Pre-Transplant Evaluation and Management of Patients with Acute Liver Failure (ALF)

Purposes of the Guideline

- **Primary purpose:** To aid in the rapid identification of those patients with possible acute liver failure (ALF) and to identify a core group of consultants with expertise in transplantation, the complications of liver disease, and/or critical care medicine who can consistently evaluate these patients within the first 24 hours of presentation.

- **Secondary Purpose:** To outline a management strategy consisting of initial orders and subsequent daily care for patients with ALF.

Early Identification

**Definition**

- **Acute Liver Failure (ALF)**
  - Hepatic illness or jaundice ≤ 26 weeks
  - Encephalopathy
  - Coagulopathy with INR ≥ 1.5

- **Acute Liver Injury (ALI)**
  - APAP
    - Acute illness < 2 weeks
    - INR ≥ 2
    - ALT ≥ 10x ULN
    - No encephalopathy
  - Non-APAP
    - Acute illness < 26 weeks
    - INR ≥ 2
    - ALT ≥ 10x ULN
    - TBili ≥ 3mg/dL
    - No encephalopathy

**Etiology**

- The etiology of ALF is important in both the prognosis of the patient as well as in the predictive index for transplantation. Common etiologies include viral (hep A, hep B, hep C, non-A, non-B) drugs including acetaminophen/toxins, unknown and other.

- Exclusion for both ALF and ALI is a history of chronic liver disease.

Timing

- In general, any patient who becomes seriously ill with ALF should be immediately considered as a potential candidate for transplantation. Listing of patients for transplantation occurs when physicians and surgeons believe that death will occur without transplantation.

- Candidacy is further determined according OSUWMC Liver Transplant Patient Selection Protocol.

Core Consultants and Additional Services

The services listed in the “core services” group should all be contacted within the first day of the patient’s hospital course.

- **Core Consultants**
  - Hepatobiliary
  - Transplant Social Work

Within 24 hours of initiating a consult to the core or additional service(s), it is expected that the attending physician will document in the medical record their evaluation and recommendations.

Management

**Admission**

- Upon recognition of condition, make an immediate consult to Hepatobiliary (specify acute liver failure), and Social Work (specify: liver transplant).

- Order STAT admission labs (Chem 10, CBC, LFTs, albumin, coag’s including):
  - ABG, arterial ammonia, arterial lactate, venous phosphate, serum osmolality, serum and urine tox screen, acetaminophen level, AFP.
  - Metabolic studies: ceruloplasmin, uric acid, iron studies, TSH, free T4.
  - Autoimmune studies: ANA, AMA, anti-smooth muscle Ab, anti-liver/kidney microsomal Ab, SPEP, quantitative immunoglobulins (IgG, IgM, IgA), Coombs.
  - Micro: blood cultures, VRE screen swabs, UA, urine cultures, CXR.
  - Viral serologies: HAV IgM, IgG Ab, HBsAg (with HBeAg, HBeAb and HDV Ab if positive), HBsAb, HBC IgM Ab, HBc IgG Ab, HBV viral load (DNA by PCR), HCV Ab (with genotype if positive), HCV viral load (RNA by PCR), HEV IgM, IgG Ab, +CMV IgM, CMV PCR, Quantiferon, +CMV IgM, HSV PCR, RPR, EBV VCA IgG Ab, +EBV PCR, varicella-zoster IgM, HIV RNA PCR, HIV serologies (with viral load and CD-4 count if positive).

- Order STAT Right Upper Quadrant Ultrasound and Liver Doppler Ultrasound

- Routine labs (Chem 10, CBC, coag’s) every 12 hours. LFTs, ammonia, and albumin daily.

- Nursing: Neuro checks every 4 hours,
• Consideration for enrollment in Acute Liver Failure Study Group Trial
  o https://clinicaltrials.gov/ct2/show/NCT00518440
  o https://clinicaltrials.gov/ct2/show/NCT02786836
• Admission medications:
  o N-acetylcysteine (NAC) for any case of known or suspected acetaminophen ingestion (should be used with caution in patients with a history of asthma or bronchospasm).
  o Consider use of NAC when diagnosis suggests hyperacute picture and for non-acetaminophen cases with hepatic Encephalopathy (HE) grade I-II.
  o Penicillin G and N-acetylcysteine (NAC) for any case of known or suspected mushroom poisoning
  o Acyclovir (5mg/kg IV every 8 hours) for any case of known or suspected herpes virus or varicella zoster
  o Hypertonic saline should be considered for a goal serum sodium level of 145-155 mEq/L in patients at highest risk for cerebral edema (serum ammonia > 150 μM, grade 3 or 4 encephalopathy, acute renal failure, patients requiring vasopressors to maintain mean arterial pressure)
    - Nephrology consult recommended to administer Hypertonic saline
  o Pantoprazole 40mg IV Q24H.
  o Strictly avoid sedation including benzodiazepines, narcotics or centrally acting anti-emetics (i.e., phenergan); nephrotoxic medications (i.e., NSAIDs, aminoglycosides) and volume overload.
  o Do not correct PT/INR unless bleeding occurring or for invasive procedure

**Daily Management**

- Neuro checks every 4 hours; for worsening mental status, alert transplant team.
- Intubate patient at onset of Grade 3-4 encephalopathy.
- Sedation should be with propofol if needed. E-T suction should be minimized.
- Maintain aspiration precautions with HOB elevated > 30° unless MAP is < 55.
- Nephrology consultation for possible initiation of CRRT in patients with oliguria and/or acute kidney injury
  o Use of CRRT in non-oliguric patients without acute kidney injury should be individualized on a case-by-case basis
- Use of intracranial pressure (ICP) monitoring should be individualized on a case-by-case basis

• In the event of intracranial hypertension or deterioration in neurologic exam (in absence of ICP monitoring), the goal should be to maintain ICP < 20 mmHg and cerebral perfusion pressure (CPP) between 60 mmHg and 80 mmHg [CPP = mean arterial pressure (MAP) – ICP].
  1. First line therapy should be use of vasopressors (norepinephrine preferred) for goal MAP > 75 mm Hg
  2. Second-line treatment is Mannitol.
     a. Mannitol is given as a 0.5 g - 1 g/kg IV bolus and can be repeated as long as serum osmolality is < 320 mmol/kg if no response in ICP.
  3. For uncontrolled intracranial hypertension (ICH), hyperventilation to PaCO₂ of 25-30 mm Hg) may be instituted to delay impending herniation.
  4. For uncontrolled ICH unresponsive to above measures, consider use of pentobarbital coma.
     a. Pentobarbital bolus (3-5 mg/kg) given and an infusion of (1-3 mg/kg/hr) is maintained. Infusion rate may be increased as blood pressure tolerates with goal of lowering ICP.

**Grading for Hepatic Encephalopathy (HE)**

(See next page.)

**Additional Tools and Resources**

- **OSUWMC Ordersets**
  o OSU IP MIC: ACUTE LIVER FAILURE [2221]
  o Acetylcysteine IV Dosing for Acetaminophen OD or non-Acetaminophen Induced Acute Liver Failure [1969]

- **Resources**
  o Access Acute Liver Failure Management Tools via Apple App Store
    • App for Acute Liver Failure Checklist
    • How to Use the ALF Checklist
    • App for Acute Liver Failure Prognostic Model
  o Intravenous N-Acetylcysteine Improves Transplant-Free Survival in Early Stage Non-Acetaminophen Acute Liver Failure
References


Quality Measures

- Orderset use
- Placement of core consults within 24 hours of admission
- Length of stay
- Mortality rate

Authors

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Guideline Approved


Disclaimer: Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.

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## Grading for Hepatic Encephalopathy

**Note:** Three or more indicators in any grade are sufficient to assign grade of encephalopathy (e.g., if the description is grade 3 in the behavior, mood, and neuromuscular categories but grade 2 for everything else, then the patient is grade 3).

<table>
<thead>
<tr>
<th></th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
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</thead>
<tbody>
<tr>
<td><strong>Level of Consciousness</strong></td>
<td>Awake</td>
<td>Level of consciousness decreased, but opens</td>
<td>Patient goes to sleep but can be aroused by</td>
<td>Comatose; no response to pain</td>
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<tr>
<td></td>
<td></td>
<td>eyes spontaneously</td>
<td>verbal and painful stimuli; does not open</td>
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<td></td>
<td></td>
<td></td>
<td>eyes spontaneously</td>
<td></td>
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<tr>
<td><strong>Orientation</strong></td>
<td>Total orientation with</td>
<td>Disoriented to time events; severe</td>
<td>Complete disorientation when aroused</td>
<td>Comatose</td>
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<tr>
<td></td>
<td>progression to confusion,</td>
<td>confusion</td>
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<td></td>
<td>then disorientation to time</td>
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<td></td>
<td>and place</td>
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<tr>
<td><strong>Intellectual Functions</strong></td>
<td>Mental clouding; slowness in</td>
<td>Amnesia for past events; psychometric test</td>
<td>Inability to make computations</td>
<td>Comatose</td>
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<tr>
<td></td>
<td>answering questions;</td>
<td>scores decrease</td>
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<td></td>
<td>impaired handwriting; subtle</td>
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<tr>
<td></td>
<td>changes in intellectual function; psychometric test scores decrease</td>
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<tr>
<td><strong>Behavior</strong></td>
<td>Forgetful, restless,</td>
<td>Decreased inhibition, lethargic</td>
<td>Bizarre behavior (rage)</td>
<td>Comatose</td>
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<tr>
<td></td>
<td>irritable, untidy, apathetic,</td>
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<tr>
<td></td>
<td>disobedient</td>
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<tr>
<td><strong>Mood</strong></td>
<td>Euphoria, depression, crying</td>
<td>Apathetic, paranoid</td>
<td>Apathy increased</td>
<td>Comatose</td>
</tr>
<tr>
<td><strong>Neuromuscular</strong></td>
<td>Muscular incoordination,</td>
<td>Hypoactive reflexes, asterixis, ataxia,</td>
<td>Cannot cooperate, nystagmus and Babinski, clonus</td>
<td>Seizures; rigidity decreases to flaccidity; dilated pupils</td>
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<td></td>
<td>tremors, yawning; insomnia</td>
<td>slurred speech</td>
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<tr>
<td><strong>EEG Abnormalities</strong></td>
<td>Mild-to-moderate abnormalities</td>
<td>Moderate-to-severe abnormalities</td>
<td>Severe abnormalities, usually slowing</td>
<td>Severe</td>
</tr>
</tbody>
</table>