Management of decompensated cirrhosis

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How are we doing at managing decompensated cirrhosis?

• NCEPOD report on identified deficiencies in the management of patients with ALD nationally
  – Only 47% of patients given “good” care

• Audit in NE England also showed patients with decompensated cirrhosis were managed suboptimally
  – 139 patients from all hospitals in the NE+NC hepatology Network
  – Overall 9% mortality and median hospital stay 15 days
  – Only 62% with ascites had tap in first 24hrs (18% had SBP)
  – 28% of subjects with renal impairment did not have nephrotoxins stopped
  – 19% of subjects with variceal bleeding did not receive terlipressin
Case

- 59 year old male
- Presented with confusion and jaundice
- Known alcoholic related liver disease
- “grade 2” varices on endoscopy Jan 2015
- Still drinking 50 units per week (cut down from >200 a year ago)
- Medications:
  - Carvedilol 6.25mg BD
  - Thiamine 100mg od
  - Spironolactone 100mg od
- Examination:
  - Pulse 72/min, BP 84/43 mmHg, Temp 37.6 °C
  - Drowsy and liver flap
  - Moderate ascites no hepatomegaly
  - Malnourished
Case - results

- **Bloods**
  - Hb 101
  - WCC 13.2
  - Platelets 69
  - PT 25 secs
  - Bilirubin 186
  - Albumin 25
  - ALT 25
  - Na 126
  - K 3.6
  - Urea 10.1
  - Creatinine 159
  - CRP 52
What is the most likely diagnosis?

1. Decompensated cirrhosis due to variceal haemorrhage

2. Acute alcoholic hepatitis

3. Decompensated cirrhosis due to spontaneous bacterial peritonitis

4. Acute portal vein thrombosis
Case

Problem list:

1. Decompensated cirrhosis
2. Alcoholic-related liver disease
3. Probable SBP
4. Acute kidney injury
5. Encephalopathy
6. Malnourished
Care bundle for the management of decompensated cirrhosis – the first 24 hours

Decompensated cirrhosis is a medical emergency with a high mortality. Effective early interventions can save lives and reduce hospital stay. This checklist should be completed for all patients admitted with decompensated cirrhosis within the first 24 hours of admission.

1. Investigations
   a) ALP [ ] IL-6 [ ] Urea [ ] ALT [ ] LDH [ ] C-Reactive [ ] Plasminogen [ ] Fractional [ ]
   b) Blood culture [ ] (if patient is suspected)
   c) Perform a chest X-ray on admission in all patients with acute decompensation and aspiration
   d) Perform a chest X-ray on admission in all patients with acute decompensation and aspiration
   e) Perform a chest X-ray on admission in all patients with acute decompensation and aspiration
   f) Perform a chest X-ray on admission in all patients with acute decompensation and aspiration

2. Alcohol – if the patient has a history of current or excess alcohol consumption
   a) Stigmata of portal hypertension
   b) Comorbidity status
   c) History of alcohol withdrawal
   d) History of alcohol withdrawal

3. Infections – if sepsis or infection is suspected
   a) Blood culture [ ] (if patient is suspected)
   b) Blood culture [ ] (if patient is suspected)
   c) Blood culture [ ] (if patient is suspected)
   d) Blood culture [ ] (if patient is suspected)

4. Acute kidney injury
   a) Serum creatinine [ ]<br>Increased on admission [ ]<br>Increased on admission [ ]<br>Increased on admission [ ]<br>Increased on admission [ ]
   b) Urea and creatinine levels [ ]<br>Urea and creatinine levels [ ]
   c) Urea and creatinine levels [ ]
   d) Urea and creatinine levels [ ]

5. GI bleeding – if the patient has evidence of GI bleeding and requires urgent intervention
   a) Protime, INR, PT [ ]<br>Protime, INR, PT [ ]<br>Protime, INR, PT [ ]
   b) Protime, INR, PT [ ]<br>Protime, INR, PT [ ]
   c) Protime, INR, PT [ ]
   d) Protime, INR, PT [ ]
   e) Protime, INR, PT [ ]
   f) Protime, INR, PT [ ]
   g) Protime, INR, PT [ ]
   h) Protime, INR, PT [ ]
   i) Protime, INR, PT [ ]
   j) Protime, INR, PT [ ]

6. Encephalopathy
   a) Look for precipitants (QI bleed, constipation, dehydration, sepsis etc.)
   b) Encephalopathy – look for appropriate level of alertness and response to stimuli
   c) If in doubt consult a confused patient and patient/relative to exclude encephalopathy
   d) Encephalopathy – look for appropriate level of alertness and response to stimuli

7. Other
   a) Various diagnostic procedures – pleural fluid analysis
   b) Hepatic encephalopathy
   c) Renal impairment
   d) GI bleeding
   e) Signs of severe hyperammonia
   f) Frequent alcohol use

Decompensated Cirrhosis Care Bundle – First 24 Hours

The recent MRC/DOH report 2013 on alcohol related liver disease highlighted that the management of some patients with decompensated cirrhosis in the UK was substandard. Admission with decompensated cirrhosis is a common medical presentation and carries a high mortality (10-20% in hospital mortality). Early intervention with evidence-based treatments for patients with the complications of cirrhosis can save lives. This checklist aims to provide a guide to help ensure that the necessary early investigations are completed in a timely manner and appropriate treatments are given at the earliest opportunity.

- Decompensated cirrhosis is defined as a patient with cirrhosis who presents with an acute deterioration in liver function that can manifest with the following symptoms:
  - Jaundice
  - Increased ascites
  - Hepatic encephalopathy
  - Renal impairment
  - GI bleeding
  - Signs of severe hyperammonia
- Frequently there is a precipitant that leads to the decompensation of cirrhosis. Common causes are:
  - GI bleeding (variceal and non-variceal)
  - Infection/sepsis (hospital-acquired bacteraemia, urinary tract infection, cholangitis etc.)
  - Alcohol use
  - Acute portal vein thrombosis
  - Development of hepatocellular carcinoma
  - Drug/alcohol use, NASH etc.
  - Sudden liver injury (sepsis or hypotension)
  - Decompensation
  - Contraindication

When assessing patients who present with decompensated cirrhosis please look for the precipitating cause and treat accordingly. The checklist is designed to optimize care at the time. When patient data is not available, please arrange for a review of the patient by the appropriate team at the earliest opportunity. Scoring of care to higher level should be considered in patients not responding to treatment within 24 hours of presentation and those with good underlying performance status at the time of presentation.

McPherson S, Frontline Gastroenterology 2016

What is “decompensated cirrhosis”?

• Deterioration in liver function in cirrhotic, that can manifest with the following:
  – Jaundice,
  – Increasing ascites,
  – Hepatic encephalopathy,
  – Acute kidney injury,
  – Signs of sepsis
What precipitates a decompensation?

- Infection/sepsis
- GI bleeding (variceal and non-variceal)
- Alcoholic hepatitis
- Acute portal vein thrombosis
- Development of hepatocellular carcinoma
- Drugs (Alcohol, opiates, NSAIDs etc)
- Ischaemic liver injury (sepsis or hypotension)
- Constipation (encephalopathy)
1. Ascitic tap sent urgently for fluid neutrophil count
2. Full septic screen sent
3. Given i.v. pabrinex
4. Monitored for alcohol withdrawal
5. Spironolactone and propranolol suspended
6. Fluid resuscitated with 1L Hartmann’s over 1 hour
7. Catheterised to monitor urine output
8. Given i.v. Vitamin K
9. Lactulose 20ml QDS commenced
Further results 1 hour later

- Ascitic neutrophil count 1100/mm³ (1.1x10⁹/L)
  - Diagnostic of SBP
- BP increased to 104/62
- Urine dip – normal
- CXR normal
What is the most appropriate treatment for SBP?

1. i.v co-amoxiclav
2. i.v co-amoxiclav and i.v albumin 1.5g/kg
3. i.v co-amoxiclav and terlipressin 1mg QDS
4. i.v co-amoxiclav and metronidazole
Infections

- Infections are common in patients with cirrhosis and have very high mortality rates
- Cirrhotics often don’t show typical signs of infection, such as pyrexia and increase CRP
- Most common infections in cirrhotics are
  - SBP
  - UTI
  - Pneumonia
  - Cellulitis
- Gram negatives and enteric bacteria most common
Spontaneous bacterial peritonitis (SBP)

- Infection of the ascitic fluid in the absence of a secondary cause
- Occurs in approximately 10% of hospitalized cirrhotics
- Usually asymptomatic
  - Can have fever and abdominal pain
- Polymorphonuclear cells >250/mm³ in ascitic fluid
  - Neut 0.25 x10⁹ on automated testing (FBC tube)
- Treat with antibiotics
  - i.v. co-amoxiclav or ciprofloxacin (oral)
  - Be guided by culture results
- Give i.v. albumin to reduce HRS
Acute kidney injury in cirrhotics

- AKI occurs in 20% of hospitalised cirrhotics
- Commonly multi-factorial,
  - pre-renal AKI (45%)
  - acute tubular necrosis or glomerulonephritis (32%)
  - HRS (23%)
  - rarely post-renal (<1%).
- Previously defined as creatinine >133 μmol/l
- Cirrhotic frequently have low creatinine levels (low muscle bulk)
- Use RIFLE/AKIN criteria to diagnose
- Hyponatraemia frequently co-exists
**Acute Kidney injury in cirrhotic**

1. Increase in serum creatinine by $\geq 26.5 \mu$mol/L within 48 hrs or
2. $\geq 50\%$ increase from baseline in the last 7 days

- Suspend diuretics and nephrotoxins
- Volume expand with albumin (1g/kg on day 1)
- Treat infections
- Exclude other intrinsic renal cause (USSK, urinalysis)

**Improvement**
- Continue treatment if appropriate

**No improvement**
- Likely Hepato-renal syndrome

- Treat with terlipressin (initially at 0.5mg QDS increasing up to 2mg QDS if no response) + albumin 20-40g/day

**HRS diagnostic criteria**
1. Cirrhosis with ascites
2. No response after 2 days of diuretic withdrawal and volume expansion with albumin (1g/kg/day)
3. Absence of shock
4. No current or recent nephrotoxic drugs
5. No macroscopic signs of structural kidney injury (no proteinuria, haematuria, normal US)

Modified from Angeli Gut 2015
Fluids in cirrhotic patients

- Albumin 5% (500ml) – volume expander
- Albumin 20% (100ml) – concentrated (paracentesis SBP etc)
- Hartmann's or Normal saline – ok to use acutely to volume expand, but don’t give litres of it as it will increase ascites
- Dextrose 5% - don’t give lots of this if the patients is hyponatraemic
- Gelofusine/isoplex – can cause immune dysfunction in cirrhotics
Hepatic encephalopathy

Main causes

- Infection
- GI bleeding
- Electrolyte disturbance
- Constipation
- Sedative drugs

Management

- Treat underlying cause
- Oral lactulose – aiming for 2-3 stools/day
- Phosphate enemas
- Rifaximin for persistent HE or >1 admission with HE

<table>
<thead>
<tr>
<th>Grades</th>
<th>Detailed Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mild confusion, euphoria, anxiety or depression, reversed sleep rhythm, slurred speech.</td>
</tr>
<tr>
<td>II</td>
<td>Drowsiness, lethargy, gross deficits in the ability to perform mental tasks, relatively moderate confusion.</td>
</tr>
<tr>
<td>III</td>
<td>Somnolent but arousable, severe confusion, inability to perform mental tasks</td>
</tr>
<tr>
<td>IV</td>
<td>Coma with (IVa) or without (IVb) response to painful stimuli.</td>
</tr>
</tbody>
</table>
• Treated with co-amoxiclav and albumin
• Renal function improved
• Encephalopathy improved
• Malnourished - commenced on NG feeding
• Once renal function normalised he was recommenced on spironolactone 100mg/day
• His BP remained low 105/65 mmHg so stayed off propranolol
• At day 10 he was planned for home, but collapsed in the toilet
Case cont

- Reviewed by F1 – strong smell of melaena in toilet

- BP 80/50 mmHg, Pulse 100/min
- Hb 68 (~100 prior)
- Platelets 86
- PT 20 secs
- Urea 6.8
- Creat 90
- Bil 124
- Alb 35
Which of the following treatments is most appropriate?

1. i.v. terlipressin

2. i.v. terlipressin and cefuroxime

3. i.v omeprazole and iv terlipressin

4. i.v. omeprazole
Case cont

• Initial management
  – Fluid resuscitated with 1L N saline over 1 hour
  – X match 6 units blood
  – Transfused 2 units of blood
  – Given 2mg terlipressin stat
  – Given 750mg Cefuroxime stat
  – Urgent endoscopy arranged
Case cont

• Initial management
  – Fluid resuscitated with 1L N saline over 1 hour
  – X match 6 units blood
  – Transfused 2 units of blood
  – Given 2mg terlipressin stat
  – Given 750mg Cefuroxime stat
  – Urgent endoscopy arranged
Terlipressin for variceal bleeding

Reduces mortality

Improves control of bleeding

Ioannou G et al. Aliment Pharmacol Ther 2003 17 53-64
Antibiotics prevent infections in cirrhotic patients with GI bleeding

**Free of infection**
Risk difference, random model
Bilateral CI, 95% for trials, 95% for MA

- Rimola 85
- Soriano 92
- Blaise 94
- Pauwels 96
- Hsieh 98
- Total

Risk difference

0.0 0.2 0.4 0.6 0.8

0.3230, p<0.001

**Survival**
Risk difference, random model
Bilateral CI, 95% for trials, 95% for MA

- Rimola 85
- Soriano 92
- Blaise 94
- Pauwels 96
- Hsieh 98
- Total

Risk difference

-0.1 0.0 0.1 0.2 0.3 0.4

0.0908, p=0.0042

**Fig. 1.** Mean percentage of patients free of infection (Der Simonian).

**Fig. 4.** Mean survival (Der Simonian).

Restrictive transfusion strategy reduces mortality from GI bleeding

Acute alcohol-related hepatitis

- Syndrome of:
  - rapid onset jaundice (<3 months),
  - liver failure,
  - systemic inflammation,
- Associated with prolonged, heavy alcohol consumption (typically >12 units/day)
- Clinical features:
  - tender hepatomegaly,
  - fever,
  - ascites,
  - encephalopathy.
Diagnosis of Alcohol-related hepatitis

• Laboratory investigations:
  – Increased AST and ALT 2-6 x ULN with
  – an AST/ALT ratio >2
  – neutrophilia
  – hyperbilirubinaemia,
  – coagulopathy.

• Differentiation between alcohol-related hepatitis and other causes of hepatic decompensation can be difficult (especially sepsis)

• Liver biopsy (usually transjugular) should be considered when doubt exists over the diagnosis
Steroids for Alcohol-related hepatitis

- 1103 participants
- Trend towards reduced 28 day mortality with Prednisolone (OR 0.72 CI 0.52 to 1.01, P=0.06)
- After correcting for baseline factors, 28 day mortality was significantly reduced by 40% (0.61, 0.41 to 0.91, P=0.02).
- Mortality was not reduced at 90 days or at one year

Thursz et al. NEJM 2015
Management of acute alcohol-related hepatitis

1. Patient with suspected alcohol related hepatitis
2. Seek and treat infections and other complications of cirrhosis
3. Calculate MDF
   - MDF ≥32 – high risk
   - MDF <32 – low risk
4. Consider liver biopsy if diagnosis is in doubt
5. Continue treatment of complications
6. Start prednisolone 40 mg
7. Assess response after 7 days with Lille scores
   - Lille score ≤0.45
   - Lille score >0.45
8. Complete 28 days of prednisolone in total
9. Stop prednisolone
10. Consider investigative treatment as part trial

McPherson BMJ 2016
Does the care bundle make a difference?

- Outcomes of implementation assessed in 3 hospitals
  - Newcastle
  - Sunderland
  - Royal Cornwall Hospital
- 228 patients with decompensated cirrhosis reviewed
- High level of usage of the care bundle
  - Increased to 90% in Newcastle
- Improvement in all aspects addressed in the Bundle
- Hospital stay reduced from 11 days to 8 days
Conclusions

- Decompensated cirrhosis is a complex multisystem disorder with a high mortality rate
- Early intervention for complications can save lives
- The NCEPOD report and regional audit has shown significant deficiencies in the management of patients with decompensated cirrhosis – WE MUST IMPROVE
- A care bundle is widely available that has been shown to improve the early management of patients with decompensated cirrhosis.
### The care bundle

#### Decompensated Cirrhosis Care Bundle - First 24 Hours

Decompensated cirrhosis is a medical emergency with a high mortality. Effective early interventions can save lives and reduce hospital stay. This checklist should be completed for all patients admitted with decompensated cirrhosis within the first 24 hours of admission.

1. **Investigations**
   - [ ] Abdominal ultrasound
   - [ ] LFT
   - [ ] Coag
   - [ ] Urine dip
   - [ ] INR
   - [ ] Pericardiocentesis
   - [ ] CT scan
   - [ ] CaSeCa
   - [ ] CaSeC
   - [ ] Do not proceed

2. Alcohol - if the patient has a history of current excess alcohol consumption
   - N/A

3. Infections - if sepsis or infection is suspected
   - N/A

4. Acute kidney injury and/or hyponatraemia
   - N/A

5. Blood pressure
   - N/A

6. Encephalopathy
   - N/A

7. Other
   - N/A

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### Decompensated Cirrhosis Care Bundle - First 24 Hours

The recent MRC/SGI report 2013 on alcohol-related liver disease highlighted that the management of some patients admitted with decompensated cirrhosis is in the UK was suboptimal. Admission with decompensated cirrhosis is a common medical emergency and carries a high mortality (10-20% in hospital mortality). Early intervention with evidenced-based treatment for patients with the complications of cirrhosis can save lives. This checklist aims to provide a guide to help ensure that the necessary early investigations are completed in a timely manner and appropriate treatment is given at the earliest opportunity.

- Decompensated cirrhosis is defined as a patient with cirrhosis who presents with an acute deterioration in liver function that can manifest with the following symptoms:
  - Jaundice
  - Increasing ascites
  - Hepatic encephalopathy
  - Renal impairment
  - GI bleeding
  - Enlarged spleen
  - Loss of appetite
  - Bowel disorders
  - Altered liver function tests
  - Hypersplenism
  - Development of hepatocellular carcinoma
  - Diabetic (alcohol, obesity, NASH etc.)
  - Intrahepatic injury (episodes or hyper tension)
  - Dehydration
  - Consideration

When assessing patients who present with decompensated cirrhosis, please look for the precipitating cause and treat accordingly. The checklist shown overleaf gives a guide to the necessary investigations and early management of these patients admitted with decompensated cirrhosis and should be completed on all patients who present with this condition. The checklist is designed to optimise a patient's management in the first 24 hours when specialist liver/gastro input might not be available. Please arrange for a review of the patient by the gastroenterologist at the earliest opportunity. Escalation of care to higher level should be considered in patients not responding to treatment when reviewed after 6 hours, particularly those with first presentation and those with good and definite performance status prior to the recent illness.

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**McPherson S, Frontline Gastroenterology 2016**