Inpatient Management of GI Bleeding

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Faculty disclosure:

I am a consultant for Boston Scientific and Medtronic, which manufacture devices used in evaluation and treatment of GI bleeding

Agenda

1. Initial resuscitation strategy in GI bleeding

2. Review medical management of upper GI bleeding prior to EGD:
   A. NG tubes, yay or nay?
   B. PPI dosing
   C. Brief mention re: scoring systems
   D. Even briefer mention of liver/variceal management

3. Review management of LGIB, including:
   A. Urgent colonoscopy
   B. Tagged RBC/angio
   C. Segmental colectomy

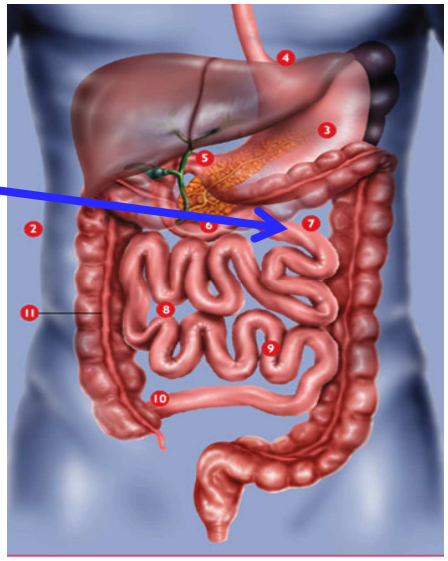
4. Small bowel bleeding- (Exactly one slide)
5. Bonus topics: Anticoagulation decisions, H.pylori eradication, PPI

Before we continue… 5 important definitions:

1.Upper GI bleeding: arising from above the Ligament of Treitz

2. Lower GI bleeding: arising from the colon

(*Midgut' bleeding or 'deep small bowel' bleeding = varying definitions)



Before we continue… 5 important definitions:

3. Overt GI bleeding
   melena, hematochezia, hematemesis….

4. Occult GI bleeding
   guaiac positive stool only

5. Obscure GI bleeding (aka 'suspected small bowel bleeding')
   recurrent bleeding from unknown source despite
   negative EGD/colonoscopy/capsule

"obscure, overt bleeding…"
"obscure, occult bleeding…"

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Resuscitation Strategies for GIB

68 y.o. male presents to ED with 3 episodes of hematochezia. BP 70/30 → 80/50 after 2L NS. Hgb 8.5 HCT 26, coags normal. Sent to ICU with 1U PRBC hanging and two 20g IVs. One additional large episode of hematochezia upon arrival to ICU.

Which of the following is NOT an appropriate next step in this patient's management?

1. Insertion of additional 16-18g IV catheters
2. Insertion of a TLC central line
3. Insertion of a cordis/trauma line
4. NG lavage
5. Two additional units PRBC

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Volume Resuscitation & IV Flow Rate:

22 gauge angiocath: 35 ml/min
20 gauge angiocath:
18 gauge angiocath:
16 gauge angiocath:
14 gauge angiocath:
Triple lumen central line:
Cordis/trauma line:

*Source: Cornell MICU Manual

Volume Resuscitation & IV Flow Rate:

22 gauge angiocath: 35 ml/min

20 gauge angiocath: 60 ml/min

18 gauge angiocath: 105 ml/min

16 gauge angiocath: 205 ml/min

14 gauge angiocath: 333 ml/min

Triple lumen central line:

Cordis/trauma line:

*Source: Cornell MICU Manual

Volume Resuscitation & IV Flow Rate:

22 gauge angiocath: 35 ml/min

20 gauge angiocath: 60 ml/min

Triple lumen central line: 68 ml/min (34ml/min + 2 x 17 ml/min)

18 gauge angiocath: 105 ml/min

16 gauge angiocath: 205 ml/min

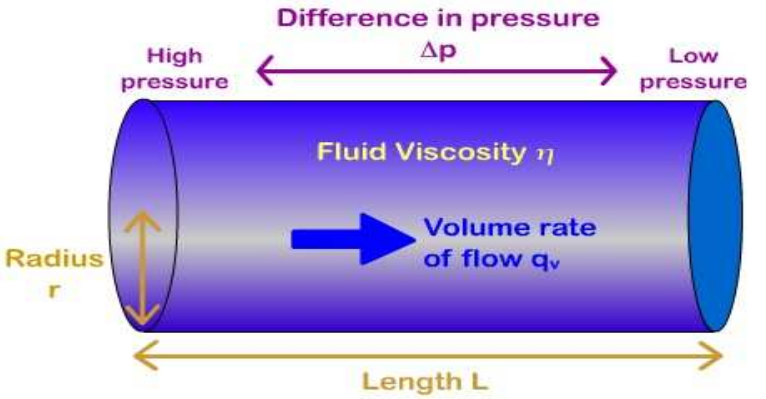
14 gauge angiocath: 333 ml/min

Cordis/trauma line: >1000ml/min

FASTER FLOW

*Source: Cornell MICU Manual

Science Section of Slide



$$\text{Blood Flow} = \frac{\Delta P\ r^4\ \pi}{\eta\ L\ (8)}$$

Δ = Change
P = Pressure
r = Radius of vessel
π = constant (3.14)
η = Viscosity of blood
L = Vessel length

Poiseuille's law [pwah-zweez]

Doctor Section of Slide

wide catheter =

much faster infusion

long catheter =

slower infusion

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

Càndid Villanueva, M.D., Alan Colomo, M.D., Alba Bosch, M.D., Mar Concepción, M.D., Virginia Hernandez-Gea, M.D., Carles Aracil, M.D., Isabel Graupera, M.D., María Poca, M.D., Cristina Alvarez-Urturi, M.D., Jordi Gordillo, M.D., Carlos Guarner-Argente, M.D., Miquel Santaló, M.D., Eduardo Muñiz, M.D., and Carlos Guarner, M.D.

921 patients with acute upper GIB randomized to:

restrictive transfusion strategy (Hgb target >7)

vs.

liberal transfusion strategy (Hgb target >9)

- all patients underwent EGD within 6 hours
- included both cirrhotic patients and peptic ulcer patients

NEJM January 2013

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

Càndid Villanueva, M.D., Alan Colomo, M.D., Alba Bosch, M.D., Mar Concepción, M.D., Virginia Hernandez-Gea, M.D., Carles Aracil, M.D., Isabel Graupera, M.D., María Poca, M.D., Cristina Alvarez-Urturi, M.D., Jordi Gordillo, M.D., Carlos Guarner-Argente, M.D., Miquel Santaló, M.D., Eduardo Muñiz, M.D., and Carlos Guarner, M.D.

Summary:

- Restrictive transfusion → lower overall mortality (5% vs. 10%) and lower risk of rebleeding (10% vs. 16%)
- Mortality benefit largest for cirrhotic patients, but also present in PUD

Limitations:

- hypovolemic shock subgroup not analyzed separately
- excluded patients with "exsanguinating bleed requiring transfusion" (i.e. best strategy for rapid bleed is rapid resuscitation- don't wait for CBC!)

NEJM January 2013

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

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The practical summary:

1. Ignore these thresholds in a 'rapid exsanguinating bleed' – these patients were excluded from the study. Blood out → blood in.

2. For the 'more stable' bleeder (in whom you actually have time to monitor labs!)- transfusing more conservatively may be beneficial.

NEJM January 2013

Upper GI Bleeding

Upper GI Bleeding

Differential Diagnosis

Common

gastric/duodenal ulcer, esophageal varices, Mallory-Weiss tear, gastritis/erosions, esophagitis, anastamotic ulcers

Less common

Cameron lesions, Dieulafoy lesions, gastric varices, GAVE, neoplasms

Rare

esophageal ulcer, aorto-enteric fistula, hemobilia, pancreatic bleeding, upper GI Crohn's disease

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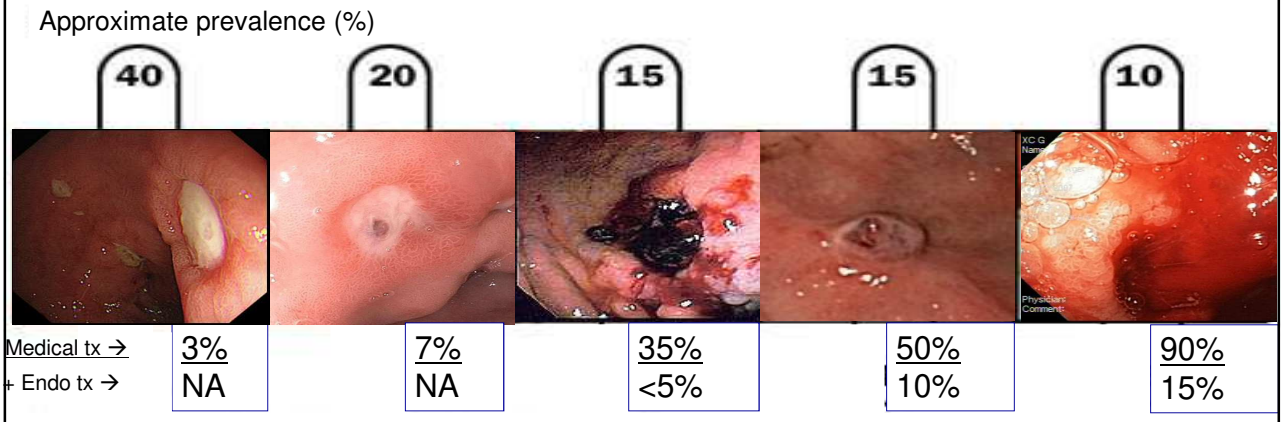
Ulcer appearance and risk of re-bleeding

"Clean based"



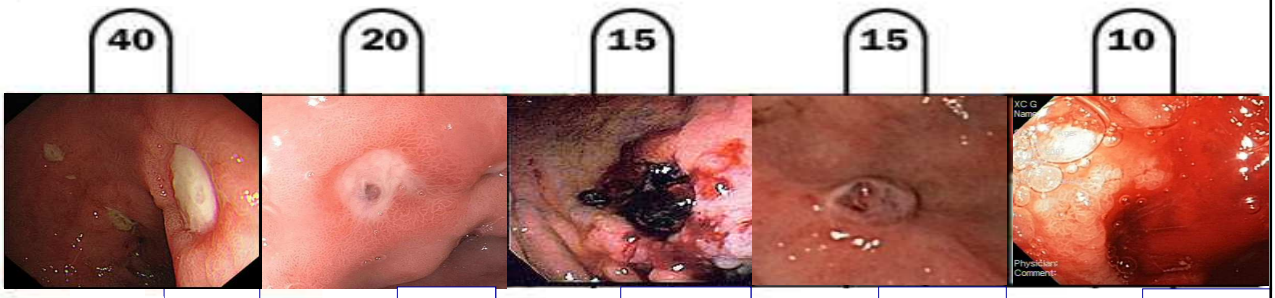
Rebleeding risk (with medical tx alone vs. + endo)

Forrest et al. Lancet 1974
Kovacs et al. Curr Treatment Gastro 2007

Ulcer appearance and risk of re-bleeding

"Pigmented spot"

Approximate prevalence (%)



Medical tx →	3%	7%	35%	50%	90%
+ Endo tx →	NA	NA	<5%	10%	15%

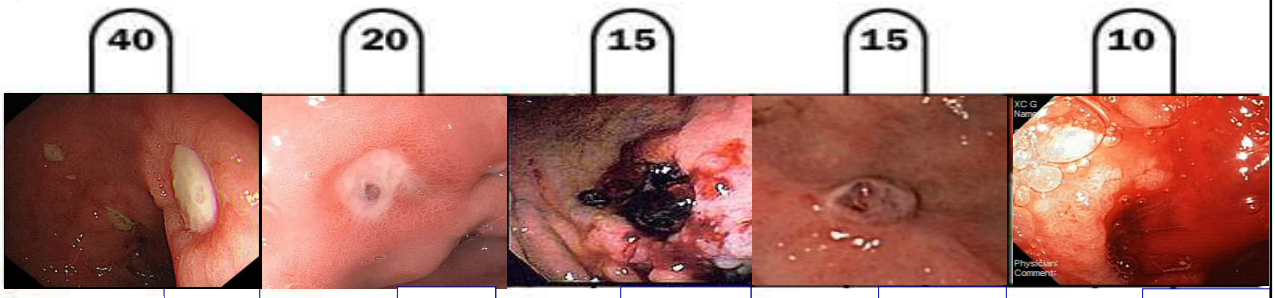
Rebleeding risk (with medical tx alone vs. + endo)

Forrest et al. Lancet 1974
Kovacs et al. Curr Treatment Gastro 2007

Ulcer appearance and risk of re-bleeding

"Adherent clot"

Approximate prevalence (%)



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Rebleeding risk (with medical tx alone vs. + endo)

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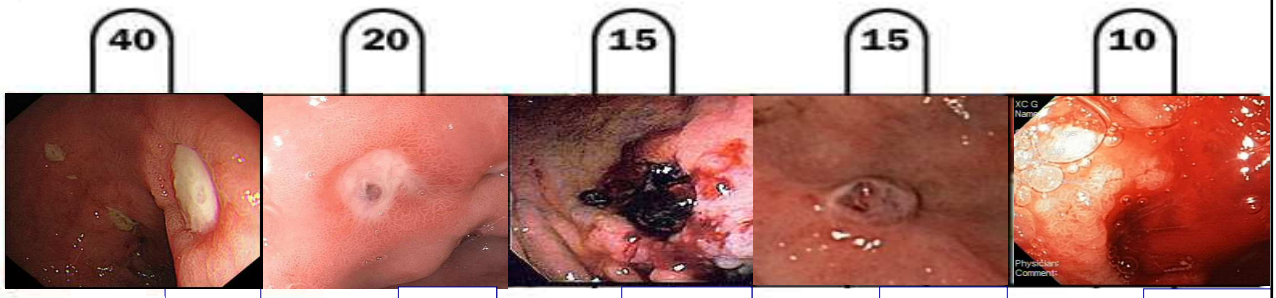
Ulcer appearance and risk of re-bleeding

"Visible vessel"

Approximate prevalence (%)



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Rebleeding risk (with medical tx alone vs. + endo)

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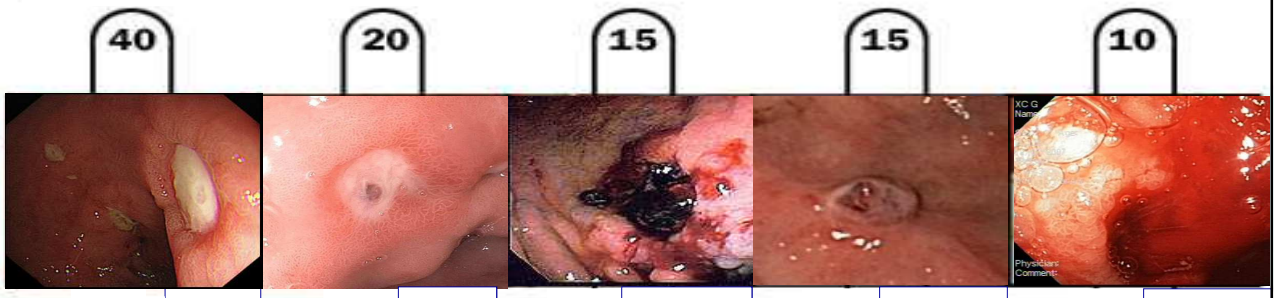
Ulcer appearance and risk of re-bleeding

"Active bleeding"

Approximate prevalence (%)



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Rebleeding risk (with medical tx alone vs. + endo)

Forrest et al. Lancet 1974
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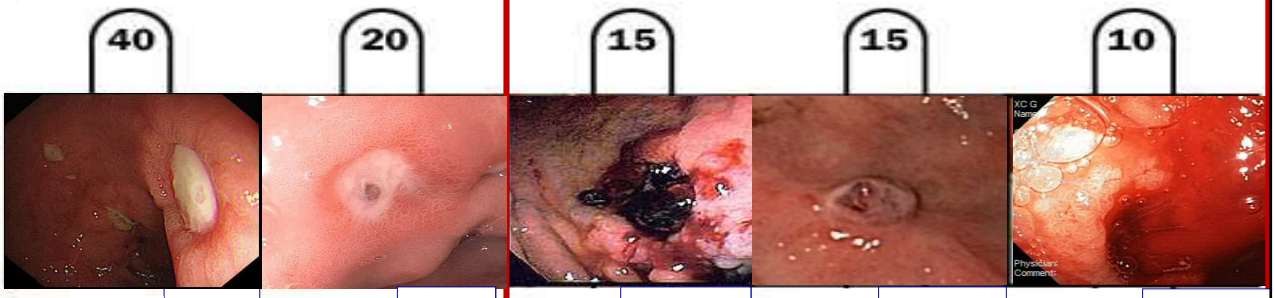
Ulcer appearance and risk of re-bleeding

Endoscopic therapy space

Approximate prevalence (%)



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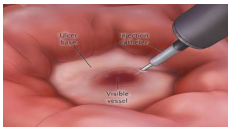
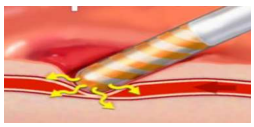
Endoscopic hemostasis techniques and tools

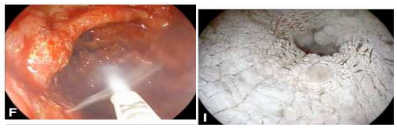


1. Injection/local vasoconstriction (temporary)

2. Clip closure of ulcer/vessel (definitive)



3. Thermal coagulation (definitive)



4. Hemospray (salvage)

Upper GI Bleeding

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Less common
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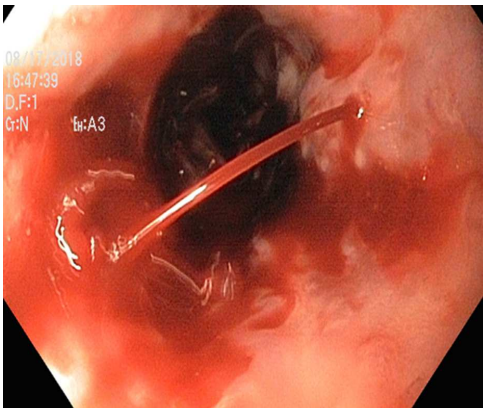
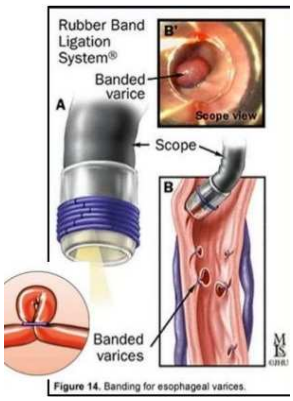
Esophageal Varices

Bleeding varix



Endoscopic banding/ligation of varices



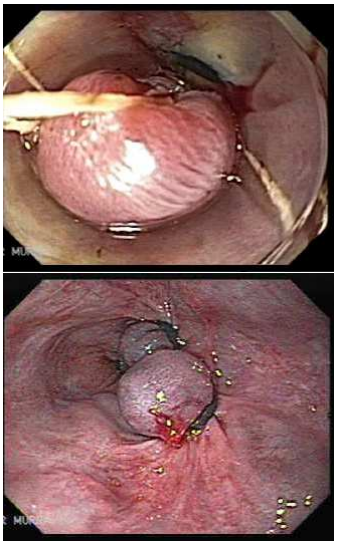
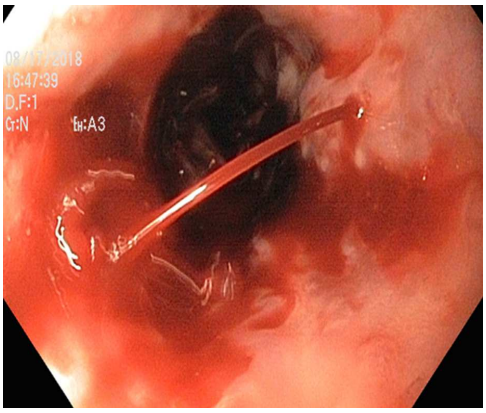


Image sources: gastrointestinalatlas.com, Boregowda et al WJGPT 2019

Esophageal Varices

Bleeding varix



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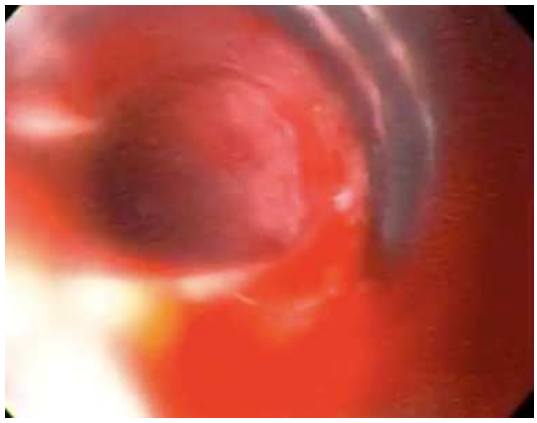

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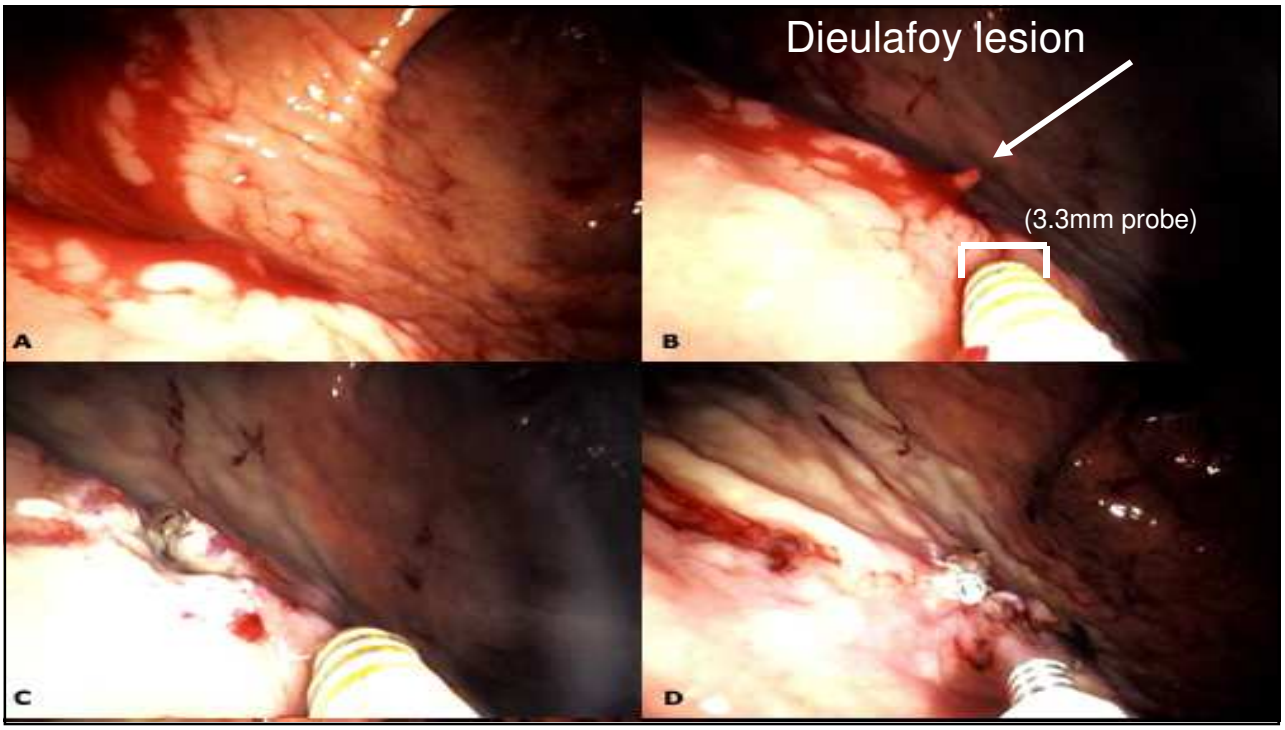
Mallory-Weiss Tear

(GE junction, view from esophagus)

Cameron Lesion (hiatal hernia)

(GE junction, view from stomach, retroflexed)



62 y.o. male presents to the ED with 6 episodes of melena. He feels lightheaded and appears pale. Blood pressure is 110/60 and HR is 115. HCT 22, platelets and coags normal. Sent to ICU with 2U PRBC hanging.

NG lavage reveals fresh red blood. A large bore central line is placed, after which the patient has an additional large episode of hematemesis.

Which of the following is NOT an appropriate next step.

1. Urgent upper endoscopy
2. Intubation for airway protection prior to EGD
3. IV pantoprazole 40mg bolus
4. 250mg IV erythromycin
5. 1g IV ceftriaxone

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5. **~~1g IV ceftriaxone~~**

How to rule-out possibility of variceal bleeding (aka decompensated cirrhosis) in 2 steps:

Step 1: Look at platelet count and INR

There isn't really a step 2. If PLT and INR are normal, then your patient doesn't have decompensated cirrhosis.

Upper GI Bleeding Management

<u>Initial approach</u>
Treat as peptic ulcer disease unless strong evidence otherwise

1) Resuscitation, triage.
2) IV or oral PPI
3) ? NG tube
4) 'Early' upper endoscopy
5) Scoring systems
6) Last ditch options: angio embolization > surgery

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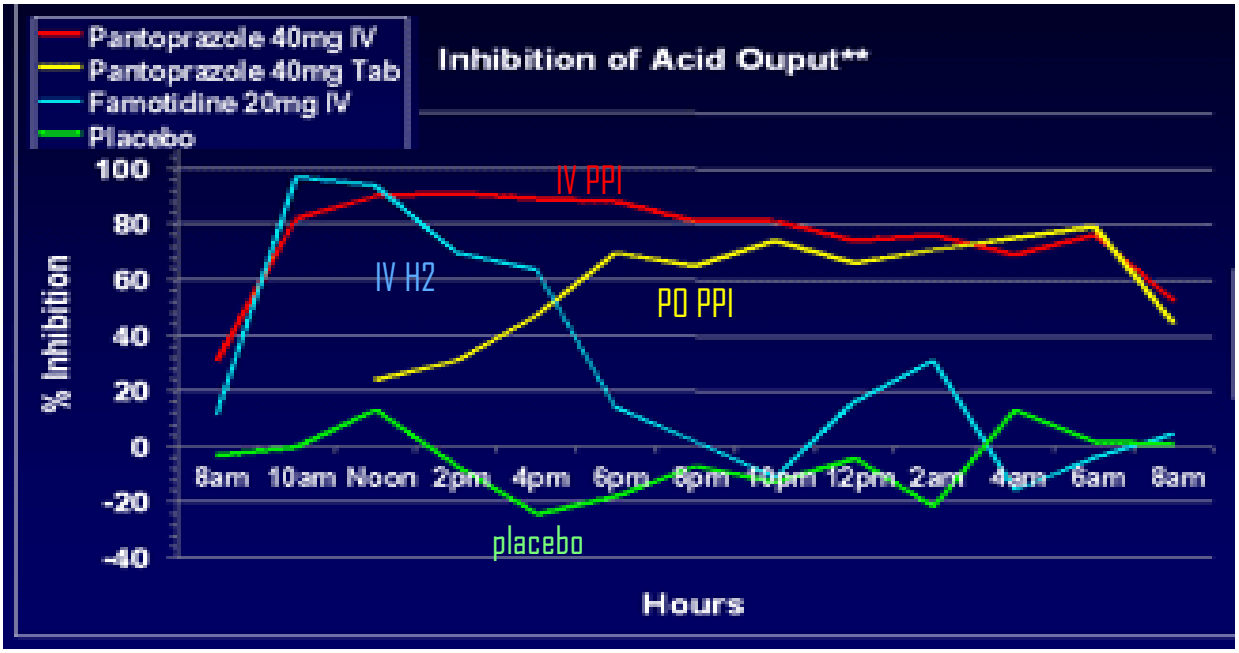
Physiologic Goals of Medical Therapy of Bleeding Ulcer

- pH>4 Prevents pepsin activation and reduces proteolytic degradation of clots
  (Good!)

- pH>6 Clot stabilization via improved platelet aggregation
  (Even Better!)



EFFECT OF INTRAVENOUS OMEPRAZOLE ON RECURRENT BLEEDING AFTER ENDOSCOPIC TREATMENT OF BLEEDING PEPTIC ULCERS

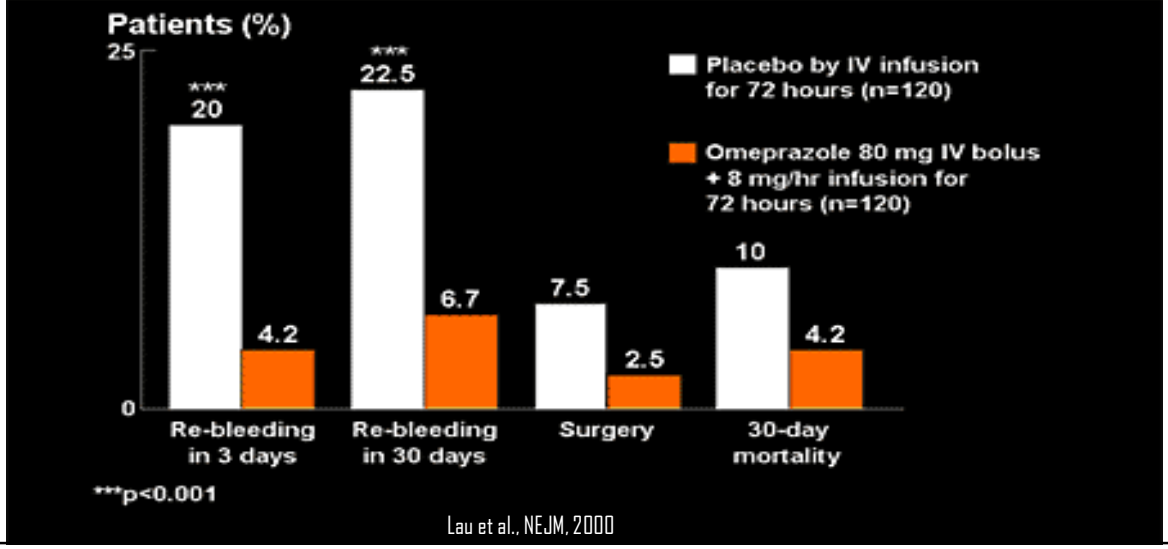
JAMES Y.W. LAU, M.B., B.S., JOSEPH J.Y. SUNG, M.D., KENNETH K.C. LEE, PH.D., MAN-YEE YUNG, B.N., SIMON K.H. WONG, M.B., CH.B., JUSTIN C.Y. WU, M.B., CH.B., FRANCIS K.L. CHAN, M.D.,

RCT : IV omeprazole (80mg x 1 + 8mg/hr gtt) vs placebo AFTER endoscopy

240 patients with endoscopic evidence of active or recent ulcer bleeding

NEJM August 2000

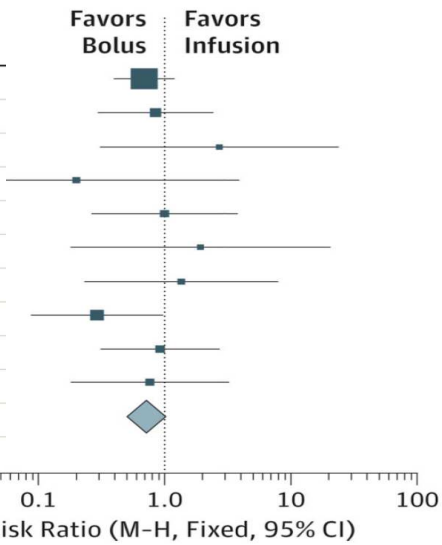
Randomized, placebo-controlled study of high dose IV omeprazole infusion in bleeding peptic ulcer



Lau et al., NEJM, 2000

Clinical equivalence between PPI bolus and infusion strategies

Source	Intermittent Bolus, No. Events	Total	Continuous Infusion, No. Events	Total
Andriulli et al,[14] 2008	19	239	28	243
Chen et al,[16] 2012	6	101	7	100
Choi et al,[17] 2009	3	21	1	19
Jang et al,[24] 2006	0	19	2	19
Javid et al,[20] 2009	4	53	4	53
Kim et al,[21] 2012	2	54	1	52
Sung et al,[25] 2012	3	105	2	95
Ucbilek et al,[26] 2013	3	37	10	36
Yamada et al,[22] 2012	4	13	5	15
Yüksel et al,[23] 2008	3	49	4	50
Total (95% CI)	47	691	64	682



Sachar et al. JAMA Internal Medicine 2014

Clinical equivalence between PO PPI vs IV PPI?

Effects of Intravenous and Oral Esomeprazole in the Prevention of Recurrent Bleeding from Peptic Ulcers after Endoscopic Therapy

Joseph J.Y. Sung, MD, PhD[1], Bing-Yee Suen, RN[1], Justin C.Y. Wu, MD[1], James Y.W. Lau, MD[1], Jessica Y.L. Ching, MPH[1], Vivian W.Y. Lee, PharmD[1], Philip W.Y. Chiu, MD[1], Kelvin K.F. Tsoi, PhD[1] and Francis K.L. Chan, MD[1]

STOMACH

118 patients who underwent endoscopic treatment of bleeding ulcer →

randomized to: IV esomeprazole (80 mg bolus + 72 hr drip) OR

oral esomeprazole (40mg bid)

Findings: Rates of recurrent bleeding at 72h, 7 days, & 30 days were comparable between oral and IV PPI. No differences in any other major outcome (transfusions, mortality etc)

Am J Gastro, July 2014

A reasonable approach for PPI in Upper GI bleeding:

For patients with ongoing melena/hematemesis who need urgent endoscopy → IV PPI 40mg BID. Continue IV if patient remains unstable and needs to be NPO. Otherwise, reasonable to switch to 40mg PO BID.

For more stable patients → single IV dose, then oral PPI 40mg PO BID

Upper GI Bleeding Management

Initial approach
Treat as PUD unless strong evidence otherwise

1) Resuscitation, triage.
2) IV or oral PPI
3) ? NG tube
4) 'Early' upper endoscopy
5) Scoring systems
6) Last ditch options: angio embolization > surgery

Upper GI Bleeding- NG tubes

"Pro" arguments:

1. Suctioning blood from the stomach may improve endoscopic visualization or reduce aspiration
2. Large amount of red blood is highly specific for large UGIB requiring early EGD

"Con" arguments:

1. Endoscopy is diagnostic/therapeutic procedure of choice, period.
2. Sensitivity/specificity of NG lavage for UGIB is inadequate to guide management (Sens 79%, Spec 55%)…

↑

(specificity is low in the setting of coffee grounds or scant red blood)

Upper GI Bleeding Management

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Timing of upper endoscopy for upper GI bleed
(aka: should I push for GI team to scope at 2am?)

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 2, 2020 VOL. 382 NO. 14

Timing of Endoscopy for Acute Upper Gastrointestinal Bleeding

RCT of 516 patients presenting with evidence of acute upper GI bleed
(how sick?: Blatchford score ≥ 12, but excluded 'hypotensive shock')

Mix of conditions: 60% PUD, 10% varices. etc

All patients received high dose PPI and appropriate resuscitation

Randomized to: → 'urgent' endoscopy (within 6 hours of GI consultation)
↘ 'early' endoscopy (6-24 hours of GI consultation)

Key outcomes: 30 day mortality, 30 day re-bleeding

The NEW ENGLAND JOURNAL of MEDICINE
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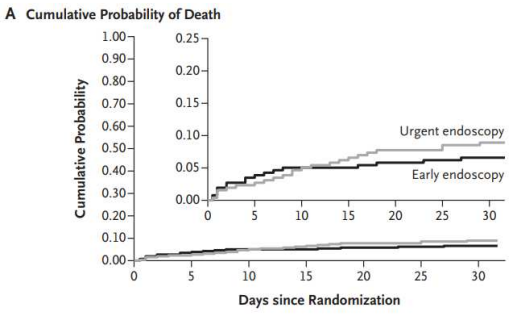
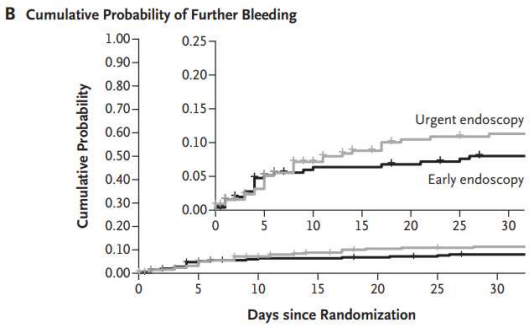
Timing of Endoscopy for Acute Upper Gastrointestinal Bleeding

Key finding: No benefit for mortality or rebleeding in pts who had EGD 'urgently' (within 6 hrs) vs. 'early' (6-24 hours). → Stabilize + PPI first… then 'early' EGD





Prokinetic prior to endoscopy in UGIB

- Prior to EGD, give erythromycin 250 mg IV (3mg/kg) over 30 minutes (prokinetic effect)
- Reasonable data to suggest better gastric clearance = reduced need for 2nd look endoscopy
- No difference in:
  - # of transfusions
  - Need for surgery
  - Length of hospital stay

(Azithromycin 500mg IV x 1 may have similar effect)

Bai et al. Aliment Pharmacol Ther. 2011;34(2):166

Upper GI Bleeding Management

<u>Initial approach</u>
Treat as PUD unless strong evidence otherwise*

1) Resuscitation, triage.
2) IV or oral PPI
3) ? NG tube
4) 'Early' upper endoscopy
5) Scoring systems
6) Last ditch options: angio embolization > surgery

UGIB scores can predict need for endo intervention +/- mortality

- Rockall Score
- AIMS 65 Score
- Blatchford Score →

..and others

At Presentation	Points
Systolic blood pressure	
100–109 mm Hg	1
90–99 mm Hg	2
<90 mm Hg	3
Blood urea nitrogen	
6.5–7.9 mmol/liter	2
8.0–9.9 mmol/liter	3
10.0–24.9 mmol/liter	4
≥25 mmol/liter	6
Hemoglobin for men	
12.0–12.9 g/dl	1
10.0–11.9 g/dl	3
<10.0 g/dl	6
Hemoglobin for women	
10.0–11.9 g/dl	1
<10.0 g/dl	6
Other variables at presentation	
Pulse ≥100	1
Melena	1
Syncope	2
Hepatic disease	2
Cardiac failure	2

Blatchford score of 0 = No need for 'intervention*'

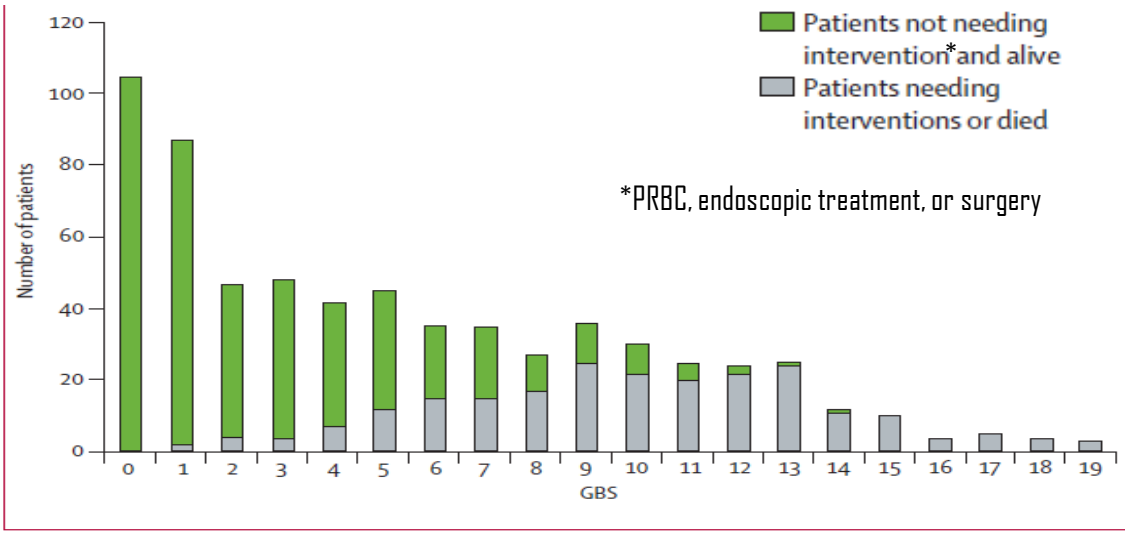


Figure 1: **Need for intervention or death by score for all four centres in phase one**

Lancet 2009

Plan B… if you suspect variceal bleed*

*Consider varices if known/suspected cirrhosis based on exam, imaging, or lab findings (low platelets, high INR)

Upper GI Bleeding

Plan B… if you suspect variceal bleed

1) Resuscitation, triage.
2) IV Octreotide (50mcg + 50mcg/hr gtt)
3) NG tube (ok to use in most cases)
4) Antibiotic treatment
5) Endoscopy for banding/injection
6) Recurrent/massive bleeding → TIPS

*Suspect varices if known/suspected cirrhosis based on exam/imaging/lab findings (low plts, low albumin, coagulopathy..)

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AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

2017 AASLD Guidelines

- Patients with cirrhosis presenting with any type of GI bleed, are at high risk for SBP and other bacterial infections
- Multiple RCTs show definitive benefit for antibiotics re: reduced risk of infection, rebleeding, death
- Best option: 1g IV ceftriaxone q24hrs

Garcia-Tsao et al. Hepatology 2017

Lower GI Bleeding

Lower GIB: Evidence Deficit

- UGIB and LGIB have fairly similar incidence and similar mortality rate… but…. LGIB has no ‘gold standard’ approach and evidence base for clinical management is relatively thin.

Lower GI Bleeding

Differential Diagnosis

Common
colonic diverticula, angioectasia

Less common
post-polypectomy bleeding, colon cancer/polyp, hemorrhoids, Meckel's, colitis (inflammatory, ischemic, radiation)

Rare
Dieulafoy's lesion, rectal varices

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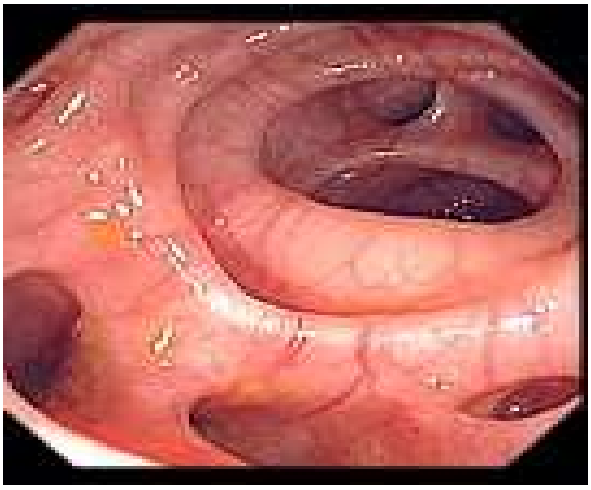
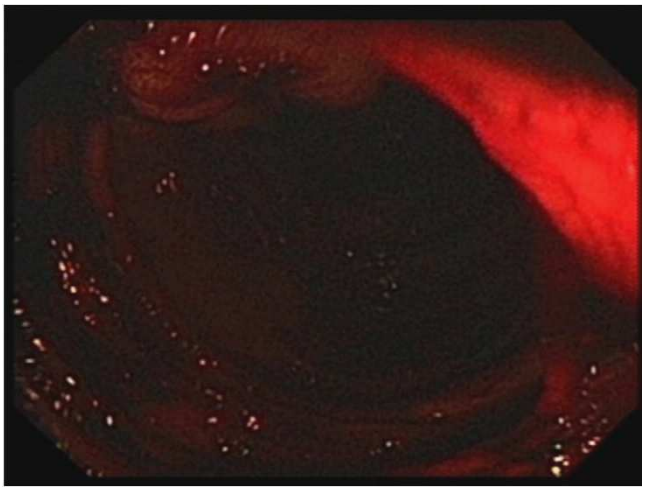
Diverticulosis

Sigmoid colon with multiple large tics



Diverticular bleed with inadequate prep



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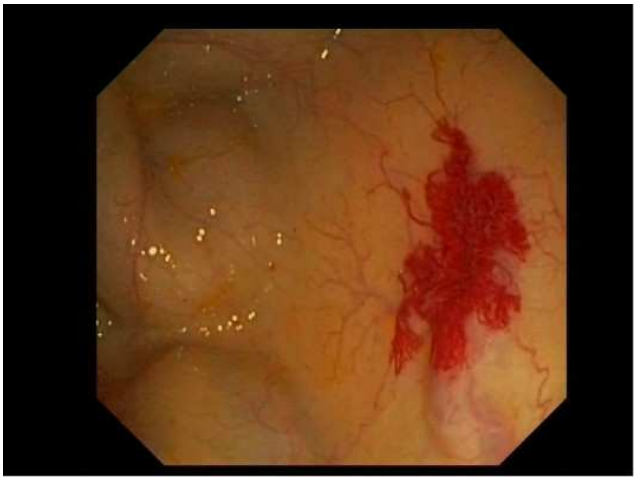
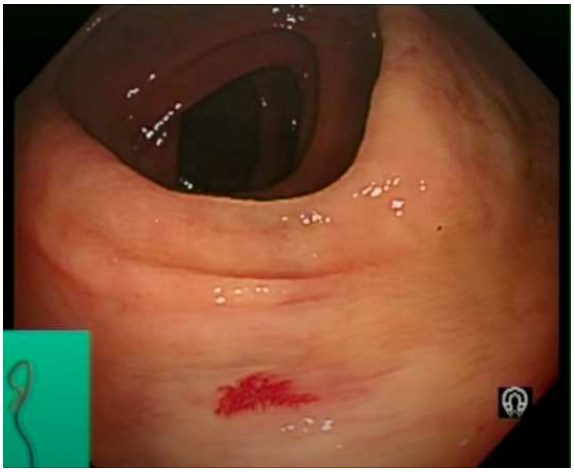
‘Angioectasia’

(sometimes incorrectly referred to as ‘angiodysplasia’ or ‘AVM’)





72 y.o. female presents to ED with 2 episodes of hematochezia. BP 100/50. HCT 34, coags normal. No prior GIB history. Last colo ~8 years ago for screening. Patient has one more episode of hematochezia on medical floor and then nothing more overnight. Colonoscopy is planned the next day.

What is the likelihood that she will leave the hospital without a definitive ‘source’ identified for her likely lower GI bleed?

1. 80%
2. 50%
3. 35%
4. 20%
5. 5%

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3. **35%**
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Lower GI bleeding Pro Tip: 30-40% of patients admitted with LGIB will be discharged without a definitive source. This is because many LGIBs (including diverticular) stop spontaneously, before the diagnostic studies occur.

The *wise* physician says...
"*Please understand that it is expected for lower GI bleeding that we may not find the source despite careful investigation..*"

The *foolish* physician says...
"*How confusing that we could not find your bleeding source*!"

Sengupta et al Mayo Clinic Proc 2015

Lower GI Bleeding

Treat as diverticular unless strong evidence otherwise*

1) Resuscitation, triage.
2) Consider NG tube lavage (r/o UGI source)
3) Careful rectal exam to evaluate for obvious fissure/hemorrhoids
4) Localization and treatment

* i.e. Post-polypectomy bleed, known large hemorrhoids, possible UGI source

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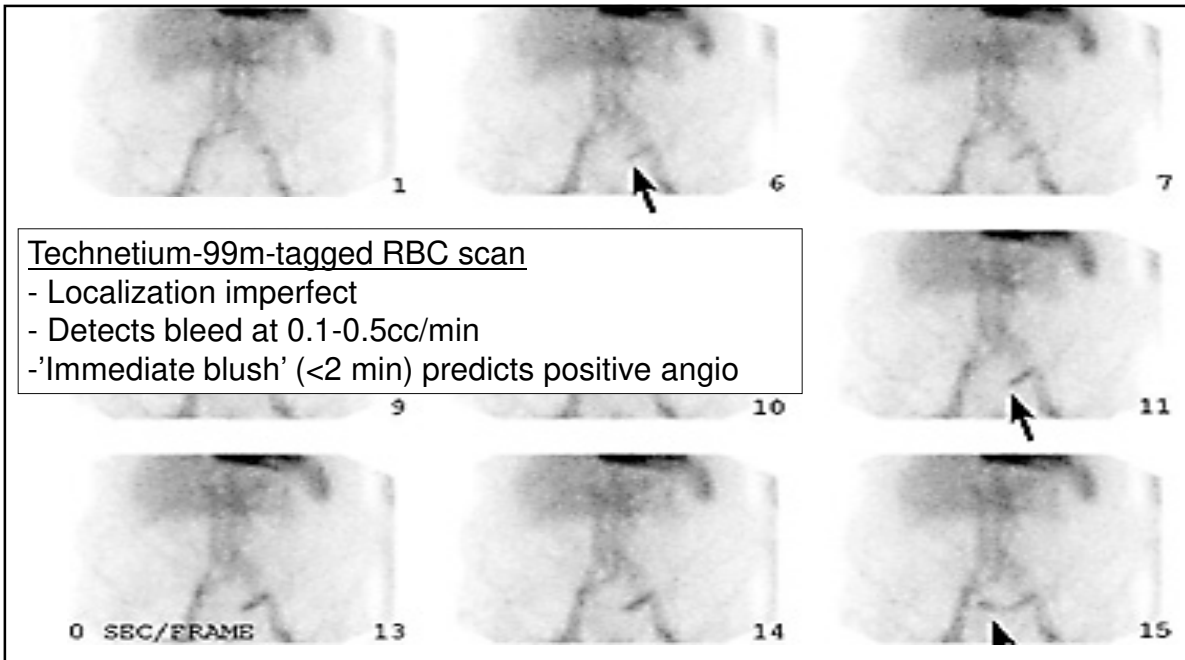
Lower GI Bleeding- localization/treatment

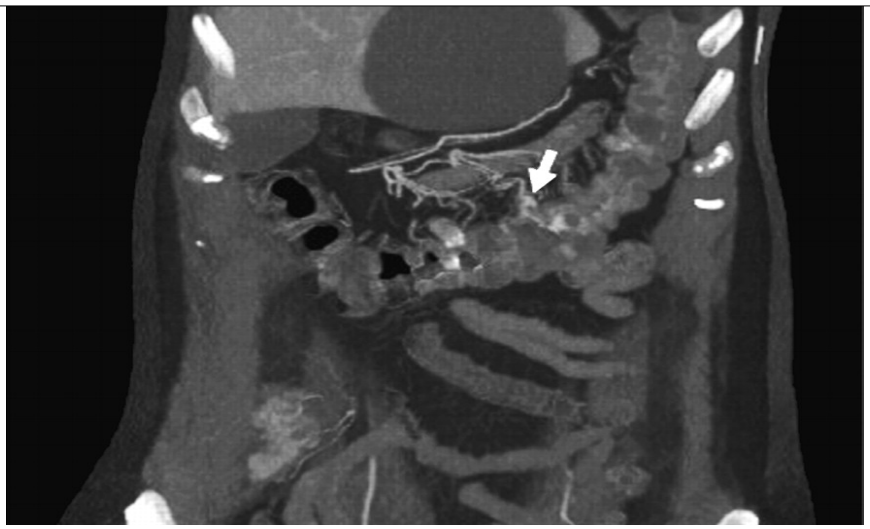
~ 6 options

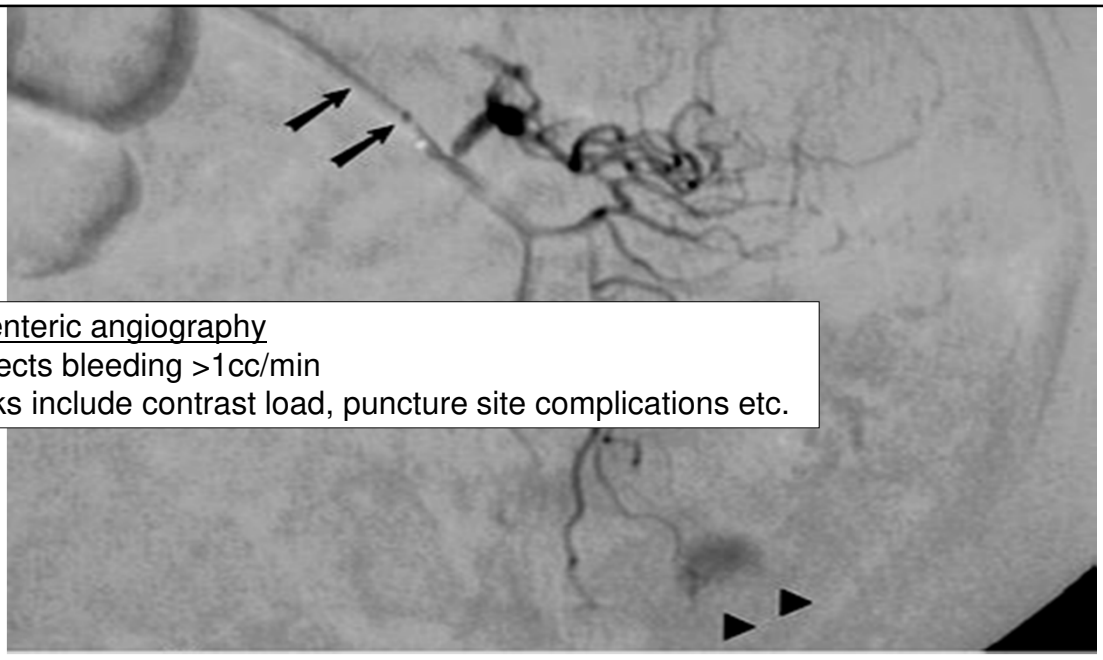
Rectal exam/anoscopy	diagnostic
Tagged RBC scan	diagnostic
CT angiography	diagnostic
IR/Angiography	diagnostic/therapeutic
Urgent colonoscopy	diagnostic/therapeutic
Surgery	last ditch option



Technetium-99m-tagged RBC scan
- Localization imperfect
- Detects bleed at 0.1-0.5cc/min
-'Immediate blush' (<2 min) predicts positive angio

CT angiography
- Increasing use as best radiologic test for localization of GIB
- Detects bleeding 0.3-0.5cc/min





Mesenteric angiography
- Detects bleeding >1cc/min
- Risks include contrast load, puncture site complications etc.

Colonoscopy

- Can detect bleeding site at “0 cc/min”
- Requires rapid prep and *willing endoscopist*
- Particularly effective for post-polypectomy bleeding, angiodysplasia
- No evidence that bowel purge ‘disrupts the clot’

“Urgent colonoscopy purge”

PO: PEG (golytely) 1 cup Q15 minutes
or
NG tube: 250 mL Q15 minutes

(4-6 L golytely total over 3-4 hours)

Published trials on ‘urgent colonoscopy’ recommend starting procedure within 2 hrs after stool/blood clearance and “within 8 hours of hospitalization or onset of hematochezia”

Green BT, et al. Am J Gastroenterol. 2005;100:2395–2402

SYSTEMATIC REVIEW AND META-ANALYSIS

Urgent colonoscopy in patients with lower GI bleeding: a systematic review and meta-analysis (CME)

Abdul M. Kouanda, MD,[1] Ma Somsouk, MD,[2] Justin L. Sewell, MD, MPH,[2] Lukejohn W. Day, MD[2]

Very low quality evidence and no randomized trial comparing, modern colonoscopy approaches vs. CT angio etc for LGIB.

Meta-analysis shows no significant differences in bleeding source localization, adverse event rates, rebleeding, transfusion requirement, or mortality between colo vs. CT angio/imaging.

GIE 2017

Suspected small bowel bleeding = 1 slide

- If EGD/colo negative, must evaluate for small bowel bleeding (most common = angioectasia, most dangerous = tumor). Capsule endoscopy is reasonable 1st step.
- Yield of capsule drops from >90% if done during active bleeding, to 33% if capsule several weeks after event (Pennazio et al. 2004).
- Use capsule as screening tool before deep enteroscopy (single/double balloon)

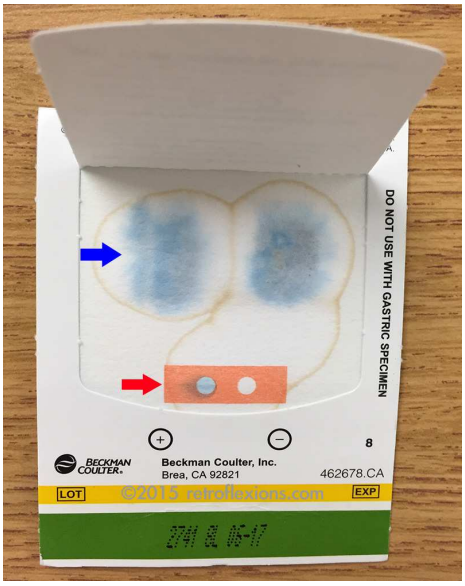
Acute GI Bleeding- 4 management pearls

1. Resuscitation requires adequate IV access (short fat peripheral IVs preferred)
2. Ulcer vs variceal bleeding? Check PLT and INR for decomp cirrhosis
3. 'Early' EGD (6-24hrs) is equivalent (?preferred) vs. 'urgent' EGD (<6 hrs)
4. Data on LGIB approach is mixed, but colonoscopy generally first line

GI bleeding bonus slides (3 key questions):

1. When is inpatient FOBT testing appropriate?
2. How long does a patient need to be on a PPI after a peptic ulcer?
3. What about patients who need to resume anticoagulation?

1) When is inpatient FOBT use appropriate?



Fecal occult blood testing in hospitalized patients

FOBT generally <u>not useful</u> to answer clinical questions in hospitalized patients and studies show even when checked, rarely changes management:

A negative result should not likely change decisions

- Clinically-suspected GIB in hospitalized patient → likely to needs endoscopy.
- If you have low concern for GIB, normal CBC... but positive guaiac? → likely false positive

Matthews et al. J. Hosp Medicine 2017 (TWDFNR series)

2) What is the appropriate duration of PPI therapy after a gastric/duodenal ulcer?

- No evidence-based answer to this question
- I typically treat for 8 weeks if there is an obvious, reversible cause (H.pylori, NSAIDs which can be avoided)
- Consider longer/lifelong treatment if there is no reversible cause, or if there is a clear need for continued NSAID use

3) What are appropriate recommendations for patients who need to resume anticoagulation?

- For majority of UGIB and LGIB patients previously on anticoagulation, anticoag should be resumed.

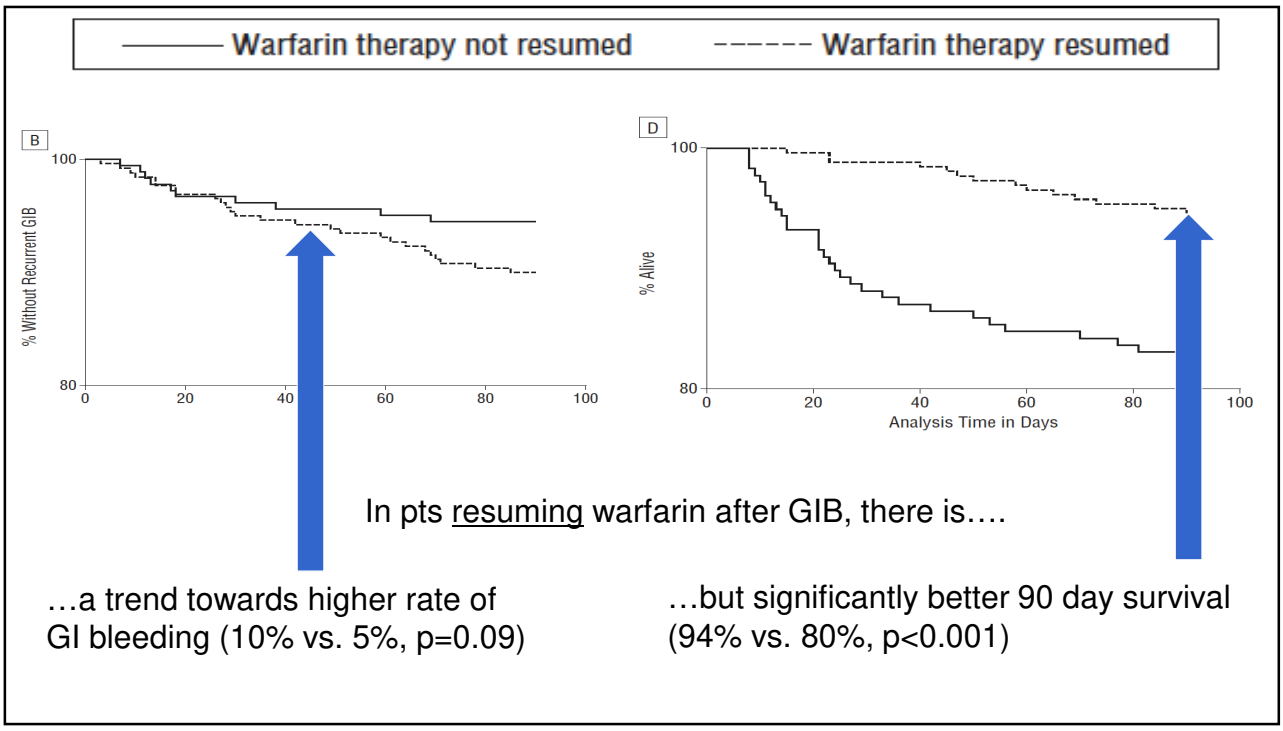
ORIGINAL INVESTIGATION

ONLINE FIRST

Risk of Thromboembolism, Recurrent Hemorrhage, and Death After Warfarin Therapy Interruption for Gastrointestinal Tract Bleeding

Daniel M. Witt, PharmD, FCCP, BCPS; Thomas Delate, PhD; David A. Garcia, MD; Nathan P. Clark, PharmD; Elaine M. Hylek, MD; Walter Ageno, MD; Francesco Dentali, MD; Mark A. Crowther, MD

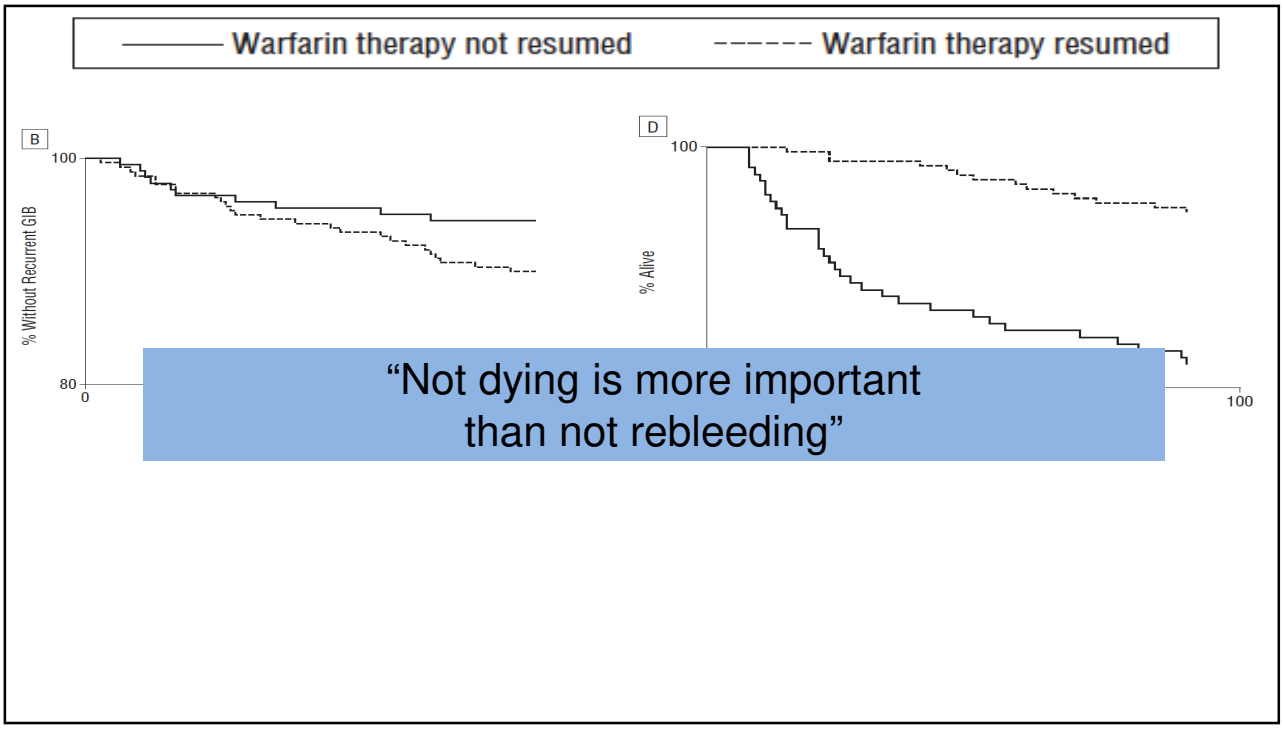
Arch Int Med 2012



In pts resuming warfarin after GIB, there is….

…a trend towards higher rate of GI bleeding (10% vs. 5%, p=0.09)

…but significantly better 90 day survival (94% vs. 80%, p<0.001)



"Not dying is more important than not rebleeding"

Thank you!

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