Liver Transplantation and ICU Issues

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Consultant Intensive Care Medicine and Liver Transplant Anaesthesia
Outline

• Scope of problem
• Liver patients on ICU
• Recognising who to refer
• Indications for transplant
• transplantation
• Outcomes
Scope of problem

Survival rates have improved for almost every disease of every organ in the last few decades, with one notable exception: liver disease. 

PERCENTAGE CHANGE IN STANDARDISED UK MORTALITY RATES (AGE 0–64) NORMALISED TO 100% IN 1970

[Bar chart showing percentage change in standardized UK mortality rates for various causes from 1970 to 2010, with liver disease showing a significant increase.]
Deaths Caused by Liver Disease in Under 65s.
Deaths from liver disease in England have reached record levels, rising by 25% in less than a decade, according to new NHS figures. Heavy drinking, obesity and hepatitis.

More deaths in men, with the highest number of fatalities in the North West.
Hospital Deaths from Liver Disease

• 1 in 11 hospital admissions for liver disease ends in a hospital death

  = 8.8% (3,040 out of 34,650)

• 1 in 72 of all hospital admissions result in hospital death

  = 1.4%, (210,170 out of 15.2 million)

April 2013
Liver Disease and ICU

• Chronic liver disease and its complications
  – Infections
  – Variceal bleeding
  – MOF
• Liver dysfunction in the ICU patient
  – Sepsis
  – Ischaemia

• Acute Liver failure
• Transplantation
Liver Disease and ICU

- **Chronic liver disease and its complications**
  - Infections
  - Variceal bleeding
  - MOF
- **Liver dysfunction in the ICU patient**
  - Sepsis
  - Ischaemia
- **Acute Liver failure**
- **Transplantation**
Liver Disease and ICU

- Chronic liver disease and its complications
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- Liver dysfunction in the ICU patient
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- Acute Liver failure

- Transplantation
Aetiology of ALF

1. Drugs:
2. Viruses:
3. Pregnancy:
4. Wilson’s disease
5. Toxins: *Amanita phalloides*
6. Budd Chiari / veno-occlussive disease
7. Others: malignancy, ischaemic
8. Seronegative, Indeterminant
Figure 3. Worldwide Causes of Acute Liver Failure.
HAV denotes hepatitis A virus, HBV hepatitis B virus, HEV hepatitis E virus, and NT not tested.
What to do in a non Liver Centre

- Make the diagnosis
- Aetiology
- Monitor: BM PT
- Supportive therapy: fluids, antibiotics, antifungal.
- Recognise the need to refer
Key points in management

- establish diagnosis
- **monitor for hypoglycaemia**
- if encephalopathy progresses beyond grade 2 protect airway
- maintain adequate intravascular volumes and add inotropes if necessary
- contact specialist centre (?need for transplantation)
- prevent / treat cerebral oedema / ICP monitoring
- aggressive surveillance and treatment of infection
- treat / support associated complications
- Early CVVH

- **DON’T CORRECT CLOTTING**
When to contact a Liver Centre

- **Adverse aetiology**
  - Drugs
  - Indeterminate cause
  - Hep B
  - Wilsons

- **Nature of paracetamol overdose**
  - Staggered, late presentation, mixed O/D
  - Associated low BMI
  - Chronic alcohol use

- **Encephalopathy**

- **Renal failure**

- **Severity of liver damage (non POD INR>1.5)**
### Guidelines for Referring Acute Liver Failure

#### Paracetamol

<table>
<thead>
<tr>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
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<tbody>
<tr>
<td>pH &lt; 7.3</td>
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<tr>
<td>INR 3.0, PT&gt;50s</td>
<td>INR 4.5, PT&gt;75s</td>
<td>INR 6.0, PT&gt;100s</td>
</tr>
<tr>
<td>Oliguria</td>
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</tr>
<tr>
<td>Creatinine &gt;200mmol/l</td>
<td>Creatinine &gt;200mmol/l</td>
<td>Creatinine &gt;300mmol/l</td>
</tr>
</tbody>
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#### Non Paracetamol

- Encephalopathy
- Hypoglycaemia
- PT>30s (>20 subacute)
- INR>2 (>1.5 subacute)
- Renal failure
- Hyperpyrexial
- Na<130
- Shrinking liver

#### Table:

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</tr>
<tr>
<td>Severe thrombocytopenia</td>
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Guidelines for Transfer

• As for any critically ill patient:
  – Experienced personnel
  – Stabilisation, will need fluids ++
  – Ideally invasively monitor

• Be prepared for a rapid deterioration

• If in doubt re encephalopathy grade, sedate and intubate

• May require inotropes
History of LTx:

- **March 1, 1963**: Thomas Starzl on a 3yr old, Bennie Solis, Died of uncontrolled bleeding
- **May 1963**: for cancer of the liver. to solve the bleeding administered huge amounts of fibrinogen. the man died three weeks later from complications due to blood clotting.
- **1967** first successful human liver transplant
- **1968** Sir Roy Calne: first European LTx
- **1970s** development of immunosuppression: cyclosporin
Leeds

- 1986: first liver transplant: Prof G Giles

- July 2007 First NHS Living Related Donor
Liver Transplants
NHS BLOOD AND TRANSPLANT
LIVER ADVISORY GROUP

Protocols and Guidelines for Adults Undergoing Deceased Donor Liver Transplantation in the UK
Listable conditions

- Cirrhosis:
  - Primary biliary cirrhosis
  - Secondary biliary cirrhosis
  - Cryptogenic
  - Alcoholic
- Non-alcoholic fatty liver disease
- Chronic active hepatitis (autoimmune)
- Chronic viral hepatitis B
- Chronic viral hepatitis C
- Congenital hepatic fibrosis
- Primary sclerosing cholangitis
- Secondary sclerosing cholangitis
- Alpha - 1-antitrypsin deficiency
- Budd-Chiari syndrome
- Wilson’s disease
- Biliary atresia
- Other congenital biliary abnormalities
- Acute/subacute fulminant hepatic failure (FHF)
- Primary hepatocellular cancer in a cirrhotic liver
- Cystic Fibrosis
- Polycystic liver disease
- Familial Amyloidosis syndromes
- Inborn errors of metabolism not in
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Types of Listing

Elective Vs Super-urgent
**Figure 7**  Deceased donor liver only transplants in the UK in adult recipients  
1 April 2006 - 31 March 2016

*Super-urgent registration categories were changed on 17 June 2015 to account for developments in treatment of patients with acute liver failure*

Source: Annual Report on Liver Transplantation 2015/16, NHS Blood and Transplant
# Indications for Super-urgent Liver Transplant

## Acute hepatic failure

- Budd-Chiari syndrome
- Serologically indeterminate
- Wilson’s disease
- HAV
- HBV
- Other virus
- Paracetamol hepatotoxicity
- Other drug toxicity
- Other

## Re-transplantation

- Primary non-function
- Non-thrombotic infarction
- Hepatic artery thrombosis
- Early graft dysfunction
- Acute vascular occlusion - venous
- Acute vascular occlusion - artery and venous
Listing Acute liver failure

Survival for different etiologies of acute liver failure

- Pregnancy related: 98%
- Hepatitis A: 67%
- Acetaminophen: 56%
- Hepatitis B: 38%
- Seronegative hepatitis: 20%
- Idiosyncratic drug reactions: 2.5%
- Wilson disease: <1%

Survival from grade 3–4 encephalopathy

Elsevier 2006: Comprehensive Clinical Hepatology
Criteria for Super Urgent Listing

• **Strict criteria:**
  – Diagnosis
  – Age
  – Clotting
  – Presence of encephalopathy
  – Renal function
Criteria for Super-urgent listing
Paracetamol Poisoning

• **Category 1:**
  – pH <7.25 more than 24 hours after overdose and after fluid resuscitation

• **Category 2:**
  – Co-existing prothombin time >100 seconds (or INR >6.5) and
  – serum creatinine >300 μmol/l or anuria, and
  – grade 3-4 encephalopathy

• **Category 3:**
  – Significant liver injury and coagulopathy and arterial lactate >5 mmol/l on admission and >4 mmol/l 24 hours later (after adequate fluid resuscitation and exclusion of other causes) in the presence of clinical hepatic encephalopathy

• **Category 4:**
  – Two of the three criteria from category 2 with clinical evidence of deterioration (eg increased ICP, FiO₂ >50%, increasing inotrope requirements) in the absence of clinical sepsis.
Criteria for Super-urgent listing
Non-Paracetamol

• PT > 100 (INR >6.7)
• or any 3 of the following:
  – unfavourable aetiology
    • sero -ve hepatitis, halothane hepatitis, drug reaction
  – Jaundice to encephalopathy >7 days
  – age <10 >40 years
  – PT > 50 (INR >3.5)
  – bilirubin >300 mmol/l
Criteria for Super-urgent listing
Re-transplant

- **Category 8**: Hepatic artery thrombosis on days 0 to 21 after liver transplantation

- **Category 9**: Early graft dysfunction on days 0 to 7 after liver transplantation with at least two of the following: AST >10,000; INR >3.0; arterial lactate >3 mmol/l; absence of bile production

- **Category 10**: The total absence of liver function (e.g. after total hepatectomy)

- **Category 11**: Any patient who has been a live liver donor (NHS entitled) who develops severe liver failure within 4 weeks of the donor operation
ELECTIVE
Types of Donor

• DBD (donor from brain death, heart beating)

• DCD (donor from cardiac death, non-heart beating)

• LRD (living related donor)
The Operation

• 6-8 hours

• Attention to detail:
  – Positioning
  – Warmth
  – Preparation

• Induction and line insertion
  – Central, A line
  – ? Bypass lines: Internal Jug and Femoral Veins
Stages

Phase I:

- dissection
- hepatectomy

- Blood Loss ++++
  - Cell saver
  - Level I

- Haemodynamic instability
Bench work on new liver
Stages

Phase II: anahepatic

- Implanation: Portal and Hepatic vein anastomosis
- Warm ischaemic time
  - ↑acidosis
  - Coagulopathy
  - ↓bld glucose
Stages

Phase III: reperfusion: (portal and hepatic)

- Fluid load as clamps removed $\rightarrow$ venous congestion $\rightarrow$ ↑ Right sided pressures
- Cardio depression
  - Vasodilatation $\rightarrow$ Hypotension $\rightarrow$ Need for vasopressors
  - Potassium load $\rightarrow$ Dysrhythmias

- Arterial and Bilary anastomosis
Post Operative

• Closure +/- drains

• ICU

• Aim to wake as soon as stable

• Total length of stay 10 -14 days

• Analgesia: PCAS

• Immunosuppression: prednisone, mycophenolate tacrolimus
  Basiliximab (simulect)

• Heparin /LMWH for 3-5 days
# Mortality (%) following liver Tx

<table>
<thead>
<tr>
<th>Time Period</th>
<th>1st elective</th>
<th>2nd elective</th>
<th>Super-urgent</th>
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<tbody>
<tr>
<td>March 1994-March 2012</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>12.5</td>
<td>26.6</td>
<td>22.7</td>
</tr>
<tr>
<td>3 year</td>
<td>18.8</td>
<td>25.7</td>
<td></td>
</tr>
<tr>
<td>5 year</td>
<td>24.9</td>
<td></td>
<td>26.4</td>
</tr>
<tr>
<td>(Full Audit period)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Last 3 yrs:</td>
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<tr>
<td>1 year</td>
<td>8.8</td>
<td>23.1</td>
<td></td>
</tr>
<tr>
<td>Last 1 yr:</td>
<td></td>
<td></td>
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<tr>
<td>90 days</td>
<td>3.5</td>
<td>8*</td>
<td>12.9</td>
</tr>
</tbody>
</table>

*In the last 12 months 46 had a second liver transplant 4 deaths within 90 days (8%)*
The Future
Questions?