Critical care in acute liver failure

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Today’s content

- Definition and classification of liver failure
- Things to consider in acute liver failure
- Things to consider in acute on chronic liver failure
Liver failure: definition

- Inability of the liver to perform its normal synthetic and metabolic function as part of normal physiology.
Clinical spectrum

Kim TY et al., Clin Mol Hepatol 2013
Acute liver failure

- Acute loss of hepatocellular function
- Systemic inflammatory response
- Multi-organ system failure

- Evidence of coagulation abnormality, usually an INR \( \geq 1.5 \), and any degree of mental alteration (encephalopathy) in a patient without preexisting cirrhosis and with an illness of < 26 weeks’ duration
Prothrombin time (PT)

- Measures of the extrinsic pathway of coagulation.
- Time it takes plasma to clot after addition of tissue factor.
- The speed is greatly affected by levels of factor VII.
- VII is synthesized in the liver
- Half-life is 3.5 hour
Why encephalopathy?

- The most serious *complication* of acute liver failure
Case

- 42/M
- Heavy alcoholics (>100 g/d)
- URI symptoms for a week
- Sleeping tendency for 3-4 days
- **Drowsy mental status**
  - TB: 5.9  AST/ALT: 1123/2678  **PT INR: 5.75**
  - Brain CT: non specific
- Referred to ER
Case description

- Mental status: semicoma
- Icteric sclera
- LAB
  - TB: 10.2  AST/ALT: 351/1180
  - BUN/Cr: 52.3/2.51  PT INR: 2.05
  - Outside (TB: 5.9  AST/ALT: 1123/2678  PT INR: 5.75)
  - ABGA: 7.51-34-54-26.8
  - Lactic acid: 6.7
  - Viral marker: HBsAg- HBsAb+, HBcIgG+, HAV IgM+, HAV IgG+, anti-HCV-
Clinical course

- HD 0
  - Emergent living donor evaluation: deferred → DDLT listing

- HD 1
  - Seizure developed → not controlled

- HD 2
  - Aggravated neurologic exam, pupil (4mm/4mm fix)

- HD 3
  - EEG (electrical inactivity) CT angiography (no intracranial arterial blood flow)
  - Brain death

- HD 7
  - Expired (multi-organ failure)
Most dangerous signal

- Cerebral edema and intracranial hypertension.

- Pathogenesis: multi-factorial
  - Osmotic disturbances in the brain
  - Heightened cerebral blood flow d/t loss of cerebrovascular autoregulation
  - Unknown
Summary

- Acute liver failure
  - Coagulopathy
  - Encephalopathy

**TABLE 5. GRADES OF ENCEPHALOPATHY**

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Changes in behavior with minimal change in level of consciousness</td>
</tr>
<tr>
<td>II</td>
<td>Gross disorientation, drowsiness, possibly asterixis, inappropriate behavior</td>
</tr>
<tr>
<td>III</td>
<td>Marked confusion; incoherent speech, sleeping most of the time but arousable to vocal stimuli</td>
</tr>
<tr>
<td>IV</td>
<td>Comatose, unresponsive to pain, decorticate or decerebrate posturing</td>
</tr>
</tbody>
</table>
Clinical spectrum: ACLF
ACL F

- No uniform definition present!
- Under hot debate!
- West vs. East
ACLF concept

Sarin et al., Hepatol Int 2014;8:453
Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the Study of the Liver (APASL) 2014

What constitutes chronic insult?

- NASH
- Chronic Hepatitis
- Cirrhosis

What constitutes the acute insult?

- Hepatotrophic insults
  - Alcohol
  - Viral
  - DILI
  - Autoimmune hepatitis
  - Wilson’s

- Non hepatotrophic insults leading to primary hepatic failure
  - Infections
  - Surgery
  - Bleed

Acute-on-chronic liver failure

- Hepatic failure
  - Jaundice to ascites
  - Coagulopathy

- Extra-hepatic organ failures
  - Hepatic encephalopathy
  - Acute Kidney injury
  - Sepsis
  - Circulatory dysfunction
The ACLF is an acute hepatic insult manifesting as jaundice (serum bilirubin >5 mg/dl) and coagulopathy (INR >1.5) complicated within 4 weeks by clinical ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease/cirrhosis, and is associated with a high 28-day mortality.
EASL-CLIF definition (28d mortality >15%)

- **ACLF grade 1.**
  - Single kidney failure
  - Single cerebral failure + Cr 1.5 and 1.9 mg/dL.
  - Single failure of the liver, coagulation, circulation, or respiration + Cr 1.5 to 1.9 mg/dL and/or mild to moderate hepatic encephalopathy,

- **ACLF grade 2:** 2 organ failures

- **ACLF grade 3:** more than 3 organ failure
Case

- M/47
- Heavy alcoholics, known HBV (no tx history)
- Vibrio sepsis
  - Septic shock
  - Rt leg cellulitis → necrosis → fasciotomy
  - Renal failure with anuria → CRRT
- HBV DNA
  - HBV DNA 8600 IU/ml → entecavir start
Case

- Comatous mental status
- Lab
  - CBC: 12940 (90%)-11.2-62k
  - PT-INR: 2.2
  - Albumin: 3.4, Total bilirubin: 14.7,
    AST/ALT:49/27
  - BUN/Cr = 33.2/0.45 (on CRRT)
- ACLF type B (infection)
Hospital course (134 days, LT at HD 71)

Infarcted regenerative nodules, S8 and S4 (4 nodules, up to 0.3x0.3x0.3 cm)

Micronodular cirrhosis, active with marked cholestasis and bile duct proliferation, clinically HBV-related.
## West vs. East

<table>
<thead>
<tr>
<th></th>
<th>EAST</th>
<th>WEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decompensated cirrhosis</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Liver failure</td>
<td>Mandatory</td>
<td>Not mandatory</td>
</tr>
<tr>
<td>Non-hepatic insults</td>
<td>Questionable</td>
<td>Yes</td>
</tr>
<tr>
<td>(e.g., varix bleeding,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>infection)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Decompensation: Varix bleeding, ascites, encephalopathy, Child-Pugh Class B

Case: LC-B, ascites → Pneumonia, complicated by renal failure  (EAST: no!)  (WEST: yes!)
“ACLF is a syndrome in patients with chronic liver disease with or without previously diagnosed cirrhosis which is characterized by acute hepatic decompensation resulting in liver failure (jaundice and prolongation of the INR) and one or more extrahepatic organ failures that is associated with increased mortality within a period of 28 days and up to 3 months from onset.”
Figure 1. Proposed unifying pathogenesis for different types of acute-on-chronic liver failure (ACLF).
268 cases screened for liver failure

167 cases included

101 cases excluded:
91 had acute liver failure (acute viral hepatitis, postop lab abnormalities, sepsis-related, toxic hepatitis, obstructive jaundice, etc.)
9 had chronic liver failure
6 were on warfarin

Type A (n=34)
Type B (n=53)
Type C (n=80)
Survival by ACLF types

Overall survival

- Type A: 81.3%
- Type B/C: 76.4%
- Type B/C: 78.8%

Transplant-free survival

- Type A: 63.6%
- Type B/C: 46.3%
- Type B/C: 50.0%

No additional mortality after initial early period for type A
Additional mortality even after 90 days for type B/C

Hong YS et al., Intrim review
Survival by ACLF type and transplantation

**Survival at 1 year**

- **Type A**
  - 90.9% vs. 71.4%
  - 36.2%

- **Type B**
  - 83.7% vs. 47.5%
  - 45.0%

- **Type C**
  - 80.0% vs. 35.0%
  - 41.2%

- **Type A**
  - At 1 year: 90.9% vs. 71.4%
  - 19.5%

**Hong YS et al., Intrim review**
### Characteristics by ACLF types

<table>
<thead>
<tr>
<th></th>
<th>Type A N=32</th>
<th>Type B N=55</th>
<th>Type C N=80</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (year)</strong></td>
<td>51.8±10.4</td>
<td>53.9±10.2</td>
<td>58.0±11.1</td>
<td>0.010</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>20 (62.5)</td>
<td>32 (58.2)</td>
<td>59 (73.8)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>PREDISPOSITION</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>HBV</strong></td>
<td>20 (62.5)</td>
<td>20 (36.4)</td>
<td>28 (35.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol</strong></td>
<td>4 (12.5)</td>
<td>25 (45.5)</td>
<td>33 (41.3)</td>
<td></td>
</tr>
<tr>
<td><strong>HCV</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>6 (7.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Autoimmune</strong></td>
<td>6 (18.8)</td>
<td>2 (3.6)</td>
<td>2 (2.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>2 (6.3)</td>
<td>8 (14.5)</td>
<td>11 (13.8)</td>
<td></td>
</tr>
</tbody>
</table>

*Hong YS et al., Intrim review*
## Characteristics by ACLF types

<table>
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<tr>
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<th>Type A</th>
<th>Type B</th>
<th>Type C</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV flare</td>
<td>16 (50.0)</td>
<td>12 (21.8)</td>
<td>4 (5.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3 (9.4)</td>
<td>19 (34.5)</td>
<td>6 (7.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HAV</td>
<td>3 (9.4)</td>
<td>1 (1.8)</td>
<td>1 (1.3)</td>
<td>0.061</td>
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<tr>
<td>Toxin</td>
<td>5 (15.6)</td>
<td>9 (16.4)</td>
<td>3 (3.8)</td>
<td>0.031</td>
</tr>
<tr>
<td>AIH flare</td>
<td>7 (21.9)</td>
<td>2 (3.6)</td>
<td>0 (0.0)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Infection</td>
<td>0 (0.0)</td>
<td>13 (23.6)</td>
<td>32 (40.0)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Varix bleeding</td>
<td>0 (0.0)</td>
<td>3 (5.5)</td>
<td>11 (13.8)</td>
<td>0.038</td>
</tr>
<tr>
<td>Other bleeding</td>
<td>0 (0.0)</td>
<td>2 (3.6)</td>
<td>6 (7.5)</td>
<td>0.21</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (9.4)</td>
<td>5 (9.1)</td>
<td>23 (28.8)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Hong YS et al., Intrim review*
# Characteristics by ACLF types

<table>
<thead>
<tr>
<th></th>
<th>Type A N=32</th>
<th>Type B N=55</th>
<th>Type C N=80</th>
<th>P-value</th>
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<tbody>
<tr>
<td><strong>RESPONSE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>MELD score</td>
<td>29.2 ± 8.4</td>
<td>27.1 ± 5.7</td>
<td>26.3 ± 6.3</td>
<td>0.11</td>
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<tr>
<td>SIRS</td>
<td>9 (28.1)</td>
<td>19 (34.5)</td>
<td>30 (37.5)</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Organ failures by CLIF-SOFA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Specific organ type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic</td>
<td>25 (78.1)</td>
<td>43 (78.2)</td>
<td>28 (35.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Coagulation</td>
<td>9 (28.1)</td>
<td>12 (21.8)</td>
<td>21 (26.3)</td>
<td>0.76</td>
</tr>
<tr>
<td>Cerebral</td>
<td>2 (6.3)</td>
<td>4 (7.3)</td>
<td>11 (13.8)</td>
<td>0.33</td>
</tr>
<tr>
<td>Renal</td>
<td>7 (21.9)</td>
<td>5 (9.1)</td>
<td>17 (21.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Circulatory</td>
<td>1 (3.1)</td>
<td>4 (7.3)</td>
<td>16 (20.0)</td>
<td>0.018</td>
</tr>
<tr>
<td>Respiratory</td>
<td>2 (6.3)</td>
<td>1 (1.8)</td>
<td>4 (5.0)</td>
<td>0.53</td>
</tr>
<tr>
<td><strong>Type of organ failure</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>None</td>
<td>7 (21.9)</td>
<td>9 (16.4)</td>
<td>28 (35.0)</td>
<td></td>
</tr>
<tr>
<td>Hepatic</td>
<td>13 (40.6)</td>
<td>26 (47.3)</td>
<td>11 (13.8)</td>
<td></td>
</tr>
<tr>
<td>Hepatic + extrahepatic</td>
<td>12 (37.5)</td>
<td>17 (30.9)</td>
<td>17 (21.3)</td>
<td></td>
</tr>
<tr>
<td>Extrahepatic</td>
<td>0 (0)</td>
<td>3 (5.5)</td>
<td>24 (30.0)</td>
<td></td>
</tr>
</tbody>
</table>

*Hong YS et al., Intrim review*
Reversibility is a concern

- 1-year of 15% & 5-year 50% mortality for grade 2-3 ascites

Reversibility? Contraindicated for LT?

Figure 1. Proposed unifying pathogenesis for different types of acute-on-chronic liver failure (ACLF).

Jalan R et al., Gastroenterology 2014;147:4
<table>
<thead>
<tr>
<th>Differences</th>
<th>ALF</th>
<th>ACLF</th>
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<tbody>
<tr>
<td>Underlying liver disease</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Definition of liver failure</td>
<td>Coagulopathy</td>
<td>Coagulopathy + Jaundice</td>
</tr>
<tr>
<td>Extrahepatic organ failure</td>
<td>Encephalopathy</td>
<td>Encephalopathy, Kidney, Lung, Circulation</td>
</tr>
<tr>
<td>Subtype</td>
<td>No</td>
<td>A, B, C</td>
</tr>
</tbody>
</table>
Summary

- Acute liver failure
  - Coagulopathy
  - Encephalopathy

- Acute on chronic liver failure
  - Chronic liver disease (type A,B,C)
  - Acute deteriorated liver function (jaundice + coagulopathy)
  - Extrahepatic organ failure (encephalopathy and others...
Take home message #1

- Definition and classification of liver failure
  - Acute liver failure
  - Acute on chronic liver failure
    - Type A
    - Type B
    - Type C
Today’s content

- Definition and classification of liver failure
- Things to consider in acute liver failure
- Things to consider in acute on chronic liver failure
Things to consider in acute liver failure

- The dangerous signal: **Encephalopathy**

- Specific management? → look for etiology

- High volume plasmapheresis?
Hepatic Encephalopathy in Chronic Liver Disease: 2014 Practice Guideline by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases

American Association for the Study of Liver Diseases *\,†
European Association for the Study of the Liver *\,†

**Definition of HE**

**Hepatic encephalopathy** is a brain dysfunction caused by liver insufficiency and/or PSS; it manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma

<table>
<thead>
<tr>
<th>Type</th>
<th>Grade</th>
<th>Time course</th>
<th>Spontaneous or precipitated</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>MHE</td>
<td>Covert</td>
<td>Spontaneous</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>Overt</td>
<td>Precipitated (specify)</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cerebral Edema/Intracranial Hypertension
Grade I/II Encephalopathy
   Consider transfer to liver transplant facility and listing for transplantation
   Brain CT: rule out other causes of decreased mental status; little utility to identify cerebral edema
   Avoid stimulation; avoid sedation if possible
   Antibiotics: surveillance and treatment of infection required; prophylaxis possibly helpful
   Lactulose, possibly helpful
Grade III/IV Encephalopathy
   Continue management strategies listed above
   Intubate trachea (may require sedation)
   Elevate head of bed
   Consider placement of ICP monitoring device
   Immediate treatment of seizures required; prophylaxis of unclear value
   Mannitol: use for severe elevation of ICP or first clinical signs of herniation
   Hypertonic saline to raise serum sodium to 145-155 mmol/L
   Hyperventilation: effects short-lived; may use for impending herniation
Why look for etiology?

- N-acetylcysteine for acetaminophen, drug, HBV
- Steroid for autoimmune hepatitis, drug
- Antiviral agents for viral hepatitis
Acute liver failure (ALF)

- Drug induced-ALF (DI-ALF)
  - Intrinsic hepatotoxin (acetaminophen...)
  - Idiosyncratic drug reactions (presumably immune-mediated liver injury due to the metabolic generation of a neo-antigen)

Smith et al., Lancet 1993;342:963; Stravitz et al., Hepatology 2011;53:517
Steroid Use in Acute Liver Failure


- Retrospective analysis
- Patients
  - AI-ALF (n = 66)
  - DI-ALF (n = 131, non-acetaminophen)
  - Indeterminate (n = 164)
- Steroid use
  - AI-ALF (25/66, 38%)
  - DI-ALF (16/131, 12%)
  - Indeterminate (21/164, 13%)

Karkhanis et al., Hepatology 2014;59:612
Steroid use in potentially immune mediated ALF

Fig. 1. Overall and spontaneous survival among different etiologies of ALF.

Karkhanis et al., Hepatology 2014;59:612
Steroid use in potentially immune mediated ALF

Karkhanis et al., Hepatology 2014;59:612
Steroid use in potentially immune mediated ALF

Karkhanis et al., Hepatology 2014;59:612
Steroid use in DI-ALF

- Data suggest.
  - High MELD patients, may not benefit from steroid
  - High AST/ALT, may help identify patients who will likely to respond from steroid

- Controversial.
High volume plasmapheresis (HVP)

- HVP can remove albumin bound toxins as well as unbound toxins, including aromatic amino acids, ammonia, endotoxin, indols, mercaptans, phenols, and other factors which may be responsible for hepatic coma, hyperkinetic syndrome, and decreased systemic vascular resistance and cerebral blood flow.

- Improved cerebral blood flow, mean arterial, pressure (MAP), cerebral perfusion pressure, cerebral metabolic rate, increased hepatic blood flow, and improvements in other laboratory parameters such as cholinesterase activity or galactose elimination capacity.
RCT that took more than 12 years

Larsen et al., J Hepatol 2016
**Guidelines on the Use of Therapeutic Apheresis in Clinical Practice—Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue**

### ACUTE LIVER FAILURE

<table>
<thead>
<tr>
<th>Incidence: &lt; 10/1,000,000/yr</th>
<th>Procedure</th>
<th>Recommendation</th>
<th>Category</th>
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<tbody>
<tr>
<td></td>
<td>TPE</td>
<td>Grade 2B</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>TPE-HV</td>
<td>Grade 1A</td>
<td>I</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of reported patients: &gt; 300</th>
<th>Procedure</th>
<th>Recommendation</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RCT</td>
<td>CS</td>
<td>CR</td>
</tr>
<tr>
<td>TPE</td>
<td>1(120)</td>
<td>40(878)</td>
<td>54(73)</td>
</tr>
<tr>
<td>TPE-HV</td>
<td>1(182)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

TPE-HV: TPE-High Volume, not available in US.
Today’s content

- Definition and classification of liver failure

- Things to consider in acute liver failure

- Things to consider in acute on chronic liver failure
Things to consider in acute on chronic liver failure

- Specific management? → look for trigger

- Critically ill patients with cirrhosis need a multidisciplinary approach
ACLF management

Trigger-specific management

Sarin et al., Hepatol Int 2014;8:453
Events known to precipitate ACLF

- Acute hepatotrophic viral infection
  - Acute hepatitis A, B, D, E
  - Reactivation of hepatitis B
- Alcoholic hepatitis
- Drug induced liver injury
- Infection
- Gastrointestinal bleeding
- Ischemia

Asrani et al., Clin Liver Dis 2014;18:561
Management of the critically ill patient with cirrhosis: A multidisciplinary perspective


J Hepatology 2016;64:717
Key recommendations for AKI

- **Replacement of**
  - isotonic crystalloids in cases of volume loss due to diarrhea or over diuresis (1D)
  - blood in cases of acute gastrointestinal hemorrhage (1D),
  - 20–25% albumin for infections (1A), suspected type-1 HRS (1A) or in cases where the cause of AKI is unclear (1D).

- **RRT indication**
  - worsening AKI, worsening fluid overload with >10% total body weight despite diuretic therapy or worsening acid-base status (1D).

Nadim et al., J Hepatology 2016;64:717
Key recommendations for Cardio-pulmonary dysfunctions

- a mean arterial pressure 60 mmHg is usually appropriate (1D).
- therapeutic paracentesis in patients with tense ascites (1A).
- careful attention and monitoring of patients, preferably with a pulmonary artery catheter (PAC) or echocardiography, during fluid resuscitation to avoid development of fluid overload (1D).
- repeated measurements of blood lactate levels even though the interpretation may be complicated by the impaired clearance in cirrhosis (1A).

Nadim et al., J Hepatology 2016;64:717
Key recommendations for choice of fluid

- Crystalloid solutions as the initial fluid of choice in volume depleted patients (10–20 ml/kg) (1C).
- Albumin (8 g/L of ascites removed) following large volume paracentesis (>5 L) (1B).
- Concentrated albumin (1.5 g/kg on day one followed by 1 g/kg on day 3) for SBP (1B). → 보험 급여 됨 (단 cr > 1mg/dL, BUN > 30mg/dL, Bilirubin > 4 mg/dL 였고 옳고 옳았다)
- Crystalloids and a proportion of 4–5% albumin may be an option for suspected bacterial infection (2D).
- Recommend against the use of hydroxyethyl starch (HES) (1B).

Nadim et al., J Hepatology 2016;64:717
nAdim et al., J Hepatology 2016;64:717

Key recommendations for shock

- norepinephrine as the first line vasopressor agent (1A).
- Vasopressin or terlipressin are appropriate second line agents for persistent hypotension (1B).
- A trial of hydrocortisone 200–300 mg/day in divided doses in patients with refractory hypotension should be started and stopped following improvement in hemodynamics (1C).
Key recommendations for antibiotics prophylaxis

- universal decontamination with intranasal mupirocin (twice daily) and chlorhexidine baths of ICU patients as part of a hospital wide plan to decrease bloodstream infections (2B).

Nadim et al., J Hepatology 2016;64:717
Key recommendations for risk of bleeding

- INR does not provide an adequate assessment of hemostasis in cirrhosis (2B).
- recommend against routine prophylactic use of fresh frozen plasma (FFP) (1B).
- maintaining platelet counts above 50 \( \times 10^9 \)/L in the presence of active bleeding (2C).
- hemoglobin transfusion trigger of 7 mg/dl (1A).
- anticoagulation with unfractionated/low molecular weight heparin in patients with occlusive portal vein thrombosis in the absence of bleeding risk factors (2C).
- maintaining fibrinogen levels >1.5 g/L in patients with significant bleeding or during invasive/surgical procedures (2C).

Nadim et al., J Hepatology 2016;64:717
Take home message #2

- ALF management
  - Encephalopathy
  - Look for etiology
  - Consider high volume plasmapheresis

- ACLF management
  - Look for trigger
  - Multidisciplinary approach for organ failures