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Overview

• Non-Variceal Upper GI Bleeding (NVUGIB)
• Variceal Upper GI Bleeding (VUGIB)
• What’s New?
  – Doppler Ultrasound Probe
  – Hemospray
  – EUS-guided Therapy for Gastric Varices
NVUGIB: Assessment

- Assess hemodynamics immediately
- Begin resuscitation as appropriate
- Transfuse to Hgb of > 7 g/dl, more for comorbidities like CAD
- Stratify into high/low risk categories to plan timing of endoscopy/discharge.


NVUGIB: When to consider early discharge

- BUN < 18.2 mg/dl
- Hgb >= 13 g/dl for men (12.0 g/dl for women)
- SBP > 110 mm Hg
- HR < 100
- No melena, syncope, cardiac failure or liver disease

If all the above criteria are met: < 1% chance of needing intervention

NVUGIB: Preparing for EGD

• IV erythromycin (250 mg 30 min before EGD) may improve yield & decrease need for repeat EGD
• IV PPI (80 mg bolus & 8 mg/hr infusion) to reduce frequency of high risk stigmata at EGD and for when EGD is delayed/contraindicated
• NG/OG lavage is optional (no benefit of iced lavage)


NVUGIB: EGD

• Usually within 24 hrs of admission
• More rapid endoscopy will allow for early discharge of lower risk patients and may improve outcomes in higher risk patients
• Properly record stigmata of hemorrhage
• Treat spurting/oozing lesions or non-bleeding visible vessels, possibly some with adherent clots (older, inpatient etc)

FINDINGS AT ENDOSCOPY

Clean Based Ulcer  Ulcer with flat spot  Ulcer with adherent clot

Visible Vessel  Active arterial bleeding

Poor inter-observer variability for all of these endoscopic stigmata except for active bleeding, even among experts!

Endoscopic Stigmata of Bleeding Peptic Ulcer: Classified as High Risk or Low Risk

Forrest Classification: (IA-III)

High Risk (seen in 1/3-1/2 UGIB):
• IA - Active spurting of blood
• IB - Oozing blood
• IIA - Visible vessel/pigmented protuberance
• IIB - Adherent clot

Low Risk:
• IIC - Flat, pigmented spots
• III - Clean based ulcers

V. Raman Muthusamy, MD, FACG

Endoscopic risk stratification

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Active bleeding</th>
<th>Non-bleeding visible vessel</th>
<th>Adherent clot</th>
<th>Flat pigmented spot</th>
<th>Clean ulcer base</th>
</tr>
</thead>
<tbody>
<tr>
<td>17% (0-49)</td>
<td>55% (17–100%)</td>
<td>43% (0–51%)</td>
<td>22% (14–36%)</td>
<td>10% (0–13%)</td>
<td>5% (0–10%)</td>
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<tr>
<td>18% (4-26)</td>
<td>35% (20–69%)</td>
<td>34% (0–56%)</td>
<td>10% (5–12%)</td>
<td>6% (0–10%)</td>
<td>0.5% (0–3%)</td>
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<tr>
<td>17% (4-35)</td>
<td>11% (0–23%)</td>
<td>11% (0–21%)</td>
<td>7% (0–10%)</td>
<td>3% (0–10%)</td>
<td>2% (0–3%)</td>
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<tr>
<td>20% (0-42)</td>
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<td>42% (19-52)</td>
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Laine et al, NEJM, 1995

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

- Epinephrine injection (1:10000)
- Contact thermocoagulation (BPEC, heater probes)
- Non-contact thermal (laser, APC)
- Endoclips
- Sclerosant injection (polidocanol, absolute alcohol)
- Fibrin glue, thrombin injection
- Saline injection (tamponade)

Combo tx superior to mono tx (epi alone) for high risk lesions
- 10% vs 18% rebleeding (Meta-analysis)

Calvet, Gastroenterol 2004; 126: 441.
Laine & McQuaid, Clinical Gastroenterology and Hepatology, 2009, p 33-47.
NVUGIB: Treatment

- NO epinephrine monotherapy!
- Use MPEC or heater probe/sclerosant (absolute ETOH)
- Clips also effective, but comparative data not as abundant
- For active bleeding, thermal therapy or epinephrine + second modality may be preferred to clips or a sclerosant alone


Endoscopic Techniques: Coaptive Thermocoagulation

- Large caliber probe (10F)
- Firm tamponade
- Bipolar (multipolar electrocautery): 15-25 Watt setting
- Heater probe: 30 joule setting
- hemostasis: > 90%
- Complications: induce bleeding 0.3%; perforation 0.5%

From Laine, NEJM 1995; 331: 717.
Time Vs. Power

Power Delivered vs. Impedance


Issues of Technique

- Increased duration increases energy delivered, coagulation depth, and surface area
- Increased force helps increase energy delivery, depth of coagulation, and surface area
- Increased watt setting increases impedance and decreased power delivered without increased depth or surface area
- Tamponade is needed to seal arteries
  - **Recommend: 15 W, 10 seconds, large coaptive force**

NVUGIB: Post-Treatment

- IV PPI (80 mg bolus + 8 mg/hr) for those with high risk stigmata
- Low risk stigmata can be treated with QD oral PPI
- Relook endoscopy only for those with clinical suspicion of rebleeding
- Consider surgery/IR if 2nd endoscopy treatment is unsuccessful.


NVUGIB: Discharge/Prevention of Recurrence

- High risk stigmata pts usually stay 3 days; start clear liquids after endoscopy
- Low risk stigmata patients can be discharged on a regular diet.
- H. pylori associated ulcers should receive H pylori therapy and may not require long-term PPI therapy
- If NSAID related, consider d/c of NSAID, dose reduction, use of a COX-2 agent, and daily PPI use.
- If ASA related, consider d/c of ASA, especially if for primary prevention. For secondary prevention, restart in 1-3 days and ensure long term PPI use.
- For idiopathic ulcers, daily PPI use is recommended

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VUGIB: Evaluation and Initial Endoscopy

- Antibiotics x 7 days for cirrhotics presenting with VUGIB
- Initiate octreotide and continue if VUGIB confirmed for 3-5 days
- EGD in < 12 hrs from admission
- Consider intubation, especially in patients with encephalopathy
- Band ligation preferred, with sclerotherapy reserved for difficult banding cases
- Cyanoacrylate, when available, is preferred over band ligation for treating bleeding gastric varices

Hwang JH et al, GIE, 80:2, 2014
VUGIB: Post-Endoscopy

- When endoscopy fails for acute variceal hemorrhage, balloon tamponade should be considered as a temporizing measure.
- When endoscopy fails for esophageal/gastric varices, recommend IR techniques for definitive therapy.
- After initial variceal treatment with banding/sclerotherapy, continue band ligation at 1-8 week intervals until variceal eradication.
- Once eradication, perform surveillance q 3-6 months to assess for recurrence.

Hwang JH et al, GIE, 80:2, 2014

Overview

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- Current Guidelines for Variceal Upper GI Bleeding
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ACG Western Regional Postgraduate Course - Las Vegas, NV
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Doppler Ultrasound Probe (DUP)

- 2.0 mm diameter
- Flexed pulse wave 20 MHz probes
- FDA Approved in 2003
- Passes through biopsy channel
- Audible output signal
- Allows for determination of:
  - Depth of blood vessel
  - Location of blood vessel
  - Arterial/venous flow


RCT of DUP in Adherent Clots

- 27 patients (14 DUP/13 standard tx)
- DUP utilized post endoscopic therapy in DUP group and additional tx done if arterial flow detected
- Patients and managing MDs blinded to therapy
- Rebleed rate of 23.1% in Control group (3/13) vs. 0% (0/14) in DUP group
- No perforations
- Ongoing study

Prior cohort study of 19 patients showed 68.4% had arterial flow under the clot compared to 18.8% post-treatment

Jensen et al, Submitted to DDW 2015
DUP Cost Analysis

- Compared DUS to Conventional Forrest Classification in managing acute peptic ulcer bleeding
- DUS saved $853-1160 per patient
- Even with high dose IV PPI, DUS saved $328-560 per patient


DUP: Summary

- Close correlation between a positive DUP signal and visualized endoscopic stigmata
- DUP positive ulcers have a higher risk of rebleeding than DUP-negative ulcers.
- An ulcer that is DUP positive after endoscopic therapy has an increased risk of rebleeding than one in which the DUP signal is negative after treatment
Hemospray (TC-325)

- Highly adsorptive
- Two mechanisms of action
  - Creates cohesive and adhesive bond in the presence of moisture (blood/tissue), creating a stable mechanical barrier
  - Increases concentration of clotting factors enhancing clot formation
- Currently, not FDA Approved


Mechanism of Action

Barkun et al, Gastroint Endosc, 77:5, 2013
**Hemospray (TC-325): Advantages**

- Non-contact
- Not absorbed and inorganic
- Can be applied over a wide area
- No resulting tissue injury


**Hemospray: Potential Safety Concerns**

- Embolization
- Allergic reaction
- Perforation due to the delivery system
- Intestinal obstruction from sloughed Hemospray
- Inhalation
- Local tissue and vascular injury
**Hemospray Technique**

- Catheter tip position 1-2 cm from lesion
- Short spray bursts of 1-2 seconds until hemostasis achieved
- Observe for 5 minutes once hemostasis achieved
- Perform second application if bleeding recurred during 5 minute observation
- Maximum 150 g hemospray (21 g/cannister)
- Failure if bleeding persisted after 2 spray sessions/150 g spray

**Hemospray (TC-325): Initial Data**

- 20 patients (19 Forrest IB/1 IA)
- Half had ulcer > 1 cm
- 85% w/ one application
- 65% w/ only one syringe used
- 95% acute hemostasis rate
- Failure was in IA patient who had a pseudoaneurysm
- Sustained hemostasis in 17/19 (89.5%) at 72 hrs
- No adverse events
Hemostatic Agents: Data Limitations

- Little data on Forrest Ia lesions (active pulsatile bleeding)
- Unclear re: benefit in non-bleeding lesions (non-bleeding visible vessel, adherent clot etc)
- ? For role in other bleeding conditions (GAVE, tumor bleeding etc)

Potential Roles of Hemostatic Agents

Barkan et al, Gastroint Endosc, 77-5, 2013
EUS-Guided Coil & Cyanoacrylate Injection for Gastric Varices

- EUS guided cyanoacrylate injection has been reported to be effective in treating gastric varices
- Reports of fatal cyanoacrylate emboli exist
- Aim to use coils and 2-octyl-cyanoacrylate (Dermabond) together to improve efficacy and reduce/eliminate embolic events


Study Parameters/Technique

- Must have > 1 cm gastric varices on EUS
- Must not be TIPS candidate or must have previously failed TIPS
- Must have active or recent gastric variceal bleeding
- 12-20 mm embolization coils used
- 1 cc of cyanoacrylate injected
- Additional injection/coiling as needed to obliterate the varices
- Follow-up EGD/EUS at 1, 3, 9, and 15 mos

Results of Coil and Glue for Gastric Varices

- 30 pts (25 IGV:5 GOV)
- Mean # GV injected per pt = 1.4
- 30/30 successful for both coiling and injection of 1.4 cc of cyanoacrylate
- No immediate complications
- 4/24 rebled, but none due to variceal bleeding
- 23/24 with gastric variceal obliteration
- Mean f/u = 193 d

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Do We Need Both?

- 30 patients
- 11 coil embolizations (ECA) vs. 19 cyanoacrylate (CYA) injections (all EUS-guided)
- 96.7% variceal obliteration (1 failure in ECA group)
- Trend to fewer sessions w/ ECA; 82% of ECA vs. 53% of CYA needed only 1 treatment
- No gastric varices recurrences
- Adverse events: 40% in CYA vs. 9.1% of ECA; Only 2 w/ symptoms in CYA group

Romero-Castro et al, Gastrointest Endosc, 78:5, 711-21.
Summary

• Recognize the importance of risk stratification and proper coaptive technique for Non-variceal UGI hemorrhage

• The DUS probe may be a cost-effective technique to reduce recurrent bleeding after endoscopic therapy

• Despite its promise, the exact utility and role of Hemospray remains to be determined

• EUS-guided therapy of gastric varices is feasible using coils, with or without cyanoacrylate