Alcoholic Liver Disease - who to admit to critical care and how to prognosticate

Clinical Problem

A 48 year old male patient presented to the Accident and Emergency (A&E) Department with a massive haematemesis. He was referred to the Intensive Care Unit (ICU) team by the gastroenterology registrar for assistance with stabilisation and endoscopy and subsequent management on ICU.

The patient had a 15 year history of Alcoholic Liver Disease (ALD) with multiple admissions to hospital and two previous admissions to ICU following variceal bleeds. He was known to still be drinking heavily. He had Child-Pugh C cirrhosis.

Management

His initial haemodynamic instability responded to fluid challenges but he was non compliant and agitated. He was transferred to theatre where he underwent endoscopy under general anaesthetic. Variceal bleeding was identified but not controllable with banding, consequently a Sengstaken tube was placed.

On his arrival on ICU he was sedated and ventilated with the Sengstaken tube in place. He was oxygenating well on 35% oxygen. He was haemodynamically stable having received 2l of crystalloid and 2 units of blood. Urine output was approximately 1ml/kg/hr.

He remained stable and underwent removal of Sengstaken and repeat endoscopy on ICU. Further variceal bands were placed. He was then successfully extubated following a sedation hold. Alcohol withdrawal was managed with chlordiazepoxide and the following day he was discharged to the gastroenterology ward.

Three days later he was re-referred to ICU by the Outreach team. He was deteriorating significantly, he had escalating oxygen requirements and was hypotensive and oliguric. On review by the ICU doctor he was saturating at 93% on 15l oxygen, he had a blood pressure of 80/40 despite fluid therapy and his urine output had been less than 0.5ml/kg/hr for 12 hours. His blood tests revealed worsening liver function and an acute kidney injury. He was confused and had a liver flap on examination. A diagnosis of sepsis due to Hospital Acquired Pneumonia (HAP) was made.

He was readmitted to ICU, sedated and ventilated, and inotropic support was initiated. It was agreed with the Gastroenterology team and family that he would be reviewed at 48 hours and a decision regarding ongoing care made at that time. Within 24 hours he was deteriorating rapidly, with escalating inotropic and oxygen requirements. He had also become anuric with a worsening metabolic acidosis. In view of the worsening multi-organ failure a decision was made, with
the understanding of the family, that initiating renal replacement therapy was inappropriate and that palliation was now the most appropriate strategy.

Support was withdrawn approximately 30 hours after ICU admission and the patient died.

Discussion

The healthcare burden of ALD is a significant and increasing problem in the United Kingdom. Hospital admissions with decompensated chronic ALD have increased by over 100% in the last 25 years. ICU admissions with ALD have tripled between 1996 and 2005 with an estimated annual cost of £14.7 million.

Previous studies have reported a very poor prognosis, for example reporting 100% mortality in sepsis. It should however be borne in mind that ALD is a spectrum of pathophysiology from hepatic steatosis through to severe cirrhosis with irreversible systemic complications. As such physiological reserve and reversibility of acute pathology will vary from patient to patient. The assessment and appropriate escalation of patients with ALD is therefore a difficult but important facet of ICU expertise.

This case was chosen to assess the evidence available to support decision making in critically ill patients with ALD, specifically who to admit and how to prognosticate.

There are a number of approaches to objective assessment of a patient with a view to prognostication or admission/escalation decision making.

- Scoring systems
- Presenting diagnosis or disease process
- Level/number of organ support

Scoring Systems

Scoring systems attempt to categorise and grade physiological and pathological variables to provide a tool for both research and clinical use.

There are a number of liver specific scoring systems, with one the most familiar being the Child-Pugh score (CPS). A more modern system is the Model for End-Stage Liver Disease (MELD) and its numerous variants. There are also several generic ICU scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE) II score and then there are organ dysfunction scores such as the Sequential Organ Failure Assessment (SOFA) score.

Cholongitas et al conducted a review of studies comparing liver specific and ICU scoring models. They found that ICU general prognostic models out performed liver specific scores. This is likely to be because the liver specific scores do not take into account the severity of injury to organs other than the liver. Of the ICU scores they found that organ dysfunction models such as SOFA correlated better
with mortality than APACHE. SOFA was shown to have an area under the Receiver Operator Curve of 0.83 – 0.89 versus 0.66 – 0.78 for APACHE.

Therefore in patients admitted to ICU with decompensated ALD SOFA is probably the most appropriate score to consider, with MELD consistently being shown to be the most appropriate of the liver specific scores.

In a study undertaken after the above review Cholongitas found that scoring at 48 hours post admission correlated with mortality better when compared with scoring at admission. This study also showed a SOFA of 10 or greater was associated with a 93% mortality.

The use of scoring systems may aid both prognostication and discussions with the parent team and family. They do not replace clinical acumen, nor do they accurately apply to all patients all of the time.

**Diagnosis**

Presenting diagnosis has an impact on mortality. Decompensated ALD typically presents to the ICU with one of four problems: gastrointestinal (GI) haemorrhage, sepsis, encephalopathy or hepato-renal syndrome.

In a UK based study by Mackle et al patients presenting with gastrointestinal haemorrhage had a 62% hospital mortality, this compares with 88% in sepsis, 33% in encephalopathy and 94% in renal failure requiring renal replacement therapy (RRT). This implies patients with an isolated GI bleed have significantly better outcomes than those presenting with sepsis or renal failure. Therefore a low threshold for admission may be appropriate, if the bleed is manageable, regardless of the severity of underlying liver disease.

Historically sepsis in decompensated ALD was reported as having a 100% mortality. More recent studies show improved, but still very poor, outcomes. As above Mackle study showed an 88% mortality in patients with sepsis and multiorgan failure. A large cohort study by Galbois et al showed improving outcomes in cirrhotic patients with septic shock, hospital mortality falling from 78% to 72% between 1998 and 2010. It should be noted that the inclusion criteria were broad in this study and included both non ALD cirrhosis and patients who did not require mechanical ventilation.

In the Mackle study the numbers of patients presenting with encephalopathy was too small to draw clear conclusions (7 patients). Other studies have suggested a mortality of approximately 50% but all are small numbers. I would postulate that patients presenting solely with hepatic encephalopathy are relatively unusual.

Hepato-renal syndrome can be difficult to diagnose in the ICU population as many patients have multiple potential risk factors for Acute Kidney Injury (AKI). As such studies are difficult to compare to directly. However prognosis appears poor. As described in the Mackle study there was a 94% mortality in patients receiving RRT for AKI. A further study created a new definition of cirrhosis
associated AKI. This was characterised by a creatinine increase of 26.4 micromoles/l in 48 hours or a >50% increase from a baseline within the last 6 months. This new definition showed irreversible cirrhosis associated AKI in hospitalised (therefore not only ICU) ALD patients was associated with an 80% 30 day mortality.

**Number of organ failures**
Number of organ systems failing may also help assess likely outcome and inform decision making. A review of mortality in critically ill ALD patients found a consistent relationship between number of organ failures and mortality. This showed a mortality of 33-45% for single organ failure, 65-75% for two organs and 90-100% for three organ failure.

Mackle et al found patients requiring mechanical ventilation with no inotrope support had only a 31% hospital mortality. This describes the patient in the case vignette on his initial admission. However, in patients who are admitted and then deteriorate there is objective evidence of worsening outcome. Mackle showed adding inotropic support to mechanical ventilation resulted in an 86% hospital mortality and the third organ failure (renal) increased this to 91%. This is in line with the case patient's second admission.

**Data quality**
All of these studies are retrospective cohort studies or systematic review there of. As such they suffer from a number of issues. Definitions, inclusion criteria and reported outcomes vary. To allow conclusions and assessment to be made patients must be categorised, for example by admission diagnosis. This may be undertaken differently between studies and even potentially within studies. Comparisons between studies and with one's own clinical practice is therefore possibly flawed. Pooled data analysis would be inappropriate.

**Lessons Learnt**
Outcomes in critically ill patients with ALD are poor but there is some evidence of improvement. Multidisciplinary assessment, SOFA, and MELD scores, presenting diagnosis and number of failing organ systems are all important aspects for consideration.

The evidence base is not of a high quality. A subjective assessment therefore has to be made. There is a consistency to the data reported by different studies that gives them credibility. It would appear that a patient presenting with an isolated GI bleed would be highly appropriate for admission. In contrast a septic patient in established multiorgan failure with a SOFA score more than 10 should prompt a multidisciplinary discussion regarding the appropriateness of escalation to ICU.

Overall a pragmatic approach seems wise. Where the suitability for escalation to ICU is questionable admission with a clearly agreed review point at 36 to 48 hours may be appropriate. This allows patients in whom reversal of the pathophysiological process is possible chance to stabilise and improve. It also
allows time for families to understand and come to terms with the situation. In patients with a rising SOFA score and/or increasing number or severity of organ system failures appropriateness of ongoing treatment needs to be then carefully considered.

Further research would prove useful. A case-matched study between patients with and without ALD would provide interesting insight into the significance of the diagnosis of ALD on outcomes. Future cohort studies should aim to use universal definitions wherever possible.

References