

**EVALUATION AND
MANAGEMENT OF
UPPER GI BLEEDING**

**ASSESS RISK OF
PATIENT WITH UGIB**

**PRE-ENDOSCOPIC INDEPENDENT
RISK FACTORS IN UGI BLEEDING**

Assessment in 74 U.K. Hospitals, 15.5 million people in 1993

- Vital signs
 - HR \geq 100, Systolic BP \leq 100
- Age
 - 60-79, \geq 80
- Comorbidities

Rockall et al. Gut 1996;38:316

MEDICAL THERAPY BEFORE ENDOSCOPY?

PRE-ENDOSCOPIC MEDICAL THERAPY

- Erythromycin to improve visibility
 - Greater proportion of mucosa visualized
 - No significant increase in diagnoses made at 1st EGD or decrease in 2nd EGDs

Gastro 2002;123:17; AJG 2006;101:1211; GIE 2002;56:174; NEJM 2007;356:1631; Lancet 1995;346:865; Lancet 1997;350:1495; Cochrane, 2005.

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 - No change in any clinical outcome

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- Octreotide for possible variceal bleeding
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- Antibiotics for cirrhotics with GI bleeding
 - Significantly reduces infection and mortality

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MANAGEMENT OF BLEEDING ULCERS

**STANDARD ENDOSCOPIC THERAPIES
 FOR ULCER BLEEDING**

- Bipolar Electrocoagulation
- Heater Probe
- Injection
 - Epinephrine
 - Sclerosant (e.g., polidocanol, ethanol)
 - Thrombin, fibrin glue (fibrinogen + thrombin)
- Clips

**CRITERIA FOR ENDOSCOPIC
 HEMOSTATIC THERAPY**

Inclusion Criteria for RCTs of Endoscopic Therapy

- Overt UGIB
- High-risk endoscopic features
 - Active bleeding
 - Nonbleeding visible vessel
 - ??Adherent clot

**FURTHER BLEEDING AFTER ENDOSCOPIC THERAPY:
 RELATION TO STIGMATA OF HEMORRHAGE**

Meta-Analysis of RCTs of Endoscopic Therapy vs. No Endoscopic Therapy

| | RR (95% CI) | NNT (95% CI) |
|-----------------------------|----------------|--------------|
| Active bleeding | 0.3 (0.2-0.4) | 2 (2-2) |
| Non-bleeding visible vessel | 0.5 (0.4-0.6) | 5 (4-6) |
| Clot | 0.3 (0.1-1.8)* | ----- |

* Statistical heterogeneity

Laine, McQuaid. CGH 2009;7:33.

APPROACH TO ULCERS WITH CLOTS

- Vigorous irrigation may expose high-risk stigmata, and remove most of patients who would have bled
- If rebleeding rate with clots is high (e.g., elderly with multiple comorbidities), endoscopic therapy may be beneficial
- PPI alone may be sufficient
 - “Intensive” PPI alone: no rebleeding in RCTs from Hong Kong (N=24), Kashmir (N=64)

Laine et al. GI Endo 1996;43:107; Bleau et al GI Endo 2002;56:1; Jensen et al. Gastro 2002;123:407; Sung et al. AIM 2003;139:237; Khuroo et al. NEJM 1997;336:1054

DUAL THERAPY VS. MONOTHERAPY FOR BLEEDING ULCERS

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- Epinephrine followed by 2nd modality is significantly better than epinephrine alone

Gastro 2004;126:441; Gut 1999;44:715; GIE 2004;60:910; Gastro 2003;125:396;GIE 2002;55:466; 1999;49:13; AJG 2003;98:2198; International Consensus Conference on NVUGIB, 2008

DUAL THERAPY VS. MONOTHERAPY FOR BLEEDING ULCERS

- Epinephrine followed by 2nd modality is significantly better than epinephrine alone
- Thermal, sclerosant, clips can be used alone
 - Uncertain if thermal plus injection therapy is better than thermal monotherapy
 - Clips plus injection therapy not documented to be better than clips alone
 - No studies assess epinephrine followed by clips

Gastro 2004;126:441; Gut 1999;44:715; GIE 2004;60:910; Gastro 2003;125:396;GIE 2002;55:466; 1999;49:13; AJG 2003;98:2198; International Consensus Conference on NVUGIB, 2008

ANTISECRETORY THERAPY AFTER ENDOSCOPIC HEMOSTASIS

ANTISECRETORY THERAPY FOR TREATMENT OF BLEEDING ULCERS

Hypothesis

- Clot formation and stability require pH of 6-7
 - Based on experimental studies of platelet aggregation, PT/PTT
- Bolus + constant infusion IV PPIs reported to maintain pH > 6 for majority of 24-hr period
 - PPI half-life very short (e.g., 1 hr)
 - Constant infusion so PPI continuously present to inhibit any newly activated pumps

Green et al. Gastro 1978;74:38; LaBenz et al Gut;1997;40:36

Symposium C: New Insights on the Evaluation and Management of GI Bleeding: Upper GI

REBLEEDING WITH BOLUS/INFUSION IV PPI AFTER ENDOSCOPIC THERAPY FOR HIGH-RISK ULCERS
 Meta-Analysis of 4 RCTs of IV PPI vs. Placebo or No Rx

| | RR (95% CI) | NNT (95% CI) |
|---------------------|-----------------|---------------|
| Further bleeding | 0.4 (0.3 - 0.6) | 12 (10 - 18) |
| Surgery | 0.4 (0.2 - 0.8) | 28 (21 - 67) |
| Urgent intervention | 0.3 (0.2 - 0.5) | 8 (7 - 12) |
| Mortality | 0.4 (0.2 - 0.8) | 45 (33 - 167) |

Laine, McQuaid. CGH 2009;7:33

ANTISECRETORY THERAPY FOR TREATMENT OF BLEEDING ULCERS
 Will Intermittent PPI Therapy Work?

- Is pH > 4 - 5 is sufficient?
 - Based on experimental studies on pepsin-induced clot lysis and platelet disaggregation
- Can frequent dosing achieve effect similar to continuous IV infusion

Patchett et al. Gut ;1989;30:1704

REBLEEDING WITH INTERMITTENT PPI AFTER ENDOSCOPIC THERAPY FOR HIGH-RISK ULCERS
 Meta-Analysis of 5 RCTs of Intermittent IV or PO PPI vs. Placebo or No Rx

| | RR (95% CI) | NNT (95% CI) |
|---------------------|-----------------|--------------|
| Further bleeding | 0.5 (0.4 - 0.8) | 10 (7 - 21) |
| Surgery | 0.6 (0.3 - 1.5) | ----- |
| Urgent intervention | 0.4 (0.1 - 1.6) | ----- |
| Mortality | 0.6 (0.2 - 2.0) | ----- |

Laine, McQuaid. CGH 2009;7:33

BOLUS + CONSTANT INFUSION IV PPI VS. INTERMITTENT PPI
Further Bleeding after Endoscopic Therapy

| | Infusion | Intermittent |
|--------------------------|----------|--------------|
| <i>Intermittent IV</i> | | |
| Hung (N=103) | 4% | 4% |
| Andriulli (N=474) | 12% | 8% |
| <i>Intermittent oral</i> | | |
| Jang (N=40) | 10% | 0 |
| Kim (N=45) | 5% | 4% |

Laine, McQuaid CGH 2009;7:33; Andriulli et al. AJG 2008;103:3011

ANTISECRETORY THERAPY FOR TREATMENT OF BLEEDING ULCERS
Will Intermittent Oral (or IV) PPIs Work?

- Clinical trial data used to guide decisions
 - Most consistent for IV PPI bolus/infusion
- Initial data on intermittent PPI encouraging

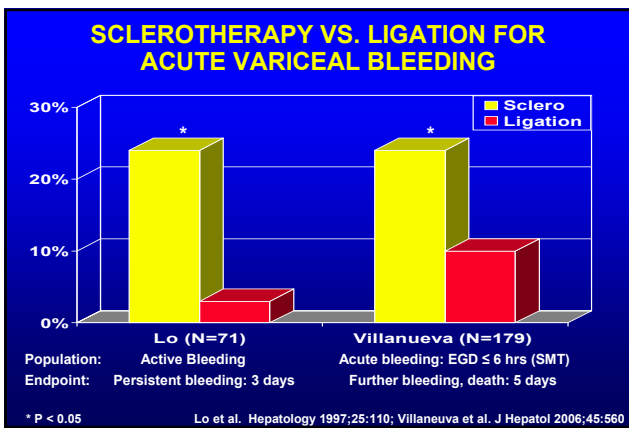
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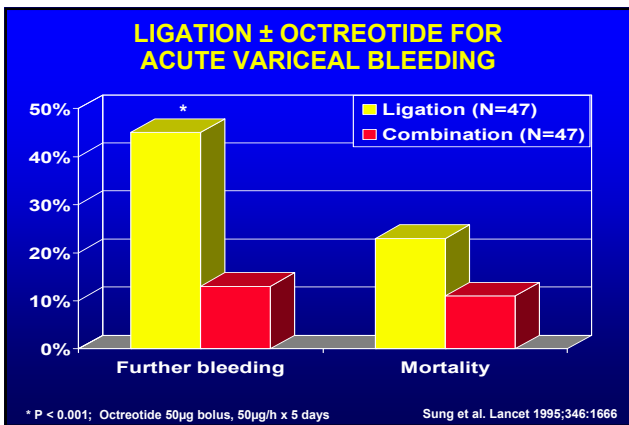
MANAGEMENT OF VARICEAL BLEEDING

MANAGEMENT OF ESOPHAGEAL VARICEAL BLEEDING

- Acute Bleeding Episode
 - Ligation
 - Vasoactive medication (e.g., octreotide)
 - Antibiotics
- Prevention of Recurrent Bleeding
 - Ligation
 - Medical therapy
 - Beta-blocker
 - ?Other medications (e.g., nitrates, carvedilol)

Garcia-Tsao et al. Hepatology 2008;47:1764



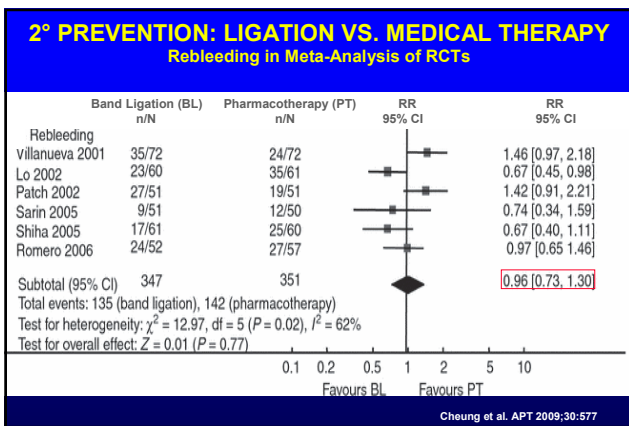


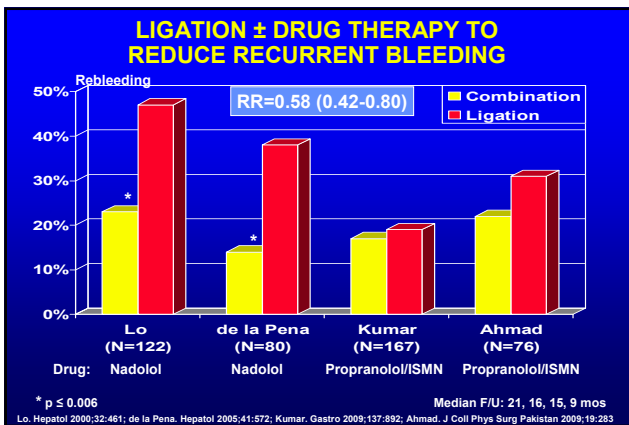
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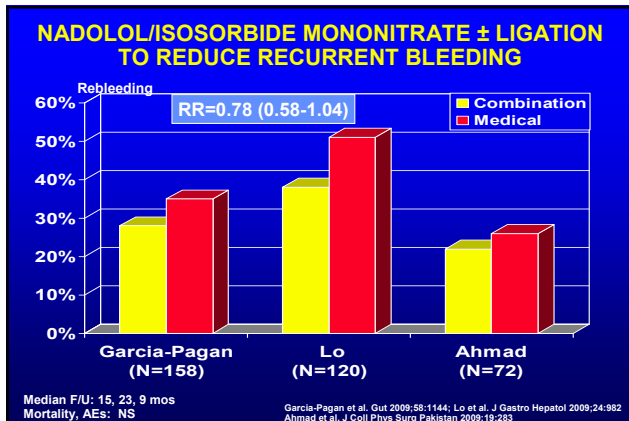
LIGATION VS. SCLEROTHERAPY Meta-Analysis of 7 Trials (N=547)

| | OR (95% CI) |
|-----------------------------|-------------------------|
| Rebleeding | 0.5 (0.4 - 0.7) |
| Due to varices | 0.5 (0.3 - 0.8) |
| Due to Rx-induced ulcers | 0.6 (0.3 - 1.1) |
| Mortality | 0.7 (0.5 - 0.98) |
| Esophageal stricture | 0.1 (0.03 - 0.3) |

6/7 trials required fewer treatment sessions with ligation to achieve variceal obliteration
Laine, Cook. AIM 1995;123:280







FAILURE OF ENDOSCOPIC AND MEDICAL THERAPY FOR VARICEAL BLEEDING

PERSISTENT OR RECURRENT BLEEDING DESPITE ENDOSCOPIC AND MEDICAL THERAPY

- More severe liver disease
 - TIPS*
- Well-compensated liver disease
 - TIPS* vs. surgical decompression

*PTFE-coated preferred to decrease shunt dysfunction, recurrent bleeding

DISTAL SPLENORENAL SHUNT VS. TIPS FOR REFRACTORY VARICEAL BLEEDING
RCT in Child-Pugh Class A/B Cirrhotics

| | DSRS (N=74) | TIPS (N=67) |
|------------------------|-------------|-------------|
| Variceal rebleeding | 5% | 10% |
| Encephalopathy | 49% | 51% |
| Mortality (2 yr; 5 yr) | 19%; 38% | 12%; 39% |
| Transplantation | 8% | 12% |
| Reintervention | 11% | 82%* |

57% Child-Pugh Class A; 44 vs. 48 mo f/u
* p < 0.001
Henderson et al. Gastro 2006;130:1643

- APPROACH TO PATIENT WITH MAJOR ULCER BLEEDING**
- Endoscopic therapy (repeat for rebleed)
 - BPEC, heater probe, injection, or clip
 - Do not use epinephrine alone
 - Constant infusion IV PPI
 - ?Intermittent oral or IV
 - Treat patients with
 - Active bleeding
 - Non-bleeding visible vessel
 - ?Adherent clot (? PPI alone)

- APPROACH TO PATIENT WITH VARICEAL BLEEDING**
- Endoscopic treatment with ligation
 - Octreotide infusion for 2-5 days
 - Long-term ligation to eradicate varices
 - Long-term β -blockers
 - TIPS if failure of medical/endoscopic therapy
 - Consider surgical decompression if well-compensated cirrhosis
