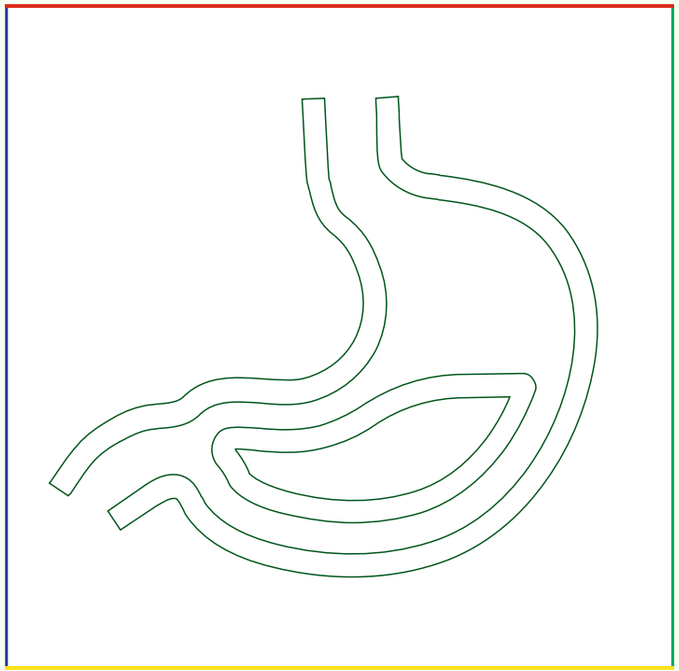
STANDARD TREATMENT GUIDELINES

MEDICAL GASTROENTEROLOGY



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STANDARD TREATMENT GUIDELINES

for

MEDICAL GASTROENTEROLOGY

Foreword

At the outset, I appreciate the work done by the respective thematic teams and coordination done by the DME. The Standard Treatment Guidelines (STG) were prepared and published in 2021 in the thick of the Covid pandemic. On the last page of these volumes the road map was mentioned. The few points are mentioned here for the recall.

"The Department of Health has been taking a systematic approach of creating and enabling multiple initiatives with a focus on prevention along with improving health care services. Health care service delivery is one of the most important services and is always seen as a barometer to assess the Governance. While it is important to develop infrastructure, an essential prerequisite is to develop systems and processes to bring in standardization in management of patient care. ……The foundation is laid and we take up the challenge to work on the unfinished agenda."

It was mentioned in the road map to have institutional mechanism to ensure updation of Standard Treatment Guidelines. The next step that was suggested was to do analysis of Karunya Arogya Suraksha Padhati (KASP) and standard treatment guidelines to work on developing a Balance Score Card to give information regarding compliance from the Hospitals and to build a "feedback loop" to improve. These initiatives remained at concept level on the last page! But following detailed discussions with Dr Vishwanathan, Director Medical Education, some of the foundational things were prioritized and given an impetus to take it to finality. In this journey, many committed doctors from various Medical Colleges of respective specialties participated. The previous coordination team members and experts were also consulted and they also participated in discussions and these Standard Treatment Guidelines are prepared.

The standard treatment guidelines will be made available in the Kerala Health portal (health.kerala.gov.in). This will enable the resource book availability not only to people within the state but to all in the country and outside our borders as well. I am confident that it will be used by students and practicing doctors. We request inputs based on the research from the Specialists and Experts. The teams shall continue to update and make any required changes in the STG by doing periodic updates.

The most important thing we all need to internalize is to have a shared vision and

work as a team to reach to a state of 'excellence'. If we take a look at the preparation of the Directorate Medical Education Management Information System, documents of each Medical Colleges, it provides information regarding 'what we are, what we do and what we aspire to do', pandemic preparedness, AMR accreditation and many more such initiatives taken on scale, which are all outcomes of collective TEAM work. This has laid a foundation for involving all the stakeholders including undergraduate and postgraduate students. This should encourage the teams in Medical Colleges to believe in themselves and build future initiatives on such a sound platform.

I express my sincere thanks to Dr Vishwanathan for his patience and bearing with relentless follow ups! I also take this opportunity to thank each and every team and their members and everyone from Directorate Medical Education and Medical Colleges who supported these initiatives.

I would like to express my sincere gratitude to all those who have contributed to publish these Standard Treatment Guidelines.

I wish all the success to DME team to make Kerala MCH as a premier knowledge hub in Medical Science.

Dr Rajan Khobragade IAS

Additional Chief Secretary
Health & Family Welfare and
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Message

Patient care today demands evidence-based, standardized, and contextually relevant clinical practice. In this regard, the publication of the **Second Edition of the Standard Treatment Guidelines** marks an important step forward in strengthening the quality, consistency, and accountability of healthcare delivery in Kerala.

The first edition laid a strong foundation for uniform clinical practice across specialties and super specialties. Since then, advances in medical knowledge, evolving treatment modalities, and the growing need for periodic updating have made it essential to revisit and refine these guidelines. The present edition reflects this commitment to continuous improvement and clinical excellence.

I am pleased to note that subject experts from various disciplines of Government Medical Colleges, private institutions and professional bodies have contributed as resource persons in the preparation of these guidelines. Their academic expertise, practical insight, and dedicated involvement have greatly enriched this edition. I deeply appreciate the sincere efforts of all the conveners, contributors, and coordinators whose collective commitment and teamwork made this publication possible.

These guidelines will serve as a valuable reference for clinicians, teachers, trainees, and healthcare institutions, helping to promote evidence-based decision-making and improve patient outcomes. I am confident that this edition will further support standardization of care and contribute to the advancement of medical education and clinical practice in the State.

I congratulate everyone involved in this commendable effort and commend this publication to all healthcare professionals.

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Contents

ABBREVIATIONS

ALF	Acute Liver Failure
ALI	Acute Liver Injury
HCC	Hepatocellular Carcinoma
HE	Hepatic Encephalopathy
HRS	Hepatorenal Syndrome
AP	Acute Pancreatitis
SAP	Severe Acute Pancreatitis
WON	Walled-Off Necrosis
UGIB	Upper Gastrointestinal Bleeding
LGIB	Lower Gastrointestinal Bleeding
ASUC	Acute Severe Ulcerative Colitis
UC	Ulcerative Colitis
IBD	Inflammatory Bowel Disease
ERCP	Endoscopic Retrograde Cholangiopancreatography
MRCP	Magnetic Resonance Cholangiopancreatography
EUS	Endoscopic Ultrasound
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
INR	International Normalized Ratio
PPI	Proton Pump Inhibitor
NAC	N-Acetyl Cysteine
SBP	Spontaneous Bacterial Peritonitis
AKI	Acute Kidney Injury
RRT	Renal Replacement Therapy
TACE	Transarterial Chemoembolization
TARE	Transarterial Radioembolization
RFA	Radiofrequency Ablation
LT	Liver Transplantation

1. UPPER GI BLEED –VARICEAL

1. SCOPE

This guideline outlines the standardized approach to the evaluation and management of acute variceal upper gastrointestinal bleeding (AVH) in adult patients with suspected or confirmed portal hypertension, particularly in the setting of cirrhosis.

It is intended for use by physicians, surgeons, emergency care providers, intensivists, and gastroenterologists involved in the acute care of such patients at secondary and tertiary healthcare facilities.

The guideline covers:

- Early recognition and risk stratification of variceal bleeding
- Initial resuscitation and hemodynamic stabilization
- Recommended laboratory and diagnostic investigations
- Pharmacological therapy including vasoactive agents and antibiotic prophylaxis
- Endoscopic management strategies
- Management of refractory bleeding
- Measures for prevention of rebleeding (secondary prophylaxis)

INTRODUCTION

Esophageal varices are present in approximately 40% of patients with cirrhosis and as many as 60% of patients with cirrhosis and ascites. Gastric varices are less common and occur in approximately 20 % of patients with cirrhosis. Ectopic varices account for less than 5 % of all varix-related bleeding episodes. Acute Variceal Hemorrhage (AVH) remains an emergent complication of cirrhosis and requires timely and effective management to prevent short-term mortality**.**The goal of resuscitation is to preserve tissue perfusion. Volume restitution should be initiated to restore and maintain hemodynamic stability. On presentation of gastrointestinal hemorrhage, those with a known or suspected history of advanced liver disease should be managed as having a portal hypertensive-related source until endoscopic confirmation. Patients presenting with AVH should be transferred to a medical care unit that provides proper levels of nursing and medical care, such as an intensive care unit.

INITIAL ASSESSMENT AND INVESTIGATIONS

INVESTIGATIONS;

1. Complete Blood Counts, Liver Function Test, PT/INR,apTT, Renal Function tests and electrolytes -The hematocrit or hemoglobin values immediately after the onset of bleeding may not reflect blood loss accurately, because it takes more than 24 to 72 hours for the vascular space to equilibrate with extravascular flui
2. ECG

GENERAL MEASURES

1. Airway Protection

- Place the patient on the side (left lateral decubitus).
- Care of the airway should be maintained as the patient is at high risk of bronchial aspiration of gastric contents and blood.
- Intubation is recommended before endoscopy in patients with altered consciousness and those actively vomiting blood
- Pulse oximetry and oxygen administration are essential to maintain adequate blood oxygen saturation

2. Role of Nasogastric tube

In patients with severe UGI bleeding, lavage with a nasogastric tube may help evacuate blood and clots from the stomach to prevent aspiration and allow adequate endoscopic visualisation.

3. Obtain an IV access

To facilitate resuscitation at least two 16 gauge cannulae should be placed, large enough to allow rapid volume expansion.

A central line should not replace a cannula.

4. Restore the circulation

- Volume expansion can usually be done with crystalloids. No benefit has been demonstrated with the use of colloids compared to crystalloids.
- Red blood cells are used to improve oxygen delivery to tissues in case of severe anemia.

A restrictive transfusion strategy is adequate in most patients with acute GI bleeding, with a hemoglobin threshold for transfusion of 7 g/dl and a target range of 7-8 gm%. The threshold for transfusion may be higher[>8gm%] in patients with massive hemorrhage or in those with underlying conditions like CAD that preclude

an adequate physiological response to acute anemia.

5. Antibiotic prophylaxis

Antibiotic prophylaxis is recommended in cirrhotic patients with acute GI bleeding because it reduces the incidence of infections (especially SBP) and improves control of bleeding and survival.

- Treatment should be initiated on presentation of bleeding and continued for up to 7 days. IV Ceftriaxone (1g/24 h) is the first choice in patients with decompensated cirrhosis. Oral quinolones (Norfloxacin 400 mg BD) should be used in the remaining patients

6. Proton pump inhibitors

Proton pump inhibitors [eg: Pantoprazole at 80mg stat and 8mg/hr infusion] should be started in all cases of UGI bleeding at predentation.Proton pump inhibitors should be discontinued once AVH has been confirmed as the bleeding source in the absence of other specific indications.

7. Nutrition and anti Hepatic encephalopathy measures

Enteral feeding should be started once the AVH episode has been controlled. The presence of variceal bands does not contraindicate the placement of a feeding tube if indicated.

In patients with AVB and hepatic encephalopathy, bouts of hepatic encephalopathy should be treated with lactulose (oral or enemas).

In patients presenting with AVB, rapid removal of blood from the gastro-intestinal tract (lactulose oral or enemas) should be used to prevent hepatic encephalopathy.

8. Vasoactive drugs

Terlipressin, somatostatin or octreotide should be initiated as soon as AVH is suspected. Starting vasoactive drugs before endoscopy decreases the incidence of active bleeding during endoscopy and facilitates endoscopic therapy, improving the control of bleeding and potentially, survival.

Drug	Recommended Dose	Duration
Terlipressin (VP analogue)	Initial 48 hours: 2mg IV every 4 hours until control of bleeding Maintenance: 1mg IV every 4 hours to prevent rebleeding	2-5 days
Octreotide (SMT analogue)	Initial IV bolus of 50 micrograms (can be repeated in the first hour if ongoing bleeding) Continuous IV infusion of 50 mcg/hr	2-5 days
Somatostatin;	Initial IV bolus 250 mg (can be repeated in the first hour if ongoing bleeding) Continuous IV infusion of 250-500 mg/hr	2-5 days

Out of the[1] 3 drugs, only terlipressin has been found to have mortality benefit.

Contraindications of terlipressin

1. Ischemic heart disease
2. Peripheral vascular disease
3. Respiratory failure
4. COPD

Adverse effects of terlipressin

1. Abdominal pain
2. Nausea
3. Loose stools
4. Hyponatremia {sodium levels need to be monitored}
5. Ischemia related events
6. Breathlessness and respiratory failure

9. Endoscopic management

- Following haemodynamic resuscitation, patients with suspected AVB should ideally undergo upper GI endoscopy within 24 hours* of presentation. If the patient is unstable, endoscopy should be performed as soon as safely possible.
- In the absence of contraindications (QT prolongation), pre-endoscopy infusion of erythromycin (250 mg IV 30-120 minutes before endoscopy) should be considered.
- Endoscopic Variceal Ligation (EVL) is the recommended endoscopic therapy for acute oesophagealvariceal bleeding.
- Endoscopic sclerotherapy can be done for patients with actively bleeding varices (if EVL is not possible.)

***As per BMJ UPDATE 2022 and ESGE 2021 Modification[Level II]**

- Endoscopic therapy with tissue adhesives (*e.g.* N-butyl-cyanoacrylate/thrombin) is recommended for acute bleeding from isolated gastric varices and type 2 gastro-oesophagealvarices that extend beyond the cardia. EUS-guided coiling is another option where available.
- If endoscopic therapy for gastric varices is not feasible, imaging to look for gastrorenal or renal shunts can be done and transluminal obliteration of varices can be performed [BRTO/PARTO/CARTO].
- Pre-emptive TIPS with polytetrafluoroethylene (PTFE)-covered stents within 72 h (ideally <24 h) is indicated in patients bleeding from oesophagealvarices and type 1/2 gastro-oesophagealvarices who meet any of the following criteria:

  Child-Pugh class C <14 points

  Child-Pugh class B >7 with active bleeding at initial endoscopy or HVPG >20 mmHg at the time of hemorrhage

10. Refractory bleeding

- Balloon tamponade due to the high incidence of adverse events, should only be used

  in refractory esophageal variceal bleeding, as a temporary bridge (for a maximum of 24 h), until definitive treatment can be instituted.
- Use of self-expanding covered esophageal metal stents (SX-ELLA Stent Danis) may be as efficacious and a safer option than balloon tamponade in refractory esophageal variceal bleeding.

11. Management of treatment failore

- Rebleeding during the first five days may be managed by a second attempt at endoscopic therapy. Persistent bleeding despite combined pharmacological and endoscopic therapy is best managed by PTFE-covered Transjugular intrahepatic portosystemic shunt (TIPS).
- Prevention of recurrent variceal hemorrhage after initial bleeding
- Secondary prophylaxis to prevent rebleeding should be instituted immediately after control of the index bleed, within 7 days from admission, because the highest risk period for rebleeding is the first 6 weeks after presentation.
- In patients who underwent preemptive TIPS, no further measures are required.
- Those who have not undergone TIPS will require secondary prophylaxis with NSBBs and endoscopic band ligation. When compared with EVL alone, the combination of EVL and NSBB reduced rebleeding in all categories of patients and improved survival in patients with CTP class B and C. EVL should not be used as monotherapy unless there is intolerance/ contraindications to beta blockers.
- NSBB should be used as monotherapy in patients with cirrhosis who are unable or unwilling to be treated with EVL
- Carvedilol, Propranolol or Nadolol may be used for secondary prophylaxis out of which carvedilol has greater effects on HVPG reduction.

References

1. AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis-2023October [Journal of Hepatology]
2. BAVENO VII-Renewing consensus in portal hypertension-November 2021
3. Sleisenger and Fordtran's Gastrointestinal and Liver diseases-11th edition

2. SPONTANEOUS BACTERIAL PERITONITIS

SCOPE

This guideline provides a standardized approach to the diagnosis and management of spontaneous bacterial peritonitis in adult patients with cirrhosis and ascites. It is intended for use by physicians, surgeons, intensivists, and emergency care providers involved in the care of such patients in secondary and tertiary healthcare settings.

The document outlines the indications for diagnostic paracentesis, criteria for diagnosis, appropriate microbiological evaluation, and evidence-based antimicrobial therapy, including considerations for community-acquired, healthcare-associated, and nosocomial infections. It also addresses the management of multidrug-resistant organisms, assessment of treatment response, use of adjunctive therapies such as intravenous albumin, and strategies for secondary prophylaxis to prevent recurrence.

This guideline does not cover secondary peritonitis requiring surgical intervention, non-cirrhotic causes of ascites, pediatric populations, or detailed long-term management of chronic liver disease. The recommendations are based on current evidence and standard hepatology practices and are adapted for practical implementation in routine clinical settings, including resource-limited environments.

INTRODUCTION

SBP is the bacterial infection of ascitic fluid without any intra-abdominal surgically treatable source of infection.It is a frequent and serious complication of cirrhotic patients with ascites.Other spontaneous infections in cirrhotic patients include spontaneous bacteremia, and SBE (infection of the hepatic hydrothorax).

The prevalence of SBP in cirrhotic hospitalised patients with ascites ranges between 10% and 30%. When first described, its mortality exceeded 90% but with early diagnosis and prompt treatment the in-hospital mortality has now been reduced to approximately 20%

Symptoms/signs specific to SBP are abdominal pain, tenderness on palpation (with or without rebound tenderness), and ileus. However, up to one-third of the patients with spontaneous infections may be entirely asymptomatic or present with only encephalopathy and/or AKI.

Spontaneous infections are typically monobacterial, with the most common (~60%) being gram-negative bacteria and with fungi representing less than 5% of infections. Recently, there has been a shift toward gram-positive and multidrug-resistant organisms (MDRO), particularly in nosocomial and health care– associated SBP.

DIAGNOSIS

SBP is diagnosed based on neutrophil count in ascitic fluid of >250/mm3. Neutrophil count is determined by microscopy, but can be substituted with a flow cytometry based automated

count. Although ascitic fluid culture positivity is not a prerequisite for the diagnosis of SBP, culture should be performed in order to guide antibiotic therapy

A diagnostic paracentesis should be carried out in all patients with cirrhosis and ascites without delay, at hospital admission to rule out SBP and it should be done even in the absence of symptoms suggestive of infection or whenever a patient (hospitalized or not) develops signs suggestive of infection.

A diagnostic paracentesis should also be performed in patients with GI bleeding, shock, fever or other signs of systemic inflammation, GI symptoms, as well as in patients with worsening liver and/or renal function, and hepatic encephalopathy.

If pleural effusion is present, a diagnostic thoracentesis should be performed when there is no ascites or when diagnostic paracentesis has ruled out SBP while bacterial infection is suspected.

Blood cultures and ascitic fluid culture should be performed in all patients with suspected SBP and should be performed before the administration of the first dose of antibiotics. Bedside inoculation of at least 10 mL of the ascitic sample into blood culture bottles increases the sensitivity of the culture to >90% in the diagnosis of SBP. A simultaneous blood samples for culture increases the possibility of isolating a causative organism.

A diagnosis of spontaneous bacterial empyema was established when the pleural fluid analysis showed a positive culture and more than 250 neutrophils/mm3 or a negative culture and more than 500 neutrophils/mm3, in the absence of lung infection

Secondary bacterial peritonitis should be suspected in case of multiple organisms on ascitic culture, very high ascitic neutrophil count and/or high ascitic protein concentration(>1g/dl) and low ascitic fluid sugar(<50mg/dl), or in those patients with an inadequate response to therapy. Patients with suspected secondary bacterial peritonitis should undergo prompt CT scanning of abdomen and early considerations for surgery.

1) Other two clinical conditions

A)Culture-negative neutrocytic ascitesrefers to individuals who have an ascitic fluid PMN count of at least 250 cells/mm3 with a negative bacterial culture. As it is generally considered to be a variant of SBP, you can treat this the same as SBP with a course of antibiotics.

B) Non-neutrocytic bacterascitesrefers to a positive bacterial culture with a normal neutrophil count in the fluid of less than 250 cells/mm3. Non-neutrocytic bacterascites may represent colonization of the ascitic fluid and typically does not require treatment unless there are other clinical signs of infection. Some cases of non-neutrocytic bacterascites may represent early spontaneous bacterial peritonitis so follow up paracentesis is recommended to see if the PMN count meets

criteria for SBP.

2) Infection with multidrug resistant organisms (MDRO)

Over the last two decades there is an alarming increase in the number of infections caused by multi-drug resistant organisms (MDROs) that are defined by an acquired non-susceptibility to at least one agent in three or more antimicrobial categories. Patients with advanced cirrhosis are highly susceptible to the development of infections caused by MDROs, because they require repeated hospitalizations. Bacterial resistance increases four fold the risk of mortality of SBP in particular, nosocomial SBP has been associated with multi-drug resistance and poor outcomes. Thus, it is crucial to separate community- acquired SBP from health care- associated and nosocomial SBP and to consider both the severity of infection and the local resistance profile in order to decide the empirical antibiotic treatment of SBP.

Extensively drug resistance (XDR) bacteria is defined by a non-susceptibility to at least one agent in all but two or fewer antimicrobial categories or to pandrug resistance (PDR) bacteria defined by a non-susceptibility to all agents in all antimicrobial categories

3) Management of SBP

Empirical i.v. antibiotics should be started immediately within 1 hour of presentation in patients with clinical suspicion of SBP. Antibiotics may be deescalated if diagnosis of SBP/SBE is not established.

a)For community-acquired SBP/SBE- third-generation cephalosporins are recommended as first-line antibiotic in areas with low rates of bacterial resistance. In areas with high rates of bacterial resistance, piperacillin/tazobactam or carbapenem should be considered.

b)Healthcare associated and nosocomial SBP is more likely to harbour resistance to antibiotics. In patients with a health care–associated or nosocomial infection or recent exposure to broad-spectrum antibiotics or who are admitted with sepsis or septic shock, empirical therapy with broad-spectrum antibiotics should be initiated as the first line.

- Patients with risk factors for MDRO - Piperacillin/tazobactam
- Patients with prior MRSA infection or positive surveillance swab for MRSA – Piperacillin/tazobactam + Vancomycin
- If known VRE (vancomycin resistant enterococci) in past or evidence of GI colonization-Daptomycin
- MDR (multidrug resistant gram negative organism)- Meropenem

- Current or recent exposure to Piperacillin/tazobactam - Meropenem+/glycopeptide(vancomycin/teicoplanin)
- Carbapenemase- producing and carbapenem-resistantnon-carbapenemase producing Enterobacteriaceae can be treated with tigecycline or with the combination of tigecycline at high doses and a carbapenem in continuous infusion.
- Addition of intravenous colistin could be necessary in severe infections.
- Renal function should be closely monitored in patients on vancomycin and colistin

4) Dosage of antibiotic regimens used for SBP Treatment

1) InjCeftriaxone 1g IV Q12H X 5-7days
2) InjCefotaxim 2g IV Q8H X 5-7days
3) InjPiperacillinTazobactam 4.5g IV Q6H X 5-7days (renal dose modification needed
4) InjMeropenem 2g IV loading dose followed by 1g IV Q8H X 5-7days (renal dose modification needed)
5) Inj Vancomycin 15-20mg/kg IV Q12H X 5-7days (renal dose modification needed , in suspected MRSA)
6) InjDaptomycin 8-12mg/kg IV Q24H X 5-7days (suspected vancomycin resistant enterococci)
7) InjTigecycline 100mg IV loading dose followed by 50mg IV Q12H X 5-7days (can consider 25mg Q12H if severe hepatic failure is suspected, no renal dose modification needed)
8) InjColistin 9MIU loading dose followed by 4.5MIU Q12H X 5-7days (renal dose modification needed , in suspected severe gram negative infections)

Severe infections caused by Pseudomonas aeuruginosa resistant to carbapenems and quinolones usually require the combination of i.v. amikacin/tobramycin or colistin plus a carbapenem/ceftazidime.

De-escalation according to bacterial susceptibility based on positive cultures is recommended to minimize resistance selection pressure.

5) Assessing treatment response

Response to empirical antibiotic therapy may be assessed by repeating diagnostic paracentesis/ thoracentesis two days after initiation. A decrease in fluid PMN <25% from baseline indicates lack of response and should lead to broadening of antibiotic coverage and further evaluation to rule out secondary bacterial peritonitis (abdominal

imaging). Repeat paracentesis/thoracentesis may be unnecessary if an organism is isolated, it Is susceptible to the antibiotic used, and the patient is improving clinically. The recommended duration of antibiotic therapy is 5-7 days

Patients with ascites PMN <250/mm3 and a positive bacteriological culture (bacterascites) in the absence of any signs of infection should not receive antibiotics, as in most cases it self-resolves or is a contaminant. A repeat diagnostic paracentesis should be performed to investigate progression to SBP. Spontaneous bacterial empyema should be managed similarly to SBP

NSBBs should be temporarily held in patients with SBP who develop hypotension (mean arterial pressure <65 mm Hg) or AKI.

6) IV Albumin in SBP

Patients with SBP should be treated with IV albumin in addition to antibiotics (1.5 g/kg at day 1 and1 g/kg at day 3). Patients with AKI and/or jaundice at time of diagnosis of SBP are more likely to benefit from albumin (Bilirubin >5mg/dl, BUN (blood urea nitrogen) >30mg/dl or Creatinine>1mg/dl)

7) Secondary prophylaxis

Patients who have recovered from an episode of SBP should receive long term prophylaxis with daily Norfloxacin 400mg. If Norfloxacin is unavailable, alternatives to Norfloxacin includes-(Ciprofloxacin 500mg/day, Rifaximin 550mg twice daily,TMP-SMX(trimethoprim sulfamethoxazole 160/800mg) one double strength tablet/day, Amoxicillin Clavulanic acid 875mg/daY. Antibiotic prophylaxis should be continued indefinitely or until ascites resolves

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1. European Association for the Study of the Liver Clinical Practice Guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *Journal of Hepatology*. 2018.
2. American Association for the Study of Liver Diseases Practice Guidance on the management of ascites and spontaneous bacterial peritonitis in cirrhosis. 2021 update.

3. HEPATIC ENCEPHALOPATHY (HE)

SCOPE

This guideline provides a standardized approach to the evaluation and management of hepatic encephalopathy in adult patients with acute or chronic liver disease. It is intended for use by physicians, surgeons, intensivists, and emergency care providers involved in the care of patients presenting with altered mental status in the setting of liver dysfunction.

The document addresses the classification of hepatic encephalopathy, identification of precipitating factors, clinical diagnosis, and appropriate use of laboratory and radiological investigations to exclude alternative causes of altered sensorium. It outlines evidence-based management strategies, including supportive care, pharmacological therapy, nutritional optimization, and prevention of recurrence.

This guideline does not cover pediatric hepatic encephalopathy, rare metabolic or congenital causes of encephalopathy, or detailed liver transplantation protocols. The recommendations are based on established clinical practice guidelines, including those from the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver, and are adapted for practical application in routine clinical practice, including resource-limited settings.

INTRODUCTION

Hepatic encephalopathy (HE) is a frequent and one of the most debilitating manifestations of liver disease. HE is a brain dysfunction caused by liver insufficiency and/or portosystemic shunting. It manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma.

Classification

Hepatic encephalopathy should be classified according to all of the following four factors

(1) According to the underlying disease, HE is subdivided into

Type A due to acute liver failure

Type B portosystemic shunt without significant liver disease

Type C to cirrhosis with or without portosystemic shunt

(2) According to the severity of manifestations. The continuum that is HE has been arbitrarily subdivided as follows – Grades 1 – 4.

(3) According to its time course, HE is subdivided into

a) Episodic HE

b) Recurrent HE denotes bouts of HE that occur within a time interval of 6 months or less.

c) Persistent HE denotes a pattern of behavioral alterations that are always present and interspersed with relapses of overt HE

(4) According to the existence of precipitating factors, HE is subdivided into

a) Non-precipitated

b) Precipitated

Precipitating factors can be identified in nearly all bouts of episodic HE type C and should be actively sought and treated when found. These include constipation, gastrointestinal bleeding, infections, hyponatremia and dehydration/diuretic overdose.

Diagnosis and Testing

The diagnosis of Overt HE (OHE) is based on a clinical examination and a clinical decision. Diagnosing cognitive dysfunction can be established from clinical observation as well as neuropsychological or neurophysiological tests. OHE still remains a diagnosis of exclusion .Therefore, as clinically indicated, exclusion of other etiologies by laboratory and radiological assessment for a patient with altered mental status in HE is warranted.

Minimal hepatic encephalopathy and Covert HE (CHE) is defined as the presence of test-dependent or clinical signs of brain dysfunction in patients with CLD who are not disoriented or display asterixis. The term ‘‘covert’’ includes minimal and grade 1 HE. The diagnosis and grading of MHE and CHE can be made using several neurophysiological and psychometric tests. Increased blood ammonia alone does not add any diagnostic, staging, or prognostic value for HE in patients with CLD. A normal value calls for diagnostic re-evaluation .

MANAGEMENT

- Initiation of care for patients with altered consciousness
- Alternative causes of altered mental status should be sought and treated.
- Identification of precipitating factors and their correction.
- Commencement of empirical HE treatment.

Patients with higher grades of HE who are at risk or unable to protect their airway need more intensive monitoring and are ideally managed in an intensive care setting. Alternative causes of altered mental status should be sought and treated.

CT brain is usually part of the diagnostic workup of first-time HE, if there is clinical suspicion of other pathology or sensorium is not improving despite anticoma measures.

Specific Approach to Overt hepatic encephalopathy - Treatment

Lactulose is the first choice for treatment of episodic OHE. 30 mL of lactulose syrup every 2 hrs until at least two to three semisolid bowel movements per day are

produced. Subsequently, the dosing is titrated to maintain two to three bowel movements per day.

Rifaximin is an effective add-on therapy to lactulose -Dose - 400 mg tds or 550 mg BD

Oral BCAAs can be used as an additional agent to treat patients nonresponsive to conventional therapy, especially to maintain nutrition.

IV LOLA can be used as an additional agent to treat patients nonresponsive to conventional therapy. L -ornithine-L-aspartate 20 g in 250 mL of 5% dextrose water and infused intravenously for four hours a day for five consecutive days .

Nutrition

Daily energy intakes should be 35-40 kcal/kg of ideal body weight .

Daily protein intake should be 1.2-1.5 g/kg/day.

Small meals or liquid nutritional supplements evenly distributed throughout the day and a late-night snack should be offered.Nasogastric tube feeding may be necessary to maintain nutrition especially in deeper stages of encephalopathy.

Prevention

Lactulose is recommended for prevention of recurrent episodes of HE after the initial episode. Rifaximin as an add-on to lactulose is recommended for secondary prevention of recurrent episodes of HE after the first episode

REFERENCES

1. Hepatic Encephalopathy in Chronic Liver Disease: 2014 AASLD guidelines , 2022 Practice Guideline by the EASL)

4 HEPATORENAL SYNDROME

SCOPE

This guideline provides a standardized approach to the evaluation and management of hepatorenal syndrome in adult patients with cirrhosis and ascites, particularly in the setting of acute kidney injury. It is intended for use by physicians, surgeons, intensivists, and emergency care providers involved in the care of patients with advanced liver disease in secondary and tertiary healthcare settings.

The document outlines the current definitions and classification of hepatorenal syndrome based on the revised criteria of the International Club of Ascites, including HRS-AKI, HRS-AKD, and HRS-CKD. It addresses early recognition, diagnostic criteria, staging of acute kidney injury, and differentiation from other causes of renal dysfunction. The guideline further provides evidence-based recommendations for management, including volume assessment, withdrawal of precipitating factors, use of vasoconstrictor therapy with albumin, monitoring of treatment response, and indications for renal replacement therapy and liver transplantation.

This guideline does not cover non-cirrhotic causes of acute kidney injury, primary renal diseases, pediatric populations, or detailed transplantation protocols. The recommendations are based on current evidence and consensus guidelines, including those from the American Association for the Study of Liver Diseases and the International Club of Ascites, and are adapted for practical application in routine clinical practice, including resource-limited settings.

DEFINITION

AKI is diagnosed by an increase in serum creatinine ≥ 0.3 mg/dl within 48 hours or ≥ 50% increase in serum creatinine that is known or presumed to have occurred within the preceding 7 days. If that is not available, the lowest stable S.Cr value obtained in the previous 3 months may be used for the diagnosis and staging of AKI. In clinical practice, the distinction between HRS-AKI and ATN is difficult. Recently, novel biomarkers have emerged in this setting and urinary neutrophil gelatinase associated lipocalin (NGAL) a marker of tubular

damage, could help to determine the type of AKI. In the recent revised ICA (international club of ascites) classification, historical terms HRS type 1 and 2 has been replaced with the terms HRS-AKI, HRS-AKD and HRS-CKD, depending on the timing and duration of kidney dysfunction.HRS for less than 90 days would be classified as HRS- AKD, while HRS persisting for more than 90 days would be classified as HRS-CKD. Patients with HRS-AKD meeting AKI criteria are classified as having HRS-AKI.

Diagnostic criteria for HRS according to ICA-AKI

1. Diagnosis of cirrhosis with ascites
2. Increase in SCr ≥ 0.3 mg/dl within 48 h or ≥ 50% from baseline value, known or presumed, to have occurred within the prior 7 days and/or UO ≤0.5 ml/kg for ≥ 6 h
3. Absence of improvement in SCr and/or UO within 24 h following adequate volume resuscitation (when clinically indicated)
4. Absence of strong evidence for an alternative explanation as the primary cause of AKI

Examples of alternative causes of AKI include septic shock requiring vasopressors, drug-induced AKI, obstruction, or acute glomerular injury

Measurement of UO, especially, outside the intensive care unit (ICU) is often inaccurate, and the frequent use of diuretics may affect interpretation; however, when possible, close monitoring of UO should be performed. However catheterization carries the risk of urinary infections.

STAGES OF AKI

Stage 1 – Increase of creatinine ≥ 0.3 mg/dl up to 2-fold of baseline

Stage 2 – Increase in creatinine between 2-fold and 3-fold of baseline

Stage 3 - Increase in creatinine > 3 fold of baseline or creatinine >4mg/dl with an acute increase ≥0.3 mg/dl or intiation of RRT

TREATMENT STRATEGIES

In a patient presenting with AKI, both risk factor and intravascular volume status should be

assessed

Intravascular volume assessment may be done by IVC measurement using point of care ultrasonogaphy. If patient has persistently low MAP, ECHO may be done.

If there is identifiable risk factors for AKI, risk factor management should be done. Risk factor management include withdrawal of nephrotoxic drugs, reduction or withdrawal of diuretics, detection and treatment of infections if present.

In those with clinical and haemodynamic evidence of intravascular volume depletion, assessment of response to fluid resuscitation should be completed within 24 h, to ensure early diagnosis and initiation of treatment for HRS-AKI.

Where volume status is equivocal and/or difficult to assess, to exclude any reduction in intravascular volume as the cause of AKI, a fluid challenge (250–500 ml of crystalloid or 1–1.5 g/kg of 20–25% albumin) may be prescribed and, if there is no improvement in SCr and/or UO within 24 h, a diagnosis of HRS-AKI should be considered.

In patients who are euvolemic or have evidence of intravascular fluid overload, 48 h of albumin infusion for the diagnosis of HRS-AKI is not appropriate and will lead to fluid accumulation.

Once HRS has been diagnosed

- Vasoconstrictors and 20% albumin are recommended in all patients meeting the current definition of AKI-HRS stage and should be expeditiously treated with vasoconstrictors and albumin

Vasopressor therapy (in addition to albumin)

a) Terlipressin— continuous IV infusion - starting dose 2 mg/day

Increase the dose of terlipressin by 2mg every 24 h if S.Cr has not decreased by 25% from baseline ,up to 12 mg/day

OR

b) Norepinephrine— given as continuous IV infusion, typically in an intensive care unit setting, starting at 0.5 mg/hour to achieve an increase in mean

arterial pressure of at least 10 mm Hg or an increase in urine output of >200 mL/4 hours. If at least one of these goals is not achieved, the dose of norepinephrine is increased every 4 hours in increments of 0.5 mg/hour up to a maximum of 3 mg/hour. Duration of vasopressor treatment is generally a maximum of 2 weeks until reversal of hepatorenal syndrome or liver transplantation

Close monitoring of volume status should be done during treatment for HRS-AKI. The dose of albumin should be adjusted daily based on patients volume status, with immediate discontinuation of albumin if there is evidence of volume overload

OR

c) Midodrine and octreotide—begin midodrine at 5-7.5 mg orally 3 times daily and increase to a maximum dose of 15 mg 3 times daily. Titrate to an MAP increase of at least 15 mm Hg; begin octreotide at 100 µg subcutaneously 3 times daily and increase to a maximum dose of 200 µg subcutaneously 3 times daily, or begin octreotide at a 25-µg IV bolus and continue at a rate of 25 µg/hr.

Contraindications and adverse effect of terlipressin – Refer - UGI bleed chapter

- Response to terlipressin or norepinephrine is defined by creatinine return to within 0.3 mg/dL of baseline over a maximum of 14 days.
- Once creatinine returns to within 0.3mg/dl of baseline continue terlipressin for 24-48 hours.
- Vasoconstrictors for HRS-AKI may be discontinued if (a) SCr returns to within 0.3 mg/dl of baseline; (b) a severe adverse reaction develops; (c) kidney function does not improve after 48 h on maximum tolerated doses; (d) RRT is indicated; or (e) maximum of 14 days of therapy
- Midodrine plus octreotide should be given only when terlipressin or noradrenaline are unavailable, but its efficacy is much lower than that of terlipressin

- In cases of recurrence of HRS-AKI upon treatment cessation, a repeat course of therapy should be given
- Terlipressin plus albumin is also effective in the treatment of HRS outside the criteria of AKI (HRS-NAKI), formerly known as HRS type II

RESPONSE TO THE TREATMENT

According to the definition of HRS-AKI, complete response to the treatment should be defined by a final serum creatinine (SCr) within 0.3 mg/dl from the baseline value, while partial response should be defined by the regression of AKI stage to a final serum creatinine SCr ≥0.3 mg/dl from the baseline value

Treatment of non-responders

- TIPS is not recommended in patients with AKI- HRS because of insufficient information
- LT is the best therapeutic option for patients with HRS regardless of the response to drug therapy
- The decision to initiate RRT should be based on the individual severity of illness
- Initiation of RRT should be made on clinical grounds, including worsening kidney function, electrolyte disturbances such as severe acidosis, hyponatremia or hyperkalemia not improving with medical management, diuretic intolerance, or increasing volume overload.
- Continuous RRT is the modality preferred to intermittent dialysis in patients who are hemodynamically unstable
- All patients with cirrhosis and AKI should be considered for urgent LT evaluation given the high short- term mortality even in responders to vasoconstrictors

PREVENTION OF HRS-AKI

- Albumin (1.5 g/kg at diagnosis and 1 g/kg on day three) should be given in patients with SBP to prevent AKI
- Albumin infusion at the time of LVP > 5L is recommended. Recommended dose of

albumin replacement is 6-8 gm for every litre of ascites removed

REFERENCES

1. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases
2. Acute kidney injury in patients with cirrhosis: Acute Disease Quality Initiative (ADQI) and International Club of Ascites (ICA) joint multidisciplinary consensus meeting, Journal of Hepatology July 202**4)**

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5. ACUTE LIVER FAILURE

SCOPE

This guideline provides a standardized approach to the evaluation and management of acute liver failure in adult patients presenting with acute liver injury, coagulopathy, and hepatic encephalopathy in the absence of pre-existing chronic liver disease. It is intended for use by physicians, surgeons, intensivists, and emergency care providers involved in the management of critically ill patients in secondary and tertiary healthcare settings.

The document outlines the diagnostic criteria for acute liver failure, early recognition, and initial stabilization measures. It includes recommendations for etiological evaluation, monitoring parameters, and comprehensive organ-specific management, including neurological, cardiovascular, respiratory, renal, metabolic, and coagulation aspects. The guideline also addresses the role of specific therapies such as N-acetylcysteine, plasma exchange, and antiviral or etiology-directed treatments, as well as indications and criteria for urgent liver transplantation.

This guideline does not cover chronic liver failure, acute-on-chronic liver failure, pediatric acute liver failure, or detailed post-transplant management protocols. The recommendations are based on established clinical guidelines, including those from the American College of Gastroenterology, American Association for the Study of Liver Diseases, European Association for the Study of the Liver, and Indian National Association for the Study of the Liver, and are adapted for practical application in routine clinical practice, including resource-limited settings.

INTRODUCTION

Diagnosis of ALF

Acute liver failure (ALF) is a life-threatening condition that occurs in patients with no preexisting liver disease and is characterized by liver injury (abnormal liver tests), coagulopathy (international normalized ratio [INR] >1.5), and hepatic encephalopathy (HE) with an illness duration of less than 26 weeks.

Patients with an acute presentation of chronic autoimmune hepatitis, Wilson disease and Budd-Chiari syndrome are considered as having ALF if they develop hepatic encephalopathy, despite the presence of a pre-existing liver disease in the context of appropriate abnormalities in liver blood tests and coagulation profile.

Immediate measures at presentation of patients with ALF to medical care.

- In patients with severe acute liver injury(ALI), screen intensively for any signs of hepatic
- encephalopathy.
- Exclude the presence of cirrhosis, alcohol induced liver injury or malignant infiltration of the liver.
- Consider whether the patient has contraindications for emergency liver transplantation (LTx)
- The finding of contraindications should not preclude transfer to a tertiary unit.
- Searching for an aetiology allows treatment to be instituted and facilitates prognostic stratification.
- Transfer to a specialised unit early if the patient has an INR >1.5 and onset of hepatic encephalopathy or other poor prognostic features.
- Early discussion with a transplant unit even if the patient does not need transfer at that time point.

*Suggested criteria for referral of cases of ALF to specialist units

Paracetamol and hyperacuteaetiologies	**Non-paracetamol**
Arterial pH <7.30 or HCO_3<18	pH <7.30 or HCO_3<18
INR >3.0day 2 or >4.0 thereafter	INR >1.8
Oliguria and/or elevated creatinine	Oliguria/renal failure or Na <130mmol/L
Altered level of consciousness	Encephalopathy, hypoglycemia or metabolic acidosis
Hypoglycemia	Bilirubin >300µmol/L (17.6mg/dl)
Elevated lactate unresponsive to fluid resuscitation	Shrinking liver size

Adapted from EASL Clinical Practical Guidelines on the management of ALF 2017

*Summary of investigation to be done in case of suspected ALF

Confirming the diagnosis and to rule out differential diagnosis	For determining etiology	For determining complications and prognosis
• LFTs (S bilirubin (T/D), SGOT/PT, s.ALP, S protein/albumin2 • PT/INR • Imaging: liver size • Transjugular liver biopsy (very limited use- before institution of immunosuppressive in suspected Autoimmune hepatitis/to rule outinfiltrative disease and malignancy and to identify patients with contraindication to LT. • Other tests as per clinical suspicion of differential diagnosis such as malaria, dengue, scrub typhus, leptospira, and other tropical infections	• Serological screen for virus infections • HBsAg, anti-HBc IgM (HBV DNA), delta if positive for HBV, anti HAV IgM, anti-HEV IgM, anti-HSV IgM, • In selected cases anti-VZV IgM, CMV, EBV, HIV, parvovirus, or VZV PCR (in immunocompromised patients) • Imaging of liver, color Doppler for hepatic and portal veins if Budd-Chiari syndrome suspected • Echocardiogram and ECG if ischemic hepatitis suspected secondary to cardiac failure • Autoimmune markers if AIH suspected: • ANA, ASMA, antisoluble liver antigen, globulin profile, ANCA • Toxicology screen in urine and paracetamol serum level are not routinely available and hence not recommend	• CBC • Procalcitonin • Cultures (respiratory, blood, urine) • Chest X-ray/ECG • Ultrasound of liver and IVC collapsibility (CT abdomen/chest required in selected cases) • RFT • Electrolytes (sodium, potassium, chloride, bicarbonate, calcium, magnesium, and phosphate) • Lipase or amylase • Arterial ammonia • Blood glucose • ECG • ABG including lactate • Thromboelastogram • Pregnancy test in selected patients

*Adapted from INASL 2020 summary of investigations to be done in case of suspected ALF

Monitoring of patients admitted with ALF

- PT/INR should be monitored at least twice a day.
- Blood sugar monitoring should be done 1–4hourly. Arterial ammonia should be monitored every 12-24 h in a patient with ALF
- Sodium levels should be monitored every 12 h and maintained between 145 - 150 meq/l.
- Urine output should be measured hourly. In case of AKI, effort should be made to define the type of injury (prerenal/HRS vs ATN)
- Surveillance cultures should be sent every 48 h or at any suspicion of infection (clinical deterioration of the patient)
- Continuous blood pressure monitoring is recommended with target MAP of 70–80 mmHg. Volume status can also be assessed though IVC diameter variability index
- Core body temperature monitoring should be done
- Routine use of invasive ICP monitoring is not recommended. Noninvasive ICP monitoring can be done in all patients with ALF.

ORGAN SPECIFIC MANAGEMENT

Neurological management

- Patients with low grade encephalopathy should be frequently evaluated for signs of worsening encephalopathy.
- Patients with grade 2 or more hepatic encephalopathy should be transferred to intensive care unit. In patients with grade 3 or 4 encephalopathy, intubation should be undertaken to provide a safe environment and prevention of aspiration.
- Regular evaluation for signs of intracranial hypertension should be performed.
- Trans-cranial Doppler and optic nerve sheath diameters are useful non-invasive monitoring tools.
- First-line treatment of increased ICP includes hyperosmolar therapy (mannitol,

hypertonic saline), hyperventilation, and CRRT.

- Hyponatremia should be avoided. The target serum sodium concentration is 145–150 mmol/L; When correction is undertaken, it should be accomplished at a slow rate, not exceeding 6–8 mmol/L in 24 hours.
- Mannitol((20%, 0.5–1 g/kg body weight) or hypertonic saline (3% saline in a bolus of 250–500 mL volume or a continuous infusion to maintain serum sodium levels below 160 mmol/L) should be administered for surges of ICP with consideration for short-term hyperventilation.
- Rifaximin/Lactulose can be given to reduce ammonia production in the intestine however no conclusive evidence for or against their use in ALF.For patients with advanced hepatic encephalopathy planning immediate liver transplantation, lactulose should be withheld due to the risk of bowel distension. There is no role for L Ornithine L Aspartate in ALF.
- Seizures including non-convulsive status should be excluded with EEG monitoring if required. If AED is required – levitriacetam/lacosamide are preferred over other agents

Cardiovascular management

- Most patients are volume depleted at presentation and require crystalloids initially for volume resuscitation.
- Volume overload is as detrimental as underfilling. Use POCUS
- Persistent hypotension requires critical care management, with application of vasopressive agents guided by appropriate monitoring techniques.
- Norepinephrine is the vasopressor of choice in refractory hypotension.
    - Initial dose 0.05-0.1mcg/kg/min .increase in increments of 0.02-0.05mcg/kg/min.Maximum dose is typically 1-2 mcg/kg/min.
- Vasopressin can be considered as second agent.
    - infusion dose of vasopressin is 0.01-0.04 units /min.

Respiratory management

- ARDS can complicate the course of ALF.
- Standard lung protective ventilator techniques should be utilized in patients with ALF.
- Avoid of excessive hyper or hypocarbia(target PCO2 of 30-40mmHg).
- Regular chest physiotherapy should be carried out and ventilator associated pneumonia should be avoided.

Gastrointestinal management

- PPIs (Inj Pantoprazole 40mg IV once daily) is given for stress ulcer prophylaxis.
- Consider stopping PPI when enteral feeding has been established due to the risk of ventilator associated pneumonia and Clostridium difficile infection
- Patients with ALF have increased resting energy expenditure therefore, enteral or parenteral nutrition are warranted. The recommended energy intake is 35–40 kcal/kg body weight/day and protein intake is 1.2–1.5 g/kg body weight/day.

Metabolic management

- Blood glucose is monitored 1- 4 hourly. 10-20% dextrose is given to prevent hypoglycemia avoiding hyperglycemia (target 150-180mg/dl)
- Hypoglycemic episodes need aggressive correction

Acute kidney injury and renal replacement therapy

- Strategies to prevent the development of AKI include: correction of hypotension, prompt treatment of infection, avoiding nephrotoxic medications and judicious use of radiological procedures that require intravenous contrast.
- Early institution of extracorporeal support (RRT) is normally instituted in the context of uremia, fluid overload and hyperkalaemia.
- In the context of ALF, however, RRT may be offered to manage acidosis, hyperammonaemia and sodium imbalance, facilitate temperature and metabolic

control.

- No anticoagulation/ regional citrate anticoagulation is recommended during RRT.
- Continuous RRT should always be undertaken in the critically ill patient with ALF as opposed to intermittent haemodialysis

Coagulation: Monitoring and management

- The routine use of fresh frozen plasma and other coagulation factors is not supported, and should be limited to invasive procedures/active bleeding. Viscoelastic testing can be done where available to guide the correction. Haemoglobin target for transfusion is 7g/dl.
- Venous thrombosis prophylaxis should be considered in the daily review

Infection management

- Regular periodic surveillance cultures should be performed in all patients with ALF.
- Prophylactic antibiotics, non-absorbable antibiotics, and antifungal have not been shown to improve survival in ALF.
- Early anti-infection treatments should be introduced upon appearance of progression of hepatic encephalopathy, clinical signs of infections, or elements of SIRS.
- Antifungal therapy in those with prolonged critical care support for multiple organ failure should be considered, as guided by the use of biomarkers (1,3 Beta-D Glucan).

Role of N-Acetyl Cysteine

- N acetyl cysteine has established role in paracetamol -ALF.
- In nonparacetamol ALF transplant free survival benefit was demonstrated in grade 1/2 hepatic encephalopathy.
- Hence N-acetyl cysteine (NAC) should be started in all patients at a dose of 150 mg/kg body weight in 250 ml 5% dextrose over 1 h, followed by 100 mg/kg doses

every 6 h over a total of 72 h.

Liver assist devices / Plasma exchange

- As per current evidences Liver support systems (biological or adsorbent) should only be used in the context of RCT
- Plasma exchange used in early encephalopathy may help to reduce ICP/transplant free survival. It can be considered as a bridge to transplant when its delayed or when it is not feasible.

Liver transplantation(OLTx)

- Those who satisfy the King College criteria should be considered for emergence liver transplantation.

Criteria for emergency liver transplantation King's College criteria

ALF due to paracetamol

1) Arterial pH <7.3 after resuscitation and >24 h since ingestion
2) Lactate >3 mmol/L after resuscitation or
3) All of The 3 following criteria:

i) Hepatic encephalopathy >grade 3

ii) Serum creatinine >3.4mg/dl

iii) INR >6.5

ALF not due to paracetamol

1) INR >6.5 or
2) 3 out of 5 following criteria:

I. Aetiology: indeterminate aetiology ,drug-induced hepatitis
II. Age <10 years or>40 years
III. Interval from jaundice to encephalopathy >7 days

IV. Bilirubin >17.5mg/dl

V. INR >3.5

- Assessment of patients with ALF for emergency LTx requires input from a multidisciplinary team with appropriate experience in this process.
- Patients with ALF, potential for deterioration and who may be candidates for LTx, should be transferred to specialist units before the onset of HE to facilitate assessment.
- Patients with ALF listed for LTx should be afforded the highest priority for donated organs.
- Irreversible brain injury is a contraindication to proceeding with LTx .
- Patients transplanted for acute HBV infection need ongoing therapy for suppression of viral replication.

Recommended treatment based on etiology of acute liver failure

Acetaminophen

1) Early gastric decontamination with 1–2g/kg of single dose activated charcoal is effective if administered within the first 4 hours after ingestion.
2) IV protocol of NAC
   - 300 mg/kg total dose
   - 1st bag 150 mg/kg/loading dose over 1 hr
   - 2nd bag 50mg/kg over 4 hr
   - 3rd bag 100mg/kg over 16hr

Extended IV protocol (Fontana 2008)

- 1st bag 50 mg/kg over 4 hr
- 2nd bag 125mg/kg over 19 hr
- Remaining bag100mg/kg over 24hr or until INR 1.5

Plasma exchange can be considered in patients with ALF.

If the above measures fail one should consider liver transplantation.

Rodenticide poisoning

- Along with the standard management of ALF ,consider plasma exchange (PLEX) in rat paste(yellow phosphorus)poisoning
- Low volume PLEX improves survival rate.
- Oral 10 mg wysolone once daily started prior to initiating PLEX and continued for 1-4 weeks.
- Prophylactic antibiotics
- If no sepsis-iv cefoperazonesulbactum
- If suspected sepsis with organ dysfunction-iv Meropenem.
- Enteral nutrition is preferred.
- In patients who are not improving to plasma exchange ,consider liver transplantation.

Drug induced liver injury

- Discontinue offending agent
- Consider NAC for early coma grade.
- Corticosteroids for those with hypersensitivity or autoimmune features
    - HEPATITIS B
- Along with standard management for ALF antivirals should be considered.
- TDF 300mg once daily or TAF 25 mg once daily or ENTECAVIR 0.5 mg once daily or according to renal clearance.
- Those who fails the above measures should be considered for liver transplantation.
    - HEPATITIS A
- Management of HAV ALF is largely supportive because no specific antiviral agent

has been proven to be effective.

- Anti cerebral edema measures.
- Plasma Exchange.
- Presence of deranged LFT and any of the following three criteria

  1) INR more than or equal to 4

  2) Worsening of INR on serial tests,after 2 doses of vit K 4 hrs apart.

  3) Altered behavior.

  Contraindication of PLEX

  1) Hemodynamic instability

  2) Sepsis

- In patients who are not improving to plasma exchange ,consider liver transplantation.
- HSV or VZV HEPATITIS
- IV acyclovir; 10-15 mg/kg every 8 hrs for 14-21 days

CMV Hepatitis

- IV Ganciclovir 5mg/Kg every 12 hrs for 14-21 days in induction phase.
- 5mg/kg once daily until resolution of symptoms as maintenance dose.
- Oral Valganciclovir
- Induction dose of 900mg twice daily for 21 days
- Maintenance dose of 900mg once daily until resolution of symptoms.

Mushroom poisoning

- Gastric lavage is recommended within 1 hour of toxin ingestion to prevent absorption.
- Activated charcoal is also recommended soon after ingestion to disrupt the

enterohepatic circulation of the amatoxin . Recommended doses are 50 g every 4 hours or 25 g every 2 hours. This can be further reduced to 12.5 g every hour for tolerability.

- IV hydration to maintain urinary output of 100–200 mL/hr for up to 4–5 days is recommended to sufficiently eliminate toxins and maintain hydration.
- IV silibinindihemisuccinate in acute amanita phalloides poisoning.
- Within the first 24 hours, patients should receive IV silibinindihemisuccinate at 20–50 mg/kg/d for 48–96 hours or alternatively, 5 mg/kg of IV silibinindihemisuccinate over 1hour, followed by 20 mg/kg/d for 6 days or until the serum transaminases normalize.
- IVpenicillin G - Continuous infusion of 1,000,000 IU/kg on day1and1,500,000IU/kg days 2and3.
- IV NAC - Dose is 150mg/kg over 15minutes, followed by 50mg/kg over 4hours,followed by 100mg/kg over 16hours.
- LT is an effective intervention for ALF due to amanita phalloides poisoning with excellent out come.

Autoimmune hepatitis

- In patients presenting with Acute severe-AIH without ALF use of IV methyl prednisolone.Dose is 0.5 to 1 mg/kg /day .
- Early evaluation for LT should be considered in patients with ALF.

HELLP/ AFLP

- Prompt delivery of fetus
- Supportive care.
- Those who fail to response even after delivery of fetus ,liver transplantation should be considered.

Budd chiari syndrome

- Anticoagulation should be done with heparin in all patients whom there is no contraindication.
- When technically feasible endovascular procedures (Angioplasty+/- stenting).
- Those who fail anticoagulation, angioplasty DIPSS/TIPSS is the preferred intervention.
- Those who fail medical/therapeutic intervention, liver transplantation should be considered.

Wilson Disease

- In patients presenting with ALF due to suspected or confirmed Wilson disease, LT evaluation should be initiated during diagnosis due to the lack of effective medical therapy.
- In ALF, copper chelation therapy is ineffective
- Plasma exchange/plasmapheresis should be considered as temporary measure for copper removal.

REFERENCES

ACG 2023 Acute liver failure guidelines, EASL Clinical Practical Guidelines on the management of acute liver failure 2017, AASLD Position Paper: The Management of Acute Liver Failure: Update 2011 Hepatology,INASL consensus statement on acute liver failure 2020,Govt of Kerala guidelines for plasma exchange in liver failure,2024

6. ALCOHOLIC HEPATITIS/ALCOHOL WITHDRAWAL SYNDROME

SCOPE

This guideline provides a standardized approach to the evaluation and management of alcohol-associated hepatitis and alcohol withdrawal syndrome in adult patients with alcohol use disorder, particularly in the setting of underlying liver disease. It is intended for use by physicians, surgeons, intensivists, and emergency care providers involved in the care of such patients in secondary and tertiary healthcare settings.

The document outlines the clinical criteria for diagnosis of alcohol-associated hepatitis, assessment of disease severity using validated scoring systems, and evidence-based management strategies including general supportive care, nutritional therapy, corticosteroid use, and adjunctive pharmacological treatments. It also addresses the management of alcohol withdrawal syndrome, including severity assessment, pharmacological therapy, and monitoring in patients with coexisting liver dysfunction. In addition, the guideline includes recommendations for relapse prevention and long-term management of alcohol use disorder in patients with alcohol-associated liver disease.

This guideline does not cover non-alcohol-related causes of liver disease, pediatric populations, or detailed liver transplantation protocols. The recommendations are based on established clinical guidelines, including those from the American College of Gastroenterology, American Association for the Study of Liver Diseases, and European Association for the Study of the Liver, and are adapted for practical application in routine clinical practice, including resource-limited settings.

Among patients with suspected heavy alcohol use and new onset or worsening jaundice, clinicians should have a high suspicion for alcoholic hepatitis (AH) given its high short-term mortality

CLINICAL CRITERIA FOR DIAGNOSIS

The NIAAA has proposed clinical criteria for the diagnosis of probable AH, which can spare severely ill patients the risk of liver biopsy. However, when the diagnosis is uncertain and 1 or more of the criteria are not met, a liver biopsy should be considered

NIAAA - grading criteria of AH
Definite AH- Histological confirmation of features of alcohol-associated hepatitis
Probable AH - Onset of jaundice within 60 d of heavy alcohol use (more than 50 g/d) for a minimum of 6 mo, serum bilirubin> 3 mg/dL, elevated AST ranging from 50 to 400 U/L, an AST:ALT ratio. 1.5, and no other cause of acute hepatitis
Possible AH - Clinical diagnosis uncertain due to another confounding etiology of liver disease or unclear history on alcohol consumption
AH, alcohol-associated hepatitis; ALT, alanine aminotransferase; AST, aspartate aminotransferase; NIAAA, National Institute of Alcoholism and Alcohol Abuse.

Criteria for diagnosis of AH – adapted from table from *ACG Clinical Guideline: Alcohol-Associated Liver Disease* 2024

ASSESSMENT OF DISEASE SEVERITY

- Once a diagnosis of AH is made, disease severity is stratified.
- Although several scoring systems are available, the model for end stage disease (MELD) score is to be used to estimate disease severity and determine eligibility for corticosteroid treatment, with scores >20 indicating severe AH and≤ 20 indicating moderate AH
- Beyond MELD, other scoring systems that have been assessed for AH include Child-Turcott-Pugh, Glasgow Alcoholic Hepatitis Score (GAHS), and Age Bilirubin International Normalized Ratio and Creatinine (ABIC).
- Previous studies showed that the combination use of MELD at baseline and the Lille score at day 7 have best discrimination and calibration for 2-month and 6-month mortality

TREATMENT

General measures

- Regardless of the severity, alcohol abstinence is the cornerstone of therapy and early management of AUD is recommended in all patients with AH
- Considering the potential risk of Wernicke's encephalopathy, supplementation with B-complex vitamins is recommended. Dose of thiamine – start with 300mg BD initially , taper and stop in 3-4 weeks .
- Patients with severe AH are at risk of developing acute kidney injury (AKI) which negatively impacts survival. Measures aimed at preventing the development of renal failure are therefore recommended. They include avoidance of diuretics and nephrotoxic drugs and volume expansion if needed.

Role of prophylactic antibiotics

- Infections are a common occurrence at presentation and during hospitalization in patients with AH , however prophylactic antibiotics are not recommended in patients with severe AH

Nutrition

- In patients with AH who are malnourished or unable to meet their caloric requirements through oral nutrition alone, the addition of oral nutritional supplements is recommended.
- In patients who remain unable to meet their caloric requirements despite oral nutritional supplements, it is recommended to use recommend enteral nutrition support (Ryles tube feeding- either continuous or intermittent ; continuous is preferred).
- A caloric intake goal of 35 kcal/kg/d with 1.2–1.5 g/kg/d of protein is recommended for patients with AH. Those patients consuming < 21 kcal/kg/d should receivenutritional support preferably through oral/enteral routes.
- Thiamine, vitamin B12, and zinc deficiencies are common in individuals with AH and

should be supplemented.

Corticosteroids

- In patients with severe AH (MELD > 20), treatment with corticosteroid therapy is recommended if there are no contraindications
- Active infection including untreated HBV infection, uncontrolled diabetes mellitus, gastrointestinal bleeding, and severe renal failure is considered contraindications to the use of corticosteroids . However, corticosteroids can be started after adequate control or reversal of infection, renal failure, and gastrointestinal bleeding.
- A careful screening for infection is recommended before initiating therapy . Complete hemogram, CRP, Cultures and chest x-ray may be taken to rule out any infections .
- Patients with severe AH and MELD scores ranging from 25 to 39 derive maximum benefit from the use of corticosteroids; careful consideration of risks and benefits is warranted if considering corticosteroids for those with MELD >50.
- Response to corticosteroid treatment can be assessed based on the Lille score at day 7 or day 4. Among nonresponders (Lille score > 0.45), corticosteroids should be discontinued.
- Lille Model Score = Exp(-R) / (1 + Exp(-R)), where: R = [3.19 - (0.101 x Age in years)] + (1.47 x Albumin in g/dL) + [0.28215 x (Bilirubin initial - Bilirubin day 7 in mg/dL)] - (0.206 x Creatinine in mg/dL) - (0.11115 x Bilirubin initial in mg/dL) - (0.0096 x Prothrombin time in seconds)
- Lille score can be easily calculated through online calculators .
- Lille score at day 4 of corticosteroid therapy has been shown to be as accurate as day 7 Lille score in predicting the outcome and response to treatment and has since been validated.
- Prednisolone and prednisone are dosed 40 mg per day for a total duration of 4 weeks.
- IV methylprednisolone (32 mg per day) is an alternative for those unable to take

medications orally. There is no evidence supporting the benefits of rapid vs slow tapering after the 4-week therapy.

N-acetyl cysteine

- NAC is recommended as an adjuvant to corticosteroids in patients with severe AH .
- A combination of prednisolone and 5 days of NAC infusion pro rides the best survival benefit at 28 days with 85% risk reduction of death from AH

Pentoxifylline

- ACG guidelines recommend against the use of Pentoxifylline for individuals with severe AH .It is also not effective as an adjuvant therapy to corticosteroids

G-CSF and microbial based therapies

- There are insufficient data to determine the role of granulocyte colony-stimulating factor (G-CSF) and microbiome-based therapies in the treatment of severe AH

Miscellaneous therapies

- Antioxidant cocktails , vitamin E , S-adenosylmethioninehave not shown benefit in severe AH.

Liver transplantation

- In patients with severe AH who are unresponsive to medical management with high risk of death, early LT for highly selected patients should be considered, according to regional and institutional protocols.
- For patients with severe AH who are nonresponsive to corticosteroids and ineligible for early LT having 4 or more organ failures, palliative therapy would be appropriate.
- Selection for LT in patients with ALD should not be based solely on an arbitrary duration of sobriety. A comprehensive psychosocial evaluation by a social worker and an addiction specialist should be used to inform transplant team decision-making.
- Early and/or heavy alcohol use is a risk for graft loss and long- term patient mortality

and requires an aggressive intervention to achieve abstinence.

ALCOHOL WITHDRAWAL SYNDROME (AWS)

AWS is a common condition affecting alcohol-dependent patients who abruptly discontinue or markedly decrease alcohol consumption. AWS is frequent in patients with AH and negatively affects survival.

Mild or moderate AWS usually develops within 6–24 hours after the last drink, and symptoms may include nausea/vomiting, hypertension, tachycardia, tremors, hyperreflexia, irritability, anxiety, and headache.

These symptoms may progress to more severe forms of AWS, characterized by delirium tremens, generalized seizures, coma, and even cardiac arrest and death. Older individuals are at greater risk for delirium tremens.

Those with moderate or severe AWS are typically monitored in an intensive care unit, where vital signs, volume status, and neurological function can be monitored closely.

SEVERITY ASSESSMENT

Severity scores for AWS such as the **Clinical Institute Withdrawal Assessment** are useful in guiding management.

CIWA-Ar score >8 indicates a moderate AWS and a score ≥15 indicates severe AWS.

Pharmacological treatment is recommended for both moderate and severe AWS.A symptom-triggered regimen or a fixed dose schedule may be used.

Clinical Institute Withdrawal Assessment of Alcohol Scale , Revised (CIWA-Ar)

Alcohol Withdrawal Assessment Scoring Guidelines (CIWA - Ar)

Nausea/Vomiting - Rate on scale 0 - 7

0 - None
1 - Mild nausea with no vomiting
2
3
4 - Intermittent nausea
5
6
7 - Constant nausea and frequent dry heaves and vomiting

Tremors - have patient extend arms & spread fingers. Rate on scale 0 - 7.
0 - No tremor
1 - Not visible, but can be felt fingertip to fingertip
2
3
4 - Moderate, with patient's arms extended
5
6
7 - severe, even w/ arms not extended

Anxiety - Rate on scale 0 - 7
0 - no anxiety, patient at ease
1 - mildly anxious
2
3
4 - moderately anxious or guarded, so anxiety is inferred
5
6
7 - equivalent to acute panic states seen in severe delirium or acute schizophrenic reactions.

Agitation - Rate on scale 0 - 7
0 - normal activity
1 - somewhat normal activity
2
3
4 - moderately fidgety and restless
5
6
7 - paces back and forth, or constantly thrashes about

Paroxysmal Sweats - Rate on Scale 0 - 7.
0 - no sweats
1- barely perceptible sweating, palms moist
2
3
4 - beads of sweat obvious on forehead
5
6
7 - drenching sweats

Orientation and clouding of sensorium - Ask, "What day is this? Where are you? Who am I?" Rate scale 0 - 4
0 - Oriented
1 – cannot do serial additions or is uncertain about date

2 - disoriented to date by no more than 2 calendar days

3 - disoriented to date by more than 2 calendar days
4 - Disoriented to place and / or person

Tactile disturbances - Ask, "Have you experienced any itching, pins & needles sensation, burning or numbness, or a feeling of bugs crawling on or under your skin?"
0 - none
1 - very mild itching, pins & needles, burning, or numbness
2 - mild itching, pins & needles, burning, or numbness
3 - moderate itching, pins & needles, burning, or numbness
4 - moderate hallucinations
5 - severe hallucinations
6 - extremely severe hallucinations
7 - continuous hallucinations

Auditory Disturbances - Ask, "Are you more aware of sounds around you? Are they harsh? Do they startle you? Do you hear anything that disturbs you or that you know isn't there?"
0 - not present
1 - Very mild harshness or ability to startle
2 - mild harshness or ability to startle
3 - moderate harshness or ability to startle
4 - moderate hallucinations
5 - severe hallucinations
6 - extremely severe hallucinations
7 - continuous hallucinations

Visual disturbances - Ask, "Does the light appear to be too bright? Is its color different than normal? Does it hurt your eyes? Are you seeing anything that disturbs you or that you know isn't there?"
0 - not present
1 - very mild sensitivity
2 - mild sensitivity
3 - moderate sensitivity
4 - moderate hallucinations
5 - severe hallucinations
6 - extremely severe hallucinations
7 - continuous hallucinations

Headache - Ask, "Does your head feel different than usual? Does it feel like there is a band around your head?" Do not rate dizziness or lightheadedness.

0 - not present
1 - very mild
2 - mild
3 - moderate
4 - moderately severe
5 - severe
6 - very severe
7 - extremely severe

TREATMENT

Benzodiazepines are the most used drugs to treat AWS. Long-acting benzodiazepines (e.g., diazepam and chlordiazepoxide) protect against seizures and delirium; short-acting and intermediate-acting benzodiazepines (e.g., lorazepam and oxazepam) are safer for patients with poor liver function .Oral administration is preferred for administration of benzodiazepines.

Patients with AWS and concomitant hepatic encephalopathy should be treated for both conditions. Benzodiazepines may precipitate and worsen hepatic encephalopathy; thus, careful monitoring and the dose titration are critical for optimal outcomes.

It should be noted that benzodiazepines carry a potential risk of abuse, and it has been

documented that patients with AUD are at higher risk. Hence clinicians should avoid the use of those drugs beyond the 10–14 initial days of treatment.

Fixed dose regimen for alcohol withdrawal in patients with ALD - Lorazepam is preferred . It is commonly given at doses of 2 mg every 6 hours for the first 24 hours followed by 1 mg every 6th hourly for 2 more days and taper and stop .

Symptom triggered regimen - Lorazepam is given as needed at a dose based on the severity of symptoms . Typical dosages are 2mg or 4 mg given only as needed .

PHARMACOTHERAPY FOR ALCOHOL USED DISORDER(AUD) – RELAPSE PREVENTION IN PATIENTS WITH ALCOHOL ASSOCIATED LIVER DISEASE(ALD)

- Pharmacotherapy of AUD is effective and is associated with reduced risk of ALD and disease progression in those with cirrhosis
- In the setting of ALD cirrhosis, the use of medication-assisted therapies is cost-effective because of benefits in reducing clinical decompensation and readmission to the hospital .
- There are 3 US Food and Drug Administration (FDA)-approved medications (**disulfiram, acamprosate, and naltrexone**) for AUD and others that have shown utility in patients that are not US FDA-approved

BACLOFEN : In patients with advanced liver disease including cirrhosis and AH, baclofen (GABA-B receptor agonist), a non-US FDA-approved drug, has been studied the most.

The medication is started in a dose of 5 mg 3 times a day, with dose escalation at 3–5-day intervals based on patient tolerance to a maximum dose of 15 mg 3 times a day.

It has been shown to safely reduce alcohol use in patients with AH and increase abstinence rates in those with ALD cirrhosis .

ACAMPROSATE:Caution should be taken in patients with concurrent kidney disease, with dose adjustment if the creatinine clearance is between 30 and 50 and avoidance if below 30 mL/min. Dose is 666mg TDS.

NALTREXONE : Both short-term and long-term acting forms of naltrexone may be used in

individuals with early ALD and in those with compensated cirrhosis but should be avoided in patients with decompensated cirrhosis or liver failure and used cautiously in patients with kidney disease . Dose is 50 mg / day orally .

DISULFIRAM: Disulfiram is contraindicated in individuals with liver disease of any spectrum because it is completely metabolized by the liver and hepatotoxic.

Idiosyncratic liver injury of an immunoallergic mechanism has been well-described with disulfiram à more common in individuals with pre-existing liver disease.

In addition, there are several medications with some benefit in relapse prevention that have not been FDA-approved for AUD treatment. These agents include gabapentin, baclofen and topiramate

Medication	Dosing	Metabolism (M) and Excretion (E)	Mechanism of Action	ALD Considerations
Naltrexone*	50 mg/d orally or 380 mg monthly sq	M: Hepatic E: Mostly renal, fecal 2%-3%	Opioid receptor antagonist	Not studied in patients with ALD Hepatotoxicity concerns
Acamprosate*	666 mg tid	M: None E: Renal	NMDA receptor antagonist	Not studied in patients with ALD No reported instances of hepatotoxicity
Gabapentin	600-1,800 mg/d	M: None E: Renal 75%, fecal 25%	Modulates GABA activity through action at presynaptic calcium channels	Not studied in patients with ALD Monitor closely for renal dysfunction and worsening mental status/sedation
Baclofen	30-60 mg/d	M: Hepatic, limited E: Renal	GABA-B receptor agonist	Single RCT in patients with ALD showed benefit
Topiramate	75-400 mg/d	M: Not extensively metabolized E: Renal	GABA action augmentation, glutamate antagonism	Not studied in patients with ALD

Drugs for relapse prevention in patients with alcohol associated liver disease

(Table adapted from *Diagnosis and Treatment of Alcohol-Associated Liver Diseases: 2019 Practice Guidance From the American Association for the Study of Liver Diseases* AASLD -2019)

REFERENCES

ACG Clinical Guideline: Alcohol-Associated Liver Disease 2024, Diagnosis and Treatment of Alcohol-Associated Liver Diseases: 2019 Practice Guidance From the American Association for the Study of Liver Diseases, EASL Clinical Practice Guidelines: Management of alcohol-related liver disease 2018

7 HEPATOCELLULAR CARCINOMA (HCC)

SCOPE

This guideline provides a standardized approach to the surveillance, diagnosis, staging, and management of hepatocellular carcinoma in adult patients, particularly those with underlying chronic liver disease and cirrhosis. It is intended for use by physicians, surgeons, oncologists, hepatologists, and multidisciplinary teams involved in the care of patients at risk of or diagnosed with HCC in secondary and tertiary healthcare settings.

The document outlines risk stratification and surveillance strategies for high-risk populations, criteria for non-invasive and histological diagnosis, and the use of standardized imaging systems. It includes staging based on validated systems such as the Barcelona Clinic Liver Cancer classification and provides evidence-based recommendations for treatment allocation, including surgical resection, liver transplantation, locoregional therapies, systemic therapies, and palliative care. The guideline also emphasizes the importance of multidisciplinary decision-making and individualized treatment planning.

This guideline does not cover pediatric liver tumors, non-hepatocellular primary liver malignancies, or detailed post-transplant management protocols. The recommendations are based on established clinical practice guidelines, including those from the European Association for the Study of the Liver, American Association for the Study of Liver Diseases, and the Indian National Association for the Study of the Liver, and are adapted for practical application in routine clinical practice, including resource-limited settings.

INTRODUCTION

Liver cancer is the sixth leading cause of cancer and the third leading cause of cancer-related deaths globally. Hepatocellular carcinoma represents about 90% of primary liver cancers and constitutes a major global health problem. Cirrhosis is an important risk factor for HCC, and may be caused by chronic viral hepatitis, chronic alcohol abuse acquired and inherited metabolic diseases. All aetiologic forms of cirrhosis may be complicated by tumour formation, but the risk is higher in patients with chronic viral hepatitis.

Surveillance

Aim of surveillance is to obtain a reduction in HCC related mortality. This is usually achieved through a diagnosis of the disease at the early stage. Patients at high risk of developing HCC as in depicted (Table 1) should be entered into a surveillance programme. An ultrasound examination of the liver every 6 months is recommended for screening of HCC. The combined use of ultrasound with / without AFP should be done. Adding of AFP increases the sensitivity to pick up HCC.

Patients on the waiting list for liver transplantation should undergo surveillance for HCC in order to detect and manage tumour occurrence or tumour response, and to help define priority policies for transplantation. Surveillance should be offered to treated patients with chronic hepatitis B who remain at risk of HCC development because of baseline factors, or those with hepatitis C virus (HCV)-induced advanced fibrosis or cirrhosis, even after achieving SVR

It is of great clinical relevance to point out that patients with HCV-associated cirrhosis and HCC treated with curative intent maintain a high rate of HCC recurrence even after subsequent DAA therapy. In these patients, close surveillance (tertiary prevention) is advised and the benefit of viral cure must be weighed against a potentially higher recurrence risk. The follow- up after HCC treatment with curative intent and subsequent successful DAA treatment implies 3–4-month imaging intervals for the first two years that can be extended to six month intervals thereafter.

Recommendations for HCC surveillance: Categories of adult patients in whomsurveillance is recommended. (Table 1)

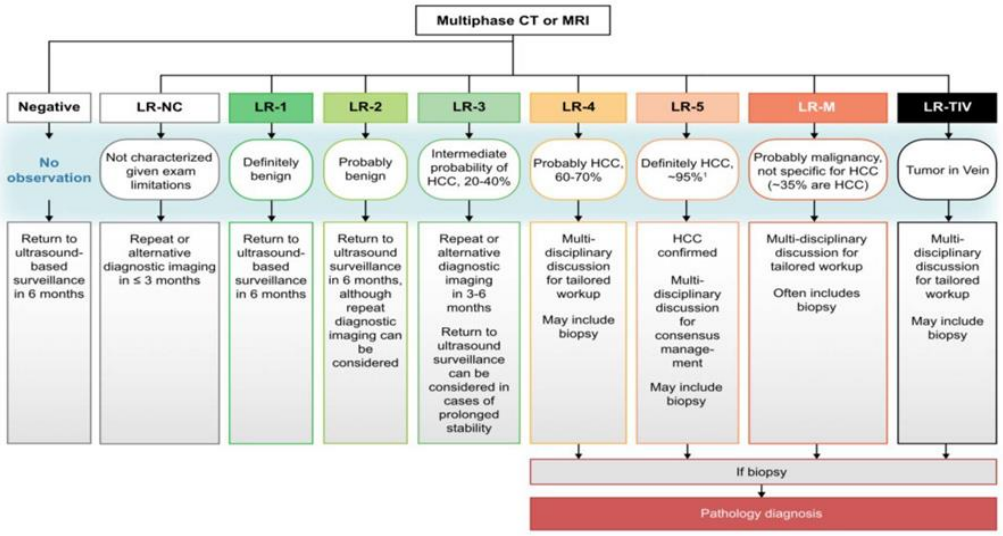
1.	Cirrhotic patients, Child-Pugh stage A and B.
2.	Cirrhotic patients, Child-Pugh stage C awaiting liver transplantation.
3.	Non-cirrhotic HBV patients at intermediate or high risk of HCC* (according to PAGE-Bclasses for Caucasian subjects, respectively 10–17 and ≥18 score

	points).
4.	Non-cirrhotic F3 fibrosis patients, regardless of aetiology may be considered for surveillance based on an individual risk assessment

Diagnosis of HCC in a cirrhotic liver

The LI-RADS should be used to favourstandardisation in the acquisition, description and reporting of liver imaging examinations. Non-invasive diagnosis of HCC should be based on the LIRADS CT/MRI. With CT/MRI, the following major imaging features are combined to reach the diagnosis: tumour size, rim and non rim arterial hyperenhancement, peripheral and non peripheral washout (in the portal venous or delayed phases on CT and MRI), enhancing capsule and threshold growth.It cannot be applied to patients <18 years old, patients with cirrhosis due to congenital hepatic fibrosis vascular disorders such as hereditary haemorrhagic telangiectasia, Budd-Chiari syndrome, chronic portal vein occlusion,cardiac congestion, or diffuse nodular regenerative hyperplasia. It cannot be applied either to pathologically proven tumours.

Those patients without cirrhosis or chronic HBV infection, current or previous HCC are considered low risk and require biopsy for diagnosis.

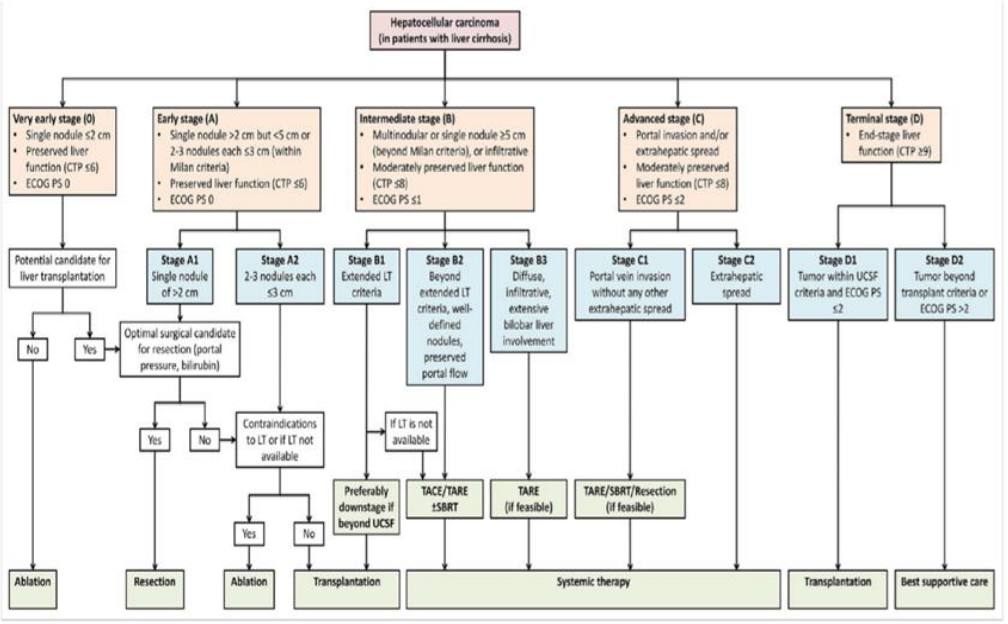


Staging systems and treatment allocation

Cancer classification is intended to establish prognosis and enable the selection of the adequate treatment for the best candidates. Staging systems for clinical decision making in HCC should include tumour burden, liver function and performance status. The BCLC staging system has been repeatedly validated and is recommended for prognostic prediction and treatment allocation.

Patients should be discussed in multidisciplinary teams to fully capture and tailor individualised treatment options.

Modified BCLC staging system and treatment strategy



Outcome prediction and treatment allocation

Patients with HCC are classified into five stages (0, A, B, C and D) according to pre-established prognostic variables, and therapies are allocated according to treatment related status. Prognosis prediction is defined by variables related to tumour status , liver function (bilirubin, portal hypertension, liver function preservation) and health

status (ECOG).

Optimal management of HCC requires the opinion and expertise of various specialists, making a coordinated multidisciplinary team (MDT) essential.

Concept of treatment stage migrationA proportion of patients in each stage do not fulfil all the criteria for the treatment allocation. In these cases, the patient should be offered the next most suitable option within the same stage or the next prognostic stage.

Response assessment

Assessment of response in HCC should be based on mRECIST for loco-regional therapies. For systemic therapies both mRECIST and RECIST1.1 are recommended. Multiphasic contrast-enhanced CT or MRI are recommended for assessment of response after resection, loco-regional or systemic therapies.

TREATMENT MODALITIES

Surgery

1. Liver resection

a) In cirrhotic liver

Indications for resection of HCC in cirrhosis should be based on multi-parametric composite assessment of liver function, portal hypertension, extent of hepatectomy, expected volume of the future liver remnant, performance status and patients' comorbidities. Perioperative mortality of liver resection in cirrhotic patients should be less than 3%. LR is recommended for single HCC of any size and in particular for tumours>2 cm, when hepatic function is preserved, and sufficient remnant liver volume is maintained. HCC presenting with two or three nodules within Milan criteria may be eligible for LR according to patient performance status, co-morbidities and preservation of liver function and remnant volume. HCC-related macrovascular invasion is a contraindication for LR. Follow-up after resection with curative intent is recommended because of high rates of treatable recurrence. Surveillance USG should be done every 3– 4 months in the first year.

b) In non-cirrhotic liver

Surgical resection is recommended as treatment of choice in patients with HCC arising in a non-cirrhotic liver.

2.Liver transplantation

LT is recommended as the first-line option for HCC within Milan criteria but unsuitable for resection. Consensus on expanded criteria for LT in HCC has not been reached. Patients beyond the Milan criteria can be considered for LT after successful downstaging to within Milan criteria, within defined protocols .Tumour vascular invasion and extrahepatic metastases are an absolute contraindication for LT in HCC.The use of marginal cadaveric grafts for LT in patients with HCC is no contraindication.

Prioritisation criteria for HCC should at least include tumour burden, tumour biology indicators, waiting time and response to tumour treatment. In LT candidates with HCC, the use of pre-transplant loco-regional therapies is recommended. Living donor LT for HCC remains an option to be explored in selected patients and in experienced centres, according to waiting list time and dynamics, and within donor-recipient double equipoise principles. The expected five-year survival rates of LT for HCC meeting conventional Milan criteria (single tumour ≤5 cm or multiple tumours ≤3 nodules ≤3 cm in size, without vascular invasion) are 65%–80%. Those beyond Milan can be offered LT only after successful down staging into Milan criteria.

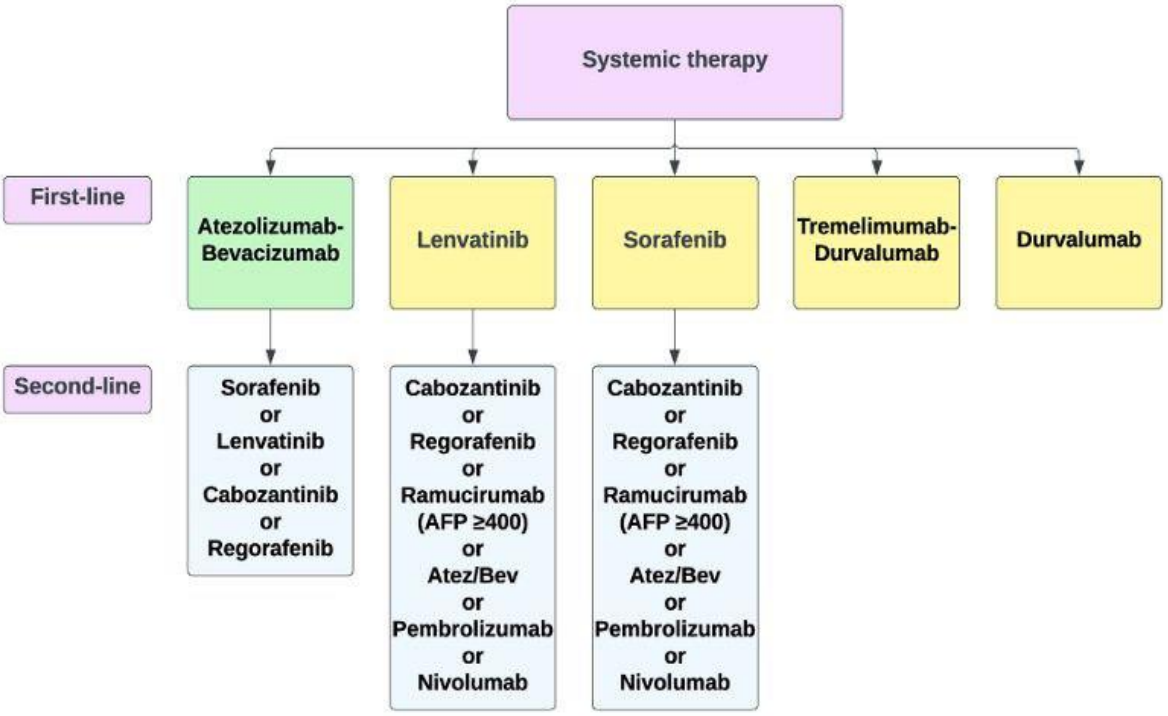
3. Locoregional therapies

Non-surgical locoregional therapies include percutaneous ablation, intraarterialembolising therapies and external beam radiation therapy (EBRT). Thermal percutaneous ablation is usually performed using radiofrequency and microwave as the source of heating energy. Embolising techniques rely on the predominantly arterial vascularisation of HCC and include bland trans arterial embolisation (TAE), conventional TACE (cTACE), drug-eluting beads TACE (DEB-TACE) and selective internal radiation therapy (SIRT), also called trans arterial radio embolization . EBRT is delivered from a linear accelerator that delivers

multiple beams of ionizing radiation to deposit high dose to the tumor, with rapid dose fall off to the surrounding normal tissues. EBRT can be considered an alternative to percutaneous ablation for single tumours within Milan criteria unsuitable for resection or transplantation, when there is a significant risk of post-ablation recurrence based on size (>3 cm) or location (in contact with large vessels). TARE can be used an accepted alternative intra-arterial therapy for intermediate-stage HCC. Selective TARE/ or radiation segmentectomy is defined as the administration of an ablative dose of Y90 microspheres to a single angiographic hepatic segment or two adjacent angiographic segments

4.Systemic therapies

Combination immunotherapies and TKIs are the mainstay of systemic therapy of HCC. Immune checkpoints include co-inhibitory molecules expressed by effector lymphocytes that prevent their overactivation. ICIs abrogate this effect and reinvigorate effector cells. ICIs used are PD-1 (nivolumab, pembrolizumab, s) or its ligand PD-L1 (atezolizumab, durvalumab); and cytotoxic T lymphocyte associated antigen 4 or CTLA-4 (ipilimumab, tremelimumab). Anti-VEGF drugs bevacizumab. In patients with advanced HCC, preserved liver function (Child-Pugh A) and ECOG performance status 0-1, combinations including at least one PD-1 or PD-L1 inhibitor should be offered, provided there are no contraindications. Combination therapy containing PD-1 or PD-L1 inhibitors should be considered first-line standard of care for those without contraindications to ICIs (and bevacizumab). Sorafenib and lenvatinib remain first-line options in these patients and both single agent durvalumab and tislelizumab may also be considered.



5. Palliative and best supportive care

Patients at BCLC D stage, who are not candidates for liver transplantation should receive palliative support, including management of pain, nutrition and psychological support.

In HCC on cirrhosis, acetaminophen (paracetamol) up to 3 g/day, depending on the severity of liver diseasecan be utilised for the management of pain of mild intensity. Non-steroidal anti-inflammatory drugs should be avoided whenever possible in patients with underlying cirrhosis. Opioids can be utilised for the management of pain of intermediate or severe intensity, paying attention to proactively avoid constipation. Bone metastases causing pain or at significant risk of spontaneous secondary fracture benefit from palliative radiotherapy.

Psycho-oncological support and adequate nutrition is recommended according to patients condition.

REFERENCES

EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatology 2018/ 2024, AASLD Practice Guidance on prevention, diagnosis and treatment of hepatocellular carcinoma 2023, INASL modification of BCLC Staging 2023

8. ACUTE CHOLANGITIS (Tokyo Guidelines 2018)

1. SCOPE

This guideline provides a standardized approach to the diagnosis, severity assessment, and management of acute cholangitis in adult patients with biliary obstruction and infection. It is intended for use by physicians, surgeons, gastroenterologists, intensivists, and emergency care providers involved in the management of such patients in secondary and tertiary healthcare settings.

The document outlines the diagnostic criteria and severity grading based on the Tokyo Guidelines 2018, and provides recommendations for initial assessment, imaging, antimicrobial therapy, and timely biliary drainage. It also includes guidance on supportive care, monitoring, and indications for referral or transfer to higher centers for advanced interventions.

This guideline does not cover chronic biliary diseases, pediatric cholangitis, or detailed surgical management of underlying biliary pathology. The recommendations are adapted for practical implementation in routine clinical practice, including resource-limited settings.

Introduction

Acute cholangitis (AC) occurs when biliary stenosis, due to various benign causes (often bile duct stones) or the presence of a tumor, results in cholestasis and biliary infection. Mortality risk is high if the condition is not treated with antibiotic therapy and biliary pressure is not immediately reduced using appropriate methods.

TG18/TG13 diagnostic criteria for acute cholangitis

Systemic inflammation A-1. Fever (> 38 °C) and/or shaking chills A-2. Laboratory data: evidence of inflammatory response B. Cholestasis B-1. Jaundice(bilirubin > 2 mg/dL) B-2. Laboratory data: abnormal liver function tests C. Imaging C-1. Biliary dilatation C-2. Evidence of the etiology on imaging (stricture, stone, stent etc.)
Suspected diagnosis: one item in A + one item in either B or C Definite diagnosis: one item in A, one item in B and one item in C
Note: A-2: Abnormal white blood cell counts (leukocytes < 4,000 or > 10,000/μL), increase of serum C reactive protein levels (CRP > 1 mg/dL), and other changes indicating inflammation B-2: Increased serum ALP, GGT) AST, and ALT levels(> 1.5 times upper limit)

TG18/TG13 severity assessment criteria for acute cholangitis

Grade III (severe) acute cholangitis "Grade III" acute cholangitis is defined as acute cholangitis that is associated with the onset of dysfunction at least in any one of the following organs/systems: 1.Cardiovascular dysfunction: hypotension requiring dopamine ≥5 mcg/kg per min, or any dose of norepinephrine 2.Neurological dysfunction: disturbance of consciousness 3.Respiratory dysfunction: PaO2/FiO2 ratio <300 4.Renal dysfunction: oliguria, serum creatinine >2.0 mg/dl 5.Hepatic dysfunction: PT-INR >1.5 6.Hematological dysfunction: platelet count <100,000/mm3
Grade II (moderate) acute cholangitis "Grade II" acute cholangitis is associated with any two of the following conditions: 1.Abnormal WBC count (>12,000/mm3, <4,000/mm3) 2.High fever (≥39°C) 3.Age (≥75 years) 4.Hyperbilirubinemia (total bilirubin ≥5 mg/dl) 5.Hypoalbuminemia (<STD 9 0.7)
Grade I (mild) acute cholangitis "Grade I" acute cholangitis does not meet the criteria of "Grade III (severe)" or "Grade II (moderate)" acute cholangitis at initial diagnosis

STD lower limit of normal value

MANAGEMENT OF ACUTE CHOLANGITIS

1. When acute cholangitis is suspected, diagnostic assessment is made using TG18/TG13 diagnostic criteria every 6-12 hours.

2. Imaging modalities capable of yielding such findings include abdominal ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP), whereas simple X-rays are not suited to diagnoses.

3. Endoscopic retrograde cholangiopancreatography is performed for the purposes of treatment (drainage), but is not suitable as first choice for diagnostic purposes.

4. Severity is repeatedly assessed using severity assessment criteria; at diagnosis, within 24 hours after diagnosis, and during the time zone of 24–48 hours

5. As soon as a diagnosis has been made, the initial treatment is provided. The treatment is as follows: sufficient fluids replacement, electrolyte compensation, and intravenous administration of analgesics and full dose of antimicrobial agents are provided

6. For patients with Grade I (mild), in most cases initial treatment including antibiotics is sufficient. However, biliary drainage should be considered if a patient does not respond to initial treatment within 24 hours. Treatment for the underlying etiology such as endoscopic sphincterotomy (EST) and subsequent choledocholithotomy may be performed at the same time as biliary drainage.

7. For patients with Grade II (moderate), early endoscopic or percutaneous transhepatic biliary drainage is indicated. If the underlying etiology requires treatment, this should be provided after the patient's general condition has improved, and EST and subsequent choledocholithotomy may be performed together with biliary drainage.

Initial management of acute cholangitis

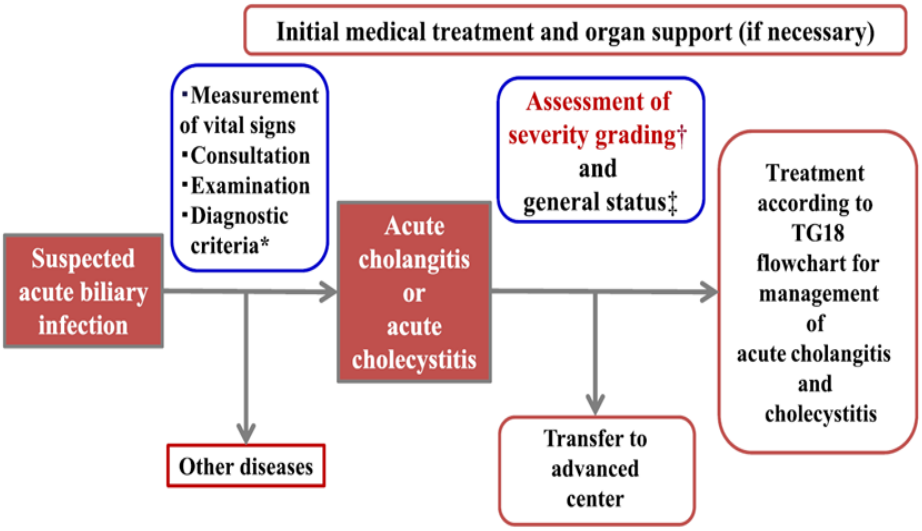


Fig. 1 TG18 flowchart for the initial response to acute biliary infection. *TG18/TG13 diagnostic criteria for acute cholangitis [4] and cholecystitis [7] should be used. †TG18/TG13 severity assessment criteria for acute cholangitis [4] and cholecystitis [7] should be used. ‡Charlson comorbidity index (CCI) [10] and the American Society of Anesthesiologists (ASA) Physical Status (PS) classification [11] should be referred to

8. For patient with Grade III (severe), organ supports (noninvasive/invasive positive pressure ventilation, use of vasopressors and antimicrobial agents, etc.) are immediately performed. Endoscopic or percutaneous transhepatic biliary drainage should be performed as soon as possible after the patient's condition has been improved by initial treatment and respiratory/ circulatory management. If treatment for the underlying etiology is required, this should be provided after the patient's general status has improved

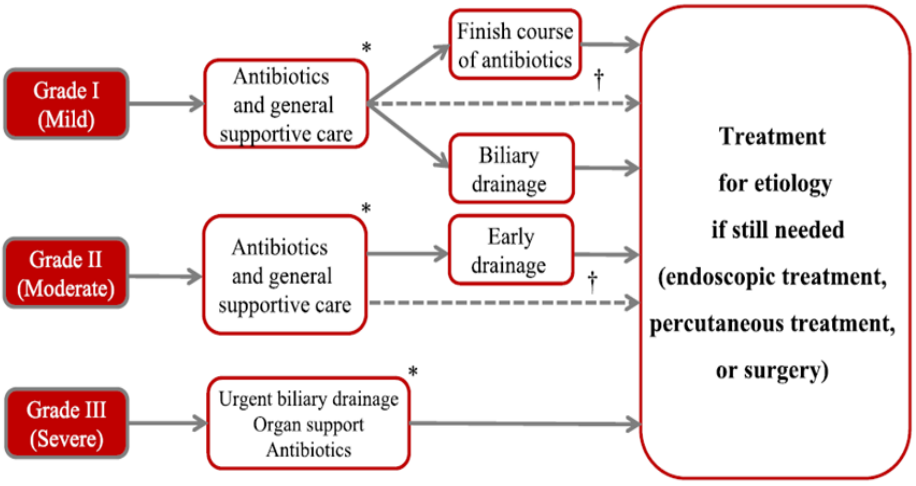


Fig. 2 TG18 flowchart for the management of acute cholangitis. Cited and modified from Miura et al. [12]. *Blood culture should be taken into consideration before antibiotics are started. Bile samples should be taken during biliary drainage and cultured. †Principles of treatment for acute cholangitis consist of antimicrobial administration, biliary drainage, and treatment of the etiology. For patients with mild or moderate choledocholithiasis, if possible the etiology should be treated at the same time as biliary drainage is performed

Tokyo Guidelines 2018: antimicrobial therapy for acute cholangitis

- The role of antimicrobial therapy for acute cholangitis is to allow patients to have elective drainage procedures other than emergency.
- Bile cultures should be obtained at the beginning of any procedure performed
- Most frequently isolated organisms are Gram negative organisms which include Escherichia coli, Klebsiellaspp.
- When selecting antimicrobial agents, targeted organisms, pharmacokinetics and pharmacodynamics, local antibiogram, a history of antimicrobial usage, renal and hepatic function, and a history of allergies and other adverse events should be considered.

Table 3 Antimicrobial recommendations for acute biliary infections

Severity	Community-acquired biliary infections			Healthcare-associated biliary infections[a]
	Grade I	Grade II	Grade III[a]	
Antimicrobial agents	Cholangitis and cholecystitis	Cholangitis and cholecystitis	Cholangitis and cholecystitis	Healthcare-associated cholangitis and cholecystitis
Penicillin-based therapy	Ampicillin/sulbactam[b] is not recommended if >20% resistance rate.	Piperacillin/tazobactam	Piperacillin/tazobactam	Piperacillin/tazobactam
Cephalosporin-based therapy	Cefazolin,[c] or Cefotiam,[c] or Cefuroxime,[c] or Ceftriaxone, or Cefotaxime ± Metronidazole[d] Cefmetazole,[c] Cefoxitin,[c] Flomoxef,[c] Cefoperazone/sulbactam	Ceftriaxone, or Cefotaxime, or Cefepime, or Cefozopran, or Ceftazidime ± Metronidazole[d] Cefoperazone/sulbactam	Cefepime, or Ceftazidime, or Cefozopran ± Metronidazole[d]	Cefepime, or Ceftazidime, or Cefozopran ± Metronidazole[d]
Carbapenem-based therapy	Ertapenem	Ertapenem	Imipenem/cilastatin, Meropenem, Doripenem, Ertapenem	Imipenem/cilastatin, Meropenem, Doripenem, Ertapenem
Monobactam-based therapy	–	–	Aztreonam ± Metronidazole[d]	Aztreonam ± Metronidazole[d]
Fluoroquinolone-based therapy[e]	Ciprofloxacin, Levofloxacin, Pazufloxacin ± Metronidazole[d] Moxifloxacin	Ciprofloxacin, Levofloxacin, Pazufloxacin ± Metronidazole[d] Moxifloxacin	–	–

Table 3 is modified and cited from the Tokyo Guidelines 2013 (TG13) [1]

[a]Vancomycin is recommended to cover *Enterococcus* spp. for grade III community-acquired acute cholangitis and cholecystitis, and healthcare-associated acute biliary infections. Linezolid or daptomycin is recommended if vancomycin-resistant *Enterococcus* (VRE) is known to be colonizing the patient, if previous treatment included vancomycin, and/or if the organism is common in the community

[b]Ampicillin/sulbactam has little activity left against *Escherichia coli*. It is removed from the North American guidelines [43, 49]

[c]Local antimicrobial susceptibility patterns (antibiogram) should be considered for use

[d]Anti-anaerobic therapy, including use of metronidazole, tinidazole, or clindamycin, is warranted if a biliary-enteric anastomosis is present. The carbapenems, piperacillin/tazobactam, ampicillin/sulbactam, cefmetazole, cefoxitin, flomoxef, and cefoperazone/sulbactam have sufficient anti-anaerobic activity for this situation

[e]Fluoroquinolones use is recommended if the susceptibility of cultured isolates is known or for patients with β-lactam allergies. Many extended-spectrum β-lactamase (ESBL)-producing Gram-negative isolates are fluoroquinolone resistant

Recommended duration of antimicrobial therapy

	Community-acquired biliary infections	Healthcare-associated biliary infections
Severity and diagnosis	Grade I, II and III cholangitis	Grade I, II, III healthcare-associated cholangitis and cholecystitis
Duration of therapy	Once source of infection is controlled, duration of 4–7 days is recommended. If bacteremia with Gram-positive cocci such as Enterococcus spp., Streptococcus spp. is present, duration of minimum 2 weeks is recommended.	If bacteremia with Gram-positive cocci such as Enterococcus spp., Streptococcus spp. is present, duration of minimum 2 weeks is recommended.

Specific conditions for extended therapy	Residual stones or obstruction of the bile tract are present, treatment should be continued until these anatomic problems are resolved. If liver abscess is present, treatment should be continued until clinical, biochemical and radiological follow-up demonstrates complete resolution of the abscess.

Transfer criteria for acute cholangitis

Severe acute cholangitis (Grade III) Patients who require emergency biliary drainage as well as critical care should be transferred immediately to a hospital where this can be provided
Moderate acute cholangitis (Grade II) Patients should be treated in a hospital where biliary drainage and systemic management can be performed. If a hospital is not equipped to perform biliary drainage, they should be transferred to a hospital where this can be provided
Mild acute cholangitis (Grade I) If a calculus is present in the common bile duct or there is no response to initial treatment (within 24 h), a similar response to that for moderate acute cholangitis should be considered

REFERENCES

1. Tokyo Guidelines 2018: Diagnostic criteria and severity grading of acute cholangitis and cholecystitis. *Journal of Hepato-Biliary-Pancreatic Sciences*. 2018.

9. ACUTE PANCREATITIS

1. SCOPE

This guideline provides a standardized approach to the diagnosis, severity assessment, and management of acute pancreatitis in adult patients presenting with acute abdominal pain and suspected pancreatic inflammation. It is intended for use by physicians, surgeons, intensivists, and emergency care providers involved in the management of such patients in secondary and tertiary healthcare settings.

The document outlines the clinical diagnostic criteria, appropriate use of laboratory and imaging modalities, and classification of disease severity based on the revised Atlanta classification. It includes evidence-based recommendations for initial resuscitation, fluid management, nutritional support, use of antibiotics, role of endoscopic interventions such as ERCP, and indications for surgical or minimally invasive procedures in complications such as necrosis and pseudocyst.

This guideline does not cover chronic pancreatitis, pancreatic malignancies, pediatric pancreatitis, or detailed long-term follow-up protocols. The recommendations are based on established clinical guidelines, including those from the American College of Gastroenterology and the revised Atlanta classification, and are adapted for practical application in routine clinical practice, including resource-limited settings.

INTRODUCTION

Acute pancreatitis (AP) is best defined physiologically as an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ system.

DIAGNOSIS

The diagnosis of AP is established by identification of 2 of the 3 following criteria:

(i) abdominal pain consistent with the disease [acute onset epigastric and/or left upper quadrant pain, often radiating to the back],

(ii) serum amylase and/or lipase level greater than 3 times the upper limit of normal, and

(iii) characteristic findings from abdominal imaging, usually using CT or MRI.

Due to limitations on sensitivity and negative predictive value, serum amylase alone cannot be used reliably for the diagnosis of AP, and serum lipase is preferred.

Routine use of abdominal CT in patients with AP is unwarranted. However, in a patient failing to improve after 48–72 hours (e.g., persistent pain, fever, nausea, and unable to begin oral feeding), CT or MRI is recommended to assess local complications such as pancreatic necrosis.

In all patients of Acute Pancreatitis, basic evaluation to identify the etiology of pancreatitis is necessary.

Severity of acute pancreatitis (2012 Atlanta classification revision of acute pancreatitis)

1) Mild acute pancreatitis
   No organ failure
   No local or systemic complications
2) Moderately SAP
   Transient organ failure (<48 hours) and/or
   Local or systemic complications without persistent organ failure
3) Severe acute pancreatitis
   Persistent organ failure (>48 hours)––single organ or multiorgan

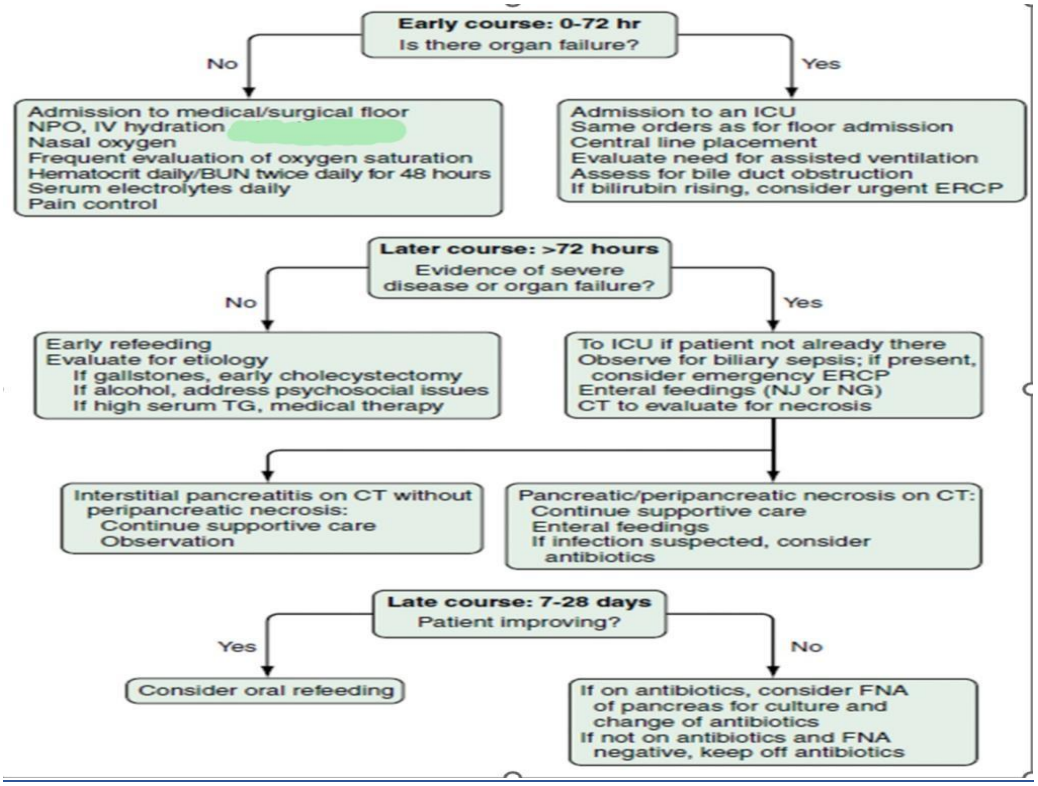
Local complications are peripancreatic fluid collections, pancreatic necrosis, and peripancreatic necrosis (sterile or infected), pseudocyst, and WON (sterile or infected).

Definition of organ failure

Three organ systems should be assessed to define organ failure: respiratory, cardiovascular and renal. Organ failure is defined as a score of 2 or more for one of these three organ systems using the modified Marshall scoring system as given below:

	Score				
Organ system	0	1	2	3	4
Respiratory (PaO_2/FiO_2)	>400	301–400	201–300	101–200	≤101
Renal*					
(serum creatinine, µmol/l)	≤134	134–169	170–310	311–439	>439
(serum creatinine, mg/dl)	<1.4	1.4–1.8	1.9–3.6	3.6–4.9	>4.9
Cardiovascular (systolic blood pressure, mm Hg)†	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH<7.3	<90, pH<7.2

Algorithm for the management of acute pancreatitis at various stages in its course.



BUN - blood urea nitrogen; ERCP – Endoscopic Retrograde CholangioPancreaticography; NG - nasogastric; NJ - nasojejunal; TG - triglycerides. (Sleisenger and Fordtran's gastrointestinal and liver disease pathophysiology, diagnosis, management. 10th edition)

MANAGEMENT

Initial management

1. Moderate intravenous hydration during the first 24–48 hours may be equally effective as aggressive hydration. In patients with no evidence of hypovolemia, an initial resuscitation rate of no more than 1.5 mL/kg of body weight per hour should be administered. The preferred crystalloid is lactated Ringer solution.
2. However, in patients with hypovolemia, clinicians should administer a bolus of 10 mL/kg.
3. Older individuals and those with a history of cardiac and/or renal disease will need caution when applying hydration.
4. When severe disease develops and/or after 24 hours, aggressive hydration may actually be harmful and goal directed hydration is recommended.
5. Fluid requirements should be reassessed at frequent intervals within 6 h of admission and for the next 24 48 h.

Ercp in AP

1. Patients with acute biliary pancreatitis and concurrent acute cholangitis should undergo ERCP. Early ERCP within the first 24 hours has been shown to decrease morbidity and mortality.
2. In the absence of cholangitis and / or jaundice, MRCP or EUS rather than diagnostic ERCP should be used to screen for choledocholithiasis.
3. Pancreatic duct stents and periprocedural rectal nonsteroidal anti-inflammatory drug (NSAID) suppositories (indomethacin 100mg) should be utilized to lower the risk of post-ERCP pancreatitis in high-risk patients.

ANTIBIOTICS IN ACUTE PANCREATITIS

1. Antibiotics should be given for an extrapancreatic infection, such as cholangitis, catheter-acquired infections, bacteremia, urinary tract infections, pneumonia .
2 .Routine use of prophylactic antibiotics in patients with severe AP is not recommended.
3. The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is not recommended.
4. Infected necrosis should be considered in patients with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7 – 10 days of hospitalization. In these patients, either (i) initial CT-guided fine-needle aspiration (FNA) for Gram stain and culture to guide use of appropriate antibiotics or (ii) empiric use of antibiotics after obtaining necessary cultures for infectious agents, without CT FNA, should be given.
5. In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis, such as carbapenems, quinolones, and metronidazole, may be useful in delaying or sometimes totally avoiding intervention, thus decreasing morbidity and mortality.

NUTRITION

In patients with mild AP, early oral feeding (within 24–48 hours) is recommended as tolerated by the patient. Initial oral feeding with low fat solid diet is preferred rather than a stepwise liquid to solid approach.In moderately severe / severe AP, enteral nutrition is recommended to prevent infectious complications. Parenteral nutrition should be avoided, unless the enteral route is not available, not tolerated, or not meeting caloric requirements . Nasogastric delivery is preferred over nasojejunal route. If enteral nutrition is administered by tube feeds, continuous infusion is preferred over cyclic or bolus administration.

ROLE OF SURGERY

1. Patients with mild acute biliary pancreatitis should undergo cholecystectomy early, preferably before discharge to prevent a recurrence of AP.

2. In a patient with necrotizing biliary AP, in order to prevent infection, cholecystectomy is to be deferred until active inflammation subsides and fluid collections resolve or stabilize.
3. Asymptomatic pseudocysts and pancreatic and / or extrapancreatic necrosis do not warrant intervention regardless of size, location, and / or extension.
4. In stable patients with infected necrosis, surgical, radiologic, and / or endoscopic drainage should be delayed preferably for more than 4 weeks to allow liquefication of the contents and the development of a fibrous wall around the necrosis (walled-off necrosis).
5. In symptomatic patients with infected necrosis, minimally invasive methods of necrosectomy are preferred to open necrosectomy.

REFERENCES

American College of Gastroenterology Guidelines: Management of Acute Pancreatitis; Am J Gastroenterol 2024, Classification of acute pancreatitis—2012: Revision of the Atlanta classification and definitions by international consensus, Gut 2013, Sleisenger and Fordtran's Gastrointestinal and Liver Disease 11th edition

10. PEPTIC ULCER BLEEDING

SCOPE

This section outlines a comprehensive, evidence-based framework for the evaluation, risk stratification, and management of non-variceal upper gastrointestinal bleeding, aligned with recommendations from bodies such as the American College of Gastroenterology and European Society of Gastrointestinal Endoscopy.

It covers the entire continuum of care, including:

- Initial assessment and resuscitation, with emphasis on early hemodynamic stabilization and appropriate transfusion strategies.
- Risk stratification tools (e.g., Glasgow-Blatchford score) to identify low-risk patients suitable for early discharge versus high-risk patients requiring urgent intervention.
- Pre-endoscopic management, including proton pump inhibitor therapy and optimization before endoscopy.
- Timing and role of endoscopy, including identification of high-risk stigmata and application of endoscopic hemostatic techniques.
- Endoscopic therapeutic modalities, such as injection therapy, thermal coagulation, clips, and newer modalities like hemostatic powders.
- Post-endoscopic management, including PPI infusion protocols, monitoring, and criteria for repeat endoscopy or escalation to interventional radiology or surgery.
- Hospitalization and discharge planning, based on bleeding risk and clinical stability.
- Secondary prevention strategies, including:
    - Helicobacter pylori infection eradication
    - NSAID and antiplatelet management
    - Long-term acid suppression therapy

  Additionally, the scope includes management considerations in special clinical scenarios, such as:

- Patients on anticoagulants and antiplatelet agents
- Recurrent or refractory bleeding
- Idiopathic ulcers

Overall, this section is intended to serve as a practical clinical guide for physicians managing UGIB in emergency, ward, and intensive care settings, facilitating timely intervention, reduction in rebleeding rates, and improved patient outcomes.

1. Initial assessment and risk stratification

- Hemodynamic status should be assessed immediately upon presentation and resuscitative measures begun.
- Blood transfusions should target haemoglobin ≥ 7 g/dl, with higher haemoglobin targeted in patients with clinical evidence of intravascular volume depletion or comorbidities such as coronary artery disease(haemoglobin ≥ 8 g/dl)

Risk assessment should be performed to stratify patients into higher and lower risk categories

Risk stratification Scoring System for Upper GI Tract Bleeding (Glasgow-Blatchford)

Risk factors at admission	Factor score
Blood urea nitrogen (mg/dL)	
18.2 to <22.4	2
22.4 to <28.0	3
28.0 to <70.0	4
>=70.0	6
Hemoglobin (g/dL)	
12.0 to <13.0 (men); 10.0 to <12.0 (women)	1
10.0 to <12.0 (men)	3
<10.0	6
Systolic blood pressure (mm Hg)	
100-109	1
90-99	2
<90	3
Heart rate (beats per minute)	
>=100	1
Melena	1
Syncope	2
Hepatic disease	2
Cardiac failure	2

Adapted from ACG peptic ulcer guidelines (2021)

*Hepatic disease and cardiac failure were not defined in the original report of the Glasgow-Blatchford score. A more recent study defined hepatic disease as known history or clinical and laboratory evidence of chronic or acute liver disease and cardiac failure as known history or clinical and echocardiographic evidence of cardiac failure.

2. Pre-endoscopic medical therapy.

a) Proton pump inhibitor therapy

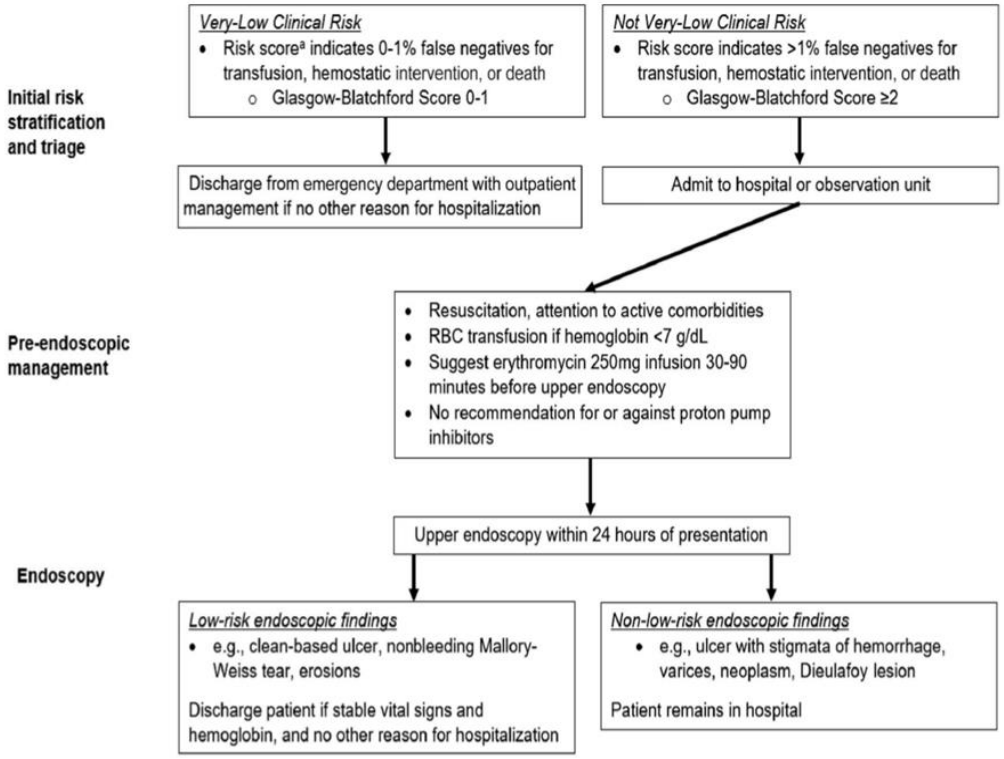
- Pre-endoscopic intravenous proton pump inhibitor (e.g., 80 mg bolus followed by 8 mg / h infusion) may be considered to decrease the proportion of patients who have higher risk stigmata of hemorrhage at endoscopy and who receive endoscopic therapy.
- If endoscopy is delayed or cannot be performed, IV PPI is recommended to reduce further bleeding.
- When available, an infusion of erythromycin before endoscopy in patients with UGIB is recommended.

b) Gastric lavage - NG or orogastric lavage is not required in patients with UGIB for diagnosis, prognosis, visualization, or therapeutic effect.

c) Timing of endoscopy

Patients with UGIB should generally undergo endoscopy as early as possible, following resuscitative efforts to optimize hemodynamic parameters and other medical problems.

Clinical algorithm for the management of peptic ulcer bleeding



3. Endoscopic management of ulcer bleed

Endoscopic diagnosis of ulcer and stigmata of recent hemorrhage

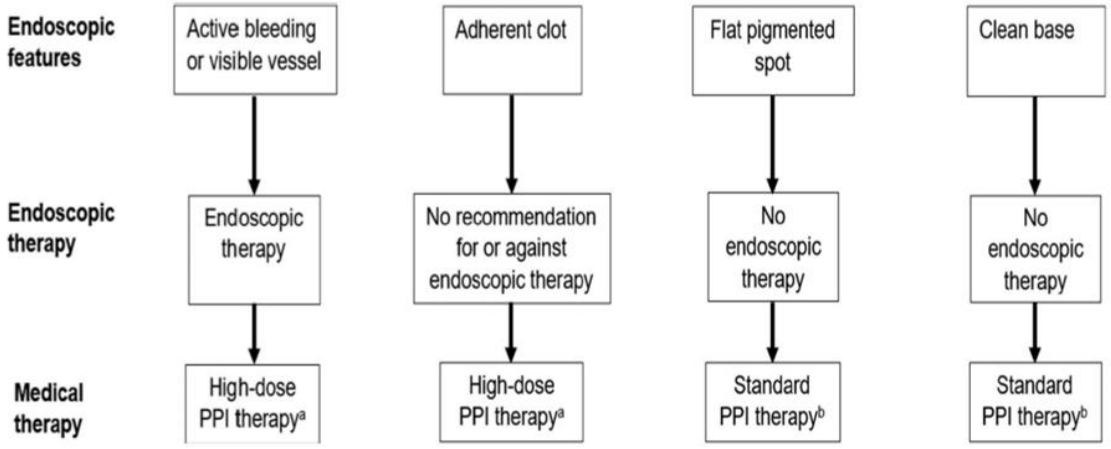
Stigmata of recent hemorrhage (SRH) should be recorded as they predict risk of further bleeding and guide management decisions. The stigmata, in descending risk of further bleeding, are active spurting, non-bleeding visible vessel, active oozing, adherent clot, flat pigmented spot, and clean base.

Forrest classification of peptic ulcer bleed

Forrest classification	
Active spurting bleeding	1 A
Active oozing bleeding	1B
Non-bleeding visible vessel	11A
Adherent clot	11B
Flat pigmented spot	11C
Clean base	111

- Endoscopic therapy should be provided to patients with active spurting or oozing bleeding or a non-bleeding visible vessel. Endoscopic therapy may be considered for patients with an adherent clot resistant to vigorous irrigation.
- Endoscopic therapy should not be provided to patients who have an ulcer with a clean base or a flat pigmented spot.

Fig: Endoscopic and medical therapy for ulcer bleeding based on endoscopic features of the ulcer.



For continuous regimen, 80-mg bolus followed by 8-mg/min infusion for 3 days is recommended. For intermittent regimens, doses of 40 mg 2 to 4 times daily for 3 days are suggested, given orally if feasible, and an initial bolus of 80 mg may be appropriate.

- Epinephrine therapy should not be used alone. If used, it should be combined with a second modality.
- Thermal therapy with bipolar electrocoagulation or heater probe and injection of sclerosant or injection of absolute ethanol are recommended because they decrease further bleeding, need for surgery, and mortality.
- Clips are recommended because they appear to decrease further bleeding and need for surgery.
- Endoscopic hemostatic therapy with hemostatic powder spray TC-325 is recommended for patients with actively bleeding ulcers.
- Over-the-scope clips as a hemostatic therapy is recommended for patients who develop recurrent bleeding due to ulcers after previous successful endoscopic hemostasis

4. Medical therapy after endoscopy

- After successful endoscopic hemostasis, intravenous PPI therapy with 80 mg bolus followed by 8 mg / h continuous infusion for 72 hr should be given to patients who have an ulcer with active bleeding, a non-bleeding visible vessel, or an adherent clot.
- Patients with ulcers that have flat pigmented spots or clean bases can receive standard PPI therapy (e.g., oral PPI once-daily).

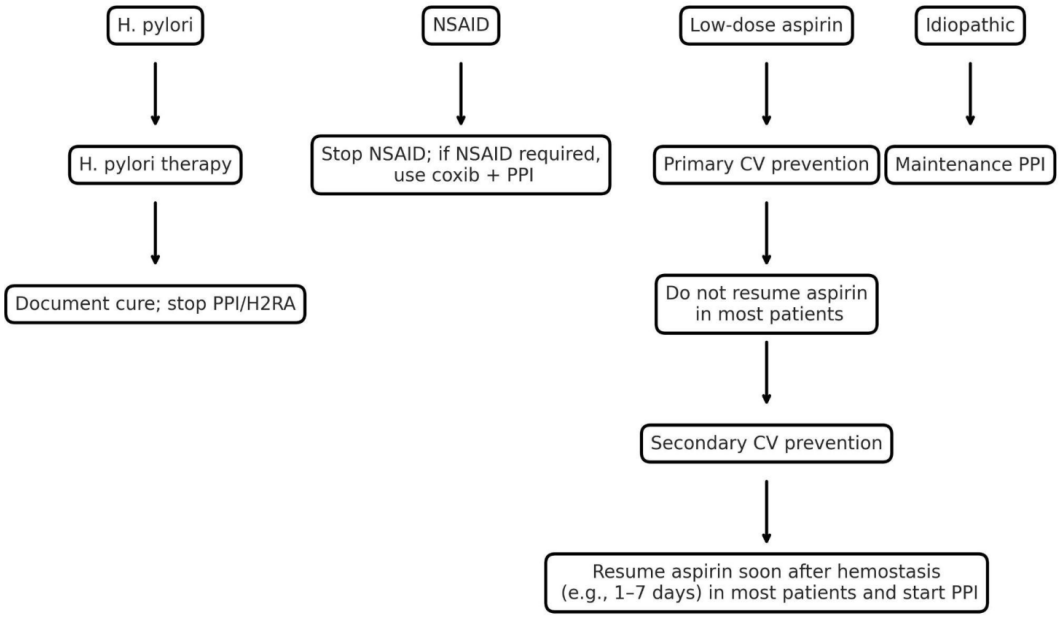
5. Repeat endoscopy

- Repeat endoscopy should be performed in patients with clinical evidence of recurrent bleeding and hemostatic therapy should be applied in those with high-risk stigmata of hemorrhage.
- If further bleeding occurs after a second endoscopic therapeutic session, interventional radiology with transcatheter arterial embolization or surgery is generally employed.

6. Hospitalization for patients with UGIB

- Patients with high-risk stigmata (active bleeding, visible vessels, clots) should generally be hospitalized for 3 days to monitor rebleeding.
- Patients with clean-based ulcers may receive a regular diet and be discharged after endoscopy once they are hemodynamically stable.

Long term prevention of recurrent bleeding ulcers



- H. pylori suspected bleeding should be tested with Invasive (Biopsy urea test, Histology) or non-invasive tests (Stool antigen test, Urea breath test). If positive for H. pylori, shall be treated with clarithromycin based triple therapy (PPI, Clarithromycin 500 mg, amoxicillin 1000 mg, each twice daily) or Bismuth based quadruple therapy (PPI twice daily , Bismuth subcitrate 120 mg 4 times daily, tetracyclin 500 mg 4 times daily and metronidazole 500 mg 4 times daily) or Vonaprazan based therapy (Vonaprzan 20 mg twice daily and amoxicillin 1000 mg

thrice daily)

- Patients with H. pylori-associated bleeding ulcers should receive H. pylori therapy. After documentation of eradication (Invasive or non-invasive tests), maintenance antisecretory therapy is not needed unless the patient also requires non-steroidal anti-inflammatory drugs (NSAIDs) or antithrombotic.
- In patients with NSAID-associated bleeding ulcers, the need for NSAIDs should be carefully assessed and NSAIDs should not be resumed if possible. In patients who must resume NSAIDs, a COX-2-selective NSAID at the lowest effective dose plus daily PPI is recommended.
- In patients with low-dose aspirin-associated bleeding ulcers, the need for aspirin should be assessed. If given for secondary prevention (i.e., established cardiovascular disease) then aspirin should be resumed as soon as possible after bleeding ceases ideally within 1–3 days and certainly within 7 days. Long-term daily PPI therapy should also be provided. If given for primary prevention (i.e., no established cardiovascular disease), antiplatelet therapy likely should not be resumed in most patients.
- For patients on warfarin who are hospitalized or under observation with acute GIB, PCC administration is recommended when available compared with FFP administration. However routine administration of FFP or factors are not recommended.
- For patients on dabigatran who are hospitalized or under observation with acute GIB, the administration of idarucizumab may be recommended when available.
- For patients on rivaroxaban or apixaban who are hospitalized or under observation with acute GIB, the administration of Andexanet alfa may be recommended when available.
- In patients with idiopathic (non-H. pylori, non-NSAID) ulcers, long-term antiulcer therapy (e.g., daily PPI) is recommended.

REFERENCES

ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding May 2021

11. ACUTE LOWER GASTROINTESTINAL BLEEDING

SCOPE

This section provides a comprehensive, evidence-based approach to the evaluation and management of acute lower gastrointestinal bleeding, in accordance with recommendations from the American College of Gastroenterology. It focuses on patients presenting with hematochezia originating from a colorectal source, while also emphasizing the need to exclude an upper gastrointestinal source in cases associated with hemodynamic instability.

The scope includes the initial clinical assessment and risk stratification of patients using validated tools such as the Oakland score, while reinforcing that clinical judgment remains paramount. It outlines principles of early hemodynamic resuscitation, appropriate transfusion thresholds, and tailored management in patients with comorbid conditions such as cardiovascular disease.

A detailed framework is provided for the management of coagulation abnormalities, including reversal strategies for anticoagulants and optimization of antiplatelet therapy, balancing the risks of bleeding and thrombosis. The role of colonoscopy as the primary diagnostic and therapeutic modality is emphasized, along with the appropriate timing of the procedure. Advanced imaging modalities such as CT angiography are included for patients with ongoing or hemodynamically significant bleeding, with guidance on escalation to interventional radiology or surgical management when required.

INTRODUCTION

Acute overt lower gastrointestinal bleeding (LGIB) accounts for 20% of all cases of gastrointestinal (GI) bleeding usually leads to hospital admission with invasive diagnostic evaluations, and consumes significant medical resources.

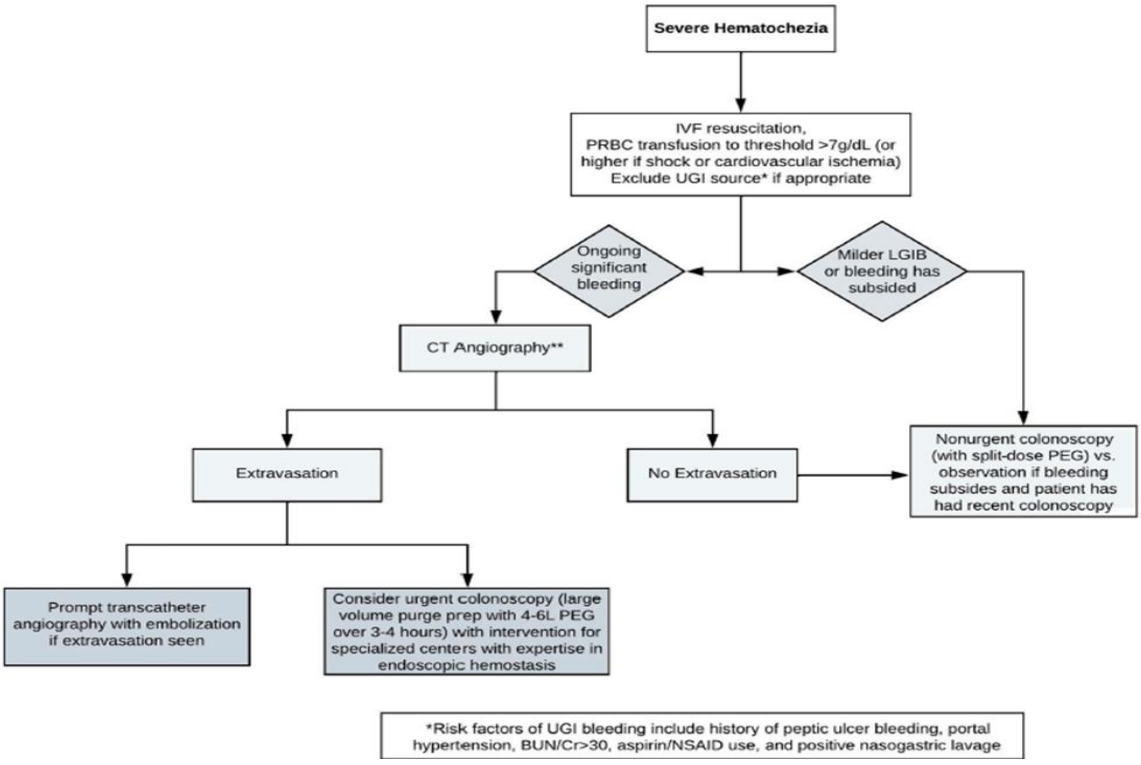
DEFINITION

Although historically LGIB has referred to a bleeding source originating distal to the ligament of Treitz, small bowel bleeding is considered a separate entity, with a distinct diagnostic and therapeutic algorithm .

For the purposes of this clinical practice guideline, LGIB refers to hematochezia or bright red

blood per rectum originating from a colorectal source.

MANAGEMENT



** Predictors of a positive CTA include the following: performance of a CTA within 4 hours of hematochezia, recent bowel resection or intervention, transfusion of >3 units of PRBC, use of antiplatelets or DOACs, tachycardia, or hypotension. For centers without interventional radiology availability, would consider performing a prompt colonoscopy after resuscitation.

Abbreviations: IVF, intravenous fluid resuscitation; PRBC, packed red blood cell; UGI, upper gastrointestinal; LGIB, lower gastrointestinal bleeding; PEG, polyethylene glycol; CT, computed tomography; DOAC, direct oral anticoagulants; BUN, blood urea nitrogen; Cr, creatinine; NSAID, nonsteroidal anti-inflammatory drugs

EVALUATION AND RISK STRATIFICATION

Hematochezia associated with hemodynamic instability may be indicative of an UGIB source, and an upper GI endoscopy should be performed. A nasogastric aspirate/lavage may be used (routine use not recommended due to poor sensitivity) to assess a possible upper GI source if suspicion of UGIB is moderate.

Risk assessment and stratification should be performed to help distinguish patients at high- and low-risk of adverse outcomes and decide upon the timing of colonoscopy and the level of care.

Oakland score </=8 predicted safe discharge. Safe discharge was defined as the absence of all of the following after presentation: rebleeding,defined as additional blood transfusion requirements or a further decrease in hematocrit concentration of 20% or more after 24 hours of clinical stability; red blood cell transfusion; therapeutic intervention to control bleeding, defined as endoscopic, radiologic, or surgical hemostasis; in-hospital death; and readmission with further lower gastrointestinal bleeding within 28 days. Risk scores should be used to supplement but not replace clinician judgment.

HEMODYNAMIC RESUSCITATION

Patients with hemodynamic instability and/or suspected ongoing bleeding should receive intravenous fluid (crystalloids) resuscitation with the goal of normalization of blood pressure and heart rate before endoscopic evaluation.

Restrictive strategy of red blood cell transfusion (threshold for transfusion at a hemoglobin level of 7 g/dL) in hemodynamically stable patients with LGIB.

A restrictive transfusion may not be applicable to patients presenting with hemorrhagic shock.

A threshold of 8 g/Dl should be considered in patients with acute coronary syndrome and GIB. (ACG 2022)

MANAGEMENT OF COAGULATION DEFECTS

Endoscopic hemostasis can be considered safe and effective in patients who have an international normalized ratio (INR) of 2.5 or less.

INR at the onset of GIB or immediately before endoscopy has not been shown to be associated with rebleeding risk, and no significant difference in rebleeding has been seen between patients with an INR of ≤2.5 compared with >2.5.

In patients with a prolonged INR who do not have SRH and endoscopic therapy is not performed, anticoagulation can be continued.

Although most patients with LGIB on VKAs are unlikely to require reversal, we suggest reversal of patients who present with a life threatening LGIB and have an INR substantially exceeding the therapeutic range. For patients on VKAs to prevent stroke in nonvalvular atrial fibrillation who require reversal, 4-factor prothrombin complex concentrate (PCC) is preferred to fresh frozen plasma (FFP) because of the rapidity of INR reduction.

In patients with minor bleeding who are unlikely to require a hospital-based intervention (e.g., Oakland score#8), oral anticoagulants may be continued if necessary.

For patients on DOACs, we suggest reversal for the small subset of patients who present with a life-threatening LGIB that does not respond to initial resuscitation and cessation of the anticoagulant alone.

For patients requiring reversal, targeted reversal agents (idarucizumab for dabigatran and andexanet alfa for apixaban and rivaroxaban) may be used if available if the DOAC has been taken within the past 24 hours.

Platelets should be administered in the setting of severe LGIB to maintain a platelet count of >30 x 10^9/L, and a higher threshold of >50 x10^9/L can be considered if endoscopic procedures are required.

There is no benefit to routine platelet transfusion for patients on antiplatelets.

For patients with LGIB on aspirin for secondary prevention, aspirin should be continued during hospitalization if possible.

Nonaspirinantiplatelets should be held initially for patients with severe hematochezia. However, for patients with recent cardiac stents within 1 year, a multidisciplinary approach should be used to determine the safety of temporarily holding antiplatelets.

For patients on dual antiplatelet therapy, aspirin should be continued if possible while the P2Y12 receptor antagonist is held; however, in patients with previous stents within a year, the P2Y12 receptor antagonists should be resumed within a maximum of 5 days because of high risk of stent thrombosis.

There is no role of administration of antifibrinolytic agents such as tranexamic acid in LGIB.

Colonoscopy

We recommend the performance of colonoscopy for most patients who are hospitalized with LGIB because of its value in detecting a source of bleeding

However, colonoscopy may not be needed in patients where bleeding has subsided, and the patient has had a high-quality colonoscopy within 12 months with an adequate bowel preparation showing diverticulosis with no colorectal neoplasia.

For patients hospitalized with LGIB requiring a colonoscopy, we recommend performing a nonemergent inpatient colonoscopy because performing an urgent colonoscopy within 24 hours has not been shown to improve clinical outcomes such as rebleeding and mortality

In patients undergoing inpatient colonoscopy, administration of 4–6 L of polyethylene glycol (PEG)-based bowel preparation has historically been recommended; however, split-dose preparation and/or the use of low-volume preparations can also be considered.

Unprepared evaluation or routine flexible sigmoidoscopy is not recommended, unless the source is known to be emanating from the anorectal area or distal colon.

CT Angiogram

Consider performing a CTA as the initial diagnostic test in patients with ongoing hemodynamically significant hematochezia. However, CTA is of low yield in patients with minor LGIB or those in whom bleeding has clinically subsided.

Patients who have a CTA demonstrating extravasation be promptly referred to interventional radiology. For specialized centers with experience in performing endoscopic hemostasis, a colonoscopy can also be considered after a positive CTA.

Transcatheter angiography[TA] should be performed promptly after a positive CTA because the greater the time delay between the two, the weaker the correlation between a bleed observed between the 2 modalities.

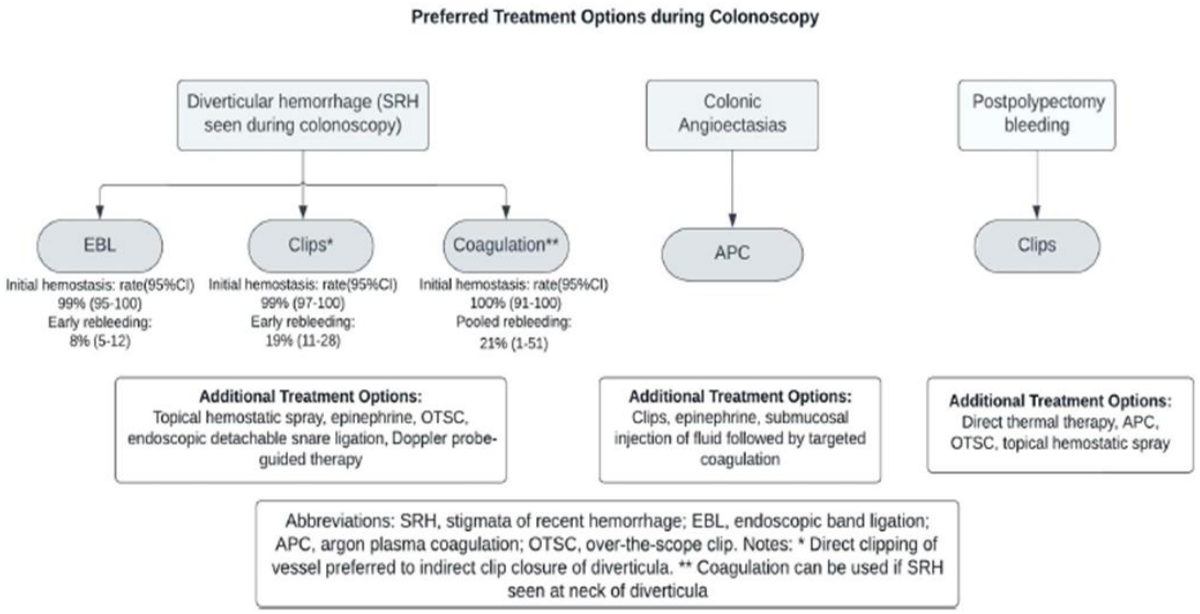
If CTA shows extravasation in the upper GI tract, then an urgent EGD should be performed.

Nuclear imaging

Not prefered due to various disadvantages and widespread availability of CTA. Only be used if CTA unavailable or contraindiacated because of high concern for contrast induced nephropathy.

Endoscopic treatment

Endoscopic therapy is recommended when finding active bleeding or SRH, irrespective of the etiology.



Role for repeat colonoscopy, angiography, and surgery

For patients experiencing rebleeding after initial hemostasis or cessation of bleeding, repeat colonoscopy can be considered depending on the patient's stability and likelihood of successful repeat endoscopic therapy. In patients with suspected recurrent diverticular bleeding with recent colonoscopy who are hemodynamically stable, observation can be considered.

In the setting of a known bleeding site and either recurrent or refractory bleeding despite endoscopic intervention, proceeding to TA with possible embolization is indicated. A previously placed endoclip can help perform a focused TA.A CTA can be considered if more precise localization is needed, followed by transcatheter arteriography.

Resumption of antiplatelet medications and risk of recurrenee

Discontinue nonaspirin NSAIDs after hospitalization for diverticular hemorrhage.

Discontinue aspirin given for primary cardiovascular prevention after hospitalization for diverticular haemorrhage given the risks of recurrent diverticular hemorrhage.

Resumption of antiplatelets should be done with consultation with cardiologist and gastroenterologist.

Resumption of anticoagulants and risk of recurrence

Resume anticoagulation after cessation of LGIB given that resumption of anticoagulation has been shown to decrease the risks of postbleeding thromboembolism and mortality.

REFERENCES

ACG Clinical Guideline: Management of Patients with Acute Lower Gastrointestinal Bleeding 2022 AMJ

12. ACUTE SEVERE ULCERATIVE COLITIS

SCOPE

This section provides a comprehensive, evidence-based framework for the diagnosis and management of acute severe ulcerative colitis, aligned with recommendations from the European Crohn's and Colitis Organisation. It focuses on patients presenting with severe disease activity requiring hospitalization and intensive medical management.

The scope includes clear diagnostic criteria based on the Truelove and Witts classification with incorporation of inflammatory markers, enabling early identification of patients with severe disease who require urgent admission. It emphasizes the importance of systematic baseline evaluation, including exclusion of infectious etiologies, early endoscopic assessment, and radiological evaluation to detect complications such as toxic megacolon.

A structured approach to initial management is outlined, centering on timely initiation of intravenous corticosteroids, meticulous supportive care, correction of fluid and electrolyte imbalances, and prevention of thromboembolic complications. The section also incorporates guidance on appropriate monitoring strategies, including daily clinical, laboratory, and radiological reassessment to detect early signs of deterioration.

The scope further addresses criteria for assessing response to therapy, particularly the use of day 3 prognostic indicators such as the Travis (Oxford) criteria to identify steroid non-responders. It provides direction for escalation to second-line or rescue therapies, including immunosuppressive and biologic agents, while ensuring timely surgical consultation for patients at risk of complications or treatment failure.

Overall, this section serves as a practical clinical guide for the management of acute severe ulcerative colitis in inpatient and critical care settings, aiming to reduce morbidity, prevent complications, and facilitate timely escalation to advanced therapies or surgical intervention when required.

INTRODUCTION

UC is a chronic idiopathic inflammatory disease of the GI tract that affects the large bowel and is a major disorder under the broad group of conditions termed inflammatory bowel

disease.

DISEASE ACTIVITY, SEVERITY, AND RISK

The definition and classification of ASUC follow the criteria of Truelove and Witts and ECCO, which also include C-reactive protein [CRP] measurement.

DIAGNOSIS OF ACUTE SEVERE UC

Patients with bloody diarrhoea ≥6/day and any signs of systemic toxicity

(tachycardia >90 bpm, fever >37.8 °C, Hb < 10.5 g/dL, ESR > 30 mm/h or an CRP > 30 mg/l) have severe colitis and should be admitted to hospital for intensive treatment.

MANAGEMENT

The standard initial therapy consists of intravenous corticosteroids.

Day 1:

Treatment:

1. Corticosteroids are given intravenously using methylprednisolone

60 mg IV in 24 hours or IV hydrocortisone 100 mg four times daily. Higher doses are no more effective, but lower doses are less effective.

2. Stop anticholinergic and antidiarrhoeal medicines, opioids and NSAIDs.
3. Stool chart (often more accurate if completed by patient); standard observations 4-6 hourly.
4. Fecal Calprotectin, Stool culture, C. difficile toxin, parasites if recent travel history.
5. Ideally unprepared limited flexible sigmoidoscopy to take place on the same day, including 2 biopsies to exclude CMV.
6. Supine AXR to exclude toxic megacolon (transverse colon diameter> 5.5 cm and systemic toxicity; rare in left-sided colitis) and assess extent (suggested by stool-free colon).If toxic megacolon is suspected, consider urgent surgical review.
7. Check routine blood tests including FBC, U&E, electrolytes, CRP or ESR.

8. Thromboprophylaxis - subcutaneous prophylactic low-molecular-weight heparin.Enoxaparin 40 mg OD.
9. IV fluids to correct and prevent dehydration.
10. IV electrolyte correction dependent on serum levels Potassium and Magnesium. Hypokalaemia is common with diarrhoea and certain steroid therapies. Hypokalaemia or hypomagnesaemia can promote toxic dilatation.
11. Potassium supplementation of at least 60 mmol/day is usually necessary.
12. Oral vitamin D.
13. Antibotics only if infection is considered or immediately prior to surgery - IV metronidazole and ciprofloxacin only if toxic dilatation or temperature > 37.8°C, following rehydration PO metronidazole if C. difficile or amoebiasis likely.
14. Request dietetic review and consider enteral nutrition.
15. Blood transfusion if Hb < 80-100 g/L (transfusion targets to be individualised based on risk e.g. if any known ischaemic heart disease).

Prebiologic screening:

1. Serological screening for hepatitis A, B, C, HIV, Epstein- Barr virus, cytomegalovirus, varicella zoster virus, and measles virus [in the absence of documented past infection or vaccination for the latter two]
2. Tuberculosis: Chest X-ray, tuberculin skin test, and interferon-gamma release.

Daily monitoring:

1. Medical review should take place on a daily basis. Colorectal surgical team and stoma-nurse review if no improvement.
2. Deterioration suggested by increasing pulse/temperature, or abdominal pain or tenderness. Senior review and colorectal surgical review should take place to assess need for emergency/urgent colectomy.
3. Supine AXR (performed daily if fever, tachycardia, tenderness, dilatation on initial films, or clinical deterioration).

4. Check FBC, electrolytes, CRP or ESR (performed daily until clinical improvement).
5. Continue IV fluids only if patient unable to maintain hydration orally or if electrolytes deranged.

Day 3:

Approximately 30% of patients fail to respond to conservative treatments. ASUC failing to respond by day 3, is judged by the Travis or Oxford criteria.

On day 3 of corticosteroid therapy, pa-tients who have a stool frequency of >8 times/day or a stool frequency of 3 times/day plus CRP >45 mg have an 85% likelihood of undergoing colectomy during the admission. If no clinical response, consider medical rescue therapy and discuss need for colectomy on or soon after day 3 in absence of improvement.

Second line therapy / Salvage therapy

The response to intravenous steroids should be best assessed by the third day; in non-responders, treatment options including ciclosporin, infliximab, tacrolimus or Tofacitinib, or surgery should be considered.

Colectomy is recommended if there is no improvement following 7 days of salvage therapy.

Nutrition

Exclusive enteral nutrition (EEN) acts as an adjunctive therapy to intravenous corticosteroids in patients with ASUC. Patients with ASUC undergoing EEN showed reduced corticosteroid failure rates.

REFERENCES

European evidence-based Consensus on the diagnosis and management of ulcerative colitis: Current management Journal of Crohn's and Colitis 2017 and 2022)