Endoscopic Hemostasis in Non-Variceal UGI Bleeding

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Etiology of Nonvariceal UGI Bleeding

- Nonvariceal UGI Bleeding
  - Peptic ulcer
  - Esophagitis/Gastritis
  - Mallory -Weiss Tear
  - Vascular ectasia
  - Dieulafoy’s
  - Tumor
  - Post sphincterotomy
  - Post polypectomy

- Hemosuccus pancreaticus
- Hemobilia
- Aortoenteric fistula

Enestvedt et al. GIE. 2008
Barkun et al. Am J Gastro. 2004
Goals of Endoscopic Therapy

• Control active bleeding
• Decrease rebleeding rates
• Improve outcomes
  – Decrease transfusion requirements
  – Decrease need for surgery
  – Decrease Length of stay
  – Decrease morbidity and mortality
  – Decrease cost

Which Lesions to Treat?

• Ulcer bleeding
  – Spurting arterial bleeding
  – Non-bleeding visible vessel
  – Adherent clot
• Mallory-Weiss tear
• Dieulafoy’s
• Vascular ectasia
• Post endoscopic sphincterotomy
• Post polypectomy
Ulcer Stigmata of Bleeding
Risk of Bleeding without Endotherapy

<table>
<thead>
<tr>
<th>Stigmata</th>
<th>Prevalence (%)</th>
<th>Rebleed (%)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial bleed</td>
<td>10</td>
<td>85-100</td>
<td>yes</td>
</tr>
<tr>
<td>Visible Vessel</td>
<td>25</td>
<td>18-55 (mean-43)</td>
<td>yes</td>
</tr>
<tr>
<td>Adherent Clot</td>
<td>10</td>
<td>8-35</td>
<td>Yes / maybe</td>
</tr>
<tr>
<td>Oozing</td>
<td></td>
<td>10-27</td>
<td>yes</td>
</tr>
<tr>
<td>Flat Red/Black Spots</td>
<td></td>
<td>&lt; 8</td>
<td>No / maybe</td>
</tr>
<tr>
<td>Clean Based</td>
<td>35%</td>
<td>&lt; 3</td>
<td>no</td>
</tr>
</tbody>
</table>

ASGE Guideline GIE 2012

Results of Endoscopic Therapy

<table>
<thead>
<tr>
<th></th>
<th>Sham (n=23)</th>
<th>MPEC (n=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemostasis</td>
<td>13%</td>
<td>90%</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Blood Transfusions</td>
<td>5.4 units</td>
<td>2.4 units</td>
<td>0.002</td>
</tr>
<tr>
<td>Emergency Intervention</td>
<td>57%</td>
<td>14%</td>
<td>0.005</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>7.2 days</td>
<td>4.4 days</td>
<td>0.02</td>
</tr>
<tr>
<td>Deaths</td>
<td>13%</td>
<td>0</td>
<td>NS</td>
</tr>
</tbody>
</table>

Compared to medical therapy
- Reduced rebleeding
- Reduced surgery
- Reduced mortality
- MPEC can be used as monotherapy

Active ulcer bleeding - 24
Mallory-Weiss Tears - 17
Vascular malformations - 3

Laine L, NEJM. 1987;316:1613
**Risk of Ulcer Rebleeding after Therapy**

<table>
<thead>
<tr>
<th></th>
<th>Medical</th>
<th>Bipolar</th>
<th>Heater Probe</th>
<th>Epi Injection</th>
<th>Inject + bipolar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spurting</td>
<td>85-100</td>
<td>12</td>
<td>22</td>
<td>-</td>
<td>18</td>
</tr>
<tr>
<td>NBVV</td>
<td>18.55 (mean-43)</td>
<td>12</td>
<td>23</td>
<td>-</td>
<td>18</td>
</tr>
<tr>
<td>Adherent Clot</td>
<td>8-35</td>
<td>35</td>
<td>35</td>
<td>38</td>
<td>0</td>
</tr>
<tr>
<td>Oozing</td>
<td>10-27</td>
<td>n/a</td>
<td>n/a</td>
<td>0</td>
<td>n/a</td>
</tr>
<tr>
<td>Flat Spots</td>
<td>&lt; 8</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Clean Based</td>
<td>&lt; 3</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

CURE data

**Adherent Clot Treatment**

Rebleeding depends on lesion below the clot

<table>
<thead>
<tr>
<th></th>
<th>Rebleeding Rate (%)</th>
<th>Rebleeding Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kahi et al, 2005</td>
<td>Laine et al, 2009</td>
</tr>
<tr>
<td>Clot removed + endo Tx</td>
<td>8.5%</td>
<td>No difference</td>
</tr>
<tr>
<td>Clot not removed</td>
<td>24.7%</td>
<td>No Difference</td>
</tr>
</tbody>
</table>

- ASGE Guideline - Individualize treatment
- Vigorous irrigation and clot falls off
  - Treat lesion
- Clot remains after vigorous irrigation
  - Pre inject with epinephrine and remove with cold snare
  - Treat lesion: thermal tx or clip
Endoscopic Options
Bleeding Ulcers

- Coagulation
  - Bipolar, Heater probe
  - APC
- Injection
  - Epinephrine
- Mechanical ligation
  - Clips

Why Endoscopic Treatment Fails?

- Anticoagulation
- Diffuse bleeding
- Difficult position
  - Posterior wall
  - Upper lesser curve
Epinephrine Injection
Bleeding Ulcers

- 21-25G injection needle
- 1:10,000 dilution standard
  - 0.5 – 1.0 cc aliquots in four quadrants
  - Large volume injection (13-20 cc)
  - Within 2-3 mm of the active bleeding point in the ulcer base
- Achieves hemostasis by
  - mechanical tamponade and vasoconstriction

Clear the view
- Use in combination with another modality
  - Epi + thermal/mechanical better than epi alone

Lin et al. GIE 2002

Thermal Therapy

- Contact
  - Compress vessel (pressure) and coagulate (heat) to seal
    - Bipolar Probe
      - 15-20W; 10 sec per tamponade
    - Heater Probe
      - 30J, 2-4 pulses per station
      - Equally effective
- Non-contact
  - APC less studied in ulcer disease
    - No difference compared to epi + heater probe in RCT

Laine et al. GIE 2008;67:502
Endoscopic Hemoclips
Bleeding ulcers

- First developed in 1975
- Olympus- Quickclip 2
- Cook- Instinct & Triclip
- Boston Scientific- Resolution
- Ovesco- Over-the-Scope Clip

Meta-analysis
Clips vs Other Endoscopic Therapy

Clips vs Heater Probe
- Favors clips
  - Recurrent bleeding
  - Emergency surgery
- Favors Heater Probe
  - Initial hemostasis

Clips vs Injection + Thermal
- Favors clips
  - Recurrent bleeding
  - Emergency surgery
- Favors Injection + Thermal
  - Initial hemostasis

Clips vs Injection
- Favors Clips
  Recurrent bleeding
  Emergency surgery
- Favors Injection
  Initial hemostasis

Yuan Y. GIE 2008;68:339
Rationale

• Results were not statistically significant
• Studies were heterogeneous
• RCT comparing clips alone with other modalities limited

Hemoclips

Situations to prefer hemoclips
  – Patients with coagulopathy or ongoing anticoagulation needs
  – Retreatment of lesions that have rebled

Difficult situations for clips
  – Lesser curve
  – Cardia
  – Posterior bulb

Yuan Y. GIE 2008;68:339
Endoscopic Hemostasis

Summary

- **Epinephrine Injection (1:10,000)**
  - Less effective than thermal or clips used when alone

- **Thermal + firm pressure**
  - Bipolar & heater probe: Equally effective
  - APC: less well studied

- **Combination: Epinephrine injection + thermal**
  - Better than epinephrine alone

- **Mechanical**
  - Clips appear to be as effective as thermal alone or combination epi + thermal


Caps in GI Bleeding

- Place target en face
- Push folds aside
- Maintain optimal field of view
- Keep correct depth of field
- Place accessory within cap
- Stabilize endoscope

Sanchez-Yague et al. GIE 2012;76:169
Caps in GI Bleeding

GAVE: APC
- Most widely studied and used treatment
- 10 case series (n=192)
- 0.5-2 L/min, 20-80W, q2=6 weeks
- About 75-86% clinical success
- Complications (mild) in 20%
- No perforations


Cappell M. Nat Rev Gastro Hep 2010;7;214
GAVE: Radiofrequency Ablation

<table>
<thead>
<tr>
<th>Treatment Surface Area</th>
<th>Electrode Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultra Long</td>
<td>520 mm² 13mm x 40mm</td>
</tr>
<tr>
<td>90 RFA</td>
<td>260 mm² 13mm x 20mm</td>
</tr>
<tr>
<td>APC</td>
<td>12 mm² n/a</td>
</tr>
</tbody>
</table>

- n = 21 pts with GAVE refractory to APC
- 18/21 (86%) transfusion independent after 6 months
- Hgb increased from 7.8 – 10.2
- Median ~ 2 treatment sessions
- 2 patients with minor acute bleeding and ulceration

McGarisk et al. GIE 2013;78:584
GAVE: Banding

- 14 patients
- EBL (9), APC (13)
- EBL 67% effective
- ETT 23% effective
- EBL fewer sessions (1.9 vs 4.7)

Wells et al. GIE 2008;68:231.

GAVE: Cryotherapy

- n = 12 patients
- 50% with complete response
- 50% partial response
- Decreased transfusion requirement 4.6 vs 1.7
- Average session time 5 minutes
- No complications

Cho et al. GIE 2008;68:895
Future Therapies

• Clotting Sprays
  – Hemospray
  – Fibrin Glue/Thrombin
  – Cyanoacrylate
• Over-the-Scope clips
• Endoluminal suturing
• Doppler guided hemostasis
• EUS-Guided angiotherapy

Hemospray

• Military Nanopowder
• Ankaferd: Turkish plant extract
  – Ganular mineral nanopowder
• Endoclot hemostatic powder
  – Privately funded Silicon Valley by surgeons and medical device experts
  – Absorbable Modified Polymers (AMP™) and a unique powder delivery system (applicator)
• TC-325 hemostatic powder- Hemospray
  – proprietary Inorganic powder
  – Hemospray powder cannot be taken in by mucosal tissues, absorption and metabolism of the powder does not occur in the body, thereby eliminating the risk of systemic toxicity
**Hemospray**

**How it works**

- **Hemospray**
- Contact with blood
  - Forms mechanical barrier
- Seals blood vessel
  - Absorbent powder increases the local concentration of clotting factors and enhances clot formation
- Clot formation
  - Powder cannot be taken in by mucosal tissues, thereby eliminating the risk of systemic toxicity
Hemospray Delivery System

- Syringe containing the Hemospray powder
- CO2 cannister
- Delivery catheter that is inserted into the working channel of the endoscope

Hemospray for Bleeding Ulcers
Prospective Trial

- Refractory bleeding ulcers
- n = 20
- Hemostasis: 19/20 (95%)
  - 1 patient had a pseudo-aneurysm requiring arterial embolization
- Recurrent bleeding 2 patients
  - Neither had active bleeding identified at the 72-hour endoscopy.
- No mortality, major adverse events, or treatment or procedure-related serious adverse events were reported during 30-day follow-up.

Hemospray for Bleeding Ulcers
Sung et al. Endoscopy 2011

- Tip of endoscope 1-2 cm from bleeding site
- Applied in 1-2 second spray bursts
- A- Bleeding gastric ulcer
- B- Catheter in place
- C- s/p hemospray tx
- D- after 3 days, ulcer base with flat pigment

Hemospray for Cancer-Related Bleeding
Chen et al. GIE 2012;75:1278

- Case series
- n = 5
- Hemostasis in all
- Rebleeding in 1 (had DIC)
Hemospray in Cancer-Related Bleeding
LeBlanc et al. GIE 2013;78:172

- n = 5
- Esophageal (2), Gastric (2), Pancreas (1)
- Hemostasis in all
- Rebleeding in 2
- Rebleeding in 1 after retreatment

- A- Bleeding gastric stromal tumor
- B- S/P Hemospray

Hemospray in Post-Therapeutic Bleeding
LeBlanc et al. GIE 2013;78:172

- n = 12
- EMR (9), Ampullectomy (2), Sphincterotomy (1)
- Hemostasis in all
- No rebleeding

- A- S/P EMR
- B- S/P Hemospray
- C- s/p ampullary resection
- D- s/p hemospray
Hemospray
Pros and Cons

• Pros
  – Non-contact
  – Simple to use
  – Covers large area

• Cons
  – Moisture can plug catheter tip
  – Loss of view after application
  – Must wash off coating for further treatment

Hemospray
Safety

• No complications reported

• Theoretical risk of CO2 gas embolization
  (low pressure venous system)

• Theoretical risk of local tissue and vascular injury
Topical Fibrin Glue and Topical Thrombin

- Fibrinogen with Factor XIII plus Human Thrombin forms clot
- Deliver through double-lumen catheter with double plunger syringe
- Not adequately studied for bleeding

Cyanoacrylate Spray
GI bleeding

- n = 6
- DU (3), Vascular ectasia (1)
- Post polypectomy (1)
- Hemostasis in all
- Rebleeding in 2
- No adverse events

- A- bleeding DU, s/p bipolar
- B- s/p hemoclip
- C- s/p cyanoacrylate

Bhat et al. GIE 2013;78:209,
Sukhpreet et al. GIE 2013;78:538
Over-the-Scope Clips

**“Bear-Claw” Type**

**“Padlock” Type**

Applicator cap on tip of scope with hand wheel to release clip

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**Over-the-Scope Clip Designs**

<table>
<thead>
<tr>
<th>OTSC Feature</th>
<th>Relevance</th>
<th>Cap size (Scope Size)</th>
<th>11mm</th>
<th>12mm</th>
<th>14mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cap size</td>
<td>Scope Size</td>
<td>11mm</td>
<td>12mm</td>
<td>14mm</td>
<td></td>
</tr>
<tr>
<td>Cap depth</td>
<td>Depth of tissue</td>
<td>3mm</td>
<td>6mm</td>
<td>3mm</td>
<td>6mm</td>
</tr>
<tr>
<td>Shape of Teeth</td>
<td></td>
<td>3mm</td>
<td>6mm</td>
<td>3mm</td>
<td>6mm</td>
</tr>
<tr>
<td>Rounded</td>
<td>Hemostasis</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Pointed</td>
<td>Perforation/ fistula</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Long pointed</td>
<td>Gastric perforation/ fistula</td>
<td>no</td>
<td>Only 6mm</td>
<td>no</td>
<td></td>
</tr>
</tbody>
</table>

Banerjee et al. GIE 2012;76:244
Over-the-Scope Clips

Over-the-Scope Clips in Acute GI Bleeding

- Compared Quickclip2, Resolution clip and OTSC in porcine model
- OTSC required:
  - Fewer clips to achieve hemostasis
  - Less time to achieve hemostasis

Kato M et al. GIE 2012;75:3
**Over-the-Scope Clip**

**Ulcer Bleeding**

- n = 7
- All prior failures
- Hemostasis in all
- 3/7 had recurrent bleeding
- One perforation

Gastric ulcer at angulus

Albert J et al. GIE 2011;74:390

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**Over-the-Scope Clip**

**GI Bleeding**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>n</th>
<th>Hemostasis</th>
<th>Rebleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal Ulcer</td>
<td>12</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Gastric Ulcer</td>
<td>6</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Mallory-Weiss Tear</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Dieulafoy</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Surgical anastomosis</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

- n = 30, 6 centers
- All prior endo failures
- Hemostasis=96%
- 2 rebleeds (6%)
  - Tx’ed with injection
- No complications

Manta et al. Surg Endos. 2013
Over-the-Scope Clips
US Initial Experience

- For GI bleeding
  - n = 7 reported
  - All prior failures
  - Hemostasis in all

Baron et al. GIE 2012;76:202

Over-the-Scope Clip
US Initial Experience

<table>
<thead>
<tr>
<th>Complication</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications in leak group</td>
<td>Generally safe</td>
</tr>
<tr>
<td>Bowel closure in 2 pts</td>
<td></td>
</tr>
<tr>
<td>Perforation in 1</td>
<td></td>
</tr>
</tbody>
</table>

Baron et al. GIE 2012;76:202
Over-the-Scope Clip
Pros and Cons

- **Pros**
  - Entraps large amount of tissue
  - Band ligation technique

- **Cons**
  - Withdraw scope to mount OTSC
  - Endoscopic view impaired
  - Suction traps fluid in cap
  - Limited scope angulation with cap

Endoluminal Suturing
“Eagle Claw”

- **Pros**
  - Close large defects

- **Cons**
  - Double channel gastroscope
  - Withdraw endoscope to mount device
  - Training needed
  - Cost
Endoscopic Doppler Ultrasound in GI Bleeding

<table>
<thead>
<tr>
<th></th>
<th>+ Doppler before endo tx (n)</th>
<th>+ Doppler after initial endo tx (n)</th>
<th>+ Doppler after initial endo tx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spurting</td>
<td>3</td>
<td>2</td>
<td>66.7</td>
</tr>
<tr>
<td>NBVV</td>
<td>19</td>
<td>7</td>
<td>36.8</td>
</tr>
<tr>
<td>Adherent clot</td>
<td>7</td>
<td>1</td>
<td>14.2</td>
</tr>
<tr>
<td>Flat spot</td>
<td>5</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Oozing</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>11</td>
<td>28.9</td>
</tr>
</tbody>
</table>

Initial Endo tx: epi (1:20,000) and/or MPEC
Additional Endo tx: MPEC and/or clip

Jensen D et al. GIE 2010;71:AB113

Endoscopic Doppler Ultrasound in GI Bleeding

<table>
<thead>
<tr>
<th></th>
<th>30 day Rebleed rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 matched controls with SRH without doppler, Endo tx by visual cues</td>
<td>28 %</td>
</tr>
<tr>
<td>38 pts with + doppler with endo tx until eradication of doppler signal</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

Jensen D et al. GIE 2010;71:AB113
EUS-Guided Angiotherapy for GI Bleeding

• EUS identify bleeding vessel
• Fine needle injection
  – Sclerosants
  – Cyanoacrylate

Small series of 5
Severe refractory bleeding
EUS-guided alcohol or cyanoacrylate injection
  – Pancreatic pseudoaneurysm,
  – Duodenal Dieulafoy
  – Duodenal ulcer
  – GI stromal tumors
Hemostasis in all
No complications

EUS-Guided Angiotherapy for GI Bleeding
Limitations

- Intraluminal blood clots
  - interfere with identification of the bleeding source
  - Interfere with EUS transmission
- Cause extraluminal bleeding
  - May need salvage angiographic or surgical intervention
- Logistics
  - Scope availability
  - Technically challenging
  - Special expertise
- Glue damage of scope

Song et al. GIE 2012;75:933

Soft Coagulation Hemostatic Forceps

- 50 Watts, 2-3 seconds

Saltzman et al. GIE 2010;72:796
**Soft Coagulation Hemostatic Forceps**

**Bleeding Ulcers**

<table>
<thead>
<tr>
<th></th>
<th>Soft Coagulation</th>
<th>Clips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemostasis</td>
<td>85%</td>
<td>79%</td>
</tr>
<tr>
<td>Recurrent Bleeding</td>
<td>2%</td>
<td>10%</td>
</tr>
</tbody>
</table>

96 patients

**J Gastro 2010;45:501**

<table>
<thead>
<tr>
<th></th>
<th>Soft Coagulation Hemostatic Forceps</th>
<th>Heater Probe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemostasis</td>
<td>67%</td>
<td>67%</td>
</tr>
<tr>
<td>Rebleeding</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Perforation</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Need for surgery</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

111 patients

**Okazaki et al. Gastroenterology 2013;144S-511**

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**Endoscopic Hemostasis in Nonvariceal Bleeding**

**Summary**

- Thermal alone, Clips alone, or Combination Epi + Clips/Thermal: effective
- Don’t use epi alone
- Clips popular but expensive
- APC for GAVE
- Future methods:
  - Hemospray promising
  - Doppler US promising