THE MANAGEMENT OF ACUTE UPPER GASTROINTESTINAL BLEEDING

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Acute Medicine Meeting
Hutt Hospital

June 21, 2015
• Common Definitions and Risk Scores in Upper Gastrointestinal Bleeding
• Epidemiology
• Basic Management
• Decision points
• Long term management
Common Definitions and Risk Scores in Upper Gastrointestinal Bleeding

• Upper GI bleeding is defined as:
  
  *Bleeding proximal to ligament of Trietz*

• Forrest Classification\(^1\) of peptic ulceration

• Rockall Score\(^2\)

• Blatchford Score\(^3\)

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\(^1\)Forrest, Finlayson, and Shearman 1974.

\(^2\)Rockall et al. 1996.

\(^3\)O. Blatchford, Murray, and M. Blatchford 2000.
FORREST CLASSIFICATION

- Grading of acuity of peptic ulceration
  - 1a Spurting bleeding
  - 1b Oozing bleeding
  - 2a Visible vessel
  - 2b Adherent clot
  - 2c Red spot
  - 3 Clean base

Rockall Score

- Pre-endoscopy and post-endoscopy score
- Designed to predict mortality

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>&lt;60 Years</td>
<td>60-79 Years</td>
<td>≥80</td>
<td>Renal/liver failure</td>
</tr>
<tr>
<td><strong>Shock</strong></td>
<td>BP ≥ 100, pulse &lt; 100</td>
<td>Pulse ≥ 100</td>
<td>BP &lt; 100</td>
<td>Disseminated malignancy</td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td>No major comorbidity</td>
<td>Heart failure, IHD, any major comorbidity</td>
<td>Renal/liver failure</td>
<td></td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Mallory Weis, No lesion seen, No SRH</td>
<td>All other diagnoses</td>
<td>Malignancy</td>
<td></td>
</tr>
<tr>
<td><strong>Major SRH</strong></td>
<td>None or dark spot</td>
<td>Blood in lumen, visible or spurting vessel, adherent clot</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table: Rockall score. SRH = stigmata of recent haemorrhage

Rockall et al. 1996.
**Blatchford score**\(^6\)

- Designed to predict combined endpoint of death, surgery, blood transfusion, performance of endoscopic therapy at endoscopy.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood Urea mmol/L</strong></td>
<td>6.5-7.9</td>
<td>8.0-9.9</td>
<td>10-24.9</td>
<td>≥25</td>
<td></td>
</tr>
<tr>
<td><strong>Hb (g/L, men)</strong></td>
<td>12.0-12.9</td>
<td>10.0-11.9</td>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hb (g/L, women)</strong></td>
<td>10.0-11.9</td>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systolic BP mmHg</strong></td>
<td>100-109</td>
<td>90-99</td>
<td>&lt;90</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pulse (per min)</strong></td>
<td>&gt;100</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td>Melaena</td>
<td></td>
<td>Syncope</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td></td>
<td></td>
<td>Hepatic disease</td>
<td>Cardiac failure</td>
<td></td>
</tr>
</tbody>
</table>

Table: **Blatchford score.**

\(^6\)O. Blatchford, Murray, and M. Blatchford 2000.
Epidemiology

- Age Standardized Incidence between 40 and 200 per 100,000 per year\(^7\)
- 30 day mortality 5-10\(^8\)
- Associated with
  - *H. pylori* infection\(^9\)
  - NSAID use\(^10\)
  - Anticoagulant use\(^11\)
  - Increasing age\(^12\)
  - Male sex\(^13\)
  - Maori ethnicity\(^14\)


\(^9\) Schöttker et al. 2012.

\(^10\) García Rodríguez L 1998.

\(^11\) Hallas et al. 2006.

\(^12\) O. Blatchford, Davidson, et al. 1997.


\(^14\) Irwin et al. 2014b.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Ulcer</td>
<td>19</td>
</tr>
<tr>
<td>Duodenal Ulcer</td>
<td>21</td>
</tr>
<tr>
<td>Gastric Cancer</td>
<td>2.5</td>
</tr>
<tr>
<td>Oesophoegal Cancer</td>
<td>0.9</td>
</tr>
<tr>
<td>Gastric Erosions</td>
<td>14</td>
</tr>
<tr>
<td>Duodenal Erosions</td>
<td>8.4</td>
</tr>
<tr>
<td>Vascular Lesion</td>
<td>3.1</td>
</tr>
<tr>
<td>Oesophoegal Varices</td>
<td>5.1</td>
</tr>
<tr>
<td>Oesophagitis</td>
<td>15</td>
</tr>
<tr>
<td>Mallory Weiss Tear</td>
<td>4.05</td>
</tr>
<tr>
<td>Normal Endoscopy</td>
<td>15</td>
</tr>
</tbody>
</table>
Basic Management Algorithm

- Safe IV access - 2 large bore lines
- Crossmatch
- Resuscitation
  - Monitor and maintain end organ perfusion
  - blood pressure, urine output, level of consciousness
- Correct coagulation defects
- PPI
- Endoscopy
- Address risk factors
  - H. pylori status
  - NSAID use
  - Antiplatelet and anticoagulant therapy
- Home!
**Decision Points**

- When to transfuse?
- PPI therapy
- Continue or stop antiplatelet therapy?
- Continue or stop anticoagulant therapy?
- Timing of endoscopy?
- What endoscopic therapy?
- Discharge criteria?
- What is a rebleeding episode?
When to transfuse?

- Evidence of massive bleeding
- Haemodynamic instability
- Haemodynamically stable anaemia?
  - Evidence in trauma and in variceal bleeding of survival benefit from lower transfusion targets\(^{15}\)
  - No clear data in undifferentiated GI bleed\(^{16}\)

\[ \rightarrow Hb < 70 \text{ g/L} \]

\(^{15}\)Hébert et al. 1999; Villanueva et al. 2013.

\(^{16}\)Villanueva et al. 2013.
## Sub-group Analysis

### B Death by 6 Weeks, According to Subgroup

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Restrictive Strategy</th>
<th>Liberal Strategy</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients/total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>23/444 (5)</td>
<td>41/445 (9)</td>
<td>0.55 (0.33–0.92)</td>
<td>0.02</td>
</tr>
<tr>
<td>Patients with cirrhosis</td>
<td>15/139 (11)</td>
<td>25/138 (18)</td>
<td>0.57 (0.30–1.08)</td>
<td>0.08</td>
</tr>
<tr>
<td>Child–Pugh class A or B</td>
<td>5/113 (4)</td>
<td>13/109 (12)</td>
<td>0.30 (0.11–0.85)</td>
<td>0.02</td>
</tr>
<tr>
<td>Child–Pugh class C</td>
<td>10/26 (38)</td>
<td>12/29 (41)</td>
<td>1.04 (0.45–2.37)</td>
<td>0.91</td>
</tr>
<tr>
<td>Bleeding from varices</td>
<td>10/93 (11)</td>
<td>17/97 (18)</td>
<td>0.58 (0.27–1.27)</td>
<td>0.18</td>
</tr>
<tr>
<td>Bleeding from peptic ulcer</td>
<td>7/228 (3)</td>
<td>11/209 (5)</td>
<td>0.70 (0.26–1.25)</td>
<td>0.26</td>
</tr>
</tbody>
</table>

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17 Villanueva et al. 2013.
PPI Therapy

- No reduction in mortality
- Reduction in rebleeding rates
- Before or after endoscopy?
  - First large randomised placebo controlled trial demonstrated no benefit of IV PPI before endoscopy \(^{18}\)
  - Hong Kong study demonstrated IV PPI after endoscopy reduces rebleeding (not mortality) \(^{19}\)

- IV or oral dosing?
  - There is evidence for oral dosing \(^{20}\)
  - Dose needs to be large enough: 40mg bd omeprazole

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\(^{19}\) Lau et al. 2000.  
Antiplatelet therapy

- Aspirin, clopidogrel
- Usually given for atherosclerotic disease
- Irreversible inhibition of COX or ADP receptors
  - Effect lasts until new platelets are formed in absence of drug (3-7 days)
- For continuation of aspirin:
  - Reduced cardiovascular mortality\textsuperscript{21}
  - Increased risk of rebleeding

\textsuperscript{21} Sung et al. 2010.
**Survival Analysis**

Log-rank test ($P = 0.005$)
Hazard ratio, 0.2 (95% CI, 0.06–0.60)

<table>
<thead>
<tr>
<th>Follow-up, d</th>
<th>Aspirin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>7</td>
<td>77</td>
<td>75</td>
</tr>
<tr>
<td>14</td>
<td>77</td>
<td>74</td>
</tr>
<tr>
<td>21</td>
<td>77</td>
<td>70</td>
</tr>
<tr>
<td>28</td>
<td>76</td>
<td>70</td>
</tr>
<tr>
<td>35</td>
<td>75</td>
<td>69</td>
</tr>
<tr>
<td>42</td>
<td>75</td>
<td>68</td>
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<tr>
<td>49</td>
<td>75</td>
<td>68</td>
</tr>
<tr>
<td>56</td>
<td>75</td>
<td>67</td>
</tr>
</tbody>
</table>

*Patients at risk, n*

Aspirin: 78 77 77 77 76 75 75 75 75
Placebo: 78 75 74 70 70 69 68 68 67

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*Sung et al. 2010.*
Anticoagulant Therapy

- Anticoagulation for AF, prosthetic heart valve, venous thromboembolism
- Cohort with high comorbidity, however lower rates of 30 day mortality\textsuperscript{23}
- No randomized controlled data regarding how to manage anticoagulation
- Status quo is to reverse warfarin anticoagulation acutely with vitamin K/FFP/prothrombinex
- Should warfarin be restarted?
  - Restarting warfarin associated with reduction in thromboembolic stroke, no increase in recurrent bleed at 90 days\textsuperscript{24}
  - For patients with AF reduced mortality over subsequent 2 years associated with restarting warfarin\textsuperscript{25}

\textsuperscript{23}Irwin et al. 2014a.
\textsuperscript{24}Sengupta et al. 2015.
\textsuperscript{25}Qureshi et al. 2014.
Timing of Endoscopy

- For endoscopic therapy to provide benefit, bleeding must be identified and successfully treated.
- The earlier, the better?
- Resource constraint for after hours procedures
- Within 24 hours\(^{26}\)
  - Reduction in rebleeding, length of stay
- Negative studies for early endoscopy (within 6 hours)\(^{27}\)
- DDW presentations 2015
  - Higher mortality with early endoscopy (<6 hours)
  - Observational studies, likely selection bias
  - Hypothesis that early endoscopy is detrimental - effect of procedural sedation? - aspiration? - inadequate resuscitation?

  - Riccardo Marmo, Stig Laursen

\(^{26}\) Cooper et al. 1999; Hwang et al. 2012.
Timing of endoscopy

- Can stratify patients and select who are likely to benefit from early endoscopy
- Rockall score\(^{28}\)
  - Predicts death
- Blatchford score\(^{29}\)
  - Predicts need for: requirement of blood transfusion, requirement of endoscopic or operative intervention to control bleeding, death, rebleeding, or a substantial fall in haemoglobin
- Waikato analysis\(^{30}\)
  - Association of presenting features with endoscopic lesions that were treated.
  - Presentation with fresh haematemesis, fresh melaena, high urea, low BP, male sex, history of peptic ulcer disease.

\(^{28}\text{Rockall et al. 1996.}\)
\(^{29}\text{O. Blatchford, Murray, and M. Blatchford 2000.}\)
\(^{30}\text{Irwin et al. 2013.}\)
**What endoscopic therapy?**

- For peptic ulceration
  - Adrenaline injection\(^{31}\)
  - Dual therapy
    - Heater probe\(^{32}\)
    - Clip placement
  - For oesophageal varices
    - sclerotherapy\(^{33}\)
    - banding\(^{34}\)

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\(^{31}\)Cook et al. 1992.


\(^{33}\)Infante-Rivard, Esnaola, and Villeneuve 1989.

\(^{34}\)Stiegmann et al. 1992.
Who is safe to discharge before or after endoscopy?

- Before endoscopy
  - Blatchford score = 0\textsuperscript{35}
- After endoscopy
  - post-endoscopy Rockall score ≤ 2\textsuperscript{36}

\textsuperscript{35}O. Blatchford, Murray, and M. Blatchford 2000; Stanley et al. 2009.
\textsuperscript{36}Rockall et al. 1996; Dulai et al. 2002.
Rebleeding episode?

- Rebleed associated with increased risk of death\textsuperscript{37}
- What is a rebleed?
  - Fresh haematemesis \textit{or}
  - Combination of
    - Ongoing melaena \textit{and/or}
    - Further drop in Hb \textit{and/or}
    - Haemodynamic instability
- Management
  - Resuscitation
  - Endoscopy/surgery/...interventional radiology

\textsuperscript{37}Rockall et al. 1996.
NON-ACUTE DECISIONS

- Test and treat for *H. pylori* if peptic ulcer disease
- Cease NSAID
- Decide ongoing anticoagulation
  - Usually restart warfarin after 1-14 days
- Decide ongoing antiplatelet therapy
- If gastric ulcer, requires repeat endoscopy to ensure ulcer healing\(^{38}\)
- Decide long term PPI\(^{39}\)

\(^{38}\) Hansson et al. 1996.
\(^{39}\) Laine and Jensen 2012.


Hwang, J. H. et al. (June 2012). “The role of endoscopy in the management of acute non-variceal upper GI bleeding”. *Gastrointestinal endoscopy* 75.6, pp. 1132–1138
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**Irwin, J. et al. (Aug. 2014b).** “Incidence of upper gastrointestinal haemorrhage in Maori and New Zealand European ethnic groups, 2001-2010”. *Internal Medicine Journal* 44.8, pp. 735–741

**Javid, G. et al. (Sept. 2001).** “Omeprazole as adjuvant therapy to endoscopic combination injection sclerotherapy for treating bleeding peptic ulcer”. *The American Journal of Medicine* 111.4, pp. 280–284


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Incidence per 100,000 per year

Age (years)

0 200 400 600 800

Sex

Male (n = 804)
Female (n = 556)