GI Bleeding: old problems and new challenges

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Disclosures

NONE

Topics to Cover

• The basics
  – Resuscitation and risk assessment
  – Epidemiology and diagnoses
  – Therapy
    • Endoscopic and medical
• New challenges and questions
  – New risks
  – New sources
  – New therapies

Resuscitate

• Isotonic IV fluids
• pRBC for HgB < 7
  – Anticipate nadir HgB
  – Individualize Tx target, but be mindful of over transfusion
• Correction of coagulopathy
  – No target data and no evidence of efficacy
• Airway
Aggressive Resuscitation

- Small RCT of standard care versus intensive resuscitation per protocol
  - No change in timing of endoscopy
  - Reduced rate of MI
  - Reduced mortality 3% versus 11%, p < 0.05

Airway Management

- Pulmonary complications a major source of morbidity and mortality
  - > new CXR infiltrates in ~ 15%
  - Significant cardiopulmonary complications in 5%
- Endotracheal intubation for altered mental status or massive upper bleed

Risk Assessment

- Hemodynamic derangement
- Age
- Comorbidities
- Hospitalized
- Red blood
- Low initial Hgb
Hospitalization

- **Admission**
  - Abnormal vital signs
  - Ongoing emesis or passage of blood/black per rectum
  - Acute anemia with HgB < 7

- **ICU**
  - Abnormal vital signs despite initial fluids
  - Moderate to severe comorbidity
  - Moderate to large volume red blood per os or rectum
  - HgB < 7 despite administration of blood

Score 0 = Low Risk

- Blatchford
  - Systolic BP > 110
  - Pulse < 100
  - Hgb ≥ 12 (women), 13 (men)
  - BUN < 6.5 mmol/L
  - Comorbidities: none

- Rebleeding < 5% and mortality < 1%

Is hospitalization needed?

Epidemiology and Incidence

- ~ 500,000 hospitalizations/yr
- Mortality = 5%
- Rebleeding 10-20%
- Need for invasive intervention other than endoscopy = 10%
- Length of stay 3-5 days
Lanas A. Time trends and impact of upper and lower gastrointestinal bleeding and perforation in clinical practice. *AJG*. 2010; 1633-41

UK 1995 (N=4137)
US-CORI 2004 (N=7822)
Canada 2002 (N=1869)
Hong Kong 2007

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>PUD</td>
<td>35%</td>
<td>21%</td>
<td>50%</td>
<td>60%</td>
</tr>
<tr>
<td>Erosive disease</td>
<td>21%</td>
<td>43%</td>
<td>10%</td>
<td>13%</td>
</tr>
<tr>
<td>MW Tear</td>
<td>5%</td>
<td>4%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Varices</td>
<td>4%</td>
<td>11%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>4%</td>
<td>1%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>AVM</td>
<td>5%</td>
<td></td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Esophagitis</td>
<td>15%</td>
<td>17% (w/erosive)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
<td></td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>No Dx Made</td>
<td>25%</td>
<td>4%</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>275</td>
<td>252</td>
<td>415</td>
</tr>
<tr>
<td>Mean age</td>
<td>70</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>Cause</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diverticulosis</td>
<td>41%</td>
<td>30%</td>
<td>41%</td>
</tr>
<tr>
<td>Rectal ulcers: stercoral, solitary ulcer</td>
<td>8%</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Postpolypectomy</td>
<td>6%</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>AVM</td>
<td>1%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>11%</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>Ischemic colitis</td>
<td>11%</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>Other colitis (IBD, infectious, radiation)</td>
<td>12%</td>
<td>15%</td>
<td>7%</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>3%</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>No source found</td>
<td>7%</td>
<td>9%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Etiology of Lower GI Bleeding: 2017
Meds at Admission

<table>
<thead>
<tr>
<th>Factor</th>
<th>Upper GI event (n=3,228)</th>
<th>Lower GI event (n=1,873)</th>
<th>Unidentified GI event (n=779)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID</td>
<td>20.8%</td>
<td>11.1%</td>
<td>17.6%</td>
</tr>
<tr>
<td>PPI</td>
<td>11.3%</td>
<td>16.6%</td>
<td>16.0%</td>
</tr>
<tr>
<td>NSAID and PPI</td>
<td>2.1%</td>
<td>3.0%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Anti-platelet therapy</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Anti-platelet and PPI</td>
<td>15.5%</td>
<td>16.9%</td>
<td>17.6%</td>
</tr>
<tr>
<td>Clear or bilious</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Coffee grounds</td>
<td>23%</td>
<td>77%</td>
<td>20%</td>
</tr>
<tr>
<td>Bloody</td>
<td>47%</td>
<td>53%</td>
<td>65%</td>
</tr>
</tbody>
</table>

Early Endoscopy

- < 24 hours, < 12 hours, < 6 hours
- Therapy
  - Especially in those with red blood, hemodynamic changes, HgB < 8
- Accurate risk assessment after specific diagnosis

NGA Poor prediction of high-risk lesion

<table>
<thead>
<tr>
<th>NGA</th>
<th>Hemodynamic instability</th>
<th>Stable VS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID</td>
<td>HRL</td>
<td>LRL</td>
</tr>
<tr>
<td>PPI</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>NSAID and PPI</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Anti-platelet therapy</td>
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<td>NS</td>
</tr>
<tr>
<td>Anti-platelet and PPI</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Forrest's classification for PU bleeding

- I-a (arterial jet)
- I-b (oozing)
- I-c (black spot)
- II-a (visible vessel)
- II-b (adherent clot)
- II-c (black base)
Endoscopic Stigmata of Bleeding Ulcers & Rebleed Risk

<table>
<thead>
<tr>
<th>Stigmata</th>
<th>Prevalence (%)</th>
<th>Rebleed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial bleed</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>Visible vessel</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Adherent clot</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Clean ulcer base</td>
<td>35</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>

Endoscopic Treatments for PUD with High-risk Stigmata (active bleeding / visible vessels)

- **Injection:**
  - Epinephrine (1:10000)

- **Thermal:**
  - Contact thermocoagulation: MPEC, heater probes

- **Mechanical:**
  - Endoclips: loops, bands

Combination is best

Epi injection + thermal or mechanical

Outcomes: Reduction in rebleed, LOS, Tx, Surgery, Mortality by ≥ 50%
Endoclips

- Applied directly or tangentially to vessel
- Minimum of 2 applied (usual 2-4)
- Limitations:
  - fibrotic base; posterior bulb or proximal stomach
  - misfires common

From Raju, GIE 2004; 59: 267.

Combination Therapy vs Monotherapy: Is It Better?

<table>
<thead>
<tr>
<th>Combination</th>
<th>Monotherapy</th>
<th># Trials / N</th>
<th>OR Rebleeding (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epi + Thermal</td>
<td>Epi alone</td>
<td>3 / 376</td>
<td>0.363 (0.177-0.727)</td>
</tr>
<tr>
<td>Epi + Clips</td>
<td>Epi alone</td>
<td>4 / 362</td>
<td>0.334 (0.177-0.629)</td>
</tr>
<tr>
<td>Epi + Thermal</td>
<td>Thermal alone</td>
<td>3 / 425</td>
<td>0.699 (0.465-1.206)</td>
</tr>
<tr>
<td>Epi + Clips</td>
<td>Clips alone</td>
<td>3 / 234</td>
<td>1.045 (0.447-2.449)</td>
</tr>
</tbody>
</table>

Pooled Rebleeding 0.597 (0.444-0.802)


Rebleeding Rates in RCT’s of Treatment of Adherent Clots

- Medical Therapy: Mayo Clinic Multicenter Trial N = 56
  - 34.3%
  - P < 0.05
- Endotherapy: UCLA CURE Multicenter Trial N = 32
  - 35.0%


Initial Treatment of Patients with Ulcer Bleeding, According to the Endoscopic Features of the Ulcer.
**Urgent vs Elective Colonoscopy**

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Definition of Urgent</th>
<th>Source Identified</th>
<th>Endoscopy</th>
<th>Mortality</th>
<th>Blood Transfusions</th>
<th>Hospital LOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caes (1986)</td>
<td>&gt; 24 hours</td>
<td>69%</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Jensen (1988)</td>
<td>6-12 hours</td>
<td>74%</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Jensen (2000)</td>
<td>6-12 hours</td>
<td>All had diverticular bleeding</td>
<td>5 vs. 3.9%</td>
<td>NS</td>
<td>Yes</td>
<td>2 vs. 3.5</td>
</tr>
<tr>
<td>Strate (2003)</td>
<td>&lt; 12 hours</td>
<td>NS</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
<td>Early time to col resulted in shorter stay</td>
</tr>
<tr>
<td>Green (2005)</td>
<td>8 hours</td>
<td>47% vs. 29%</td>
<td>22% vs. 30%</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Laine (2005)</td>
<td>&lt; 12 hours</td>
<td>78% vs. 67%</td>
<td>82% vs. 34%</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Urgent Colonoscopy: UCLA Experience**

- Urgent colonoscopy after rapid purge
- Diagnostic yield
  - 80%: endoscopic
  - treatment in 40%
  - complications in 0%
- Retrospective Results
  - angio rate from 50 to < 5%
  - BE rate from 25 to 0%
  - surgery rate from 20 to < 5%
  - LOS from 10 to 5 days and ICU stay from 3 to 1 day
  - Cost reduced $10,000 per patient
Bleeding diverticula (n=3) Rx’d with Gold Probe (10-15W, 1 sec pulses X 6-18 pulses)

Savides et al. GIE 1994;40:70-72

Vascular ectasia

http://www.gastrointestinalatlas.com/imagenes/Dosangiodisplasias.jpg

What if bleeding persists or recurs?
Nuclear Medicine as a Prelude to Angiography

  - 160 patients, 1989-1994
  - 86 positive scans → 47 underwent angiography
  - Look for “blush” on nuclear medicine
  - Grp 1 (33) blush < 2 min → 20/33 positive angio
  - Grp 2 (14) blush > 2 min → 13/14 (-) angio
  - Immediate blush should go to angio; if > 2 min—colonoscopy or observe
CT angiography

Angiography

- Diagnosis
  - Femoral access
  - 5 Fr catheters with steerable wires
  - Selective access of SMA, IMA catheterization (sometimes celiac)
  - Endoscopic identification/mark of bleeding lesion with clips facilitates
- Endovascular therapy
  - Vasopressin infusion no longer used
  - Sub-3 Fr catheter placed to most peripheral arteries
    - Microcoils (1-2 mm) for colon
    - Polivinyl microspheres (350-500 μm) for small intestine

Meta-analysis of Angiography for LGIB


- Included:
  - 7 cases series; all with ≥ 10 pts with major LGIB tx’ed with attempted embolization
- Results:
  - Median 30 d rebleeding rate: 14% (0-75)
    - Rebleed w/ Non-diverticular source: 45% (OR 3.4 vs diverticular bleeding)
    - 75% of rebleed w/in 3.5 days

Triage after Endoscopy

- Immediate/early discharge in low risk patients
- Optimal length of stay in patients who require admission
- Data are scant in LGIB
Early Endoscopy-based Triage: Three RCT’s

- Lee J, GIE 1999
  - N = 110: ER EGD vs routine admission
  - ER EGD: 46% immediate discharge; no rebleeds
  - LOS 1 vs 2 days; costs reduced 40%

- Cipolletta L, GIE 2002
  - N=464 pts underwent EGD w/in 12 hrs: 95 (20%) low risk.
  - Randomized to early discharge vs hospital care
  - Recurrent bleeding: 2% both groups
  - Costs: 90% reduction

- Bjorkman D, GIE 2004
  - N=99: ER EGD vs routine admission
  - ER EGD: 40% recommended for discharge; ER only discharged 10%

Early EGD Reduces LOS

Cooper GS et al. Medical Care 1998;4:462
Cooper GS et al. Gastrointest Endos 1999;49:145

Medical Therapy

Meta-Analysis: RCTs of PPI vs Placebo After Endoscopic Therapy of Ulcers with High-risk Stigmata

<table>
<thead>
<tr>
<th>Endoscopic Therapy Followed by High-dose IV PPI</th>
<th>Placebo</th>
<th>PPI</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebleeding</td>
<td>5.2%*</td>
<td>12.8%</td>
<td>0.39 (0.18-0.87)</td>
</tr>
<tr>
<td>Surgery</td>
<td>5.2%*</td>
<td>9.4%</td>
<td>0.53 (0.31-0.89)</td>
</tr>
<tr>
<td>Mortality</td>
<td>5.7%</td>
<td>5.6%</td>
<td>0.98 (0.25-3.77)</td>
</tr>
</tbody>
</table>

Endoscopic Therapy Followed By Oral or Low-dose IV PPI vs Placebo

<table>
<thead>
<tr>
<th>Rebleeding</th>
<th>Placebo</th>
<th>PPI</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.2%*</td>
<td>17.2%</td>
<td>0.52 (0.35-0.78)</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>6.6%</td>
<td>9.9%</td>
<td>0.59 (0.33-1.05)</td>
</tr>
<tr>
<td>Mortality</td>
<td>2.4%</td>
<td>2.4%</td>
<td>1.00 (0.42-2.35)</td>
</tr>
</tbody>
</table>

Leontiadis G, BMJ 2005
21 RCTs, 2915 pts
Consult 1: Anticoagulation in a patient with GI Bleeding

- 82 year old man is admitted with an upper GI bleed and syncope. Cause is a spurting duodenal ulcer. Bleeding is stopped with endoscopic clip. Hgb 13 to 8 g/dl. IV then oral PPI given. HP negative.
- PMH: Chronic afib on warfarin with stable dose and therapeutic INR. + HTN and DM. No prior of stroke, liver, renal disease, CHF or ETOH use, + ASA 81 mg/day
- CHADS2 = 3, HAS-BLED = 4
When to resume anticoagulation?

1. As soon as hemostasis achieved.
2. At discharge, so within 3-7 days.
3. After 7 days, but before 30 days.
4. After 30 days.
5. Never again.

Best Available Data

  - 1129 patients, up to 5 year follow-up
  - Restartion of warfarin decreases TE (HR, 0.71, 0.56-0.90), decreases mortality (HR, 0.67, 0.56-0.81), does not increase risk for GI bleed (HR, 1.18, 0.94-1.50)
  - <7 days, TE (0.76, 0.37-1.59), Mortality (0.56, 0.33-0.90), GIB (3.27, 1.82-5.91)

  - Prospective, 197 patients, 74% warfarin, median LOS = 5 days, 90 day follow up
  - Restart of anticoagulation at discharge: TE within 90 days (HR, 0.12, 0.006-0.81), mortality (HR, 0.6, 0.2-1.9), GIB (2.17, 0.86-6.7)

Similar data with ASA

- UGIB (Sung JJ Ann Int Med 2010)
  - 156 CV patients with UGIB
  - Endo Rx and PPI
  - ASA v placebo
    - Rebleed at 30 days, 10.3% v 5.4%
    - Mortality at 8 weeks, 1.3% v 12.9%

- LGIB (Chan FK Gastro 2016)
  - 295 CV patients with LGIB
  - Retrospective study ASA v none
  - 5 year follow up
    - GIB 18.9% v 6.9%
    - CV event 22.8% v 36.5%
    - Death 8.2% v 26.7%
Take home message: Bleeding leads to pro-thrombotic state leads to high ischemic risk.

Immediate re-initiation of therapy
- EGD with hemostasis can be achieved with no adverse events with INR up to at least 2.5
- High risk of TE event
- Judgement that hemostasis achieved and durable
- Mitigation of other issues that impact on bleed risk
- Close observation and patient/family participation possible
- Adequate red cell reserve

Comments on DOACs
- Risk factors: age, renal fxn, other comorbidities, prior history, anti-plt drugs
- Topical anti-coagulation, but…
- MGIB rates/outcomes are similar with warfarin except in pts > 75 or low CrCl
- GIB with DOACs more likely to be SB/colon
- Risk mitigation with PPI possible
- Reversal needs to be individualized and impact on outcomes remains uncertain
  - Praxbind and other Mabs, prothrombin complex

Consult 2: Obscure (small bowel) GI bleeding
- 64 year old man with HTN and DM is transferred with recurrent melena and a transfusion requirement. He does not use ASA/NSAIDs or anticoagulants. BUN/creatinine is 35/1.4.
- Since admission to an outside hospital he has had 4 episodes of melena and a transfusion requirement of 4 units of prbc to maintain his Hb ~ 9g/dl. His vital signs have remained stable without any hypertension or tachycardia.
- Prior to transfer he underwent EGD and colonoscopy and both exams were normal. His colon prep was excellent and the ileum was intubated.
Soon after transfer the melena recurs and he requires 2 more units of blood. What test should be done next?

1. Repeat EGD
2. RBC scintigraphy
3. CT enterography
4. CT angiography
5. Conventional angiography
6. Video capsule endoscopy
7. Balloon enteroscopy

Relevant Data
ACG, ASGE Clinical Guidelines. AJG, 2015; GIE, 2016

- Repeat EGD: + in 25%
- RBC scintigraphy: + in 20-80%
- CT enterography: + in 20-40%, but yield higher in the young, IBD, SBO, complements VCE
- CT angiography: + 60-90% during active bleed, bleed threshold = scintigraphy and < conventional angiogram by 3-4 fold
- Conventional angiography: + 50-80% in those with + CTA or RBC scan, hemodynamic instability, > 5 units/24 hours
- Video capsule endoscopy: + 40-90%, PPV 95%, NPV 85-100% (rebleeding after negative study < 20%)
- Balloon enteroscopy: + in 40-80%, therapy in 30-70%, total endoscopy in 85%, serious complications < 1%, DBE = SBE

CF-LVAD

- M Gibbs rate of 15-50%
  - Meds, acquired vWB disease, plt dysfunction, loss of pulse pressure leads to ectasias
- > 2/3 source is SB
- Rebleed rate > 50%
- Early capsule, balloon enteroscopy associated with better outcomes