both ALF and ACLF. Two studies showed that in patients with ACLF, when plasma-exchange-based liver support systems were used, there was improvement in biochemistry. They further concluded that PLEX in patients with ACLF improved survival at 30 and 90 days in nontransplant patients. Further research warrants that well-designed randomized controlled trials are needed to ascertain the optimal amount and duration of PLEX and assess if the use of high-volume plasma exchange (HVPE) can be extrapolated to patients with ACLF.[5]

Beran did a systematic review and meta-analysis on PLEX for ALF and ACLF. They analyzed 20 studies, including 5,705 ACLF patients. Patients treated with PLEX have improved 30- and 90-day survival. PLEX may be considered in patients who are not ideal candidates for liver transplant or as a bridge to them.[7]

Swaroop compared ACLF patients managed with SMT alone and SMT plus TPE. Mortality at 30 and 90 days was the primary outcome. A total of 1,151 patients were

JAYPEE BROTHERS

included in this study; 864 patients had ACLF and 287 patients had acute decompensation with no organ failure. In the propensity score-matched analysis, 38 patients were selected in both groups. They found that patients treated with SMT plus TPE had lower 30-day mortality (21% vs. 50%; $p = 0.008$), but no significant difference in mortality at 90 days in both groups. They concluded that TPE may improve short-term survival but does not significantly impact long-term survival.[8]

Kumar did an updated meta-analysis of ACLF patients treated with TPE. It included 5,336 ACLF patients with 2,724 patients receiving PLEX therapy. They concluded that a significant 1-month, 3-month, and up to 1-year survival benefit was noted among patients with ACLF treated with PLEX compared to SMT. Skin rash and allergic reactions in 14% of patients were the most common adverse reactions.[9]

AUTHORS' VIEWPOINT

Jonas Schumacher studied the impact of therapeutic PLEX on organ function in patients with ACLF. It was a retrospective, propensity-score-matched, single-center cohort study. Depending on the severity, short-term mortality varies from 20% in ACLF grade 1 to 80% in ACLF grade 3. Worsening grade and (CLIF-C)-ACLF criteria after 3–7 days of full organ support are associated with even poorer outcomes. TPE is a safe extracorporeal procedure that separates a patient's blood from its soluble components and substitutes them with fresh frozen plasma alone or in combination with albumin, and this ratio is determined by the coagulation markers. It is an established treatment for diseases driven by antibodies associated with severe systemic inflammation. TPE positively influences the immune system, coagulation, micro-circulation, and endothelial permeability.

They evaluated the effects of TPE in ACLF, with the primary endpoint being 28-day transplant-free survival while also assessing 90-day transplant-free survival, changes in parameters of organ function, and CLIF-C scores in patients treated with TPE. They included ACLF patients defined by the European Foundation for the Chronic Liver Failure consortium criteria who received TPE treatment between August 2016 and July 2024, aged more than 18 years. To be enrolled in the study, they must survive more than 24 hours after the first TPE. They excluded patients who were included in an interventional clinical trial and had active extrahepatic malignancy or hepatocellular carcinoma beyond the Milan criteria. They used propensity score matching (PSM) to match the remaining 21 patients in the TPE group to the SMT group in a 1:1 ratio. The 28-day transplant-free survival rates were 70% (14/20) in the TPE group versus 45% (9/20) in the SMT group, and at 90 days, survival rates were 30% (6/20) in both groups ($p = 0.426$). Out of 21 patients, 17 in the TPE group and 15 in the SMT group were unresponsive to SMT. One patient in the TPE group and five patients in the SMT group underwent liver transplant. Six patients in both groups were alive at 90 days post diagnosis of ACLF. The most common causes of death in both groups were sepsis and disease progression. They suggested that TPE may benefit selected subgroups of ACLF patients who are not responsive to standard medical care.

REVIEWERS' VIEWPOINT

Severe systemic inflammation is the hallmark and main driving force of ACLF, resulting in multiorgan failure and increased mortality. TPE has been shown to provide survival benefit in multiple retrospective cohort studies. Most previous studies have used

JAYPEE BROTHERS

APSL or Chinese criteria to define ACLF and have been performed in Asian populations. However, in this study, the authors used EF-CLIF criteria, which have been shown to have a stronger correlation with patient prognosis and outcomes in a European subset of the population. The majority of patients in this study had alcohol-related disease. After 7 days of being unresponsive to medical therapy, when these ACLF patients underwent TPE, there was a significant improvement in short-term transplant-free survival at 28 days. There was significant improvement and stabilization of organ dysfunction, like coagulopathy, hepatic encephalopathy, reducing serum bilirubin levels, vasopressor support, and mechanical ventilation. Various limitations and factors introduce biases in this study, which significantly affect the generalizability of the findings. These factors include a single-center study, a small sample size, significant selection bias, and being retrospective.

CONCLUSION

There is significant available evidence on display, showing that TPE helps improve short-term mortality in patients not responding to SMT, acting as a strong bridge to potentially eligible patients for liver transplant. There might not be a significant long-term survival benefit, and as a bridge to the potential recovery of these patients. There is a need to do a more well-designed prospective randomized controlled clinical trial with high-volume patients in multiple centers to establish and strengthen the level of evidence and grade of recommendation for protocolized treatment in the form of volume of exchange, appropriate timing, and duration of exchange.

ARTICLE 2

Addition of Midodrine to Albumin Reduces the Incidence of Complications of Large-volume Paracentesis: An RCT Comparing Midodrine, Terlipressin, and Albumin[10]

Kulkarni AV, Maiwall R, Arora V, Jindal A, Thomas S, Ali R, et al. Addition of midodrine to albumin reduces the incidence of complications of large-volume paracentesis: an RCT comparing midodrine, terlipressin, and albumin.

Hepatol Int. 2025;19(5):1231-41.

CLINICAL QUESTION

This study addresses a pressing clinical challenge: Whether the addition of vasoconstrictors—specifically oral midodrine or terlipressin—to standard albumin therapy can reduce the incidence of complications, particularly paracentesis-induced circulatory dysfunction (PICD), in cirrhotic patients undergoing large-volume paracentesis (LVP) for refractory ascites.

WHAT IS ALREADY KNOWN?

Annually, standard medical therapy becomes refractory in 10% of decompensated cirrhotic patients.[11]

- LVP is a standard and effective treatment for patients with refractory ascites in

JAYPEE BROTHERS

decompensated cirrhosis, but is frequently complicated by PICD, which highly contributes to mortality and morbidity.[12]

- Albumin infusion helps prevent PICD by maintaining intravascular oncotic pressure but is not fully protective. Studies show 18–31% of patients still develop PICD despite albumin use.[12]
- Vasoconstrictors like terlipressin (a V1a receptor agonist) and midodrine (an α1-adrenergic agonist) have shown potential in preventing PICD by reducing splanchnic vasodilation.[13]
- Long-term use of albumin in patients with cirrhosis prolongs survival and aids in control of ascites to maintain serum albumin concentrations which is of paramount importance in patients with cirrhosis to improve outcomes.[14]
- Previous studies mostly compared vasoconstrictors to albumin, but no large randomized controlled trial (RCT) had evaluated vasoconstrictor + albumin versus albumin alone or directly compared midodrine versus terlipressin in combination with albumin.
- Midodrine, being oral, offers a promising outpatient solution. Terlipressin is typically intravenous and may pose administration limitations.[15]

STUDY DESIGN

- *Type:* Prospective, open label, RCT
- *Design:* Single-center, 1:1:1 randomization into three groups
- *Trial name:* VITAL Trial (Vasoconstrictors and Infusion of Therapeutic Albumin for LVP)
- *Study period:* May 2017 to April 2018
- *Groups:*
  - *Group I:* Albumin alone
  - *Group II:* Albumin + Terlipressin
  - *Group III:* Albumin + Midodrine
- The trial aimed to test whether vasoconstrictors plus albumin would reduce PICD and other complications more effectively than albumin alone.

POPULATION STUDIED (INCLUDING DEMOGRAPHICS)

- *Sample size:* 165 patients with cirrhosis and refractory ascites
- *Age:* 18–80 years
- *Gender:* 85% male across groups
- *Etiology of cirrhosis:*
  - Alcoholic: 42%
  - Nonalcoholic steatohepatitis (NASH): 32%
  - Viral/Other: Remaining
- *Severity of disease:*
  - Predominantly Child–Pugh class C
  - Mean MELD score: 14–15
- *Baseline characteristics:*
  - Similar distribution of prior AKI, hepatic encephalopathy (HE), and laboratory values
  - No significant intergroup differences in hemodynamics, serum albumin, creatinine, sodium, or plasma renin activity (PRA) at baseline

STUDY OUTCOMES

- *Primary outcome:* Incidence of PICD
  - Defined as a >50% increase in PRA to >4 ng/mL/h by day 6 post paracentesis
- *Secondary outcomes:*
  - *Incidence of complications:* Acute kidney injury (AKI), hyponatremia, hepatic encephalopathy
  - 28-day survival
  - Repeat paracentesis frequency
  - Hospitalization rates and duration
  - Hemodynamic changes [mean arterial pressure (MAP), heart rate (HR)]
  - Adverse events related to therapy

JAYPEE BROTHERS

New Issue Addressed

This study uniquely investigates the benefit of combining vasoconstrictors with albumin rather than using either alone.[16] It also directly compares midodrine versus terlipressin, which has not been done before in an RCT.

AUTHORS' VIEWPOINT

The authors conclude that:

- While PICD incidence was not significantly reduced with vasoconstrictor use, the addition of oral midodrine significantly reduced the incidence of complications such as AKI and hyponatremia.
- Midodrine was well tolerated, easy to administer orally, and most importantly suitable for outpatient settings. Also, it has fewer side effects, more patient acceptance maintaining hemodynamics, and also fewer complications as compared to terlipressin.[16]
- Terlipressin did not show a significant advantage over midodrine and was associated with a higher rate of adverse events.
- In high-risk patients (advanced cirrhosis, Child–Pugh C, prior AKI), midodrine + albumin is a practical, safe, and viable option to reduce LVP-related complications and adverse events.

STRENGTHS OF THE STUDY

- First comparative trial of midodrine versus terlipressin with albumin till date
- Randomized controlled design with clear eligibility and exclusion criteria
- Robust statistical analysis including multivariate regression and ROC curves
- Focus on real-world endpoints such as complications and hospitalization
- Standardized paracentesis technique and follow-up
- Use of PRA and MAP to objectively define PICD

REVIEWER'S VIEWPOINT

This study fills a critical gap in the management of refractory ascites. Although the primary endpoint (PICD by PRA) did not differ significantly, clinically relevant outcomes—particularly AKI, hyponatremia, and hospitalization—favored the midodrine + albumin group.

Advantages:

- It is practical for daycare/outpatient settings.
- Oral midodrine is patient-friendly and avoids IV therapy risks.
- It demonstrated reduction in complications and paracentesis frequency.
- It is statistically sound with good follow-up adherence.

Limitations:

- Open-label design may introduce bias.
- Short follow-up (28 days) prevents long-term outcome evaluation.
- Unequal dosing protocols (midodrine for 3 days; terlipressin for 16 hours).
- PRA as a surrogate endpoint is variable and not always reliable.
- PRA may not be readily available.

Despite these limitations, the clinical benefit of midodrine is clear and the trial paves the way for practice change.

IMPACT ON CURRENT PRACTICE AND TAKE-HOME MESSAGE

Clinical Impact

- Midodrine (7.5 mg TID for 3 days) + albumin can be safely recommended for cirrhotic patients undergoing LVP to reduce complications
- Especially useful in resource-limited or outpatient settings, where IV therapy and monitoring are not feasible
- Potential to reduce hospitalizations, prevent AKI, and improve quality of care in advanced liver disease

JAYPEE BROTHERS

Take-home Message

In cirrhotic patients undergoing LVP, oral midodrine combined with albumin significantly reduces postparacentesis complications, even if PICD (by PRA) is not significantly different. This strategy is effective, safe, and ready for implementation in real-world settings.

Future Directions

- Multicentric, double-blinded, placebo-controlled trials
- Long-term follow-up to assess survival, transplant-free interval, and cost-effectiveness
- Equal duration dosing comparison of midodrine versus terlipressin
- Incorporation of quality of life (QoL) measures
- Explore better markers for PICD beyond PRA
- Consider evaluating midodrine as long-term therapy in ascites-prevention strategies

ARTICLE 3

Hyperbilirubinemia at Hospitalization Predicts Nosocomial Infection in Decompensated Cirrhosis: Data from ATTIRE Trial[17]

Fuller H, Tittanegro TH, Maini AA, China L, Rhodes F, Salles NB, et al. Hyperbilirubinemia at hospitalization predicts nosocomial infection in decompensated cirrhosis: Data from ATTIRE trial.

Hepatol Commun. 2025;9:e0648.

INTRODUCTION

Cirrhosis is a condition in which the healthy liver is replaced by scar tissue, which prevents its normal functioning. Hepatic circulation is impaired, leading to functional impairment and progressing to liver failure. Decompensated cirrhosis is an acute deterioration in hepatic function in a patient with cirrhosis and is characterized by hepatic encephalopathy, jaundice, ascites, coagulopathy, variceal hemorrhage, or hepatorenal syndrome.[18]

It is important to determine the underlying cause of hepatic decompensation, which is commonly in the form of infections, gastrointestinal bleeding, high-alcohol intake, and drug-induced hepatic injury. Bilirubin is a breakdown product of heme, and in its insoluble unconjugated form, bilirubin is transported to the liver loosely bound to albumin, where it is converted into soluble conjugated bilirubin for excretion in bile. Hence, measuring the bilirubin levels in the serum estimates the excretion and conjugation capacity of the liver. Total serum bilirubin levels are important in prognostic models like the Child–Turcotte-Pugh (CTP) and the model for end-stage liver disease (MELD). The APASL and EASL guidelines use elevated bilirubin levels as a definition for hepatic failure.[19]

Nosocomial infections are a serious threat to patients with liver cirrhosis. Cirrhosis-associated immune dysfunction has been proposed as a potential for an increased

JAYPEE BROTHERS

risk of infections. There are also structural changes in the reticuloendothelial system, leading to impaired and restricted response to pathogens. The most prevalent sites of nosocomial infections are spontaneous bacterial peritonitis (SBP), urinary tract infections, and pneumonia, along with an increased risk of bloodstream spread with subsequent infections.[20]

PAST RESEARCH AND CLINICAL PROBLEM

Various biomarkers, such as procalcitonin levels, C-reactive protein, neutrophil cluster of differentiation, elevated bilirubin levels, MELD score, and neutrophil to lymphocyte ratio, have been used to identify nosocomial infections in patients with decompensated cirrhosis. Early prediction and identification of nosocomial infections are important to decrease morbidity and mortality, but the widespread use of prophylactic antibiotic therapy does not seem to provide a mortality benefit and increases the risk of antimicrobial resistance.

In 2013, Pleguezuelo worked on diagnosing and managing bacterial infections in decompensated cirrhosis. Due to altered and impaired immunity in cirrhotic patients, there is an increased risk of bacterial translocations. The life-threatening infections in patients with decompensated cirrhosis are SBP, followed by urinary tract infections, pneumonia, endocarditis, and skin and soft-tissue infections. Severe liver failure, variceal bleeding, low ascitic protein level, and prior episodes of SBP are the common risk factors for the development of infection in patients with cirrhosis. They suggested the use of antibiotic prophylaxis in hospitalized patients with a history of gastrointestinal hemorrhage, ascites, and SBP.[21]

Bajaj in 2020 studied the determinants of developing a nosocomial infection and evaluated their influence on 30-day outcomes in a large prospective, multicenter, inpatient cohort with cirrhosis. They included 2,864 patients, of whom 436 developed nosocomial infections. The patients with nosocomial infections were more likely to be infected at admission and had advanced cirrhosis. Hospital-acquired infections also increased the rates of ACLF, death, and transplant regardless of admission infections. They concluded that nosocomial infections are prevalent in patients with advanced cirrhosis. Higher MELD and SIRS scores are associated with nosocomial infection; all hospitalized cirrhotic patients require strict vigilance and prevention.[22]

Xu et al. researched the influence of acute decompensation (AD) events upon admission on the subsequent risk of nosocomial infections. In this study, they evaluated 419 patients with cirrhosis and AD. 91 patients developed nosocomial infections. 52.7% of patients had jaundice and 37.4% had bacterial infections at admission, compared to patients without nosocomial infections. The presence of nosocomial infections increases the 28-day mortality rates. They concluded that patients having jaundice at admission had an increased risk of nosocomial infections, which also increased the mortality. Using antibiotic prophylaxis might be beneficial in such a subset of patients.[23]

Xu et al. conducted a retrospective case–control study to identify risk factors for nosocomial infections in patients undergoing artificial liver support. 174 patients were included in this study. They found that total serum bilirubin levels, the number of invasive procedures, and blood transfusions were independent risk factors,

JAYPEE BROTHERS

and hemoglobin (Hb) was a protective factor for nosocomial infection in these patients.[24]

AUTHORS' VIEWPOINT

Fuller did this study in 2024 to find out if in patients with decompensated cirrhosis, hyperbilirubinemia at hospitalization can predict nosocomial infection. In patients with decompensated cirrhosis, nosocomial infection is a major cause of morbidity and mortality. However, available evidence regarding antibiotic prophylaxis to reduce infection is not very assuring. The ATTIRE trial included patients with decompensated cirrhosis and compared human albumin infusions with standard care. In the ATTIRE trial, widespread prophylactic use of antibiotics was noticed, but it did not result in a reduction of nosocomial infections. They did a follow-up study in patients of the ATTIRE trial, examining baseline clinical characteristics that predicted the development of nosocomial infection to guide a more precise approach to antibiotic prophylaxis that may help in reducing antibiotic resistance and improve patient outcomes.[17]

They also performed a subgroup analysis of patients to find out if serological markers of inflammation, bacterial translocation, infection, and lipid metabolomics on the first day of hospitalization could predict the subsequent development of nosocomial infection. Among 777 patients of decompensated cirrhosis, and randomized to the ATTIRE trial, 211 patients were diagnosed with infection at presentation. 203 out of 563 patients with no infection were already on antibiotics, and 360 patients neither had infection nor were on antibiotic treatment on hospitalization. Among these, 73 patients developed nosocomial infection, and the absence of any signs of nosocomial infection was observed in 287 patients. The common sites of nosocomial infections were the respiratory tract (29%), urinary tract (13.7%), SBP, skin, and soft tissue (8% each), and 31.5% remained unknown. The median time to diagnosis of infection was 6 days.

They found that the only clinical characteristic that differed in patients developing nosocomial infections was having a median value of serum bilirubin of 125 and 103 μmol/L in patients without nosocomial infections ($p = 0.02$). A threshold serum bilirubin level of >188 μmol/L had a specificity of 80% for the prediction of subsequent nosocomial infection, though the sensitivity for the same was only 36%. The use of proton-pump inhibitors, nonselective beta-blockers, prednisolone, or albumin had no impact on the development of nosocomial infection. But there was a higher incidence in patients treated with rifaximin. Plasma lipid metabolomics predicted, but the use of serological biomarkers of infection, bacterial translocation, and inflammation did not predict nosocomial infection.

REVIEWERS' VIEWPOINT

This study included a large cohort from a UK multicenter clinical trial, with the primary endpoint as the diagnosis of nosocomial infection, and the selection criteria avoided the potential confounders of community-acquired infection or antibiotic prescription at the time of admission. Bajaj studied the incidence and impact of nosocomial infections in hospitalized patients with cirrhosis. They included 2,864 patients in this trial, of which 436 (15%) developed nosocomial infection.[22] They concluded that nosocomial infections in cirrhotic patients are associated with poor outcomes. In this study, almost 20% of patients developed nosocomial infections and had a threefold

JAYPEE BROTHERS

increase in 28-day mortality and a twofold increase in mortality at 90 days.

Kutmutia, in 2023, concluded that almost 50% of the antibiotics at study entry were given without a diagnosis of infection. It did not improve the mortality rates and overall risk of hospital-acquired infections.[25] This study also supports limiting the use of prophylactic antibiotics in patients with serum bilirubin levels >188 μmol/L, which could reduce antibiotic misuse and could be a key inclusion criterion for a pragmatic clinical trial to prevent nosocomial infections. The majority of patients in this study cohort had alcohol-associated liver dysfunction; such patients typically have greater serum bilirubin levels, so these results might not be extrapolated to other causes of liver disease. They have no data on liver biopsy for this study. The data regarding the microorganisms cannot be considered comprehensive, and the majority of the patients included in this study were ward-based, so the application of this data to critically ill patients in the intensive care unit must be done with caution.

CONCLUSION

In the ATTIRE trial, the patients at hospitalization were not diagnosed with infection nor treated with antibiotics, and serum bilirubin levels of >188 μmol/L predicted nosocomial infection. Lacking a validation cohort, the primary analysis of the results of the randomized controlled trial (ASEPTIC) can provide more strength to the present study outcomes. The biomarkers did not improve the predictive ability, and these data can be used to reduce the administration of antibiotic prophylaxis, aid antibiotic stewardship, and also in developing trial designs to investigate use in high-risk patients.

ARTICLE 4

Acute-on-Chronic Liver Failure (ACLF): The 'Kyoto Consensus'—Steps from Asia[26]

Choudhury A, Kulkarni AV, Arora V, Soin AS, Dokmeci AK, Chowdhury A, et al. Acute-on-chronic liver failure (ACLF): the 'Kyoto Consensus'-steps from Asia.

Hepatol Int. 2025;19:1-69.

INTRODUCTION

Acute-on-chronic liver failure (ACLF) is characterized by acute decompensation of chronic liver disease and is associated with extrahepatic organ failures, carrying a very high short-term mortality in the absence of liver transplantation (LT). Almost half the cases of ACLF have no identifiable trigger; alcohol associated and chronic viral hepatitis are the most common underlying liver diseases, and others, like sepsis, drugs, and relapse of chronic viral hepatitis, are the common precipitating factors.[27] There are different consortia involved in managing these patients in different parts of the world. There have been various definitions proposed worldwide, and literature supports these definitions to be equally effective in their

JAYPEE BROTHERS

respective subsets of cohorts in identifying patients with high mortality.

The four major consortia are (1) APASL ACLF Research Consortium (AARC), (2) European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF), (3) North American Association for the Study of the End Stage liver Disease (NACSELD), and (4) Chinese Group on the Study of Severe Hepatitis B (COSSH), and one from the society is the American Association for the Study of Liver Disease (AASLD).[28,29] These variations have manifested various challenges in the diagnosis, management, and research of ACLF due to varying inconsistencies across different areas and populations. There has been significant progress in the understanding of treatment strategies; the treatment is largely limited to bridge therapies and LT. Lack of a unified definition is a major hindrance to research in liver-directed therapies, which can actually improve patient outcomes in these sick patients.

PAST RESEARCH AND CLINICAL PROBLEM

A working party on ACLF was set up by the Asian Pacific Association for the Study of the Liver (APASL) in 2004 to study and analyze the various aspects of this problem and further develop consensus guidelines on ACLF relevant to the disease pattern and clinical practice. The development of these consensus guidelines involves a rigorous process of reviewing all the available published literature on ACLF; with an effort to define the acute insults to liver, the underlying chronic liver disease, and the hepatic failure of ACLF; surveying the present approaches for the diagnosis and treatment of ACLF; deliberating contentious issues; and developing a consensus statement by the working party. They concluded that ACLF is a distinct clinical entity, with characteristic hemodynamic alterations in cirrhotic patients, including increased portal pressure and cardiac output, a dilated and hyporesponsive peripheral circulation, increased portosystemic shunting, and a reduced renal blood flow. The need for a liver biopsy must be individualized, as it is quite helpful in assessing the presence and degree of hepatic fibrosis and/or cirrhosis. The prognostic scores for ACLF, including MELD (model for end-stage liver disease), CPT (Child–Turcotte-Pugh), SOFA (sequential organ failure assessment), and APACHE (acute physiology and chronic health evaluation) scores, are generally not different in patients with varying etiologies of ACLF.[30]

Bajaj et al., in view of variability in definitions by different consortia, suggested this definition of ACLF as a potentially reversible condition in patients with chronic liver disease with or without cirrhosis, having high potential for multiple organ failure and mortality within 3 months in the absence of treatment of the underlying liver disease, liver support, or LT. ACLF is associated with elevated serum bilirubin levels and coagulopathy; the associated presence of renal, lung, circulatory, or brain failure supports the diagnosis. EASL-CLIF sequential organ failure assessment score or NACSELD organ failures score is used for assessing the severity. Preventing precipitating factors such as infections and alcohol is a priority in improving the prognosis of these individual organ failures (brain, circulatory, renal, respiratory, and coagulation). The judicious use of antibiotics and antifungal medications is required, and these are best managed in the critical care unit; some also benefit from early LT, but the futility of listing patients with poor prognosis must be considered.[31]

JAYPEE BROTHERS

Luo et al. published a review on ACLF—far to go, with defining ACLF as a life-threatening clinical syndrome that develops in patients with acute deterioration of chronic liver disease. Alcohol-related cirrhosis is the most common cause of chronic liver disease, with bacterial infections being the most important precipitant in the Western world. In the Asian-Pacific population, the hepatitis B virus is the most common etiology, and its reactivation is the most common precipitant of ACLF. They concluded that ACLF is still a major challenge in the field of hepatology, with current therapeutic management relying on supportive therapy for organ failure, evolving research strategies on bridge therapies, and LT.[32]

The variability in definitions has also accounted for substantial confusion among multidisciplinary teams caring for ACLF patients. This is also a major hindrance to improving outcomes in these patients. A uniform definition based on global, prospectively collected, and validated data is essential, which can provide a sufficient theoretical basis for standardized clinical treatment. To develop a comprehensive definition, patients with chronic liver disease (with or without cirrhosis), with any type of precipitating factor, and extra-hepatic organ failures should be included. APASL, through AARC, took up this challenge and initiated a worldwide collaboration to develop a new consensus on ACLF that would be relevant to patients universally. The AARC invited scientists and opinion leaders worldwide, including those not affiliated with any existing consortium, to contribute unbiased perspectives. They involved a systematic, multilayered methodology to identify and seek solutions for the most critical and controversial aspects of ACLF. A universally accepted definition would be crucial for education, research in liver-directed therapies, and improving patient outcomes. Sixteen most important, controversial questions and areas were identified, following multiple virtual meetings.

AUTHORS' VIEWPOINT

The authors' viewpoint and salient features of the KYOTO consensus are as follows:[26]

- *ACLF definition:* To bring global acceptability, they proposed to classify ACLF into type A and type B. Type A ACLF includes components from APASL, COSSH, Japanese, AASLD, and Mexican criterias. It included patients with a first-time acute insult causing liver failure in a patient with an underlying chronic liver disease or cirrhosis. Patients with previous decompensation or extrahepatic insults were excluded. It can be reversible and is associated with high (30–40%) 28-day mortality.

  Type B ACLF includes components from EASL-CLIF, AASLD, and NACSELD. These included patients with type A, as well as those with previous decompensation and hepatic and extrahepatic insults leading to organ failures, including infection, and is associated with high (40–50%) 28-day mortality.
- *The concept of ACLF and the impact of sepsis on the natural history of cirrhosis:*
  - Compensated and decompensated cirrhosis are the two stages of cirrhosis. Decompensation is defined as the development of encephalopathy, variceal bleed, or ascites in patients with cirrhosis, and acute decompensation is the development of cirrhosis-related complications within 4 weeks of onset, requiring urgent treatment. Liver-related decompensated cirrhosis is the most common cause of mortality.

JAYPEE BROTHERS

- Removal or control of inciting causes in defining re-compensation, which pertains to alcohol abstinence in alcohol-associated liver disease, suppression of viral load in hepatitis B, sustained virological response in hepatitis C, suppression of disease activity in autoimmune disease for ≥1 year in patients with decompensated cirrhosis, coupled with improvement in the tests of the liver function, is suggestive of re-compensation. The reversal of parameters defined for ACLF is an important therapeutic goal, as it will help decongest the transplant list.
- The chances of bacterial infection as a precipitant of ACLF are unlikely in patients with definitive evidence of hepatotropic acute insult. These can be considered if there is no other identifiable cause of decompensation. The presence of infections and associated extrahepatic organ failures causes a worsening of 30-day mortality and poor response to treatment. Clinical examination, biochemistry, and using the quick SOFA score can help identify early deterioration and sepsis in these patients. Use of procalcitonin and acute-phase reactant levels can aid in the early diagnosis of sepsis and subsequent treatment.

▪ *Defining the underlying chronic liver disease and the impact of acute insult:*

- In a patient presenting with ACLF, chronic hepatitis and/or significant fibrosis without cirrhosis should be taken as a chronic liver disease. Metabolically associated fatty liver disease and metabolic-associated steatohepatitis in ACLF with significant fibrosis should be considered as chronic liver disease. For making a diagnosis of chronic liver disease and cirrhosis, detailed history, physical examination, laboratory tests, and endoscopic or radiological investigations must be considered. All subsequent episodes of ACLF should be evaluated and managed like the index patients of ACLF.
- With changing trends, alcohol is now the most common cause for acute hepatic injury as well as for the underlying chronic liver disease in Asia. Drug-induced liver injury, autoimmune hepatitis (AIH), and nonalcoholic steatohepatitis have shown an increasing trend. HBV infection–reactivation of hepatitis B-induced ACLF, as well as acute HAV/ HEV/ HCV-induced ACLF, shows a decreasing trend over a period of time in particular areas. Patients with diabetes mellitus or obesity have increased mortality with ACLF.
- As a strong recommendation, they suggested that alcohol-associated hepatitis, alcohol-associated ACLF, and jaundice in a patient with decompensated cirrhosis are distinct clinical entities based on pathophysiology and management. AIH is not a rare cause of ACLF. Corticosteroids are the drug of choice in patients with AIH and AIH ACLF (grades I and II), with no contraindications. In a proportion of patients with compensated chronic liver disease, variceal bleeding can lead to ACLF and is associated with increased mortality. Transjugular intrahepatic portosystemic shunt (TIPS) reduce the risk of developing ACLF. The diagnosis of drug-induced

JAYPEE BROTHERS

ACLF is very challenging, and the prognosis of severe drug-induced ACLF is poor in the absence of LT.

- *Prognostic scores and treatment of ACLF:*
  - The severity scores must be assessed on days 0, 3, 7, and 14 to identify individuals requiring urgent liver transplants, and the prognostic models specific for ACLF predict mortality at days 30 and 90. The AARC score is a validated scoring system for ACLF and is more accurate in comparison with MELD/MELD-Na, CLIF-SOFA, and SOFA scores for patients with ACLF.
  - Liver biopsy is important in distinguishing ACLF from acute liver failure. It is especially beneficial for patients in whom the presence and stage of underlying chronic liver disease and/or the cause of chronic liver disease are unclear. A transjugular liver biopsy helps in diagnosing/confirming the cause of acute injury, especially in patients with doubtful clinical diagnostic parameters. With increased emerging trends, drug-induced liver injury and alcohol-associated hepatitis require liver biopsy-based diagnostic confirmation. They concluded that liver histology in conjunction with clinical severity scores should be used for prognostication of these patients.
  - Nutritional assessment should be done using conventional methods in patients with ACLF, and these patients must receive 30–35 kcal/kg/day (actual body weight corrected for ascites) or 1.3× resting energy expenditure/kg (ideal body weight as per height) and 1.2–1.5 g/kg of protein per day, preferably through the oral route. If the individual fails to achieve a caloric intake of 21 kcal/kg/day per oral feed, then enteral nutrition through the nasogastric/nasojejunal tube is recommended. It is suggested to use a carbohydrate-rich, late-evening snack in these patients and omega-3 fatty acid infusions for the prevention of sepsis.
  - A 2-log reduction in hepatitis B virus DNA levels after 2 weeks of treatment therapy is associated with improved survival. Potent antiviral drugs, such as tenofovir alafenamide, tenofovir disoproxil fumarate, or entecavir, should be started immediately in all HBV-infected ACLF patients at presentation.
  - They recommended using corticosteroids for alcohol-related ACLF patients who have evidence of alcohol-associated hepatitis. Corticosteroids can also be used in patients with related AIH and biopsy-proven drug-induced ACLF who have evidence of AIH. Patient selection for a short course of steroid therapy should be made, using scoring systems like MELD and AARC, and close monitoring for and managing potential complications, such as infections and gastrointestinal bleeding, should be done. It is preferred not to use prophylactic antibiotics.
  - Therapeutic plasma exchange (TPE) may be used in patients with ACLF as a bridging modality to liver transplant, with the number of sessions and type of plasma exchange being determined clinically. Currently available artificial liver support systems, including Molecular Adsorbent Recirculating System (MARS, have not shown a survival advantage, and their use is not recommended in patients with ACLF.

JAYPEE BROTHERS

- Liver transplant is the only definitive therapy for grades II and III ACLF, and these patients should be transplanted as soon as possible. The benefit of transplant in ACLF should be assessed based on the severity of the acute liver injury, the reversibility of an underlying liver disease, and the prognosis of associated extrahepatic organ failure. The patient outcomes of LT for ACLF are similar to LT for non-ACLF, but it is associated with a more tremulous course.

They made a strong recommendation with an availability of a moderate level of evidence that the presence of uncontrolled sepsis with or without two or more organ failures, advanced azotemia or increase in creatinine by 300% from baseline or the need for renal replacement therapy, PaO_2/FiO_2 ratio below 150 mm Hg, a noradrenaline dose exceeding 1 μg/kg/min, and/or serum lactate levels >4 mol/L to be considered as conditions for temporary unsuitability for liver transplant. The following scores: AARC >13, COSSH ACLF II score of <7 or >10, CLIF-C >64, and TAM score >1 indicate futility of liver transplant in ACLF. The transplant outcomes in living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT) are comparable at 1 year, and patients should have demonstrable psychological stability following a thorough psychosocial assessment before being considered for a liver transplant.

REVIEWERS' VIEWPOINT

Acute-on-chronic liver failure in the Western and Eastern regions has been defined, including different subsets of patients, because of which the diagnosis remains a contentious issue. Variations in diagnostic criteria among different guidelines have sparked significant debates, with discrepancies being observed in defining severe liver dysfunction. The KYOTO Consensus tried to address a long-standing need for clarity and standardization, with special focus on improved communication, research comparability, and possibly translating into better patient outcomes. An attempt at unifying definition and classification balances inclusivity (APASL) with clarity on prognosis (ESAL-CLIF) and also provides actionable subtyping to guide urgency and management. Though strong recommendations are made, the available evidence is low and requires validation across diverse settings, especially the resource-limited ones. However, these different definitions seem to be a continuum, with patients developing APASL ACLF (liver failure), progressing to organ involvement (EASL-CLIF), and then finally succumbing to multiorgan failures (NACSELD).

The spectrum of decompensation in patients with chronic liver disease or cirrhosis is extensively explained. The prognosis and scoring system endorse scores validated for ACLF-specific contexts and also emphasize close dynamic monitoring to detect early changes in deterioration or the path to recovery. Frequent scoring use may strain the resource-limited, further highlighting the uncertainty that MELD–ACLF combination has a low strength of recommendation. It provides a comprehensive treatment framework with integrated intensive care-level supportive care, early and aggressive management of infection, bridging therapies such as TPE, and disease-specific interventions, including the use of antivirals for HBV and steroids in a specific subcohort of patients [alcohol-associated hepatitis-induced ACLF/drug-induced liver injury (DILI)]. On the nutritional aspect, they

JAYPEE BROTHERS

advocate structured strategies with a calorie requirement of 30–35 kcal/kg/day (1.2–1.5 g protein/kg/day), early enteral nutrition, and omega-3 supplementation to reduce the risk of sepsis. Though the nutritional targets are well defined, high-quality data on outcomes related to specific feeding strategies are still lacking.

It also encourages exploration of fecal microbiota transplant (FMT), regenerative approaches [granulocyte colony-stimulating factor (G-CSF), mesenchymal stem cells (MSCs)], and immune-modulating treatments, though the majority remain in the investigational stage. The main focus of future research can include studying a timeline and sequence of the reversal of ACLF; natural history of recompensated cirrhosis, and its impact on ACLF; risks and benefits of albumin therapy; safety and efficacy of nonselective beta-blockers; role of TIPS as a bridging modality in intractable ascites and variceal bleeding; nutritional strategies as an improvising therapy and improvement in survival; and role of N-acetylcysteine (NAC) in preventing drug-induced hepatotoxicity in patients of ACLF.

CONCLUSION

This article presents a valuable, timely, sincere, and extensive effort to unify regional perspectives and clarify the definition, diagnosis, and management of ACLF within the Asian cohort. A certain group of Western investigators, not in complete agreement with many of the observations and definitions reported, strongly supports the attempt to harmonize the existing diagnostic criteria of ACLF. In continuum, they recommend planning a large international prospective longitudinal study with this specific aim. The main strength of this consensus lies in the collaborative approach and the attempt to bridge gaps between Eastern and Western clinical frameworks. However, while it provides a foundational step forward, the article would benefit from more robust data integration and critical engagement with alternative viewpoints. Moving ahead, the success of the KYOTO Consensus will depend on its clinical and practical applicability, global harmonization, and the extent to which future research can validate and refine its recommendations across diverse patient populations.

ARTICLE 5

A Review of Gut Failure as a Cause and Consequence of Critical Illness: Consensus Article[33]

Soranno DE, Coopersmith CM, Brinkworth JF, Factora FNF, Muntean JH, Mythen MG, et al. A review of gut failure as a cause and consequence of critical illness.

Crit Care. 2025:29;91. https://doi.org/10.1186/s13054-025-05309-7

INTRODUCTION

In critical ill patients, intestinal permeability increases permitting translocation of bacteria and/or bacterial products. At a cellular level, the epithelial function is altered causing increased epithelial cell death and decreased

JAYPEE BROTHERS

proliferation due to compromise of the homeostasis of the epithelial monolayer. Loss of the gut microbial community's taxonomic diversity and appearance of new virulence factors cause dysbiosis which activates maladaptive pro- and anti-inflammatory signals leading to both tissue damage and susceptibility to infections. Crosstalk occurs between the gut and every major organ system. Splanchnic vasoconstriction and dysfunctional gut/gastrointestinal (GI) failure is often the first in a cascade of events leading to multiorgan dysfunction syndrome (MODS).[34]

CLINICAL QUESTION

The key role of the gut in critical illness was the subject of the 10th Perioperative Quality Initiative meeting. The authors (who were a part of this conference) summarized the current state of the literature, and key knowledge gaps were identified for future study as there are very few reliable measures of gut function in critical illness and therapeutic strategies have not been shown to conclusively demonstrate benefit, and care is still largely supportive.[33]

METHODOLOGY

The Perioperative Quality Initiative Group convened in Cleveland, Ohio, on June 24, 2023, to summarize what is known and establish future research directions related to the gut in critical illness. The authors performed a comprehensive literature review, summarized the literature, and identified key knowledge gaps.

WHAT DOES LITERATURE TELL US

- *Healthy gut:*
  - *Gastrointestinal tissue:* Microbial incursions into host tissues is taken care of by the innate and adaptive immune cells in the lamina propria which acts a barrier. Intestinal epithelial cells (IEC) line the gut, and these immune cells maintain the gut microbiota in a commensal state.[35]
  - *Microbiota:* The gut microbiota primarily consists of bacteriophages infecting bacteria which are called gut microbiota/gut microbiome; the density and complexity increase along the GI tract. They extract energy from ingested food, regulate molecules used in communication between the gut and other organs, and fight pathogens.[36]
  - *Gut–mucosal barrier:* A single cell layer epithelium separates the gut content from the human host. The time from cell birth to cell death of the secretory stem cells is 3–5 days and they differentiate into hormone-producing enteroendocrine cells, mucus-producing goblet cell, chemosensory tuff cells, and defensin-producing Paneth cell. The intestinal barrier is regulated to prevent microbes from leaving the lumen. Epithelial damage is the only unrestricted pathway for intact bacteria to cross the lumen other than direct cellular invasion and transcytosis.[37]
  - *Blood supply and lymphatics:* Areas supplied by mesenteric vessels are compromised early in stress/shock states so that the vital organs (heart, lungs, and liver) remain perfused. The capillaries and venules form a looped counter-current pattern in the submucosal plexus. When perfusion is reduced, the tip of the microvilli gets hypoxic leading to apoptosis and necrosis in epithelial cells. The lymphatic system of the gut is also a

JAYPEE BROTHERS

unidirectional connection between the gut and the body.[38]

GI Tract in Critical Illness

Gut injury can originate in the gut lumen or from a site outside the gut. The common causes of gut failure in critical illness are compromised GI blood supply, lymphatic dysfunction, epithelial damage, and alterations in the gut microbiota.

- *Blood supply:* In a healthy state, 25–30% of the cardiac output and oxygen delivery at rest is delivered to the splanchnic organs. During stress or hypovolemia, to maintain the blood pressure and perfusion of the vital organs, the alpha-adrenergic receptors are activated causing the smooth muscle to contract leading to splanchnic vasoconstriction, reducing the blood flow to the splanchnic organs **(Table 1)**. When this insult to the gut is prolonged, it can lead to ischemia and damage to the intestinal mucosa. Hemodynamic changes occur when 10–15% of the blood volume is lost; however, one should be aware that as little as 5% of blood loss can lead to gut mucosal hypoperfusion.[39]

TABLE 1: Distribution of blood flow in critical illness.

Nonstress	*Organ*	*Stress*
100%	Lung	100%
4–5%	Heart	↑
13–15%	Brain	↑
25–30%	Splanchnic	↓↓↓
20%	Kidney	↓
15–20%	Muscle	↓
3–5%	Skin	↓
3–5%	Bone and fat	↓

Note: During stress states/critical illness, blood flow is redistributed away from the gut to favor perfusion of the heart, brain, and lungs.

- *Gut epithelium*
  - *Epithelial cells:* Epithelial cell apoptosis increases, proliferation decreases, and migration slows in septic patients. Prevention of gut epithelial apoptosis by targeted antiapoptotic therapy prevents sepsis-associated hyperpermeability and improves survival in preclinical models of both *Pseudomonas* pneumonia and intra-abdominal sepsis.[40]
  - *Junctions between epithelial cells:* Critical illness causes compromise of the epithelial barrier integrity leading to increased permeability in all interepithelial pathways.
  - *Microbiota:* Microbes with the GI tract can primarily be responsible for gut failure or can be responsible for perpetuating or increasing the illness after the gut fails.
  - *Microbial virulence:* Bacteria that infect the GI tract and those that first infiltrate another site in the body and then migrate to the GI tract are called true pathogens or acquired microbes. Critical illness can also activate the virulent mechanisms in the normally commensal gut microbes. Changes in the available resource, stress signals or damaged bacteria, or host signals of damage and inflammation initiate new genetic programs which allow the bacteria to adapt, survive, damage host tissue, trigger inflammation, and activate innate and adaptive immunity.[40]
  - *Microbial dysbiosis:* In sepsis/critical illness, there is a significant change in the taxonomy of the gut bacteria community due to antibiotics, changes in nutrition, and various interventions, which is associated

JAYPEE BROTHERS

with an increased risk of adverse outcomes. The consistent feature of critical illness is a decrease in taxonomic diversity and loss of short-chain fatty acid production. Dysbiotic communities predominantly have Enterobacteriaceae (especially proteobacteria) and *Enterococcus* spp. It is difficult to assess whether dysbiosis is a cause or a consequence of a disease in the GI tract.[41]

- *Consequence of GI failure:*
  - *Microbial translocation:* This can be active that allows bacteria to cross the barrier or passive when the barrier itself fails. Severe epithelial damage allows the bacteria to drift across, and these bacteria anchor within the cells causing physical damage and buildup of toxins at the cell surface activating the cellular microbe-associated molecular pattern (MAMP) sensors.
  - *Local response to gut barrier failure:* Bacteria interact with the innate and adaptive immune systems activating the host defenses to contain the infection and repair the intestinal barrier.
  - *Release of extracellular vesicles (EV):* EVs are released when the gut barrier fails, and they have immunostimulatory or immunoregulatory functions where either T-cell activation occurs or there is release of transforming growth factor-beta (TGF-β).
  - *Innate immune response:* Neutrophils and macrophages are activated in the intestinal lamina propria when there is gut barrier disruption due to epithelial cell injury. When antimicrobials dysregulate microbes, they exacerbate the pro-inflammatory response and the damage to the gut increases. Recent evidence suggests that intestinal macrophage activation during sepsis depends on the barrier function where they act to restrain inflammatory response and macrophages largely influence gut dysbiosis and epithelial dysfunction.
  - *Adaptive immune response:* When the mucosal barrier fails, the number of CD4+ T cells increase dramatically to counter intestinal inflammation, stimulate intestinal stem cell proliferation, facilitate epithelial restoration, and aid in healing of the gut by secreting immunoglobulin A (IgA) and down-regulating chemokines.[42]
  - *Dissemination of translocated material:* The gut lymphatic system not only acts as a passage for the transfer of pathogens from the gut to the distant organs, but also contributes to the systemic inflammatory response by spreading the proinflammatory cytokines to other parts of the body, thereby playing a dual role.[43] Microvascular dysfunction in sepsis causes increased permeability, fluid and protein leakage, and formation of microthrombi which further compromises the blood flow. Pathogens that breach the gut barrier are carried in the bloodstream to distant organs. Lymphatic dysfunction impairs the clearance of inflammatory mediators and immune cells which continues the vicious inflammatory cycle.
  - *Systemic response to gut barrier failure:* Systemic spread of intestinal content leads to widespread inflammation and bacteremia causing release of MAMPS and damage-associated molecular patterns (DAMPS) leading to MODS.

JAYPEE BROTHERS

Secondary infections in the later stages of sepsis could be due to the anti-inflammatory pathway response. Hepatic sinusoidal endothelial cells play an important role in the integrity of the gut–liver barrier axis. In both cirrhosis and sepsis, intra-abdominal hypertension occurs due to increase in intestinal permeability and bacterial translocation, decreasing the perfusion pressure and increasing gut edema which can lead to ischemia, further increasing gut failure. The microbiota may also affect the blood–brain barrier and activate the vagal nerve stimulus to the spleen which activates the cholinergic receptors on macrophages to decrease the release of pro-inflammatory cytokines. The type and amount of neurotransmitters delivered from the gut change in sepsis leading to altered mentation.

- *Lipopolysaccharides (LPS)/endotoxin release from the compromised gut:* LPS is a microbe-derived mediator of critical illness. Systemic effects of LPS include deleterious effects on the cardiac, pulmonary, hepatic, renal, vascular, and neurological systems as well as the metabolome **(Table 2)**.

- *Diagnosing GI failure:*
  - *Clinical assessment of GI function:* Signs of GI failure are nonspecific, and it is difficult to diagnose GI failure in critical illness due to the large number of functions that the GI tract performs and the lack of clinically measurable indicators of GI function. A large international effort recently proposed a core outcome set for daily monitoring of GI function in all critically ill patients as no standardized method for daily monitoring of GI function exists in the intensive care unit (ICU)—abdominal distension, bowel dilatation, intra-abdominal pressure, abdominal pain, stool passage, vomiting, GI bleeding (upper and lower), use of parenteral

TABLE 2: Downstream effects of endotoxemia.

Organ system	*Effects*
Neurological	• Brain inflammation • Neurodegeneration • Memory deficits
Pulmonary	• Lung inflammation • Pulmonary hypertension • Free radical and oxidative stress
Cardiac	• Impaired contractility • Inflammation • Oxidative stress • Impaired energy metabolism • Impaired autophagy
Hepatic	• Hepatic necrosis • Hepatitis • Acute liver failure • Hepatic fibrosis • Cirrhosis • Chronic liver failure
Endothelium	• Glycocalyx damage • Platelet aggregation • Leukocyte infiltration • Capillary leak • Intravascular volume contraction
Renal	• Sepsis-induced AKI • Sepsis-associated AKI • Inflammation • RAAS dysfunction • Mitochondrial dysfunction
Metabolism	• Insulin resistance • Obesity • Diabetes mellitus • Deficit in energy production

(AKI: acute kidney injury; RAAS: renin-angiotensin-aldosterone system)

Note: Endotoxemia results in systemic sequelae, impacting numerous organ systems and may result in multiorgan dysfunction.

JAYPEE BROTHERS

nutrition due to intolerance of enteral nutrition (EN), prokinetics, postpyloric feeding due to gastroparesis, lower GI paralysis, gastroparesis, and intolerance to EN.[44]

- *Assessing the gut–microbial barrier:* Plasma citrulline, a marker of functional enterocyte mass, and plasma or urinary intestinal fatty acid-binding protein (I-FABP), a marker of enterocyte injury, have been proposed as measures of gut barrier integrity and shown promise in small clinical trials. However, they are not available real time for clinical use; assays are time consuming and not widely available. Plasma citrulline levels normalize in renal dysfunction with low enterocyte functional mass and glutamine deficiency even with normal intestinal activity. Zonulin dysregulation has been reported in a wide range of diseases associated with mucosal barrier failure, including sepsis. sCD14 has been used as a surrogate marker for bacterial translocation and gut barrier dysfunction, and even as a potential target for developing monoclonal antibodies to treat sepsis as it is produced primarily by macrophages and hepatocytes as part of the innate immune surveillance for LPS and endotoxemia.[45] Both are, however, nonspecific and raised levels are seen in various other clinical conditions.

■ *Treating GI failure:*

- *Supportive GI care:*
  - *Nutrition:* Even though EN is important for recovery of the damaged gut, various factors should be considered including how unstable is the patient, vasopressor dose and agent(s), route of administration of EN (gastric vs. postpyloric), formulation of EN, amount of EN (trophic vs. full feeds), and the underlying disease process.
  - *GI perfusion:* It depends on cardiac output, intravascular volume, and vascular tone and is vital for delivery of oxygen and nutrients and removal of toxic metabolic by-products from the gut mucosa. Euvolemia and restoring intravascular blood volume should precede the use of moderate- to high-dose vasopressors.[46]
  - *Inflammation and immune activation:* Even though therapies to treat sepsis are not selective for the gut inflammation and immunity in critical illnesses, these can restore gut homeostasis.
  - *Pattern recognition receptor blockade:* Anti-TREM-1 therapeutics, nangibotide (also known as LR12), has undergone both phase 2a and phase 2b (ASTONISH) trials for use in patients with septic shock. The preclinical results with nangibotide were very promising, and early trials suggested that it was safe in patients. However, a recent phase 2b trial failed to achieve the primary outcome of improvement in Sequential Organ Failure Assessment (SOFA) score across all patients.[47]
  - *Decreasing cytokine production or blocking function:* Cytokine production and release can be suppressed using corticosteroids, recombinant human activated protein C, drugs targeting Janus kinases

JAYPEE BROTHERS

(JAK), and several monoclonal antibodies. Corticosteroids have shown to improve survival in both randomized controlled studies and meta-analyses in septic shock (and more recently community-acquired pneumonia) and are recommended by international consensus guidelines.[48]

- *Manipulating the cellular components of inflammation and immunity:* The unique feature of neutrophils and macrophages that mediate directional migration has been manipulated in some animal models in which reduction of inflammation has been seen. Stimulating phagocytes and increasing leukocyte recruitment have also been attempted in models of abdominal sepsis.
- *Gut–mucosal barrier:* Therapies to restore gut barrier are related to reinforcing the junction between epithelial cells. Larazotide acetate, a single-chain eight amino acid zonulin antagonist, has shown to restore intestinal barrier function in celiac disease, but a large phase 3 clinical trial was ceased due to poor results.
- *Microbes and their components:*
  - *Probiotics:* They are live microorganisms that are introduced into the body and are thought to provide a health benefit to the host. Even though the largest meta-analysis on probiotics in critical illness included 65 randomized controlled trials, with 8,483 patients demonstrating that probiotics may reduce the risk of ventilator-associated pneumonia, healthcare-associated pneumonia, ICU length of stay, hospital length of stay, and duration of invasive mechanical ventilation (all with low certainty), the post hoc sensitivity analyses without a high risk of bias studies negated the beneficial effect of probiotics on nearly all outcomes including mortality (moderate certainty).[49]
- *Fecal microbial transplantation (FMT):* FMT is the transfer of an entire intestinal microbial community from a healthy donor to a diseased recipient. It has been used successfully for recurrent *Clostridia difficile* colitis. Antibiotics must be ceased prior to FMT, which is frequently difficult to do in the ICU setting because initiation or continuation of antibiotics will almost certainly alter the microbiome after FMT.[50]
- *Selective digestive tract decontamination (SDD):* SDD aims to prevent or eradicate oropharyngeal and intestinal carriage of pathogens without adversely impacting the remaining microbiome of the patient. The data supporting its use is compelling with drastically reduced respiratory tract infections, fewer infections, and decreased mortality. However, most studies are a decade old and are in settings with low antimicrobial resistance.
- *Extracorporeal blood purification (EBP):* This is performed via hemadsorption or plasmadsorption, adsorptive extracorporeal therapies impact immune dysfunction via nonselective removal of cytokines, pathogens, endotoxin, and inflammatory factors.

JAYPEE BROTHERS

The EUPHRATES randomized controlled trial did not demonstrate improvement in 28-day survival from hemadsorption EBP in patients with septic shock and elevated LPS levels.[51]

- *Antibiotics, vaccines, immunoglobulin, and monoclonal antibodies:* Early treatment with antibiotics remains the mainstay of treatment for bacterial infection. Monoclonal antibodies, especially recombinant monoclonal antibodies, are a more modern version of vaccination and hyperimmune serum.

REVIEWERS' VIEWPOINT

This review gives novel insights and advancements about GI failure:

- The review presents new insights into the cellular and molecular mechanisms underlying gut barrier failure, including the role of tight junctions, apoptosis, and cellular signaling pathways.
- It explores the potential for targeted therapies aimed at preserving barrier integrity and modulating the microbiome, mentioning therapies like antiapoptotic treatments and permeability modulation strategies, though noting limitations in large-scale clinical trials.
- The article also discusses the impact of gut dysbiosis on distant organs and systems beyond the gut, like its influence on atherosclerosis through metabolites like trimethylamine-N-Oxide (TMAO), highlighting the far-reaching effects of gut failure.

IMPACT ON CURRENT PRACTICE AND TAKE-HOME MESSAGE

- The review underscores the significant challenges in diagnosing gut failure due to the lack of specific diagnostic tests for gut function.
- It emphasizes the need for developing and validating reliable diagnostic tools to detect gut dysfunction early and guide targeted interventions.
- The article stresses the importance of identifying key molecular mechanisms of gut barrier failure for future therapeutic development and designing novel strategies, potentially involving personalized approaches based on patient-specific GI tolerance and function.
- It points toward the need for further research to evaluate the efficacy of novel therapeutic interventions, including adjunctive therapies targeting gut permeability and microbiome restoration.

REFERENCES

1. Schumacher J, Henschler R, Buhmann R, Petros S, Weidhase L, Veelken R, et al. Exploring the Impact of Therapeutic Plasma Exchange on Organ Function in Patients With ACLF: A Retrospective, Single-center Propensity Score-matched Cohort Study. J Clin Exp Hepatol. 2025;15(5):102550.
2. Amin A, Mookerjee RP. Acute-on-chronic liver failure: definition, prognosis, and management. Frontline Gastroenterol. 2019;11(6):458-67.
3. Blasco-Algora S, Masegosa-Ataz J, Gutiérrez-García ML, Alonso-López S, Fernández-Rodríguez CM. Acute-on-chronic liver failure: Pathogenesis, prognostic factors and management. World J Gastroenterol. 2015;21(42):12125-40.
4. Moreau R, Tonon M, Krag A, Angeli P, Berenguer M, Berzigotti A, et al. EASL Clinical Practice Guidelines on acute-on-chronic liver failure. J Hepatol. 2023;79(2):461-91.
5. Tan EX, Wang MX, Pang J, Lee GH. Plasma exchange in patients with acute and acute-on-chronic liver failure: A systematic review. World J Gastroenterol. 2020;26(2):219-45.
6. Stahl K, Busch M, Fuge J, Schneider A, Manns MP, Seeliger B, et al. Therapeutic plasma

JAYPEE BROTHERS

exchange in acute on chronic liver failure. J Clin Apher. 2020;35(4):316-27.
7. Beran A, Mohamed MFH, Shaear M, Nayfeh T, Mhanna M, Srour O, et al. Plasma exchange for acute and acute-on-chronic liver failure: a systematic review and meta-analysis. Liver Transpl. 2024;30(2):127-41.
8. Swaroop S, Arora U, Biswas S, Vaishnav M, Pathak P, Agarwal A, et al. Therapeutic plasma-exchange improves short-term, but not long-term, outcomes in patients with acute-on-chronic liver failure: a propensity score-matched analysis. J Clin Apher. 2023;38(4):376-89.
9. Kumar SE, Sithamparapillai K, Choudhury AK, Bharadwaj PK, Trebicka J, Karvellas CJ, et al. Therapeutic plasma exchange in patients with acute-on-chronic liver failure improves survival—An updated meta-analysis. Hepatol Int. 2025;19(2):213-24.
10. Kulkarni AV, Maiwall R, Arora V, Jindal A, Thomas S, Ali R, et al. Addition of midodrine to albumin reduces the incidence of complications of large-volume paracentesis: an RCT comparing midodrine, terlipressin, and albumin. Hepatol Int. 2025;19(5):1231-41.
11. Kulkarni AV, Rabiee A, Mohanty A. Management of portal hypertension. J Clin Exp Hepatol. 2022;12:1184-99.
12. Gines A, Fernández-Esparrach G, Monescillo A, Vila C, Domènech E, Abecasis R, et al. Randomized trial comparing albumin, dextran 70, and polygeline in cirrhotic patients with ascites. Gastroenterology. 1996;111:1002-10.
13. Singh V, Dheerendra PC, Singh B, Nain CK, Chawla D, Sharma N, et al. Midodrine vs albumin for PICD prevention. Am J Gastroenterol. 2008;103:1399-405.
14. Caraceni P, Riggio O, Angeli P, Alessandria C, Neri S, Foschi FG, et al. Long-term albumin in decompensated cirrhosis (ANSWER trial). Lancet. 2018;391:2417-29.
15. Wong F, Pappas C, Curry MP, Reddy KR, Rubin RA, Porayko MK, et al. Terlipressin plus albumin for HRS. N Engl J Med. 2021;384:818-28.
16. Solà E, Solé C, Simón-Talero M, Martín-Llahí M, Castellote J, Garcia-Martínez R, et al. Midodrine and albumin in transplant candidates. J Hepatol. 2018;69:1250-9.
17. Fuller H, Tittanegro TH, Maini AA, China L, Rhodes F, Becares Salles N, Mukhopadhyay S, Moore B, O'Brien A. Hyperbilirubinemia at hospitalization predicts nosocomial infection in decompensated cirrhosis: Data from ATTIRE trial. Hepatol Commun. 2025;9(4): e0648.
18. Mansour D, McPherson S. Management of decompensated cirrhosis. Clin Med (Lond). 2018;18(Suppl 2):s60-5.
19. Sarin SK, Choudhury A, Sharma MK, Maiwall R, Al Mahtab M, Rahman S, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL): an update. Hepatol Int. 2019:13(4):353-90.
20. Schultalbers M, Tergast TL, Simon N, Kabbani AR, Kimmann M, Zu Siederdissen CH, et al. Frequency, characteristics, and impact of multiple consecutive nosocomial infections in patients with decompensated liver cirrhosis and ascites. United European Gastroenterol J. 2020;8(5):567-76.
21. Pleguezuelo M, Benitez JM, Jurado J, Montero JL, De la Mata M. Diagnosis and management of bacterial infections in decompensated cirrhosis. World J Hepatol. 2013;5(1):16-25.
22. Bajaj JS, O'Leary JG, Tandon P, Wong F, Garcia-Tsao G, Kamath PS, et al. Nosocomial Infections Are Frequent and Negatively Impact Outcomes in Hospitalized Patients with Cirrhosis. Am J Gastroenterol. 2019;114(7):1091-100.
23. Xu X, Yu X, Gong K, Tu H, Yao J, Lan Y, et al. Acute decompensation events differentially impact the risk of nosocomial infections and short-term outcomes in patients with cirrhosis. Front Med (Lausanne). 2022; 9:962541.
24. Zhang X, Qin D, Liu G, Li F, Peng J, Xiang Y. Risk factors of nosocomial infection in patients who underwent artificial liver support system: a retrospective case-control study. Eur J Gastroenterol Hepatol. 2023;35(5):604-8.

JAYPEE BROTHERS

25. Kutmutia R, Tittanegro T, China L, Forrest E, Kallis Y, Ryder SD, et al. Evaluating the Role of Antibiotics in Patients Admitted to Hospital with Decompensated Cirrhosis: Lessons from the ATTIRE Trial. Am J Gastroenterol. 2023;118(1):105-13.
26. Choudhury A, Kulkarni AV, Arora V, Soin AS, Dokmeci AK, Chowdhury A, et al. Acute-on-chronic liver failure (ACLF): the 'Kyoto Consensus'-steps from Asia. Hepatol. Int. 2025;19:1-69.
27. Hernaez R, Sola E, Moreau R, Ginès P. Acute-on-chronic liver failure: an update. Gut. 2017;66:541-53.
28. Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology. 2013;144(1426–1437):1437.e1421-9.
29. Karvellas CJ, Bajaj JS, Kamath PS, Napolitano L, O'Leary JG, Solà E, et al. AASLD Practice Guidance on Acute-on-chronic liver failure and the management of critically ill patients with cirrhosis. Hepatology. 2024;79:1463-502.
30. Sarin SK, Kumar A, Almeida JA, Chawla YK, Fan ST, Garg H, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the study of the liver (APASL). Hepatol Int. 2009;3(1):269-82.
31. Bajaj JS, O'Leary JG, Lai JC, Wong F, Long MD, Wong RJ, et al. Acute-on-chronic liver failure clinical guidelines. Am J Gastroenterol. 2022;117(2):225-52.
32. Luo J, Li J, Li P, Liang X, Hassan HM, Moreau R, et al. Acute-on-chronic liver failure: far to go-a review. Crit Care. 2023;27(1):259.
33. Soranno DE, Coopersmith CM, Brinkworth JF, Factora FNF, Muntean JH, Mythen MG, et al. A review of gut failure as a cause and consequence of critical illness. Crit Care. 2025:29;91.
34. Kellum JA, Palevsky P, Mehta R, Bellomo R, Ronco C. Acute dialysis quality initiative: methodology. Curr Opin Crit Care. 2002;8:500-1.
35. Kim HJ, Li H, Collins JJ, Ingber DE. Contributions of microbiome and mechanical deformation to intestinal bacterial overgrowth and inflammation in a human gut-on-a-chip. Proc Natl Acad Sci USA. 2016;113:E7-15.
36. Hou K, Wu ZX, Chen XY, Wang JQ, Zhang D, Xiao C, et al. Microbiota in health and diseases. Signal Transduct Target Ther. 2022;7:135.
37. Odenwald MA, Turner JR. The intestinal epithelial barrier: a therapeutic target? Nat Rev Gastroenterol Hepatol. 2017;14:9-21.
38. Cifarelli V, Eichmann A. The intestinal lymphatic system: functions and metabolic implications. Cell Mol Gastroenterol Hepatol. 2019;7:503-13.
39. Hamilton-Davies C, Mythen MG, Salmon JB, Jacobson D, Shukla A, Webb AR. Comparison of commonly used clinical indicators of hypovolaemia with gastrointestinal tonometry. Intensive Care Med. 1997;23:276-81.
40. Diard M, Hardt WD. Evolution of bacterial virulence. FEMS Microbiol Rev. 2017;41:679-97.
41. Miniet AA, Grunwell JR, Coopersmith CM. The microbiome and the immune system in critical illness. Curr Opin Crit Care. 2021;27:157-63.
42. Gomez-Bris R, Saez A, Herrero-Fernandez B, Rius C, Sanchez-Martinez H, Gonzalez-Granado JM. CD4 T-cell subsets and the pathophysiology of inflammatory bowel disease. Int J Mol Sci. 2023;24(3):2696.
43. Deitch EA. Gut lymph and lymphatics: a source of factors leading to organ injury and dysfunction. Ann N Y Acad Sci. 2010;1207(Suppl 1):E103-111.
44. Bachmann KF, Jenkins B, Asrani V, Bear DE, Bolondi G, Boraso S, et al. Core outcome set of daily monitoring of gastrointestinal function in adult critically ill patients: a modified Delphi consensus process (COSMOGI). Crit Care. 2024;28:420.
45. Gabarin RS, Li M, Zimmel PA, Marshall JC, Li Y, Zhang H. Intracellular and extracellular lipopolysaccharide signaling in sepsis: avenues for novel therapeutic strategies. J Innate Immun. 2021;13:323-32.
46. Myles PS, Bellomo R, Corcoran T, Forbes A, Peyton P, Story D, et al. Restrictive versus

JAYPEE BROTHERS

liberal fluid therapy for major abdominal surgery. N Engl J Med. 2018;378:2263-74.
47. Francois B, Lambden S, Fivez T, Gibot S, Derive M, Grouin JM, et al. Prospective evaluation of the efficacy, safety, and optimal biomarker enrichment strategy for nangibotide, a TREM-1 inhibitor, in patients with septic shock (ASTONISH): a double-blind, randomised, controlled, phase 2b trial. Lancet Respir Med. 2023;11:894-904.
48. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med. 2021;49:e1063-143.
49. Sharif S, Greer A, Skorupski C, Hao Q, Johnstone J, Dionne JC, et al. Probiotics in critical illness: a systematic review and metanalysis of randomized controlled trials. Crit Care Med. 2022;50:1175-86.
50. Limketkai BN, Hendler S, Ting PS, Parian AM. Fecal microbiota transplantation for the critically Ill patient. Nutr Clin Pract. 2019;34:73-9.
51. Dellinger RP, Bagshaw SM, Antonelli M, Foster DM, Klein DJ, Marshall JC, et al. Effect of targeted polymyxin B hemoperfusion on 28-day mortality in patients with septic shock and elevated endotoxin level: the EUPHRATES Randomized Clinical Trial. JAMA. 2018;320:1455-63.

JAYPEE BROTHERS

for detailed information on critical care books, visit our website www.ejaypee.com, for detailed information on critical care books, visit our website www.ejayp

Yearbook of
CRITICAL CARE 2025
HICS Initiative

The field of intensive care is very dynamic, and new evidence emerges almost on a daily basis. Keeping pace with all the new information, analyzing and assimilating it, and implementing its gist is the key to the practice of evidence-based medicine. The Hyderabad Intensive Care Symposium (HICS) has been at the forefront of bringing such information into the midst of keen learners of intensive care every year. However, the time constraints of a didactic meeting make it impossible to convey every advance and guideline. The team therefore took upon itself the task of compiling all the major and interesting publications of the last 12 months and having them analyzed for publication. The end result is this *Yearbook of Critical Care*.

- Comprehensive review of all major publications from July 2024 to July 2025
- Experienced and seasoned teachers as reviewers
- Systemwise compilation
- Reviewers' opinion at the end of each section
- Handy format

Srinivas Samavedam MD DNB FRCP FNB EDIC FICCM is currently the Chief Intensivist, Ramdev Rao Hospital, Hyderabad, Telangana, India. He is the President of the Indian Society of Critical Care Medicine (2025–2026) and has more than 20 years of experience as a practicing Intensivist and more than 15 years as a Teacher. He has been an Examiner for several critical care examinations and has a strong passion in sharing knowledge. He has served as the General Secretary and Vice President of the Indian Society of Critical Care Medicine (ISCCM) in the past.

Ganshyam Jagathkar MD FNB FICCM is currently the Director, Department of Critical Care, Medicover Hospitals, Hyderabad, Telangana, India. He has been the Organizing Secretary of the popular HICS symposium since inception. His passion for teaching students in a simple and crisp manner has made him a popular figure among students and young intensivists. He is currently serving as the Vice President of the Indian Society of Critical Care Medicine (ISCCM).

Buy from ejaypee

JAYPEE BROTHERS

Shelving Recommendation
CRITICAL CARE

ISBN 978-93-7202-675-7

9 789372 026757