Gastrointestinal Bleeding Etiologies, Management, and the Interplay with Anticoagulant and Antiplatelet Agents in the Peri-Procedural Period

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Disclosures

• No relevant disclosures

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  – AbbVie
  – Cook Endoscopy
Learning Objectives

• Delineate the differential diagnoses of gastrointestinal bleeding, and differentiate upper GI bleeding, small bowel bleeding, and lower GI bleeding

• Explore management strategies in gastrointestinal bleeding, with a focus on non-variceal upper GI bleeding

• Recognize the different classes of anticoagulant and antiplatelet agents

• Understand patient and peri-procedural risk factors for bleeding and thrombosis

• Discuss appropriate antithrombotic agent management for elective and urgent GI procedures
Differential Diagnoses of Gastrointestinal Bleeding
Upper vs. Small Bowel vs. Lower GI Bleeding

• **Upper:** Esophagus to Ligament of Treitz

• **Small Bowel:** Ligament of Treitz to Terminal Ileum

• **Lower:** Cecum to Anus
Clinical Presentation of GI Bleeding

- Coffee-ground emesis
- Hematemesis
- Melena
- Hematochezia/Bright Red Blood Per Rectum

- Heme + stool, with or without iron deficiency anemia
- Iron deficiency anemia with or without heme + stools

**NOT** Acute GI Bleeding
# Upper GI Bleeding Etiologies

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Estimated Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptic Ulcer Disease</td>
<td>20-50%</td>
</tr>
<tr>
<td>Gastroduodenal Erosions</td>
<td>8-15%</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>5-15%</td>
</tr>
<tr>
<td>Varices/Portal Hypertension</td>
<td>5-20%</td>
</tr>
<tr>
<td>Mallory-Weiss Tears</td>
<td>8-15%</td>
</tr>
<tr>
<td>Vascular Malformations (AVMs, GAVE, Dieulafoy’s, Osler Weber Rendu)</td>
<td>≈ 5%</td>
</tr>
<tr>
<td>Other Conditions (i.e. Malignancy, etc.)</td>
<td>Remainder (Up to 5%)</td>
</tr>
</tbody>
</table>

Further Upper GI Bleeding Etiologies...

<table>
<thead>
<tr>
<th>Etiology of Acute Upper Gastrointestinal Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ulcerative or erosive</strong></td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
</tr>
<tr>
<td>Idiopathic</td>
</tr>
<tr>
<td>Drug induced</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>Nonsteroidal antiinflammatory drugs</td>
</tr>
<tr>
<td>Infectious</td>
</tr>
<tr>
<td>Helicobacter pylori</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td>Stress-induced ulcer</td>
</tr>
<tr>
<td>Zollinger Ellison Syndrome</td>
</tr>
<tr>
<td>Esophagitis</td>
</tr>
<tr>
<td>Peptic</td>
</tr>
<tr>
<td>Infectious</td>
</tr>
<tr>
<td>Candida albicans</td>
</tr>
<tr>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>Miscellaneous</td>
</tr>
<tr>
<td><strong>Pill-induced</strong></td>
</tr>
<tr>
<td>Amlodipine</td>
</tr>
<tr>
<td>Trazodone</td>
</tr>
<tr>
<td>Quinidine</td>
</tr>
<tr>
<td>Potassium chloride</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>Nonsteroidal antiinflammatory drugs</td>
</tr>
<tr>
<td><strong>Portal hypertension</strong></td>
</tr>
<tr>
<td>Esophageal varices</td>
</tr>
<tr>
<td>Gastric varices</td>
</tr>
<tr>
<td>Duodenal varices</td>
</tr>
<tr>
<td>Portal hypertensive gastropathy</td>
</tr>
<tr>
<td><strong>Arterial, venous, or other vascular malformations</strong></td>
</tr>
<tr>
<td>Idiopathic angiomas</td>
</tr>
<tr>
<td>Osler-Weber-Rendu syndrome</td>
</tr>
<tr>
<td>Dieulafoy’s lesion</td>
</tr>
<tr>
<td>Watermelon stomach (gastric antral vascular ectasia)</td>
</tr>
<tr>
<td>Radiation-induced telangiectasia</td>
</tr>
<tr>
<td>Blue rubber bleb nevus syndrome</td>
</tr>
<tr>
<td><strong>Traumatic or post-surgical</strong></td>
</tr>
<tr>
<td>Mallory-Weiss tear</td>
</tr>
<tr>
<td>Foreign body ingestion</td>
</tr>
<tr>
<td>Post-surgical anastomosis</td>
</tr>
<tr>
<td>Aortoenteric fistula</td>
</tr>
<tr>
<td>Post gastric/duodenal polypectomy</td>
</tr>
<tr>
<td><strong>Tumors</strong></td>
</tr>
<tr>
<td>Benign</td>
</tr>
<tr>
<td>Leiomyoma</td>
</tr>
<tr>
<td>Lipoma</td>
</tr>
<tr>
<td>Polyp (hyperplastic, adenomatous, hamartomatous)</td>
</tr>
<tr>
<td><strong>Malignant</strong></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Gastrointestinal stromal tumor</td>
</tr>
<tr>
<td>Lymphoma</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
</tr>
<tr>
<td>Carcinoid</td>
</tr>
<tr>
<td>Melanoma</td>
</tr>
<tr>
<td>Metastatic tumor</td>
</tr>
<tr>
<td>Miscellaneous</td>
</tr>
<tr>
<td>Hemobilia</td>
</tr>
<tr>
<td>Hemosuccus pancreaticus</td>
</tr>
</tbody>
</table>
# Small Bowel Bleeding Etiologies

## Common Causes

<table>
<thead>
<tr>
<th>&lt; 40 y/o</th>
<th>&gt; 40 y/o</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>Angioectasias (AVMs)</td>
</tr>
<tr>
<td>Meckel’s Diverticulum</td>
<td>NSAID Ulcers, Erosions, Diaphragms</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>Neoplasms</td>
</tr>
<tr>
<td>Dieulafoy’s Lesions</td>
<td>Dieulafoy’s Lesions</td>
</tr>
<tr>
<td>Polyposis Syndromes</td>
<td></td>
</tr>
</tbody>
</table>

### Malignant Neoplasm Types:
- Primary small bowel adenocarcinoma
- Primary neuroendocrine tumors (carcinoid, GIST)
- Small bowel lymphoma
- Metastases: melanoma, renal cell carcinoma, lung and breast

## Rare Causes

- Aorto-enteric Fistula
- Radiation Enteritis
- Celiac Disease
- Autoimmune Enteropathy
- Henoch-Schoenlein Purpura
- Small Bowel Varices
- Portal Hypertensive Enteropathy
- Amyloidosis
- Blue Rubber Bleb Nevus Syndrome
- Pseudoxanthoma Elasticum
- Osler-Weber-Rendu Syndrome
- Kaposi’s Sarcoma with AIDS
- Plummer-Vinson Syndrome
- Ehlers-Danlos Syndrome
- Hemobilia & Hemosuccus Pancreaticus
- Inherited Polyposis Syndromes (FAP, Peutz-Jeghers)
Small Bowel Bleeding Management: ACG 2015

1. Suspected small bowel bleeding
   - Occult
     - Treat accordingly
     - Positive
       - Repeat endoscopy if warranted
         - Negative
           - Proceed with small bowel evaluation
   - Overt
     - Repeat endoscopy if warranted
     - Negative
     - Specific management: push or deep enteroscopy surgery ± intraoperative enteroscopy

2. Possible obstruction
   - No obstruction
     - VCE
       - Positive
         - Specific management: push or deep enteroscopy surgery ± intraoperative enteroscopy
     - Negative
       - CTE/MRE
         - Negative—no obstruction
         - Positive
           - Further evaluation warranted
             - Consider repeat endoscopy/VCE/Meckel’s scan/surgery ± intraoperative enteroscopy
       - Negative
         - Observation/iron supplements
         - Observation/iron supplements
         - Observation/iron supplements
Brisk or Massive Suspected Small Bowel Bleeding Management: ACG 2015

1. Brisk/massive suspected small bowel bleeding

2. Unstable
   - Stabilize patient

3. Red cell scan or CT angiography
   - Positive
     - Angiography
       - Positive
         - Embolization
   - Negative
     - Specific management enteroscopy vs surgery and intraoperative enteroscopy
# Lower GI Bleeding Etiologies

<table>
<thead>
<tr>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diverticular Bleeding</td>
</tr>
<tr>
<td>Ischemic Colitis</td>
</tr>
<tr>
<td>Angioectasias (AVMs)</td>
</tr>
<tr>
<td>Hemorrhoids</td>
</tr>
<tr>
<td>Colorectal Neoplasia/Malignancy</td>
</tr>
<tr>
<td>Post-Polypectomy Bleeding</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
</tr>
<tr>
<td>Infectious Colitis</td>
</tr>
<tr>
<td>NSAID Colopathy</td>
</tr>
<tr>
<td>Radiation Proctopathy</td>
</tr>
<tr>
<td>Stercoral Ulcer</td>
</tr>
<tr>
<td>Rectal Varices</td>
</tr>
<tr>
<td>Dieulafoy’s Lesions</td>
</tr>
</tbody>
</table>
Lower GI Bleeding Management: ASGE 2014

- **Occult Bleed**
  - Colonoscopy
    - Negative colonoscopy
      - EGD
        - UGI symptoms
          - EGD
    - EGD

- **Melena**
  - EGD
    - Negative EGD
      - Colonoscopy

- **Scant intermittent Hematochezia**
  - Age < 40 years; No alarm symptoms/risk factors
    - Flexible Sigmoidoscopy
      - Negative
        - Colonoscopy
    - Age > 50 years; Alarm symptoms/risk factors
      - Colonoscopy

- **Severe Hematochezia (see algorithm 2)**
Severe Hematochezia Management: ASGE 2014

Severe Hematochezia

Resuscitation & Evaluation
Physical Exam/Orthostatics
CBC/Coags/Type & Crossmatch
Consider NGT lavage

Consider nasogastric tube

Positive aspirate or risk factors for UGI lesion

Negative or nondiagnostic aspirate

Purge prep

Persistent bleeding

Massive Bleeding

Surgical consult

Angiography (RBC scan)

Refractory bleeding

Successful embolization

Observe

Massive Bleeding

Surgical consult

Angiography (RBC scan)

Refractory bleeding

Successful embolization

Observe

EGD

Colonoscopy

Negative

Positive

UGI Algorithm

Endoscopic Therapy (Epinephrine Injection Bipolar Coagulation Argon Plasma Coagulation Hemoclips)
UGI Bleeding Incidence Has Decreased and Survival Has Improved

Non-Variceal UGI Hemorrhage Incidence: 108/100k (1994) → 78/100k (2009)

### Nationwide Trends in UGI Bleeding Hospitalizations and the Role of Endoscopy

<table>
<thead>
<tr>
<th></th>
<th>1989</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-Hospital Upper Endoscopy Rate</td>
<td>70%</td>
<td>85%</td>
</tr>
<tr>
<td>Endoscopic Therapy Rate</td>
<td>10%</td>
<td>27%</td>
</tr>
<tr>
<td>Early Endoscopy Rate</td>
<td>36%</td>
<td>54%</td>
</tr>
<tr>
<td>Median Length of Hospital Stay</td>
<td>4.5 days</td>
<td>2.8 days</td>
</tr>
<tr>
<td>Median Total Hospitalization Charges</td>
<td>$9249</td>
<td>$20,370</td>
</tr>
</tbody>
</table>
Risk Factors for Upper GI Bleeding

• Peptic Ulcer Disease:
  – NSAIDs/ASA
  – *Helicobacter pylori* infection
  – Tobacco smoking = ??
  – Steroids and EtOH are NOT independent risk factors
  – Psychological stress = ??

• Stress Ulcers: intubation > 48h, increased intracranial pressure, burns >35% TBSA

• Esophagitis: supine position (especially in bedbound patients)

• Mallory Weiss Tears: after wretching

• Varices: risks for liver disease or portal hypertension

https://medlineplus.gov/ency/article/000206.htm
Management of Gastrointestinal Bleeding
Diagnostic Tools for Localization of GI Bleeding

- Upper Endoscopy (EGD)*
- Video Capsule Endoscopy
- Enteroscopy*
- Colonoscopy*
- CT Angiography
- Nuclear Medicine Bleeding Scan
- Angiography*
- Surgery*

*May Be Therapeutic As Well
Initial Assessment of Upper Gastrointestinal Bleeding
GI Bleeding Initial Patient Assessment & Risk Stratification

- Immediate assessment of hemodynamics: Stable vs. Unstable
- Examine the patient (including digital rectal examination)
- Insert 2 large bore peripheral IVs and start volume resuscitation
- Labs: CBC (beware of false norms if hemoconcentrated), type and cross, CMP (BUN/Cr, LFTs), PT/INR/PTT
- Blood Transfusions:
  - Target Hgb $\geq 7$ g/dL ($\geq 10$ g/dL if active cardiac conditions)
- Risk Stratification: High-Risk vs. Low-Risk
  - Patient Triage (ICU, Inpatient, Outpatient)
  - Timing of Endoscopy
- Consult appropriate colleagues: GI, ICU, IR, Surgery
### Glasgow Blatchford Score (GBS) for UGI Bleed Management Risk Stratification

**Table 1: Admission risk markers and associated score component values**

<table>
<thead>
<tr>
<th>Admission risk marker</th>
<th>Score component value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea (mmol/L)</td>
<td></td>
</tr>
<tr>
<td>≥6.5 &lt;8.0</td>
<td>2</td>
</tr>
<tr>
<td>≥8.0 &lt;10.0</td>
<td>3</td>
</tr>
<tr>
<td>≥10.0 &lt;15.0</td>
<td>4</td>
</tr>
<tr>
<td>≥15.0</td>
<td>5</td>
</tr>
<tr>
<td>Haemoglobin (g/L) for men</td>
<td></td>
</tr>
<tr>
<td>≥120 &lt;130</td>
<td>2</td>
</tr>
<tr>
<td>≥130 &lt;140</td>
<td>3</td>
</tr>
<tr>
<td>≥140 &lt;150</td>
<td>4</td>
</tr>
<tr>
<td>≥150</td>
<td>5</td>
</tr>
<tr>
<td>Haemoglobin (g/L) for women</td>
<td></td>
</tr>
<tr>
<td>≥100 &lt;120</td>
<td>2</td>
</tr>
<tr>
<td>≥120</td>
<td>3</td>
</tr>
<tr>
<td>≥140</td>
<td>4</td>
</tr>
<tr>
<td>≥160</td>
<td>5</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>100–109</td>
<td>1</td>
</tr>
<tr>
<td>90–99</td>
<td>2</td>
</tr>
<tr>
<td>&lt;90</td>
<td>3</td>
</tr>
<tr>
<td>Other markers</td>
<td></td>
</tr>
<tr>
<td>Pulse ≥100 (per min)</td>
<td>1</td>
</tr>
<tr>
<td>Presentation with melena</td>
<td>2</td>
</tr>
<tr>
<td>Presentation with syncope</td>
<td>3</td>
</tr>
<tr>
<td>Hepatic disease</td>
<td>4</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>5</td>
</tr>
</tbody>
</table>

**Diagram 2: ROC curve**

- Glasgow Blatchford score: AUROC 0.86
- Admission Rockall score: AUROC 0.66
- Full Rockall score: AUROC 0.70
- AIMS65: AUROC 0.68
- PNED: AUROC 0.69

Patients with presentation GBS ≤ 1 in UGI Bleed can be safely discharged from the Emergency Room\(^2\)

GBS ≤ 1: Sens 98.6%, Spec 34.6%, PPV 96.6%, NPV 56.0%

Pre-Endoscopic Management of Upper Gastrointestinal Bleeding
Pre-Endoscopic Medical Therapy for UGI Bleeding

• Volume Resuscitation
• Blood Transfusion
• Proton Pump Inhibitors
• Prokinetic Agents
• Nasogastric Tube and Lavage??
• Endotracheal Intubation??

• Special Scenario: Suspected Variceal Bleeding
Improved Survival with Restrictive Transfusion Strategy for Acute UGI Bleeds


Time After Bleed (Days)

Overall Survival (%)

Hgb goal > 7 g/dL
Restrictive strategy

P=0.02 by log-rank test

Liberal strategy
Hgb goal > 9 g/dL
**Improved Survival with Restrictive Transfusion Strategy for Acute UGI Bleeds**

<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>

- **ACG Recommendation**: Transfusion goal of Hemoglobin > 7 g/dL (> 10 g/dL if active cardiac disease)
- **DON’T FORGET**: Platelets, Fresh Frozen Plasma, Cryoprecipitate if needed

The Benefit of Proton Pump Inhibitor Use Before Endoscopy

- ACG & ASGE Guidelines recommend IV PPI before Endoscopy
- **PPI Dosage**: 80 IV bolus x1 followed by 8 mg/hr IV drip
- IV PPI is also recommended to decrease further bleeding if endoscopy will be delayed or cannot be performed

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PPI Group</th>
<th>Controls</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebleeding Rate</td>
<td>13.9%</td>
<td>16.6%</td>
<td>0.81 (0.61-1.09)</td>
</tr>
<tr>
<td>Need for Surgery</td>
<td>9.9%</td>
<td>10.2%</td>
<td>0.96 (0.68-1.35)</td>
</tr>
<tr>
<td>Mortality</td>
<td>6.1%</td>
<td>5.5%</td>
<td>1.12 (0.72-1.73)</td>
</tr>
<tr>
<td>High-Risk Stigmata Lesions</td>
<td>37.2%</td>
<td>46.5%</td>
<td>0.67 (0.54-0.84)</td>
</tr>
<tr>
<td>Need for Endoscopic Treatment at Index Endoscopy</td>
<td>8.6%</td>
<td>11.7%</td>
<td>0.68 (0.50-0.93)</td>
</tr>
</tbody>
</table>

Prokinetic Agents: The Role and Benefit of Pre-Endoscopic Erythromycin

<table>
<thead>
<tr>
<th>Erythromycin vs. No Erythromycin (N=598)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate Gastric Mucosal Visualization</td>
<td>OR 4.14 (2.01-8.53); p&lt;0.01</td>
</tr>
<tr>
<td>Need for Second Look Endoscopy</td>
<td>OR 0.51 (0.34-0.77); p&lt;0.01</td>
</tr>
<tr>
<td>Length of Hospital Stay</td>
<td>Mean difference -1.75 days (-2.43 to -1.06); p&lt;0.01</td>
</tr>
</tbody>
</table>

- ACG Guidelines (2012): Use erythromycin 250 mg IV 30-120 minutes before endoscopy
- ASGE Guidelines (2012): Use erythromycin if high-probability of fresh blood
- Limited data on Metoclopramide to suggest efficacy

Myth Busters: Nasogastric Tube Placement and Lavage

• **NOT Recommended**

• NGT lavage not required to make diagnosis or as a prognosticator
  – Positive lavage: blood or coffee ground material
  – “Negative lavage”: Presence of Bile (Not clear fluid)
  – High false negative rate

• Nasogastric aspiration/decompression of limited efficacy for clearance/visualization

• No documented therapeutic effect for hemostasis of ice cold water lavage
Prophylactic Endotracheal Intubation in UGI Bleeds

**Indications:**
- Massive hematemesis
- Altered mental status
- Airway protection

**Considerations:**
- Potential risk of aspiration pneumonia
- Potential risk of cardiac adverse events (shock)
Special Scenario: Suspected Variceal Bleeding

- **Warning Signs**: cirrhosis/portal HTN, EtOH, elevated LFTs, jaundice, thrombocytopenia, coagulopathy, ascites, prior varices
- PPI: 80mg IV bolus x1 then drip 8 mg/hr
- Octreotide: 50mcg IV bolus x1 then drip 50 mcg/hr (continue for 3-5 days if variceal bleed on EGD)
- Antibiotics: IV ceftriaxone 1g q24h or quinolone or broader to start then may switch eventually to PO to complete 7 day course
- Platelets: Consider transfusion if < 50,000
- Correct Coagulopathy: Consider transfusing FFP if INR > 1.5-2.0
- Consider endotracheal intubation
- Consult colleagues early: GI, ICU, IR for possible TIPS

Endoscopic Assessment and Management of Upper Gastrointestinal Bleeding
Endoscopic Management of UGI Bleeds: Factors to Consider

• Timing: When to Perform Endoscopy?

• Endoscopic Therapy:
  – Conventional Methods vs. New Techniques

• Methods to Decrease Rebleeding
Timing of Upper Endoscopy: The 24 Hour Window

ACG 2012 Guideline Recommendation:¹

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

Better Outcomes if EGD Within 24 Hours:²

• Study of 1.8 Million UGI Bleeds in NIS 2007-13
• 3x increased risk of death without EGD (3.0 vs. 8.5%)
• 50% lower mortality if EGD within 24 hours vs. later
• Early EGD (< 24 hours) → decreased morbidity, shorter LOS, and lower total hospital costs

Optimal Timing of Endoscopy Within 24 Hours: Emergent vs. Urgent Endoscopy

• Emergent endoscopy (< 6-8 hours) vs. Urgent endoscopy (8-24 hours): ¹⁻³
  – Retrospective series of 860 patients
  – Increased endoscopic therapy in emergent group
  – No differences in rebleeding rate, length of stay, transfusion requirements, need for surgery, or mortality

• Emergent Endoscopy (<12 hours) if: ⁴⁻⁷
  – Initial hemodynamic instability
  – Hematemesis or suspected active bleeding
  – AFTER stabilization and resuscitation
  – Potential benefit for high-risk patients (incl. variceal)⁷

Forrest Classification of Peptic Ulcers

IA

IB

IIA

IIB

IIC

III
# Forrest Classification of Peptic Ulcers and Prevalence

<table>
<thead>
<tr>
<th>Stigmata of Recent Hemorrhage</th>
<th>Forrest Classification</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Spurting Bleeding</td>
<td>IA</td>
<td>12% (Spurting + Oozing)</td>
</tr>
<tr>
<td>Active Oozing Bleeding</td>
<td>IB</td>
<td></td>
</tr>
<tr>
<td>Non-Bleeding Visible Vessel</td>
<td>IIA</td>
<td>8%</td>
</tr>
<tr>
<td>Adherent Clot</td>
<td>IIB</td>
<td>8%</td>
</tr>
<tr>
<td>Flat Pigmented Spot</td>
<td>IIC</td>
<td>16%</td>
</tr>
<tr>
<td>Clean Base</td>
<td>III</td>
<td>55%</td>
</tr>
</tbody>
</table>

### Natural History of Further Bleeding, Surgery and Mortality Based on Stigmata of Recent Hemorrhage

<table>
<thead>
<tr>
<th>Stigmata</th>
<th>Further Bleeding (N=2994)</th>
<th>Surgery for Bleeding (N=1499)</th>
<th>Mortality (N=1387)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Bleeding</td>
<td>55% (17-100%)</td>
<td>35% (20-69%)</td>
<td>11% (0-23%)</td>
</tr>
<tr>
<td>Non-Bleeding Visible Vessel</td>
<td>43% (0-81%)</td>
<td>34% (0-56%)</td>
<td>11% (0-21%)</td>
</tr>
<tr>
<td>Adherent Clot</td>
<td>22% (14-36%)</td>
<td>10% (5-12%)</td>
<td>7% (0-10%)</td>
</tr>
<tr>
<td>Flat Pigmented Spot</td>
<td>10% (0-13%)</td>
<td>6% (0-10%)</td>
<td>3% (0-10%)</td>
</tr>
<tr>
<td>Clean Ulcer Base</td>
<td>5% (0-10%)</td>
<td>0.5% (0-3%)</td>
<td>2% (0-3%)</td>
</tr>
</tbody>
</table>
## Risk of Recurrent Bleeding Without Endoscopic Therapy Based on Stigmata of Recent Hemorrhage

<table>
<thead>
<tr>
<th>Stigmata</th>
<th>Risk of Recurrent Bleeding Without Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Arterial Bleeding (Spurting)</td>
<td>Approaches 100%</td>
</tr>
<tr>
<td>Ulcer Oozing (Without other stigmata)</td>
<td>10-27%</td>
</tr>
<tr>
<td>Non-Bleeding Visible Vessel</td>
<td>Up to 50%</td>
</tr>
<tr>
<td>Non-Bleeding Adherent Clot</td>
<td>8-35%</td>
</tr>
<tr>
<td>Flat Spot/Pigmented Spot</td>
<td>&lt; 8%</td>
</tr>
<tr>
<td>Clean Base</td>
<td>&lt; 3%</td>
</tr>
</tbody>
</table>

Merit Endoscopic Therapy

Recommended Management Based on Ulcer Stigmata

- **Active bleeding**
  - Endoscopic therapy
  - NNT=2
  - RR 0.29 (0.20-0.43)
  - IV PPI Bolus and Infusion x 72h
  - NNT=12, RR 0.40 (0.28-0.59)

- **Non-bleeding visible vessel**
  - Endoscopic therapy
  - NNT=5
  - RR 0.49 (0.40-0.59)
  - IV PPI Bolus and Infusion x 72h
  - NNT=12, RR 0.40 (0.28-0.59)

- **Adherent clot**
  - May consider endoscopic therapy
  - RR 0.31 (0.06-1.77)
  - IV PPI Bolus and Infusion x 72h
  - NNT=12, RR 0.40 (0.28-0.59)

- **Flat pigmented spot or clean base**
  - No endoscopic therapy

- **Flat pigmented spot or clean base**
  - Oral PPI daily

**Post-EGD IV PPI:** Surgery NNT=28, RR 0.43 (0.24-0.76); Mortality NNT=45, RR 0.41 (0.20-0.84)

---

Traditional Endoscopic Therapeutic Modalities

- **Injection (epinephrine 1:10,000)**
  - NOT to be used as monotherapy
  - Further bleeding: RR 1.72 (1.08-2.78), NNT=9

- **Thermal (contact): Bipolar (Gold) or Heater Probes**
  - Further bleeding: RR 0.44 (0.36-0.54), NNT=4
  - Initial hemostasis: RR 11.70 (5.15-26.56)
  - Surgery/Mortality: RR 0.58 (0.34-0.98), NNT=33

- **Thermal (non-contact): Argon Plasma Coagulation (APC)**

- **Mechanical: Hemoclips, Banding Devices if Varices**

- **Combination Therapy Preferred**
  - Epinephrine + Thermal or Mechanical
  - Further bleeding: RR 0.34 (0.23-0.50), NNT=5

Emerging Endoscopic Therapy Modalities

- New types of hemoclips and loop devices
- Over-the-scope clips
- Monopolar cautery
- Ablation
- Hemostatic Sprays
- Endoscopic Suturing
- Endoscopic Ultrasound Guided Therapies

https://hemospray.cookmedical.com
https://synecticsmedical.co.uk
https://apolloendo.com/overstitch/
Hemospray® Mechanism and Efficacy

- Immediate Hemostasis Efficacy: 92.3% (95% in High-risk Forest 1a/1b lesions)
- Rebleeding Rate at 7 days: 20.6% overall (25% in high-risk lesions)

https://hemospray.cookmedical.com/
Hemospray® Performance Data

- “GRAPHE” Registry of 202 UGI bleed patients treated with Hemospray for first-line (46.5%) or rescue (53/5%) therapy\(^1\)

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Immediate Hemostasis</th>
<th>Recurrent Bleeding at Day 8</th>
<th>Need for Further Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer: Forrest IA</td>
<td>93.3% (14/15)</td>
<td>66.7% (10/15)</td>
<td>60% (9/15)</td>
</tr>
<tr>
<td>Ulcer: Forrest IB</td>
<td>95.3% (41/43)</td>
<td>31.7% (13/41)</td>
<td>27.5% (11/40)</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>100% (7/7)</td>
<td>28.6% (2/7)</td>
<td>28.6% (2/7)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>95.1% (58/61)</td>
<td>25% (14/56)</td>
<td>27.8% (15/54)</td>
</tr>
</tbody>
</table>

- Prospective international multicenter study of 314 pts treated with Hemospray\(^2\)

<table>
<thead>
<tr>
<th>Clinical Outcome</th>
<th>Monotherapy</th>
<th>Combination Therapy</th>
<th>Rescue Therapy</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Hemostasis</td>
<td>92%</td>
<td>89%</td>
<td>86%</td>
<td>0.35</td>
</tr>
<tr>
<td>Rebleeding</td>
<td>7.3%</td>
<td>10%</td>
<td>19%</td>
<td>0.08</td>
</tr>
<tr>
<td>30-Day Mortality</td>
<td>25.4%</td>
<td>15%</td>
<td>22%</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Hemospray© Additional Considerations

- Special expertise & equipment not required

- Potential uses in malignant bleeding and locations not amenable to endoscopic therapy

- Effective only in lesions with active bleeding (oozing or spurting)

- Second treatment modality or repeat endoscopy needed if high-risk lesion

Photos courtesy of Cook Medical, Inc.
Over The Scope Clips (OTSC)

- OTSC is a cap-mounted device with clip deployed similar to banding device

- Potential Benefits: Larger mucosal defects or bleeding from a lesion in a difficult position

- Limited performance data to date:
  - Technical Success: approaches 100%
  - Clinical Success: approximately 70-90%
  - Improved performance if used as first-line as opposed to rescue therapy
  - RCT of 66 pts showing OTSC in treating recurrent bleeding peptic ulcers has decreased risk of rebleeding than “standard therapy” (6% vs. 42%; p<0.001)

https://synecticsmedical.co.uk
R. Conigliaro, M. Frazzoni. Diagnosis and Endoscopic Management of Digestive Diseases, 2017; DOI 10.1007/978-3-319-42358-6_2.
Endoscopic Doppler Probe

- Doppler (sound-only) probe passed through the working channel of the endoscope
- **Goal**: localize vessels and confirm eradication of flow after endoscopic therapy

**RCT of 148 UGI bleeds comparing rebleeding rate of endoscopically (visually) guided only hemostasis (Control) vs. Doppler probe guided**

<table>
<thead>
<tr>
<th>Forrest Classification</th>
<th>Control Rebleeding Rate</th>
<th>Doppler-Guided Rebleeding Rate</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active arterial bleeding</td>
<td>5/10 (50%)</td>
<td>4/14 (28%)</td>
<td></td>
</tr>
<tr>
<td>Non-bleeding visible vessel</td>
<td>7/27 (26%)</td>
<td>4/26 (15%)</td>
<td></td>
</tr>
<tr>
<td>Adherent clot</td>
<td>4/16 (25%)</td>
<td>0/12 (0%)</td>
<td></td>
</tr>
<tr>
<td>Flat pigmented spot</td>
<td>3/16 (19%)</td>
<td>0/16 (0%)</td>
<td></td>
</tr>
<tr>
<td>Oozing arterial bleeding</td>
<td>1/7 (14%)</td>
<td>0/4 (0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>20/76 (26%)</strong></td>
<td><strong>8/72 (11%)</strong></td>
<td><strong>0.02</strong></td>
</tr>
</tbody>
</table>

Special Scenario:
Esophageal Variceal Bleeding

• Endoscopic Variceal Ligation/Banding Ideal
• Endoscopic Injection of Sclerotherapy
• Medical Management:
  – IV PPI, Octreotide, Antibiotics
• Beta-blockers long-term
• Balloon Tamponade: temporize if endoscopic failure
• IR for TIPS/BRTO if treatment failure or gastric varices

Post-Endoscopic Management of Upper Gastrointestinal Bleeding
Post-Endoscopic Management: ACG 2012 Guidelines

• PPI IV Bolus and Infusion x 72h if high-risk stigmata present; oral daily PPI if flat spot/clean based ulcer
  – Question of benefit of PPI infusion (8mg/h) vs. intermittent 40mg IV q12h
  – Intermittent PPI (IV or oral) risk of further bleeding vs. placebo: RR 0.53 (0.35-0.78); no difference in surgery or mortality

• Routine second-look endoscopy 24h post-EGD with endoscopic therapy is not recommended

• Repeat endoscopy if clinical evidence of recurrent bleeding

• After second therapeutic EGD, if evidence of further bleeding, recommend interventional radiology angiography/embolization, or surgery

### Rebleeding Predictors After Endoscopic Intervention

<table>
<thead>
<tr>
<th>Predictor</th>
<th># of Studies</th>
<th>Odds Ratio Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic Instability</td>
<td>5</td>
<td>2.2-3.6</td>
</tr>
<tr>
<td>Comorbid Illness</td>
<td>2</td>
<td>7.6</td>
</tr>
<tr>
<td>Active Bleeding</td>
<td>5</td>
<td>1.6-14</td>
</tr>
<tr>
<td>Ulcer Size &gt; 2 cm</td>
<td>4</td>
<td>1.8-4.6</td>
</tr>
<tr>
<td>Posterior Duodenal Ulcer</td>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td>Lesser Curvature Gastric Ulcer</td>
<td>2</td>
<td>2.7</td>
</tr>
</tbody>
</table>

- Possible Signs of Rebleeding: Recurrent overt GI bleeding, drop in H/H, hemodynamic instability, drop in CVP, drop in urine output.
When to Discharge and When to Feed?¹

High-Risk Stigmata (active bleeding, visible vessels, clots):
- **Hospitalize**: 3 days (72h of IV PPI) if no rebleeding
  - RCT of 764 pts at 91 centers in 16 countries with ulcer bleed with high-risk stigmata: 24% rebled after 3 days, 6% rebled after 7 days²
- **Diet**: Clear liquids after endoscopy x 48h
  - Guidelines vs. Practice??

Clean-Based Ulcers, Erosive Disease, Mallory-Weiss Tears (Lack of data on pigmented spots):
- **Hospitalize**: Discharge after EGD if:
  - H/H and Vitals stable
  - No other significant comorbidities
  - Safe/monitored environment to be discharged to
- **Diet**: Regular diet after endoscopy
  - RCT of 258 pts with immediate refeeding of regular diet vs. delayed refeeding (clear liquids at 36h and regular diet at 48 h) with no significant differences (rebleeding rate 4% vs. 5%)³

Management to Prevent Recurrent Ulcer Bleeding

- **H. pylori**
  - **H. pylori** therapy
  - Document cure; stop PPI/H2RA

- **NSAID**
  - Stop NSAID; if NSAID required, use coxib+ PPI

- **Low-dose aspirin**
  - Primary CV prevention
  - Do not resume aspirin in most patients

- **Idiopathic**
  - Secondary CV prevention
  - Resume aspirin soon after hemostasis (e.g., 1–7 days) in most patients and start PPI

- **Maintenance PPI**

- Rebleeding Rates without Therapy (follow up range of 6 months – 7 years): 15-42%²⁻¹⁰

Anticoagulant and Antiplatelet Agent Classes and Characteristics
The management of antithrombotic agents for patients undergoing GI endoscopy

PubMed ID: 26621548
Anticoagulant Use Is Frequent and Increasing

- Prevalence of Atrial Fibrillation in the United States:
  - 2.6 million → 12 million by 2050\(^1\)

- 900,000 incident or recurrent, fatal and nonfatal Venous thromboembolism (VTE) events annually in the U.S.\(^2\)

- Total annual cost from VTE (including lost earnings from premature mortality): $13-27 billion as of 2011\(^3\)

- Over 30 million warfarin prescriptions annually in the U.S. → $158 million per quarter in 2010\(^4\)

- Direct Oral Anticoagulants (DOACs): 62% of new anticoagulant Rx by 2013 → approximately $10 billion annually by 2016\(^5,6\)

---

Anticoagulant Development

DOACs: Direct Oral Anticoagulants including Direct Factor Xa Inhibitors & Direct Thrombin Inhibitors
Types of Anticoagulant Agents

**Goal**: Interfere with the Native Clotting Cascade

- **Vitamin K Antagonists**
  - Warfarin (Coumadin)

- **Direct Factor Xa Inhibitors**
  - Rivaroxaban (Xarelto)
  - Apixaban (Eliquis)
  - Edoxaban (Savayasa)

- **Heparin Derivatives**
  - Unfractionated
  - Low molecular weight:
    - Enoxaparin (Lovenox), Dalteparin (Fragmin)
  - Fondaparinux (Arixtra)

- **Direct Thrombin Inhibitors**
  - Dabigatran (Pradaxa)
  - Hirudins
  - Argatran (Acova)

*Acosta RD, et al. Gastrointest Endosc 2016;83(1):3-16*
Direct Oral Anticoagulants Are Being Increasingly Used

![Graph showing office visits from 2009 to 2014 for various anticoagulants.

- All Anticoagulants
- Warfarin
- All DOACs
- Apixaban
- Rivaroxaban
- Dabigatran]
Use of Direct Oral Anticoagulants vs. Warfarin in A-Fib
# Anticoagulant Agents: Duration of Action & Reversal Options

<table>
<thead>
<tr>
<th>Specific Agent(s)</th>
<th>Duration of Action</th>
<th>Reversal for Elective Procedure</th>
<th>Reversal for Urgent Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>5 days</td>
<td>Hold</td>
<td>Vitamin K, PCC</td>
</tr>
<tr>
<td>Unfractionated Heparin</td>
<td>IV: 2-6 hours</td>
<td>Hold</td>
<td>Protamine sulfate</td>
</tr>
<tr>
<td></td>
<td>SQ: 12-24 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Molecular Weight Heparin</td>
<td>24 hours</td>
<td>Hold</td>
<td>Protamine sulfate; consider rVIIa</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>36-48 hours</td>
<td>Hold for at least 36 hours</td>
<td>Protamine sulfate; consider rVIIa</td>
</tr>
<tr>
<td>Direct Factor Xa Inhibitors</td>
<td>Onset: 1-4 h</td>
<td>Hold 1-4 days pending CrCl</td>
<td>Charcoal (if intake within 2-3h); nonactivated or activated PCC</td>
</tr>
<tr>
<td>Direct Thrombin Inhibitors</td>
<td>Onset: 1-3 h; T½: 13-27 h</td>
<td>Hold 1-6 days pending CrCl &amp; Proc. Bleed Risk</td>
<td>Charcoal (if intake within 2-3h); nonactivated or activated PCC; Hemodialysis</td>
</tr>
</tbody>
</table>

**New Antidotes:**
- Dabigratran (Pradaxa): Idarucizumab (Praxbind)
- Apixaban (Eliquis): Andexanet Alpha → FDA Fast Track
- Edoxaban: Aripazine (PER 977) → FDA Fast Track


Types of Antiplatelet Agents

**Goal:** Decrease platelet aggregation → prevent thrombus formation

- **Thienopyridines**
  - Clopidogrel (Plavix)
  - Prasugrel (Effient)
  - Ticlodipine (Ticlid)
  - Ticagrelor (Brillinta)

- **Aspirin/NSAIDs**

- **Protease-Activated Receptor-1 (PAR-1) Inhibitors**
  - Vorapaxar (Zontivity)

- **Glycoprotein IIb/IIIa Receptor Inhibitors**
  - Abciximab (ReoPro)
  - Eptifibatide (Integrillin)
  - Tirofiban (Aggrastat)
### Antiplatelet Agents: Duration of Action & Reversal Options

<table>
<thead>
<tr>
<th>Specific Agent(s)</th>
<th>Duration of Action</th>
<th>Reversal for Elective Procedure</th>
<th>Reversal for Urgent Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>7-10 days</td>
<td>N/A</td>
<td>Hold; can give platelets</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>Variable</td>
<td>N/A</td>
<td>Hold</td>
</tr>
<tr>
<td>Dipyridamole (Persantine)</td>
<td>2-3 days</td>
<td>Hold</td>
<td>Hold</td>
</tr>
<tr>
<td>Cilostazol (Pletal)</td>
<td>2 days</td>
<td>Hold</td>
<td>Hold</td>
</tr>
<tr>
<td>Thienopyridines</td>
<td>3-14 days (Clopidogrel 5-7 days)</td>
<td>Hold</td>
<td>Hold</td>
</tr>
<tr>
<td>GP IIb/IIIa Inhibitors</td>
<td>1-2 seconds – 24 hours</td>
<td>N/A</td>
<td>Hold; Hemodialysis (Tirofiban)</td>
</tr>
<tr>
<td>PAR-1 Inhibitor</td>
<td>5-13 days</td>
<td>Hold</td>
<td>Hold</td>
</tr>
</tbody>
</table>

Antithrombotic Agents and Endoscopy: Risk of GI Bleeding
Risk of GI Bleeding in Complex Antithrombotic Therapy

- Complex Antithrombotic Therapy: ASA + thienopyridine (i.e. clopidogrel) and/or warfarin\(^1\)

- GI bleeding in patients on Complex Antithrombotic Therapy: \(\text{NNH} = 42\)\(^2-5\)

- Further increased risk of GI bleeding in patients on triple therapy: ASA + clopidogrel + warfarin: \(\text{NNH} = 12.5\)\(^6,7\)

- Risk of bleeding with adding direct oral anticoagulants (DOACs) to patients on dual antiplatelet therapy after acute coronary syndromes (ACS) is high\(^8\):
  - Systematic review & Meta-analysis of 7 placebo-controlled RCTs of 31,286 pts
  - Pooled Odds ratio 3.03; 95% CI 2.20-4.16
  - Absolute Risk 0.9%; 95% CI 0.7%-1.1%

### GI Bleeding in Elderly Patients with Complex Antithrombotic Therapy (78,133 Patients)

<table>
<thead>
<tr>
<th>CAT-Related Events: 1 Year NNH</th>
<th>Anticoagulant + Antiplatelet Agent (Not Aspirin)</th>
<th>Aspirin + Antiplatelet Agent</th>
<th>Aspirin + Antiplatelet Agent (DAPT)</th>
<th>Aspirin + Antiplatelet Agent + Anticoagulant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper GI Bleeding NNH (95% CI)</td>
<td>65 (24-379)</td>
<td>56 (22-231)</td>
<td>93 (34-544)</td>
<td>52 (20-210)</td>
</tr>
<tr>
<td>Lower GI Bleeding NNH (95% CI)</td>
<td>19 (11-37)</td>
<td>15 (9-30)</td>
<td>18 (10-37)</td>
<td>23 (13-49)</td>
</tr>
<tr>
<td>Transfusion NNH (95% CI)</td>
<td>43 (21-128)</td>
<td>16 (9-31)</td>
<td>51 (24-182)</td>
<td>25 (14-50)</td>
</tr>
<tr>
<td>Hospitalization NNH (95% CI)</td>
<td>39 (18-121)</td>
<td>34 (16-89)</td>
<td>67 (30-214)</td>
<td>45 (21-126)</td>
</tr>
</tbody>
</table>

DOAC-Related GI Bleeding

Patient characteristics elevating risk of DOAC-Related bleeding:
• Age > 65 (vs. warfarin matched cohort) with further increase if Age > 75\(^1\)

• Renal impairment: DOACs have partial renal clearance so decreased GFR increases DOAC half-life\(^2\)
  – Dose adjustments for renal impairment unclear\(^3\)

• Hepatic Disease: all DOACs have partial hepatic clearance\(^4\)
  – Do not use if baseline coagulopathy
  – No dose adjustment for dabigatran or apixaban if Child-Pugh A; caution if Child-Pugh B

• Low body weight < 50kg\(^5\)

• **Estimated 13,600 – 23,800 DOAC-related GI bleeds annually**\(^4\)

---

Are We Becoming Cardio-Gastroenterologists?
Key Factors to Consider

1. Urgency of the Procedure

2. Bleeding Risk of the Procedure

3. Effect of the Antithrombotic Agent on Bleeding Risk

4. Risk of Thromboembolism due to Peri-Procedural Interruption of the Antithrombotic Agent
Procedure Related Risk of Bleeding

Patient Related Risk of VTE
<table>
<thead>
<tr>
<th>Higher Risk Procedures</th>
<th>Low Risk Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypectomy</td>
<td>Diagnostic EGD/colonoscopy with Biopsy</td>
</tr>
<tr>
<td>Endoscopic Mucosal Resection</td>
<td>Push Enteroscopy</td>
</tr>
<tr>
<td>Endoscopic Submucosal Dissection</td>
<td>Diagnostic Balloon-Assisted Enteroscopy</td>
</tr>
<tr>
<td>Ampullary Resection</td>
<td>Capsule Endoscopy</td>
</tr>
<tr>
<td>Sphincterotomy: Biliary or Pancreatic</td>
<td>ERCP (including Stenting &amp; Dilation) without Sphincterotomy</td>
</tr>
<tr>
<td>Treatment of Varices</td>
<td>Argon Plasma Coagulation</td>
</tr>
<tr>
<td>Endoscopic Hemostasis</td>
<td>Barrett’s Ablation</td>
</tr>
<tr>
<td>Tumor Ablation</td>
<td></td>
</tr>
<tr>
<td>Therapeutic Balloon-Assisted Enteroscopy</td>
<td></td>
</tr>
<tr>
<td>EUS with FNA*</td>
<td>EUS without FNA</td>
</tr>
<tr>
<td>Cystgastrostomy</td>
<td></td>
</tr>
<tr>
<td>Pneumatic or Bougie Dilation</td>
<td>Enteral Stent Placement***</td>
</tr>
<tr>
<td>PEG Placement**</td>
<td></td>
</tr>
<tr>
<td>PEJ Placement</td>
<td></td>
</tr>
</tbody>
</table>
Risk of Thromboembolism Varies by Patient & Anticoagulation Indication

• **Atrial Fibrillation:** CHADS-VASc Score of ≥2 (high-risk for thromboembolism > 2.2%/year)\(^1\)

• **Mechanical heart valves**\(^2\)

• **Venous thromboembolism**\(^2\)

• **Cardiac Stents**\(^3\): High-risk to stop Antiplatelet if:
  - Drug-eluting stent placement ≤ 12 months
  - Bare metal stent (BMS) placement ≤ 1 month
  - Acute coronary syndrome with BMS ≤ 12 months

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Antithrombotic Agent Management for Elective GI Procedures
Anticoagulation Cessation for Elective Procedures

- If finite short period of time for anticoagulation (i.e. s/p Bare Metal Stenting or after VTE), **delay** elective procedures until anticoagulation is no longer indicated\(^1\)

- Carefully weigh risks/benefits and consult specialists in patients needing longer-term anticoagulation (i.e. s/p Acute Coronary Syndrome or Drug-Eluting Stent)\(^2,\!^3\)

- Anticoagulation may be unable to be stopped in some patients

- Absolute risk of embolic event when stopping anticoagulation for 4-7 days: 1%\(^2,\!^4\)

- Re-initiate of anticoagulation (if with warfarin) within 4-7 days of cessation to prevent additional thromboembolic risk\(^5\)

- **ASGE Recommendation**: Continue anticoagulation in low-risk (of bleeding) procedures and stop for high-risk procedures (with bridge therapy if patient at high-risk for thromboembolism)\(^1\)

Bridge Therapy for Elective Procedures

- Patients on warfarin may be bridged with unfractionated heparin or LMWH

- RCT of 1884 pts with non-valvular A-Fib (low VTE risk) of heparin bridge vs. no bridge:\(^1\)
  - Major Bleeding Events: 3.2% vs. 1.3%
  - Arterial Thromboembolism: 0.3% vs. 0.4%

- Patients who do not require bridge therapy:\(^2,3\)
  - A-fib with CHADS-VASC < 2, bileaflet mechanical aortic valve

- Patients at high-risk for VTE should be bridged:\(^1-3\)
  - A-fib with CHADS-VASC ≥2
  - Valvular A-fib
  - A-fib with history of CVA
  - Mechanical heart valves
  - LVAD
  - Recent VTE
  - A-fib with CHF
  - Post-ACS

Anti-Platelet Agent Cessation for Elective Procedures: Joint Recommendations from ACC/ACG¹

• Avoid stopping antiplatelet agents after cardiac cath with stenting

• Avoid stopping clopidogrel (even if ASA continued) within first 30 days post-PCI with DES or BMS

• Defer elective procedures up to 12 months post-DES placement if clinically acceptable

• Perform endoscopic procedures with higher bleeding risk 5-7 days post-clopidogrel cessation, while continuing ASA

• Resume clopidogrel and ASA once procedural hemostasis achieved. Consider loading dose of clopidogrel if high-risk patient.

• Continue anti-platelet therapy if planned procedure is low bleeding risk

Antithrombotic Re-Initiation Post-Elective Procedures

• Weigh risk of bleeding post-procedure, the specific antithrombotic agent and its onset of action

• Resume anticoagulants ASAP, and antiplatelet agents once hemostasis achieved\(^1\)

• Re-initiation of warfarin or heparin after colonoscopy associated with increased risk of bleeding within 1 week of polypectomy (OR 5.2; 95% CI 2.2-12.5)\(^2\)

• AHA/ACC guidelines recommend restarting warfarin within 24 hours post-procedure if valvular heart disease and low thromboembolic risk, and heparin bridging if high risk\(^3\)

• Limited data on re-initiation of DOACs post-GI procedures
  — Maximal drug effect within 2-4 hours

• If DOACs cannot be restarted within 24 hours and high thromboembolic risk, consider heparin bridge\(^4,5\)

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5. Dzik WS. Transfusion 2012.
Endoscopy for Acute Bleeding and Acute Coronary Syndromes (ACS)
Endoscopy for Acute Bleeding on Anticoagulation

- Endoscopic therapy for UGI bleeds is effective in anticoagulated patients
  - 95% initial success rate in 246 patients with INR of 1.3-2.7\(^1\)

- Normalization of INR prior to endoscopy does NOT reduce risk of rebleeding but delays time to procedure\(^{1,2}\)

- INR at time of endoscopy is not predictive of rebleeding\(^3\)
  - Systematic review of 1869 non-Variceal UGI bleeds

- Reversal of warfarin with FFP or Prothrombin Complex +/- vitamin K\(^{2,4,5}\)

- **Recommendation**: Reasonable to perform endoscopy in bleeding patients with INR < 2.5\(^2\)

Reversal of Antiplatelet Agents in Acute GI Bleeding

- If serious or life-threatening bleeding: can stop agent or give platelets
- Resumption needed in most patients after endoscopic bleeding control
- ASA induced PUD: Restarting ASA + PPI better than clopidogrel monotherapy for recurrent GI bleed prevention\(^1,2\)
- Resumption of cardiac ASA after PUD bleeding: RCT of 156 patients on PPI + ASA 80mg vs. Placebo\(^3\):
  - No significantly increased 30-day rebleeding risk (10.3% vs. 5.4%; 95%CI -3.6-13.4)
  - Increased 30-day mortality if ASA not resumed (1.3% vs 12.9%)
- **Recommendation:** Resume antiplatelet agents once hemostasis achieved\(^4,5\)

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Role of Urgent Endoscopy in Patients with Acute Coronary Syndromes or Recent Stenting

- 1-3% of patients with ACS will have a GI bleed during their index hospitalization\(^1\)-\(^4\)

- 4- to 7-fold increased risk of in-hospital mortality if GI bleed in ACS patients vs. ACS without GI bleed\(^2\),\(^3\)

- Patients with UGI bleed leading to acute MI are more likely to require endoscopic therapy vs. patients with GI bleed after an acute MI (OR 3.9; 95% CI 1.8-8.5, p<0.004)\(^4\)

- EGD for significant overt GI bleeding in setting of acute MI prior to cardiac catheterization\(^5\):
  - Decreased mortality if EGD prior to Cath: 97 vs. 600 per 10,000 pts
  - Fewer non-fatal complications if EGD before Cath: 1271 vs. 6000 per 10000 pts
  - Endoscopy 1\(^{st}\) not beneficial in occult GI bleeding and acute MI

Take Home Points

1. Recognize the different types of gastrointestinal bleeding

2. Appreciate the importance of initial volume resuscitation, medical therapy, and endoscopic therapy in the diagnosis and management of acute upper GI bleeds

3. Understand the urgency and bleeding risk of the planned GI procedure

4. Identify the effect of the antithrombotic agent on bleeding risk and the effect of stopping that agent on the patient’s risk of thromboembolism

5. This is a team effort: When in doubt, consult the appropriate colleague
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