GI bleeding

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Objectives

• To identify high risk patients
• To understand the value of medical therapy of bleeding peptic ulcers
• To know the role of endoscopic therapy for control of GI bleeding
• To provide optimal management of patients with upper GI bleeding
Initial assessment and risk stratification

- Assess hemodynamic status immediately
- Insert 2 large bore IVs and begin resuscitation
- Blood transfusions
  - Target hemoglobin ≥ 7 g/dl
    (>10 g/dl if intravascular volume depletion or CAD)
  - Target INR < 2.5
- Risk stratify into higher- and lower-risk categories
  - Patient triage
  - Timing of endoscopy

Laine L, Jensen D. Am J Gastroenterol 2012;107:345

Survival according to transfusion strategy

Impact of anticoagulation and therapeutic endoscopy

- 233 patients post successful therapeutic endoscopy
- 44% of patients had an INR >1.3 (95% <2.7)

**Rebleeding Rate**
- 23% in anticoagulated patients (INR >1.3)
- 21% in patients with normal coagulation (INR <1.3)

- INR is not a predictor of: rebleeding, length of stay, transfusions, surgery, or mortality

**Endoscopic therapy is appropriate in mildly to moderately anticoagulated patients**


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**Initial assessment and risk stratification recommendations**

“Early risk stratification, by using validated prognostic scales”

- International Consensus Guidelines

“Risk assessment should be performed to stratify patients into higher and lower risk categories”

- ACG 2012 Practice Guidelines
  
  Barkun A. Ann Intern Med 2010;152:101;
  Laine L, Jensen D. Am J Gastroenterol 2012;107:345
Upper GI bleeding risk assessment scores

- Identify high-risk patients
- Direct resources to high-risk patients
- Timing of endoscopy and discharge
- Improve outcomes
- Not widely used
  - Need to calculate
  - Some require endoscopic information

Barkun A. Ann Intern Med 2010;152:101

Mortality increases with higher ASA score

Marmo R et al. Gastrointest Endosc 2012;75:263-72
Quality and endpoints of GI bleeding risk scores (before 2011)

- **Rockall Risk Score**
  - (Gut 1996;38:316-21)
  - Assesses mortality
  - Incorporates clinical and endoscopic data

- **Glasgow Blatchford Risk Score**
  - (Lancet 2000;356:1318-21)
  - Assesses need for intervention
  - Incorporates only information available at initial presentation

De Groot NL et al. Endoscopy 2012;44:731-9
### Rockall Scoring System

<table>
<thead>
<tr>
<th>Score / Variable</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</td>
<td>70-79</td>
<td>&gt;80</td>
<td>-</td>
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<tr>
<td><strong>Shock</strong></td>
<td>None</td>
<td>Tachy (p&gt;100)</td>
<td>Hypotension (SBP&lt;100)</td>
<td>-</td>
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<tr>
<td><strong>Comorbidity</strong></td>
<td>No major comorbidity</td>
<td>-</td>
<td>CHF, CAD</td>
<td>Any other, Renal or liver failure, metastatic cancer</td>
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<tr>
<td><strong>Endoscopic Diagnosis</strong></td>
<td>MWT, No SRH</td>
<td>All Other</td>
<td>Upper GI cancer</td>
<td>-</td>
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<tr>
<td><strong>Endoscopic Major SRH</strong></td>
<td>None or spot</td>
<td>-</td>
<td>Clot, vessel or spurting</td>
<td>-</td>
</tr>
</tbody>
</table>

*Rockall Gut 1996;38:316-21*

### Predictive Value of Rockall Score

![Graph showing the predictive value of Rockall score]
**Glasgow Blatchford risk scoring system**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Points</th>
<th>Variable</th>
<th>Value</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (mg/dL)</td>
<td>&gt;18.2 and &lt;22.4</td>
<td>2</td>
<td>Systolic BP</td>
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<tr>
<td></td>
<td>&gt;22.4 and &lt;28</td>
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<td>90-99</td>
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<td>&gt;28 and &lt;70</td>
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<td></td>
<td>&lt;90</td>
<td>3</td>
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<tr>
<td></td>
<td>&gt;70</td>
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<td>Other Markers</td>
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<td>Hgb men (g/dL)</td>
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<td>Heart rate</td>
<td>&gt;100</td>
<td>1</td>
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<tr>
<td></td>
<td>&gt;10 and &lt;12</td>
<td>3</td>
<td>Melena</td>
<td></td>
<td>1</td>
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<tr>
<td></td>
<td>&lt;10</td>
<td>6</td>
<td>Syncope</td>
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<td>2</td>
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<tr>
<td>Hgb women (g/dL)</td>
<td>&gt;10 and &lt;12</td>
<td>1</td>
<td>Cardiac</td>
<td></td>
<td>2</td>
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<tr>
<td></td>
<td>&lt;10</td>
<td>6</td>
<td>Liver</td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>


**AIMS65 risk score**

- Uses data routinely available at initial evaluation
- 187 hospitals from the state of Pennsylvania:
  - 45% teaching and 55% non-teaching
  - 75% urban and 25% rural
  - 24% with bed size >300, 51% with 100-300 beds, 25% with <100 beds
- Derived from 29,222 cases of UGIB in 2004-2005
- Validated in 32,504 UGIB cases in 2006-2007

Saltzman JR. Gastrointest Endosc 2011;74(6):1225-9
Components of the AIMS65 score

1. Albumin <3.0 mg/dL
2. INR >1.5
3. Mental status change (GCS <15)
4. Systolic blood pressure <90
5. Age >65 years

Mortality correlates with AIMS65 score

Area under ROC curve=0.80
Mortality: AIMS65 vs. GBRS


Is there a role for NG lavage?

- Retrospective study of propensity-matched patients with upper GI bleeding receiving NG lavage (193 patients) or no NG lavage (193 patients)

Results:
- NG lavage associated with shorter time to endoscopy (hazard ratio 1.49)
- Bloody NG aspirate associated with high-risk lesions
- NG lavage did not affect main study outcomes of mortality, LOS, surgery, or transfusions

Conclusion: NG lavage should not be routinely performed in patients with upper GI bleeding

Huang ES et al. Gastrointest Endosc 2011;74(5):971-80
Pallin DJ, Saltzman JR. (editorial) Gastrointest Endosc 2011;74(5):981-4
NG tube lavage recommendations

“NG or orogastric lavage is not required in patients with upper GI bleeding for diagnosis, prognosis, visualization, or therapeutic effect”

- ACG 2012 Practice Guidelines

Laine L, Jensen D. Am J Gastroenterol 2012;107:345-60

Capsule endoscopy (CE) to triage upper GI hemorrhage

- Prospective study of CE vs. NG tube and EGD findings
- 49 patients (3 no CE and 5 did not tolerate NG tube)
- Blood detected more by CE than NG tube (p=0.04)
  - CE 15/18 (83.3 %)
  - NG tube 6/18 (33.3 %)
- Peptic/inflammatory lesions identified by CE and EGD
  - CE 27/40 (67.5 %)
  - EGD 35/40 (87.5 %; p=0.10, OR 0.39 95%CI 0.11-1.15)
- Capsule endoscopy reached the duodenum in 45/46 patients (98 %)
- Capsule endoscopy in ED may facilitate patient triage

Gralnek IM. Endoscopy 2013; 45(1):12-9
Medical therapy: Upper GI bleeding

• Antacids
• H$_2$-receptor antagonists
• Octreotide
• Proton pump inhibitors

Guideline recommendations: pre-endoscopic

• If endoscopy will be delayed or cannot be performed, IV PPI is recommended to reduce further bleeding
• Pre-endoscopic IV PPI (e.g., 80 mg bolus followed by 8 mg / h infusion) may be considered to decrease the proportion of patients who have higher risk stigmata of hemorrhage at endoscopy and who receive endoscopic therapy. However, PPIs do not improve clinical outcomes such as further bleeding, surgery, or death.

Conditional recommendation
Laine L, Jensen D. Am J Gastroenterol 2012;107:345-60
Guideline recommendations: post-endoscopic

- After successful endoscopic hemostasis, IV PPI therapy with 80 mg bolus followed by 8 mg/h continuous infusion for 72 h should be given to patients who have an ulcer with active bleeding, a non-bleeding visible vessel, or an adherent clot.
- Patients with ulcers that have flat pigmented spots or clean bases can receive standard PPI therapy (e.g., oral PPI once daily).

Strong recommendation

Laine L, Jensen D. Am J Gastroenterol 2012;107:345-60

Continue aspirin after control of peptic ulcer bleed

Sung JJ. Ann Intern Med 2010;152:1-9
Detection of bleeding lesions: We can only treat what we see

- Double or large channel endoscopes
- External large suction device
- IV erythromycin
- Water pump/jet
- Lavage pre-endoscopy
- Hydrogen peroxide
Role of erythromycin before endoscopy in UGI bleeding

- IV erythromycin powerful prokinetic
- Erythromycin 3 mg/kg or 250 mg IV over 30 minutes 1-hour before upper endoscopy
- Quality of gastric exam significantly better
- Decreased need for repeat upper endoscopy
- No difference in:
  - Length of hospital stay
  - Need for surgery
  - Adverse events

Barkun AN et al. Gastrointest Endosc 2010;72:1138
Role of erythromycin in UGIB

“Intravenous infusion of erythromycin (250 mg ~30 min before endoscopy) should be considered to improve diagnostic yield and decrease the need for repeat endoscopy”

- ACG 2012 Practice Guidelines

Laine L, Jensen D. Am J Gastroenterol 2012;107:345-60

Timing of endoscopy

“Early endoscopy (within 24 hours of presentation) is recommended for most patients with acute upper gastrointestinal bleeding”


“Patients with upper GI bleeding should generally undergo endoscopy within 24 hours of admission, following resuscitative efforts to optimize hemodynamic parameters”

Upper endoscopy in acute gastrointestinal bleeding

- **Diagnosis:** 90-95% sensitive at locating bleeding site
- **Prognosis:** Likelihood of persistent or recurrent bleeding can be predicted
- **Therapy:** Provides therapeutic options (injection, cautery or clip)
- **Safe:** Morbidity <0.1% (50% cardiopulmonary)

### Indications for endoscopic therapy

<table>
<thead>
<tr>
<th>Stigmata</th>
<th>Endoscopic Therapy?</th>
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</thead>
<tbody>
<tr>
<td>Active bleeding</td>
<td>Yes</td>
</tr>
<tr>
<td>Non-bleeding visible vessel</td>
<td>Yes</td>
</tr>
<tr>
<td>Adherent clot</td>
<td>+/-</td>
</tr>
<tr>
<td>Flat spot</td>
<td>No</td>
</tr>
<tr>
<td>Clean ulcer base</td>
<td>No</td>
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</table>

Laine L, Jensen D. Am J Gastroenterol 2012;107:345-60
Rebleeding rates in RCT’s of treatment of adherent clots

<table>
<thead>
<tr>
<th>Medical Therapy</th>
<th>Endoscopic Therapy</th>
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</thead>
<tbody>
<tr>
<td>Mayo Clinic (N=55)</td>
<td>34.3%</td>
</tr>
<tr>
<td>UCLA CURE (N=32)</td>
<td>35.3%</td>
</tr>
</tbody>
</table>


Role of endoscopic therapy and adherent clots

"Endoscopic therapy may be considered for patients with an adherent clot resistant to vigorous irrigation. Benefit may be greater in patients with clinical features associated with a higher risk of rebleeding e.g., older age, concurrent illness, inpatient at time bleeding began”

- ACG 2012 Practice Guidelines

Laine L, Jensen D. Am J Gastroenterol 2012;107:345-60
Endoscopic therapeutic options

- Injection
- Thermal (contact)
  - Heater probe
  - Bipolar probe
  - Monopolar
- Thermal (non-contact)
  - Argon plasma coagulation
- Mechanical
  - Hemoclips
  - Banding
  - Combination

Injection

- Reduce blood flow by local tamponade
- Vasoconstricting agents reduce blood flow
  - Epinephrine 1:10,000 - 1:100,000
- Various agents can be injected
  - Sclerosants
    - Ethanolamine
    - Polidocanol
  - Ethanol
  - Tissue adhesives
    - N-butyl-2-cyanoacrylate (Histoacryl)
    - Fibrin glue
    - Thrombin

Injection monotherapy not recommended

Park WG. Gastrointest Endosc 2007;66:343
Thermal therapy

- Bi-polar (bicap) commonly used
- Coaptive coagulation: Compress vessel and then coagulate to seal vessel
- Larger 10 French probes more effective than smaller 7 French probes
- 15-20 Watts for multiple 8-12 second pulses
- Optimal therapy is 4-6 pulses

Combination therapy

- Inject first with dilute epinephrine
- Combine with thermo-coagulation therapy
- May also combine injection with hemoclips

Combination therapy is safe and effective

Monopolar cautery

- **Monopolar device**
  - Designed for endoscopic bleeding
  - Flat jaws for grasping
  - Rotational ability
  - Grounding pad required

- **Optimal settings (stomach)**
  - 50 Watts for 2 or 3 seconds

Role of monopolar cautery in the management of upper GI bleeding needs to be determined

Saltzman JR et al. Gastrointest Endosc 2010;72(4):796

Hemoclips for upper GI bleed

- Meta-analysis of 15 RCT’s of 1156 patients (mostly peptic ulcer disease patients)
  - 390 clips alone
  - 242 clips and injection
  - 359 injection alone
  - 165 thermocoagulation with or without injection

- **Hemoclips superior than injection therapy alone**
  - Definitive hemostasis 86.5% vs. 75.4%

- **Hemoclips comparable to thermal coagulation**
  - Definitive hemostasis 81.5% vs. 81.2%

Sung JJ et al. Gut 2007;56:1364
Combination therapy vs. hemoclips study

- Prospective randomized controlled trial of acute non-variceal upper GI bleeding
- All patients on high dose proton pump inhibitors

**Primary control**

- [Bar chart showing comparison between hemoclips and combination therapy.]
- P = 0.45

**Rebleeding rate**

- [Bar chart showing comparison between hemoclips and combination therapy.]
- P = 0.49

Saltzman J. Am J Gastroenterol 2005;100:1503

When to use hemoclips

**Ideal for hemoclips**
- Lesion pliable
- Lesion accessible
- ≤ 2 mm vessel
- ≤ 2 cm ulcer defect

**Difficult for hemoclips**
- Indurated or fibrotic base
- Challenging locations
  - Lesser curve stomach
  - Posterior wall stomach
  - Posterior duodenum
### Available hemoclips in 2013

<table>
<thead>
<tr>
<th></th>
<th>Olympus</th>
<th>Boston Scientific</th>
<th>Cook</th>
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<tbody>
<tr>
<td>Trade name</td>
<td>Quickclip-2</td>
<td>Resolution</td>
<td>Instinct</td>
</tr>
<tr>
<td>Open-close</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Rotate</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Clip diameter</td>
<td>11 mm</td>
<td>11 mm</td>
<td>16 mm</td>
</tr>
<tr>
<td>MRI conditional approval</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Endpoint of endoscopic therapy

Wong RC. Gastroenterology 2009;137:1897
Doppler signal before and after endoscopic therapy

Application of Doppler guided hemostasis has the potential to help reduce ulcer rebleeding

Jensen DM. DDW 2010

New hemostasis techniques to treat upper GI bleeding

- Hemostatic sprays
- Large hemoclips
### Topical hemostatic agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Trade Name</th>
<th>Composition</th>
<th>Mechanism of action</th>
<th>Approved human application</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anjulafer BloodStopper</td>
<td>Standardized herbal mixture</td>
<td>Forms protein network, aggregates RBCs, activates clotting cascade</td>
<td>Dental procedures, ambulance, first aid services, schools, fast hemostasis</td>
<td>Tampons, sprays, ampoules</td>
<td></td>
</tr>
<tr>
<td>TC-325</td>
<td>Hemospray</td>
<td>Granular mineral-based</td>
<td>Adsorbs H₂O, mechanical tamponade, activates clotting cascade</td>
<td>Recently approved for nonvariceal GI bleed in Canada, Hong Kong, Europe</td>
<td>CO₂ pressurized handheld canister (20 g)</td>
</tr>
<tr>
<td>EndoClot</td>
<td>EndoClot</td>
<td>Absorbable modified polymers</td>
<td>Absorbs H₂O and concentrates cells, activates clotting cascade</td>
<td>Intended for adjuvant hemostatic therapy</td>
<td>Pressurized air compressor</td>
</tr>
</tbody>
</table>

RBC, Red blood cells.

Barkun A et al. Gastrointest Endosc 2013;77:692-700
Hemostatic nanopowder spray

Mechanism of action:
- Tamponade (rapid velocity application)
- Dehydration of fluid within blood
- Activation of clotting cascade
- Activation of platelets

Aims: To assess the efficacy and safety of a novel hemostatic nanomaterial in short and long term hemostasis in a survival GI bleeding animal model

Conclusions: Endoscopic application of this nanopowder is safe and highly effective in achieving hemostasis in an anticoagulated severe GI bleeding animal model

Giday SA. Endoscopy 2011;43:296
<table>
<thead>
<tr>
<th>Bleeding Indication</th>
<th>Procedure Details/Outcomes</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Acute Hemostasis</td>
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</tr>
<tr>
<td><em>Forrest Scope</em></td>
<td>Ulcer Location</td>
<td>procedure</td>
</tr>
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<td>Melena</td>
<td>1b Duodenum</td>
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</tr>
<tr>
<td>Melena</td>
<td>1b Duodenum</td>
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<tr>
<td>Hematemesis, Melena</td>
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<td>1b Stomach</td>
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</tr>
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<td>Yes</td>
</tr>
<tr>
<td>Melena</td>
<td>1b Duodenum</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Human hemostatic spray initial trial**
Sung JUY, Endoscopy 2011;43:291
Spray to treat bleeding

- Post - endoscopic intervention with 12/12 patients successfully stopped
  - Esophageal EMR: 5 patients
  - Duodenal EMR: 4 patients
  - Ampullary resection: 2 patients
  - Biliary sphincterotomy: 1 patient
- Malignant bleeding - 10/10 patients stopped, but 20% rebleeding

Leblanc S et al. Gastrointest Endosc 2013;78:169-175
Chen T1, et al. Gastrointest Endosc 2012;75:1278-81

Barkun A et al. Gastrointest Endosc 2013;77:692-700
Hemospray considerations

- Effective only in actively oozing or spurting bleeding lesions
- Does not require special expertise
- Can be rapidly used if bleeding occurs after polypectomy or sphincterotomy
- May be effective in difficult locations
- Second treatment modality needed if high risk of rebleeding
- Potential role for malignant bleeding
The bear claw: over-the-scope clip (OTSC)

Kirschniak A. Gastrointest Endosc 2007;66:162

OTSC results for GI bleeding after prior failures

<table>
<thead>
<tr>
<th>GI tract</th>
<th>Bleeding lesion</th>
<th>n</th>
<th>No. OTSC, N/T</th>
<th>Primary hemostasis, n</th>
<th>Rebleeding, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper</td>
<td>Duodenal ulcer</td>
<td>12\textsuperscript{a}</td>
<td>3/9</td>
<td>11</td>
<td>1</td>
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<tr>
<td></td>
<td>Gastric ulcer</td>
<td>6\textsuperscript{b}</td>
<td>2/4</td>
<td>6</td>
<td>1</td>
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<tr>
<td></td>
<td>Mallory-Weiss</td>
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<td></td>
<td>Dieulafoy</td>
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<td>2/0</td>
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<td>0</td>
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<td>Colonic diverticulum</td>
<td>1</td>
<td>1/0</td>
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</tbody>
</table>

OTSC over-the-scope clip, GI gastrointestinal, N nontraumatic, T traumatic, EMR endoscopic mucosal resection, ESD endoscopic submucosal dissection

\textsuperscript{a} Forrest 1a = 5; Forrest 1b = 4

\textsuperscript{b} Forrest 1a = 2; Forrest 1b = 2

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<tr>
<td></td>
<td>Gastric ulcer</td>
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<td>ESD</td>
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<td>1/1</td>
<td>0</td>
<td>0</td>
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<td>Colonic diverticulum</td>
<td>1</td>
<td>1/1</td>
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</tbody>
</table>

Primary hemostasis:
- 97% (29/30)

Rebleeding:
- 7% (2/30 pts)

Upper GI bleeding summary

- Resuscitate promptly, but do not over transfuse
- Incorporate GI bleeding risk scores in practice
- Provide effective medical therapy
- Overcome limitations of endoscopic visualization by using several methods
- Perform endoscopy within 24 hours
- Use effective endoscopic treatments (hemoclips and combination therapies)
- Further improvements are coming