Acute GI Bleeding:

A few things that we “know”
A few things that we need to “know”
and
Guidance on using Guidelines

Surgery Resident Teaching Conference

February 25th 2011

Walter Smalley MD MPH

- Focus on Non Variceal GI Hemorrhage
- Evaluation and triage
  - Who needs to be in ICU ?
  - Who can be discharged on Day 0 ?
- Resuscitation
  - What is the best practice and how can we encourage implementation ?
- Medical therapy
  - How useful are PPI's ?
- Endoscopy
  - How early ?
  - What do we do when we get there ?

- Diagnose Upper GI bleeding
- Triage according to risk
- Stabilize patient : Start Resuscitation
- Call GI and Surgery early
- Initiate empiric therapy

Virtually immediately (minutes) the job of internist/ hospitalist/ surgeon

- Decide about timing of endoscopy
- Make diagnosis
- Treat underlying condition

Hours: the job of GI and surgery

- If GI bleeding is acute
  - call the GI fellow on call ASAP
  - do not wait until the morning.

- Optimizes patient care
- Optimizes utilization of resources for the patient and the rest of the hospital

Is this an Upper GI bleed ?

- Diagnostic value

Red blood from

mouth or rectum > History > exam >> labs, xrays

Evaluation: Clinical Bleeding History

- Hematemesis
  - Vomiting (“Not spitting”, “coughing”)
  - “Coffee grounds” ?
    - likely not important in absence of other findings
    - Should we quit teaching medical professionals about “coffee grounds” ?
  - Guaiac of emesis or NG aspirate?
    - Will offer a cash reward for anecdotal evidence of benefit
- Melena
  - Black (NOT “dark”), tarry, “metallic” odor
  - Needs to be in the gut 4-6 hours
  - Hematochezia and shock may mean UGI bleed

OBSERVATIONS ON THE ORAL ADMINISTRATION OF CITRATED BLOOD IN MAN.

II. The Effect on the Stools.*

By Leon Schiff, M.D.,
Associate Professor of Medicine, University of Cincinnati Medical School,
Richard J. Stevens, M.D.†
Formerly Assistant in Medicine, University of Cincinnati Medical School,
and
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Instructors in Medicine, University of Cincinnati Medical School,
Cincinnati, Ohio.

(From the Department of Internal Medicine, University of Cincinnati Medical School, and the Gastric Laboratory of the Cincinnati General Hospital.)

In the management of patients with hematemesis or melena it is important to determine the severity of the hemorrhage and whether

* Read by title before the meeting of the American Society for Clinical Investigation, Atlantic City, May 5, 1941. This work was aided by a grant from Parke, Davis & Co., through the coöperation of Dr. E. A. Sharp.

† Justin A. Rollman Fellows in Internal Medicine, 1938-1939, and 1937-1938, respectively.

Lessons from the literature – part 1

The Amount of Blood Necessary to Produce a Tarry Stool. The subjects used in this study consisted of 3 normals and 15 ward patients varying in age from 23 to 72 who, with one exception, were free of digestive tract disease. Citrated venous blood, 2 to 3 weeks' old, was mixed with 100 to 200 cc. of charged artificial Vichy water* to help disguise the taste and was then administered orally. Before the blood was given to any subject, at least two of his stools were found to be of normal color. A regular diet was allowed, and drugs known to discolor the stools were prohibited. When blood was given more than once, an interval of 10 days was allowed to elapse before the succeeding dose was administered. When a tarry stool was once obtained, no more blood was given.

** "normals" were persons willing to drink blood and examine feces for medical science

- >100 cc blood to make tarry stool
- 200 - 1000 cc blood in upper GI tract to make hematochezia (red blood from rectum)

- Bloody stools plus signs of hypovolemia should increase the concern for a massive upper GI bleed

- Lessons from the literature
  - Useful information from (really) old fashioned bedside investigation that could not be done again

Evaluation: HPI related to bleeding risks

- Previous GI Bleeding history
- Duration of bleeding
  - acute history more ominous than chronic history
- Pain
  - Not particularly helpful in absence of perforation
  - ~30% bleeding ulcers have no antecedent pain
- Symptoms of hypovolemia
  - Dizziness/Orthostasis
  - Mental status changes
  - Angina/dyspnea

Evaluation: History/Comorbidities

- Predictors of GI bleed related mortality
  - Liver disease
  - Coronary artery disease
  - Renal disease
  - Malignancy
  - COPD

Evaluation: Previous Surgery

- AAA repair with graft
- Other vascular repairs ?

- Need to rule out aortoenteric fistula now
- Patient should have EGD/CT within minutes
- “Call us in triage”

Evaluation: Medications

- NANSAIDs
  - Increase risk 3-4X baseline
  - Low dose ASA 2-3X
  - Risk increases to 16-20X on coumadin+NSAID
- Clopidogrel: might be more important than ASA
- Coumadin
  - Why are they on it ? How high is the thrombotic risk ?
  - Primary prophylaxis in afib is a low priority in setting of acute bleed
- Ethanol use

Evaluation: Physical exam - I

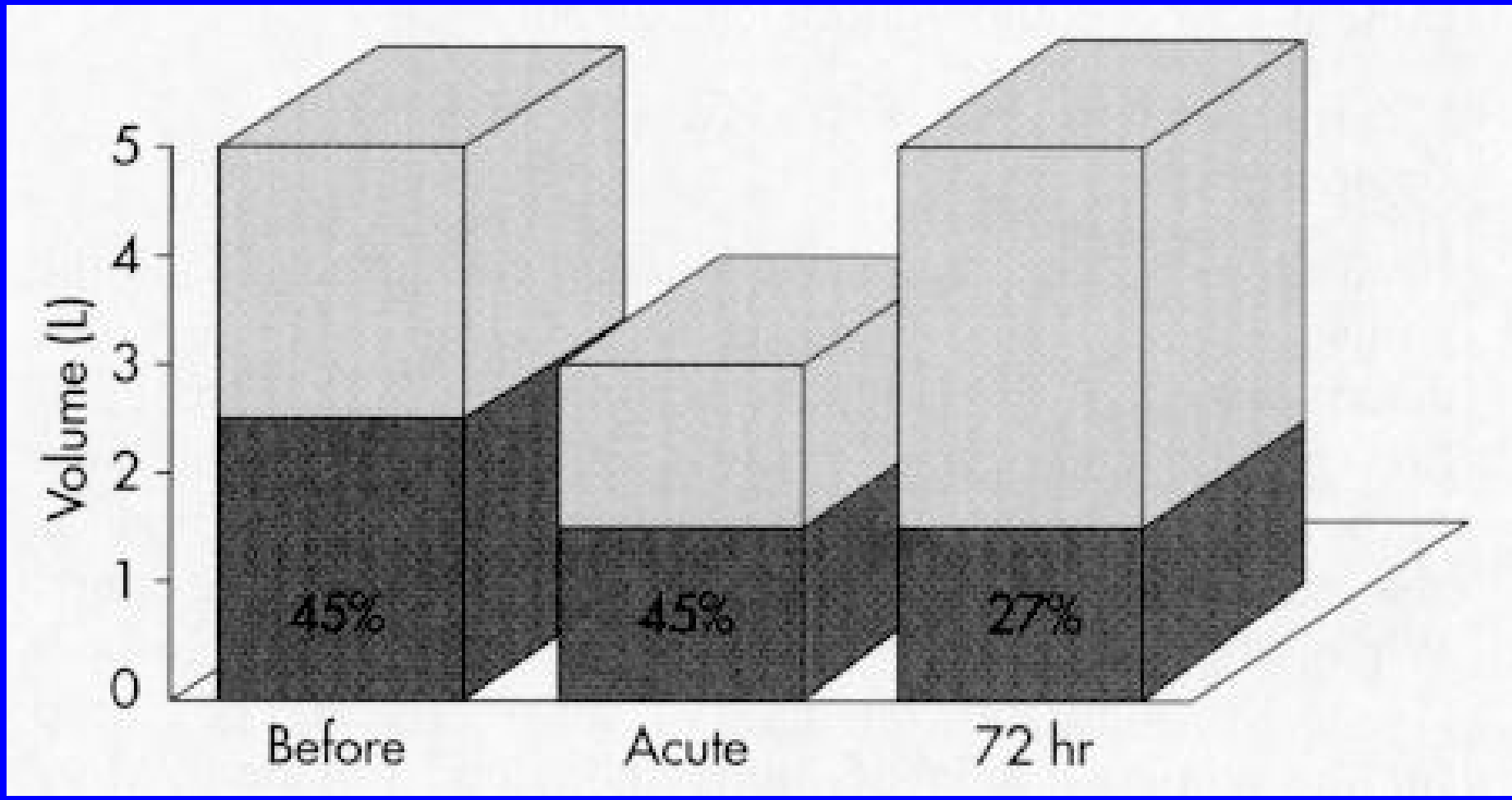
- Vital signs
  - Resting HR
  - Orthostatics: Hypovolemia
    - Orthostasis (drop 20 mm Hg, Increase in HR ~20)
    - Requires a ~20%volume loss
    - Capillary refill time

Table 3 Hypovolaemic shock: symptoms, signs, and fluid replacement

Blood loss (ml)	<750	750–1500	1500–2000	>2000
Blood loss (%bv)	<15%	15–30%	30–40%	>40%
Pulse rate	<100	>100	>120	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate	14–20	20–30	30–40	>35
Urine output	>30	20–30	30–40	<35
Mental status	Slightly anxious	Mildly anxious	Anxious and confused	Confused and lethargic
Fluid replacement	Crystalloid	Crystalloid	Crystalloid and blood	Crystalloid blood

Adapted from Grenvick A, Ayres SM, Holbrook PR, *et al. Textbook of critical care*, 4th edition. Philadelphia: WB Saunders Company, 40–5.

HCT may not drop acutely



Evaluation: Physical exam - II

- Oxygenation: can this person tolerate conscious sedation without intubation ?
- Mentation :
  - Can this person consent to invasive procedures ?
- Abdominal exam:
  - Are there signs of peritonitis ?
- Rectal exam: is there red blood ?
- Peripheral signs of “cold” shock
- Urine output

Evaluation: admission labs

- PCV
- Platelets
- PT/INR
- BUN/Cr.
- Metabolic profile : is acidosis present ?
- Type and Screen
  - Blood type and screen for major Ab
  - Requires ~30 minute more work once decision to crossmatch for transfusion is made
- Type and crossmatch : reserves a unit of blood for a patient

Annals of Internal Medicine | CLINICAL GUIDELINES

International Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding

Alan N. Barkun, MD, MSc (Clinical Epidemiology); Marc Bardou, MD, PhD; Ernst J. Kuipers, MD; Joseph Sung, MD; Richard H. Hunt, MD; Myriam Martel, BSc; and Paul Sinclair, MSc, for the International Consensus Upper Gastrointestinal Bleeding Conference Group*

Description: A multidisciplinary group of 34 experts from 15 countries developed this update and expansion of the recommendations on the management of acute nonvariceal upper gastrointestinal bleeding (UGIB) from 2003.

Methods: The Appraisal of Guidelines for Research and Evaluation (AGREE) process and independent ethics protocols were used. Sources of data included original and published systematic reviews; randomized, controlled trials; and abstracts up to October 2008. Quality of evidence and strength of recommendations have been rated by using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria.

Recommendations: Recommendations emphasize early risk stratification, by using validated prognostic scales, and early endoscopy (within 24 hours). Endoscopic hemostasis remains indicated for high-risk lesions, whereas data support attempts to dislodge clots with hemostatic, pharmacologic, or combination treatment of the underlying stigmata. Clips or thermocoagulation, alone or with epinephrine injection, are effective methods; epinephrine injection alone is not recommended. Second-look endoscopy may be useful in selected high-risk patients but is not routinely recommended. Preendoscopy proton-pump inhibitor (PPI) therapy may downstage the lesion; intravenous high-dose PPI therapy after successful endoscopic hemostasis decreases both rebleeding and mortality in patients with high-risk stigmata. Although selected patients can be discharged promptly after endoscopy, high-risk patients should be hospitalized for at least 72 hours after endoscopic hemostasis. For patients with UGIB who require a nonsteroidal anti-inflammatory drug, a PPI with a cyclooxygenase-2 inhibitor is preferred to reduce rebleeding. Patients with UGIB who require secondary cardiovascular prophylaxis should start receiving acetylsalicylic acid (ASA) again as soon as cardiovascular risks outweigh gastrointestinal risks (usually within 7 days); ASA plus PPI therapy is preferred over clopidogrel alone to reduce rebleeding.

Ann Intern Med. 2010;152:101-113. www.annals.org

For author affiliations, see end of text.

* For a list of voting participants, see **Appendix 1**, available at www.annals.org.

- Evidence Based Medicine
  - "What is known" is based on editorial consensus

  - H pylori did not cause ulcers until the editors of Lancet decided that H pylori might cause ulcers

- Evolution of teaching clinical sciences
  - Pre 1985 — How to read an article
  - Circa 1985 — How to read a metanalysis
    Term "EBM" appears
  - Now: — How and when to follow Clinical Practice Guidelines

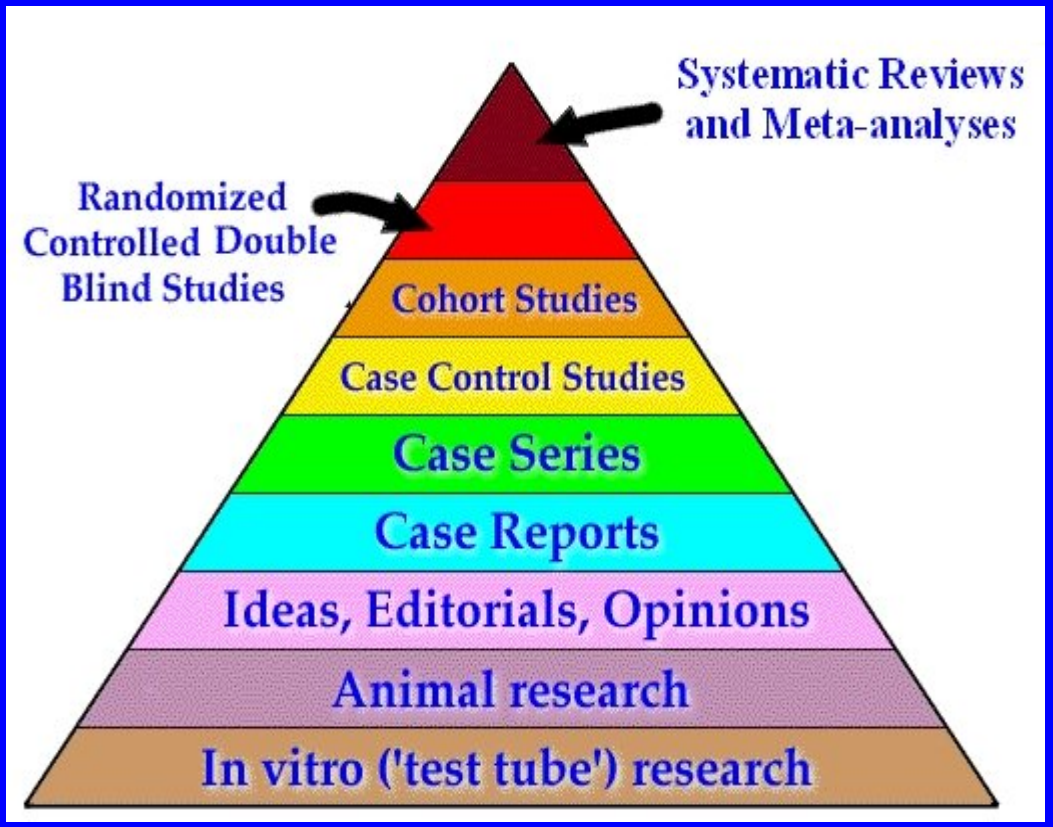
The Quality Based Pyramid of Information

Pyramid Level

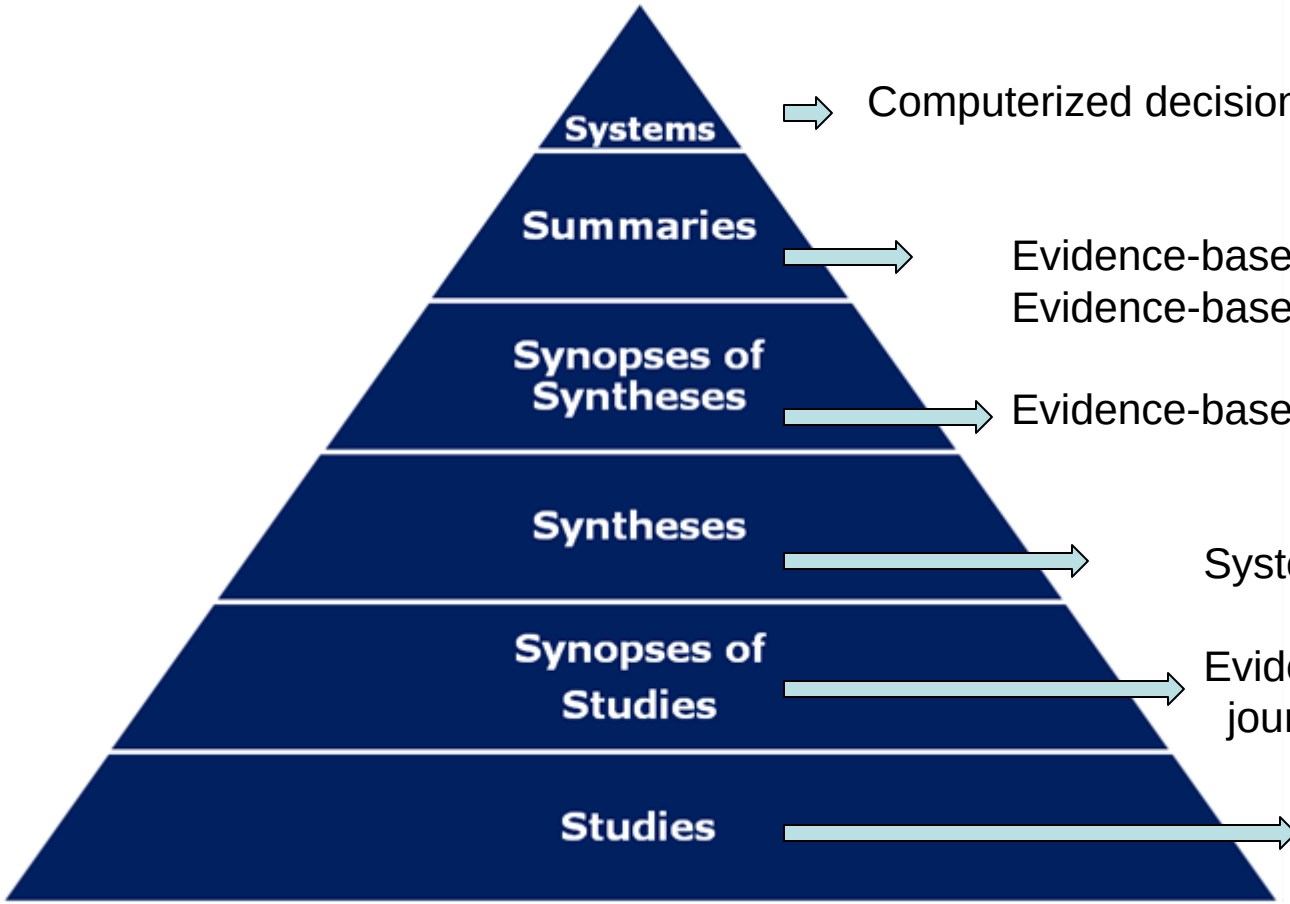
Validity increases

Work increases

Relevance may increase or decrease



The Value Based Information Pyramid



Computerized decision support systems

Evidence-based clinical practice guides
Evidence-based textbooks

Evidence-based abstraction journals

Systematic reviews

Evidence-based abstraction journals

Original articles

Use of Clinical Practice Guidelines

- High level practitioners should be able to evaluate CPGs
  - Validity
  - Applicability to specific care environments
  - Applicability to specific patients incorporating characteristics and preferences

- This will be a skill set that will differentiate medical doctors from other practitioners

“ Performing a coronary bypass isn’t difficult…..knowing when to do it is what is difficult…..”

Guideline development

- Multidisciplinary panel
- Gather and synthesize evidence
- Grade evidence
- Develop specific guidelines
- Distribute and implement guidelines
- Measure effect of guidelines

- GRADE Guidelines
  - "guidelines on guideline development"
  - http://www.gradeworkinggroup.org

Methodology of Guideline development

- Expert panels
  - Vote on items or arrive at consensus by formal or informal methods
  - Prone to undue influence by strong personalities
  - BOGSAR technique
    - “Bunch of guys sitting around a room”

- Delphi Panels
  - Specific questions reviewed anonymously by members
  - Answers combined anonymously by leaders
  - Questions and answers resubmitted
  - Process repeated
  - Designed to eliminate domination by strong panel members

Evaluation of a Clinical Practice Guideline

- Were all important options and outcomes identified?
  - What is the outcome of interest ?
    - Explicitly stated: Mortality ? Quality of life ? Costs ?

- Was an explicit and sensible process used to indentify, select and combine the evidence ?
  - Description of techniques used to gather best evidence

Adapted from: JAMA 274(7). 570-574

Evaluation of a Clinical Practice Guideline

- Is the guideline likely to account for recent developments?
  - Is the information up to date ?

- Has the guideline been subjected to peer review and testing ?
  - Often open for comment/editorial – Peer review
  - Effect of implementing clinical practice guidelines only rarely done

- How likely is it that the authors have a vested interest?
  - Personal or “corporate”

Adapted from: JAMA 274(7). 570-574

Evaluation of Clinical Practice Guidelines

- Is the primary objective of the guideline consistent with the objectives you have for your patients

- Are the primary recommendations applicable to your patients?
  - Does patients have access to recommended options ?

Adapted from: JAMA 274(7). 570-574.

Evaluation of Clinical Practice Guidelines

- Are practical clinically important recommendations made?

- How strong are the recommendations?
  - Grading schemes need to be explicit
  - Variety of schemes

- What is the impact of uncertainty associated with the evidence and values used in the guidelines?
  - Would new evidence from an RCT likely change the recommendation ?

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Sources and Searches

Literature searches included MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and ISI Web of Knowledge, with manual searches of bibliographies of key articles and proceedings of abstracts of major gastroenterology meetings held in the last 5 years (from the American College of Gastroenterology, Digestive Disease Week, and United European Gastroenter-

Explicit discussion on the search strategy used to find best evidence

randomized clinical trials, which available, and performed meta-analyses (when applicable) before the meeting. They derived search terms from previous Cochrane meta-analyses on nonvariceal UGIB and through discussions with the methodologists in the group, and the terms were then approved by the entire group. An independent research assistant performed the searches and summarized them by using standardized report forms. These were in turn reviewed by both methodological and content experts and approved by the entire group. Search strings and Quality of Reporting of Meta-analyses (QUOROM) diagrams for each of the statements are available on request.

Review and Grading of Evidence

Initially, 3 members of the group (Drs. Rostom, Malfertheiner, and Barkun) rated the level of evidence available and the strength of each recommendation by

Explicit discussion on the process used to grade the evidence

ratings after further review. The group considered health benefits, side effects, and risks, as well as cost data (when available). Seven new or updated meta-analyses were performed for the meeting, relating to statements A6, A8, B3, B11, C3, D6, and E4 (**Appendix Tables 2** and **3**, available at www.annals.org), by using a similar process as that for obtaining search string results. Most of these (for statements A6 [21], A8 [22], B11 [23], C3 [24], and D6 [25]) were presented at Digestive Disease Week 2009. All are available on request.

Group Processes

All participants identified statements to be modified, gaps in the previous recommendations, and the need for any new statements. Using a modified Delphi process, an organizing committee (chaired by Dr. Barkun) generated a list of new and old statements and circulated it electronically to all participants through 2 iterations before the meeting (26, 27). Participants anonymously voted on which statements they felt warranted discussion at the

Explicit discussion on the process used to make decisions on recommendations (voting, consensus, etc)

mary data and discussed individual studies at participants' request.

The group held a 2-day consensus conference in October 2008, chaired by a nonvoting member (Dr. Hunt), where data were presented and the grade attributed to the evidence was modified as needed and voted on by each participant. A statement was accepted if more than 75% of participants voted a, b, or c (agree strongly, agree moderately, or just agree) on a 6-point scale (with d, e, and f, being just disagree, disagree moderately, and disagree strongly, respectively). A working group drafted the manuscript, which was then reviewed and approved by all participants.

Ethics

The conference was guided by existing ethics standards of medical institutions (28–30) and supplemented by additional procedures. An unconflicted ethics consul-

Explicit discussion potential conflict of interests, including a member by member accounting and also an explanation of who is funding the process

24 months before the meeting were obtained a priori from all voting participants and included in conference materials. The ad hoc advisory committee identified one third of the statements (7 of 21) as having the potential for conflict of interest. Before discussion of the identified statements, participants were asked openly to vol-

Appendix Table 1. **Grading Criteria Used for Quality of Evidence and Recommendations**

Grade of recommendation	Benefit vs. risk and burdens	Methodologic quality of supporting evidence	Implications
Do it or don't do it			
Grade 1A: Strong recommendation, high-quality evidence	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Grade 1B: Strong recommendation, moderate-quality evidence	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Grade 1C: Strong recommendation, low or very low-quality evidence	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Probably do it or probably don't do it			
Grade 2A: Weak recommendation, high-quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Grade 2B: Weak recommendation, moderate-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Grade 2C: Weak recommendation, low or very low-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

Adapted from Guyatt et al. (20) and Atkins et al. (19). RCT=randomized controlled trial

Explicit explanation of grading scheme

1(do or don't), 2 (probably do or don't): Benefits vs risks

A,B,C : quality of evidence

Ann Intern Med. 2010;152:101-113.

2010 consensus Guidelines for UGI Bleeding in Annals

A statement was accepted if more than 75% of participants voted either
A - agree strongly
B - agree moderately
C - just agree

D- just disagree
E - disagree moderately
F- disagree strongly

A working group drafted the manuscript, which was then reviewed and approved by all participants.

Ann Intern Med. 2010;152:101-113.

- Conference included gastroenterologists, surgeons, family doctors, ER doctors

- Sponsored by Canadian Government and relevant societies from Canada, Asia and Europe

- Evidence search and initial evaluation done by organizers by GRADE process
  - Which included a Delphi panel etc……

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Who needs to be in a monitored bed or in the ICU ?

Statement A2

Prognostic scales are recommended for early stratification of patients into low- and high-risk categories for rebleeding and mortality. (Agree, 97% [Vote: a, 56%; b, 35%; c, 6%; d, 3%]. Grade: Low, 1c, “do it”)

Ann Intern Med. 2010;152:101-113.

Triage according to risk

- Essential history and physical < 5 minutes
- Goals
  - Identify high risk patients who need ICU care
  - Identify low risk patients who might be discharged from ED or GI lab after EGD

Appendix Table 2. **Summary of Statistically Significant Predictors of Death as Assessed by Multivariate Analyses in Studies within the Past 10 Years***

Risk Factor (Reference)	Range of Odds Ratios for Increased Risk†
Clinical factors	
Age (1, 4, 32, 49, 56)	
60–69 y	3.5 [1.5–4.7]
≥75 y	4.5–12.7
>80 y	5.7 [2.9–10.2]
Shock or low blood pressure (1, 4, 32, 33, 49)	1.18–6.4
ASA classification (4, 58)	2.6–9.52
Comorbid conditions (0 vs. ≥1) (1, 4, 32, 49)	1.19–12.1
Continued bleeding or rebleeding (4, 32, 49, 56, 58)	5.29–76.23
Presentation of bleeding	
Blood in the gastric aspirate (4, 32, 34, 56)	0.43–18.9
Hematemesis (1)	2.0 [1.1–3.5]
Red blood on rectal examination (4)	2.95 [1.29–6.76]
Onset of bleeding while hospitalized for other causes (4)	2.77 [1.64–4.66]
Laboratory factors	
Elevated urea level (1)	5.5–18
Serum creatinine level >150 μmol/L (32)	14.8 [2.6–83.5]
Elevated serum aminotransferase levels (32, 33)	4.2–20.2
Sepsis (33)	5.4 [1.5–19.6]
Endoscopic factors	
Major stigmata of recent hemorrhage (49)	NA

* ASA = American Society of Anesthesiologists; NA = not available.
† Values in square brackets are 95% CIs.

Risk stratification/ Triage

Clinical features

- History
- Exam
- Labs

Endoscopic features

Ann Intern Med. 2003;139:843-857. www.annals.org

Which patients need to be in a monitored bed or in the ICU ?

- What we know –
  - Several formulas used to predict poor outcomes
    - Rockall Score
    - Blatchford Score
    - Several others
  - Several recurrent themes that predict bad outcomes

Example

70 yo

Hematemesis

HR 110

CHF

Table 1 The Rockall risk scoring system

Variable	Score 0	1	2	3
Age (years)	<60	60–79	≥80	
Shock	"No shock": pulse <100 + systolic BP≥100 mm Hg	"Tachycardia": pulse ≥100 + systolic BP ≥100 mm Hg	"Hypotension": systolic B < 100 mm Hg	
Comorbidity	No major comorbidity		Cardiac failure, ischaemic heart disease, any major comorbidity	Renal failure, liver failure, disseminated malignancy
Diagnosis	Mallory Weiss tear, no lesion identified and no SRH/blood	All other diagnoses	Malignancy of upper GI tract	
Major SRH	None or dark spot only		Blood in upper GI tract, adherent clot, visible or spurting vessel	
"Translation" of our comorbidity scale				
Comorbidity	No or mild coexisting illnesses (e.g. ECG abnormalities without symptoms)	Moderate coexisting illnesses (e.g. hypertension stable with medication)	Severe coexisting illnesses (diseases which need immediate treatment: e.g. cardiac failure)	Life threatening diseases (e.g. end stage malignancies, renal failure)

Major SRH, major stigmata of recent haemorrhage (active bleeding or visible vessel); GI, gastrointestinal; BP, blood pressure.

Table 2 Distribution of patients in the risk score groups, calculated with the Rockall risk score, for the Rockall validation sample and for our own patient group

Risk score	Predicted probabilities* Rebleeding (%)	Predicted probabilities* Mortality (%)	Rockall's validation sample Number of patients	Rockall's validation sample Rebleeding (%)	Rockall's validation sample Mortality (%)	Vreeburg's validation sample Number of patients	Vreeburg's validation sample Rebleeding (%)	Vreeburg's validation sample Mortality (%)
0	4.9	0	48	4.2	0	11	9.1	0
1	3.4	0	131	4.6	0	36	3.8	0
2	5.3	0.2	142	7.7	0	71	8.5	1.4
3	11.2	2.9	162	11.7	1.8	145	13.8	7.6
4	14.1	5.3	176	15.3	8.0	175	11.4	9.7
5	24.1	10.8	199	24.6	10.6	178	16.3	10.7
6	32.9	17.3	137	27.0	11.7	142	22.5	17.6
7	43.8	27.0	96	40.6	25.0	107	20.6	24.3
8+	41.8	41.1	89	37.1	40.4	86	26.7	46.5
Total	18.9	10.0	1180	18.9	9.7	951	16.4	13.9

*Predicted probabilities based on observed percentages in original patient sample (Rockall, table V(B)[13]).

E M Vreeburg, C B Terwee, P Snel, E A J Rauws, J F W M Bartelsman, J H P vd Meulen and G N J Tytgat

Gut 1999;44;331-335

Identifying high risk patients : ICU ?

- Elderly
- HGB <8, PCV < 25
- Recurrent hematemesis, hematochezia
- Hemodynamic instability
- Comorbidities
  - Heart
  - Lungs
  - Kidney
  - Liver
- Strongly consider ICU admission
  - Must justify non unit admission

Identifying low risk patients:

Who can be sent home from triage or discharged from ICU or floor ?

- Patient characteristics
  - Non of the pre endoscopy factors that require ICU or monitored bed
- EGD findings
  - low risk findings: MW tear, esophagitis, ulcer with clean base

Table 1. Controlled Trials Relating to Timing of Endoscopy for *Low-Risk* Patients With Nonvariceal Upper Gastrointestinal Tract Hemorrhage*

Source, y	Patients	Design	Comparison	Exclusion Criteria	Patient Outcome Measure	Conclusion
Lee et al,[20] 1999	110 "Stable" patients with NVUGIH admitted to university ED	Randomized trial	Prompt upper endoscopy in ED vs direct admission with delayed upper endoscopy	History of variceal bleeding, cirrhosis, portal hypertension, hemodynamic instability, coagulopathy, history of UGIH within previous month, unable to consent or refused upper endoscopy	Mortality, rebleeding, need for surgery, readmission	Prompt upper endoscopy allowed immediate discharge of 46% with no complications or readmissions at 30 d
Campo et al,[26] 1998	83 "Low-risk" patients with NVUGIH presenting to community hospital	Randomized trial	Outpatient vs inpatient care of low-risk patients undergoing upper endoscopy within 12 h of presentation	Variceal bleeding, hemodynamic instability, visible vessel or adherent clot on upper endoscopy, poor accessibility to hospital, lack of adequate home support	Mortality, rebleeding	No complications in outpatient group with 7-d follow-up
Brullet et al,[27] 1998	20 Patients with NVUGIH and nonbleeding visible vessel on upper endoscopy presenting to community hospital	Randomized trial	Outpatient vs inpatient care of selected patients with nonbleeding visible vessel treated by endoscopic epinephrine injection within 12 h of presentation	Hemodynamic instability, peptic ulcer >10 mm, poor accessibility to hospital, lack of adequate home support	Mortality, rebleeding	No mortality in either group, and 1 episode of successfully treated rebleeding in outpatient group with 7-d follow-up
Almela et al,[28] 1999	983 Patients with NVUGIH admitted to university ED	Prospective nonrandomized study	Outpatient vs inpatient care of all comers undergoing prompt upper endoscopy in ED	Variceal bleeding, hemodynamic instability, stigmas of recent hemorrhage, unable to have upper endoscopy	Mortality, rebleeding, need for surgery	3 Deaths (1.5%) and 1 successfully treated rebleeding in outpatient group at 30 d
Hussain et al,[29] 1995	92 Patients with peptic ulcer bleeding presenting to health maintenance organization hospital	Before-and-after study	Outcomes of patients treated before and after implementation of early-discharge protocol requiring upper endoscopy within 12 h of presentation	Not stated	Need for surgery, length of stay	"Patients with clear ulcer base may be managed on outpatient basis"
Rockall et al,[30] 1997	3957 Patients with UGIH presenting to 45 hospitals	Before-and-after study	Outcomes of patients treated before and after implementation of national early-discharge protocol encouraging upper endoscopy within 24 h of presentation	Age <16 y	Mortality, length of stay, time to upper endoscopy	Patients underwent upper endoscopy more frequently and earlier after guidelines in place without change in severity-adjusted mortality

**UGIH indicates upper gastrointestinal tract hemorrhage; NVUGIH, nonvariceal UGIH; and ED, emergency department.*

In low risk patients….

low risk EGD findings..

Might mean early discharge or no admission

- 3 RCTs
- Consistent results from all studies

Arch Intern Med. 2001;161:1393-1404

Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial

John G. Lee, MD, Samuel Turnipseed, MD, Patrick S. Romano, MD, MPH, Heather Vigil, BS, Rahman Azari, PhD, Norman Melnikoff, MD, Ronald Hsu, MD, Douglas Kirk, MD, Peter Sokolove, MD, Joseph W. Leung, MD

Sacramento, California

Background: **Many patients with upper gastrointestinal (GI) bleeding have a benign outcome and could receive less intensive and costly care if accurately identified. We sought to determine whether early endoscopy performed shortly after admission in the emergency department could significantly reduce the health care use and costs of caring for patients with nonvariceal upper GI bleeding without adversely affecting the clinical outcome.**

Methods: **All eligible patients with upper GI bleeding and stable vital signs were randomized after admission to undergo endoscopy in 1 to 2 days (control) or early endoscopy in the emergency department. Patients with low-risk findings on early endoscopy were discharged directly from the emergency department. Clinical outcomes and costs were prospectively assessed for 30 days.**

Results: **We randomized 110 consecutive stable patients with nonvariceal upper GI bleeding during the 12-month study period. The baseline demographic features, endoscopic findings, and the clinical outcomes were no different between the two groups. However the findings of the early endoscopy allowed us to immediately discharge 26 of 56 (46%) patients randomized to that group. No patient discharged from the emergency department suffered an adverse outcome. The hospital stay (median of 1 day [interquartile range of 0 to 3 days] vs. 2 days [interquartile range of 2 to 3 days], $p = 0.0001$) and the cost of care ($2068 [interquartile range of $928 to $3960] versus $3662 [interquartile range of $2473 to $7280], $p = 0.00006$) were significantly less for the early endoscopy group.**

Conclusions: **Early endoscopy performed shortly after admission in the emergency department safely triaged 46% of patients with nonvariceal upper GI bleeding to outpatient care, which significantly reduced hospital stay and costs. (Gastrointest Endosc 1999;50:755-61.)**

Approximately 300,000 patients are hospitalized each year in the United States for treatment of upper GI bleeding. Most such bleeding arises from nonvariceal sources including peptic ulcer disease, Mallory-Weiss tear, and esophagitis and stops without specific intervention in 80% of cases.[1] Although the mortality of upper GI bleeding has remained fairly constant over the last 20 years, very few patients now bleed to death because effective endoscopic methods for achieving hemostasis are readily available.

Patients with nonvariceal upper GI bleeding who have active hemorrhage, shock, serious comorbid illness (e.g., myocardial infarction), and/or recurrent bleeding are usually observed in the intensive care unit because of increased risks of morbidity and mortality.[1-5] The first three groups can be triaged easily using historical and clinical criteria, but the risk of recurrent bleeding is more difficult to predict using clinical criteria readily available on admission. Endoscopic findings are helpful in predicting the outcome of patients with nonvariceal upper GI bleeding.[6-15] Patients with active bleeding or stigmata of recent hemorrhage experience continued or recurrent bleeding in up to 50% of cases, whereas patients with low-risk endoscopic lesions (e.g., a clean based gastric, duodenal, or esophageal ulcer, Mallory-Weiss tear, esophagitis, gastritis, or duodenitis) have a negligible risk of further bleeding.[1] There is a growing body of data showing that patients with such low-risk endoscopic findings can be discharged safely within 24 to 48 hours of admission, or even managed as outpatients.[16-22]

Although endoscopic findings can be used to accurately triage patients with upper GI bleeding, some patients with a negligible risk of recurrent bleeding are admitted unnecessarily to the intensive care unit or even to the hospital because endoscopy is usually

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Presented in part during the Digestive Disease Week in 1997, Washington, D.C., and 1998 New Orleans, Louisiana.

Supported in part by grants from the American Digestive Health Foundation and the Hibbard E. Williams Research Award from the University of California, Davis Health System.

Reprint request: John G. Lee, MD, Division of Gastroenterology, UC Davis Medical Center, 4150 V St., Room 3500, Sacramento, CA 95817; fax: 916-734-7908; e-mail: jgllee@ucdavis.edu.

 0016-5107/99/$8.00 + 0 **37/1/101045**

- RCT
- Patient randomized after ER attending decides to admit
- Among those who met inclusion criteria:
- Randomize to:
  - Early EGD (1-2 hours)
  - Normal care (1-2 days)

Exclusion criteria for this study

- comorbid illness requiring intensive care
- hemodynamic instability after resuscitation by infusion of 2 L of fluid
    - heart rate greater than 115 beats/min,
    - systolic blood pressure less than 90 mm Hg, or diastolic blood pressure less than 60 mm Hg)
- known or suspected variceal source,
- coagulopathy
    - (use of any anticoagulant or thrombolytic agents)
    - platelet count less than 50,000
    - international normalized ratio more than 1.5
- upper GI bleeding within the preceding 1 month
- age less than 18 years.

Table 3. Study outcomes

Outcome	Control group (n = 54)	Emergent endoscopy group (n = 56)	*p* Value
Transfusion requirement (units)	1.1 ± 1.7	1.2 ± 2.4	0.44
Hospital stay: median days (interquartile range)	2 (2-3)	1 (0-3)	0.0001
Recurrent hemorrhage: No. (%)	3 (5.6)	2 (3.6)	0.63
Repeat endoscopy: No. (%)	4 (7.4)	4 (7.1)	0.98
Surgery: No. (%)	1 (1.9)	2 (3.6)	0.99
Readmission: No. (%)	8 (14.8)	4 (7.1)	0.21
Unplanned visits to any physician: No. (%)	13 (24.5)	5 (8.9)	0.031
Death: No. (%)	2 (3.7)	0	0.54
Total median costs: dollars (interquartile range)	3662 (2473-7280)	2068 (928-3960)	0.00006

Plus-minus values are means ± SD.

46% discharged immediately after EGD: number needed to scope to avoid one admission ~2

Identifying low risk patients: Who can be sent home from triage ?

- No hemodynamic instability
- Limited hematemesis
- Few/No comorbid conditions
- Good support system

- Consider “Triage” endoscopy
  - EGD with MW tear or ulcer with clean base
- Consider outpatient management
- RCT evidence to suggest this is safe

Who needs to be in a monitored bed or in the ICU ?

Statement A2

Prognostic scales are recommended for early stratification of patients into low- and high-risk categories for rebleeding and mortality. (Agree, 97% [Vote: a, 56%; b, 35%; c, 6%; d, 3%]. Grade: Low, 1c, “do it”)

My personal assessment of guideline:
The data supports using a systematic approach for triage and possible discharge

Ann Intern Med. 2010;152:101-113.

NG Tube ?

Recommendation 4: In selected patients, the placement of a nasogastric tube can be considered because the findings may have prognostic value. Recommendation: B (vote: a, 40%; b, 36%; c, 24%); Evidence: II-3

C= accept with major reservations

From previous version of guidelines by Barkun et al. from Annals 2003

Studies Cited in the UGI Bleeding Guidelines (Barkun et al)

	Cuellar RE, et al. Arch Intern Med. 1990 Jul; 150(7): 1381-4.	Perng et al. Am J Gast. 1994 Oct; 89(10): 1811-4	Aljebreen et al. Gastro. End. 2004;59:172-8.
	Hospital series: signs of UGI bleeding and ulcers on EGD n=62	Hospital series with bleeding ulcer n=314	National Registry UGI bleeding all sources N=520
NG interpretation for predicting outcome	Fellows interpretation of NG aspirate showing active bleeding predicts Active bleeding	Coffee grounds or blood predicts Bleeding or NBVV	Bloody aspirate predicts High risk lesion
Sensitivity	0.79	0.59	0.48
Specificity	0.55	0.62	0.76
PVP	0.53	0.47	0.45
PVN	0.80	0.73	0.78
Likelihood ratio (positive)	1.8	1.5	2.0

Studies in recent metanalysis of NG tube aspirate in ER patients with melena or hematochezia without hematemesis

Table 3
Operating Characteristics of Nasogastric Aspiration and Lavage in Diagnosing Upper GI Hemorrhage in Patients With Hematochezia or Melena Without Hematemesis

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	LR+	LR–
Aljebreen et al., 2004[15]*	68 (57–78)	54 (45–61)	41 (33–50)	78 (69–85)	1.44	0.61
Cappell, 2005[17]	84 (70–93)	82 (57–96)	93 (81–98)	64 (43–80)	4.74	0.2
Witting, et al., 2004[18]	42 (32–51)	91 (83–95)	81 (69–90)	61 (53–68)	4.44	0.65

GI = gastrointestinal; LR+ = likelihood ratio of a positive test; LR– = likelihood ratio of a negative test; NPV = negative predictive value; PPV = positive predictive value.
*Information obtained by contacting authors.

Gold standard was EGD finding of in all studies

ACADEMIC EMERGENCY MEDICINE 2010; 17:126–132

Nasogastric tubes

- Indicated for decompression
- Not therapeutic in GI bleeding
- Not that effective in lavage as prep for endoscopy
  - (compared to large bore orograstric tubes)
- Not diagnostic (enough) in GI bleeding ?
  - Sensitivity < 80% for important UGI bleeding or high risk lesion
- My view – not useful. Will not be requested by GI at the VA. (Because Drs. Fiske and Awad agree with me).

(We probably know enough, we disagree about how to use what we know)

NG Tube ?

Recommendation 4: In selected patients, the placement of a nasogastric tube can be considered because the findings may have prognostic value. Recommendation: B (vote: a, 40%; b, 36%; c, 24%); Evidence: II-3

C= accept with major reservations

From previous version of guidelines by Barkun et al. from Annals 2003

My assessment of the guideline: the data does not support the use of NG tube to identify high risk patients because I have a higher demand for sensitivity than the authors of the guidelines.

This is what I emphasize to the Surgery housestaff and GI Fellows

- **Diagnose Upper GI bleeding**
- **Triage according to risk**
- Stabilize patient : Start Resuscitation
- Call GI and Surgery early
- Initiate empiric therapy

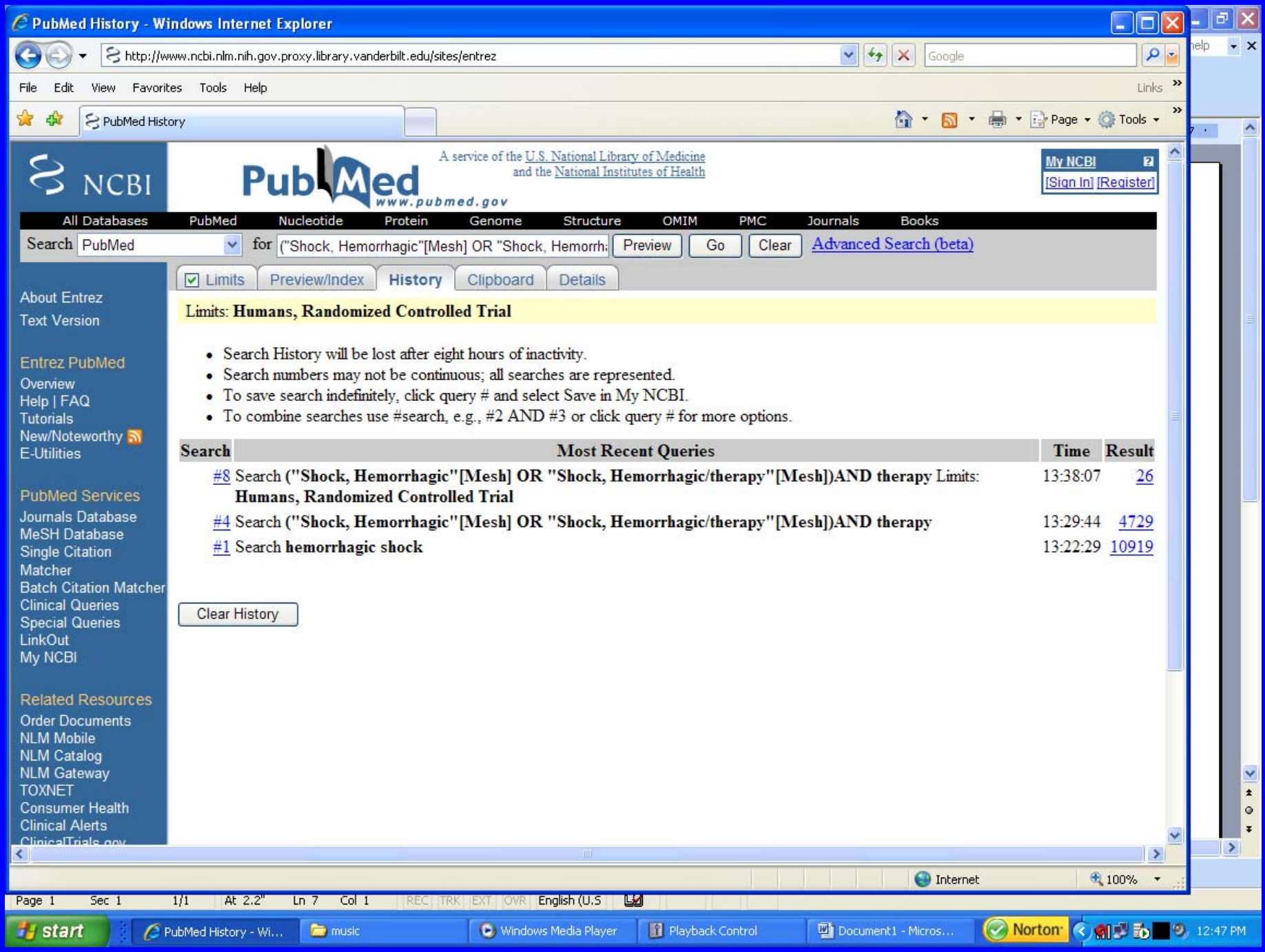
Virtually immediately (minutes) the job of internist/ hospitalist

- Decide about timing of endoscopy
- Make diagnosis
- Treat underlying condition

Hours: the job of GI and surgery

Initial Treatment

- Large bore IV access, multiple sites
  - Don’t let central access delay other interventions
- Volume replacement
- Consider Pressors
- Start Oxygen (especially if conscious sedation is anticipated)
- Transfusion goals
  - PCV > 25% and stable, >30% if Hx. CAD
  - INR < 1.5
  - Platelets >50K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Consumer Health
Clinical Alerts
Limits: Humans, Randomized Controlled Trial
Search History will be lost after eight hours of inactivity.
Search numbers may not be continuous; all searches are represented.
To save search indefinitely, click query # and select Save in My NCBI.
To combine searches use #search, e.g., #2 AND #3 or click query # for more options.
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Statement A4

Blood transfusions should be administered to a patient with a hemoglobin level of 70 g/L or less.

(Agree, 100% [Vote: a, 59%; b, 35%; c, 6%].

Grade: Low, 1c, “do it”)

Controversy

Parachute approach to evidence based medicine

Malcolm Potts, Ndola Prata, Julia Walsh, Amy Grossman

Waiting for the results of randomised trials of public health interventions can cost hundreds of lives, especially in poor countries with great need and potential to benefit. If the science is good, we should act before the trials are done

In 2003 Smith and Pell published an entertaining but profound article titled: "Parachute use to prevent death and major trauma due to gravitational challenge."[1] They used the lack of randomised controlled trials in testing parachutes to show that situations still exist where such trials are unnecessary. We argue that the parachute approach, where policies are set based on good science but without randomised trials, is often more suitable in resource poor settings. We use the examples of oral rehydration therapy, male circumcision to prevent HIV infection, and misoprostol for postpartum haemorrhage to show how an overemphasis on randomised controlled trials in poor settings poses important ethical and logistic problems and may incur avoidable deaths.

Childhood diarrhoea and oral rehydration therapy

In 1980 childhood diarrhoea was killing an estimated 4.6 million children annually.[2] Treatment with an intravenous drip is life saving but requires health facilities. Studies from 1977 onwards showed that infant diarrhoea could be treated with oral rehydration.[3] The World Health Organization initiated a highly successful programme of oral rehydration therapy in 1981

concluded circumcision slowed heterosexual HIV transmission.[11]

In 2003 in a Johannesburg township began a randomised controlled trial in which over 3000 informed volunteers aged 18 to 24 years were randomly allotted to immediate circumcision or circumc
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Sometimes it's best just to jump in

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Postpartum haemorrhage and misoprostol

Worldwide, postpartum haemorrhage is the leading cause of maternal death, and most of those who die are women in developing countries delivering at home

School of Public Health, University of California, 314 Warren Hall, Berkeley, CA 94720, USA

Malcolm Potts
Bixby professor,

Treatment of hemorrhagic shock: Liberal or Conservative Pressor therapy ? Liberal or Conservative volume resuscitation ?

- Goal directed therapy (MAP, etc) is an attractive concept but has not been proven outside setting of septic shock
- Pressors may have some role – there is very little comparative, human data in the setting of treating NVUGIH
- In general start with aggressive volume resuscitation
  - Crystalloid (20 ml per kg)
  - Blood when needed, ready
- We need to know more about optimal resuscitation for GI hemorrhage (in humans)

Statement A4

Blood transfusions should be administered to a patient with a hemoglobin level of 70 g/L or less.

(Agree, 100% [Vote: a, 59%; b, 35%; c, 6%]. Grade: Low, 1c, “do it”)

My assessment: Yes, despite the lack of RCT evidence I agree it is a good thing to treat shock……

- **Statement A8**
- *Preendoscopic PPI therapy may be considered to downstage the endoscopic lesion and decrease the need for endoscopic intervention but should not delay endoscopy.*
- (Agree, 94% [Vote: a, 32%; b, 38%; c, 24%; d, 3%; e,3%]. Grade: Moderate, 1b, “do it”)

What about acid suppression ?

- What should be the outcomes for treatment of NVUGIH ?
- Primary endpoints
  - Mortality
  - Major Morbidity
    - Need for an operation

- Secondary endpoints
  - Transfusion
  - Hospital days
  - Costs (medical/non medical, direct and indirect, patient/payor/societal perspectives)
  - “Control of bleeding”

Acid Suppression
(Smalley : GI conference circa July 2008)

- There is good evidence that acid suppression may decrease
  - rebleeding rates
  - surgical rates
- There is very little evidence that it saves lives

- A mortality benefit would be a difficult to meet standard to meet

REVIEW ARTICLE

CURRENT CONCEPTS

Management of Acute Bleeding from a Peptic Ulcer

Ian M. Gralnek, M.D., M.S.H.S., Alan N. Barkun, M.D., C.M., M.Sc., and Marc Bardou, M.D., Ph.D.

From the Department of Gastroenterology and Gastrointestinal Outcomes Unit, Rambam Health Care Campus and Rappaport Faculty of Medicine, Technion Israel Institute of Technology, Haifa, Israel (I.M.G.); the Divisions of Gastroenterology and Clinical Epidemiology, McGill University Health Centre, McGill University, Montreal (A.N.B.); and INSERM Centre d'Investigations Cliniques Plurithématique, Centre Hospitalier Universitaire du Bocage and Institut Fédératif de Recherche Santé, Sciences et Techniques de l'Information et de la Communication, Université de Bourgogne — both in Dijon, France (M.B.). Address reprint requests to Dr. Gralnek at the Department of Gastroenterology and Gastrointestinal Outcomes Unit, Rambam Health Care Campus, Bat Galim, Haifa 31096, Israel, or at i_gralnek@rambam.health.gov.il.

N Engl J Med 2008;359:928-37.

ACUTE UPPER GASTROINTESTINAL HEMORRHAGE, WHICH IS DEFINED AS bleeding proximal to the ligament of Treitz, is a prevalent and clinically significant condition with important implications for health care costs worldwide. Negative outcomes include rebleeding and death, and many of the deaths are associated with decompensation of coexisting medical conditions precipitated by the acute bleeding event.[1] This review focuses specifically on the current treatment of patients with acute bleeding from a peptic ulcer.

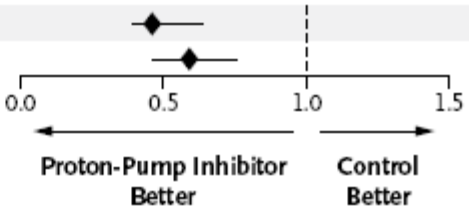
EPIDEMIOLOGY

The annual rate of hospitalization for acute upper gastrointestinal hemorrhage in the United States is estimated to be 160 hospital admissions per 100,000 population, which translates into more than 400,000 per year.[2] In most settings, the vast majority of acute episodes of upper gastrointestinal bleeding (80 to 90%) have nonvariceal causes, with gastroduodenal peptic ulcer accounting for the majority of lesions.[3] A number of studies have suggested that the annual incidence of bleeding from a peptic ulcer may be decreasing worldwide,[4] yet other recent population-based estimates have suggested that the incidence is about 60 per 100,000 population,[5] with an increasing proportion of episodes related to the use of aspirin and nonsteroidal antiinflammatory medications. Moreover, peptic ulcer bleeding is seen predominantly among the elderly, with 68% of patients over the age of 60 years and 27% over the age of 80 years.[6] Mortality associated with peptic ulcer bleeding remains high at 5 to 10%.[1,3] Estimated direct medical costs for the in-hospital care of patients with bleeding from a peptic ulcer total more than $2 billion annually in the United States.[7]

CLINICAL PRESENTATION

A Rebleeding and Surgery

Group	Proton-Pump Inhibitor	Control
	no. of patients/no. of events	
Rebleeding	1026/111	1031/189
Surgery	1081/38	1103/71



B Death

Group	Proton-Pump Inhibitor	Control
	no. of patients/no. of events	
All patients	1040/20	1062/38
With endoscopic hemostasis	954/17	969/32
Without endoscopic hemostasis	86/3	93/6

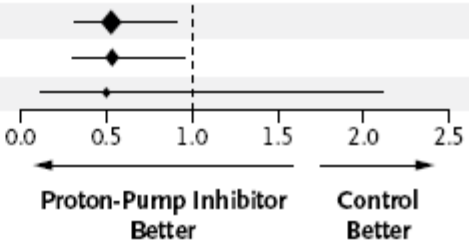


Figure 3. Effect of Proton-Pump Inhibition in Peptic-Ulcer Bleeding.

Forrest plots show the efficacy of the use of proton-pump inhibitors in decreasing the rates of rebleeding and surgery (Panel A) and death (Panel B). Rates of death are shown for all patients and for those who have either undergone endoscopic hemostasis or not undergone endoscopic hemostasis. The diamonds represent odds ratios (with the size of the diamonds proportional to the number of patients), and the horizontal lines represent 95% confidence intervals. Data are from Leontiadis et al.[57]

Proton pump inhibitor treatment for acute peptic ulcer bleeding (Review)

Leontiadis G I, Sharma V K, Howden C W

THE COCHRANE COLLABORATION®

Lesson from the literature: Sometimes things get quoted in strange ways

Authors' conclusions

PPI treatment in PU bleeding reduces rebleeding and surgery compared with placebo or H2RA, but there is no evidence of an overall effect on all-cause mortality.

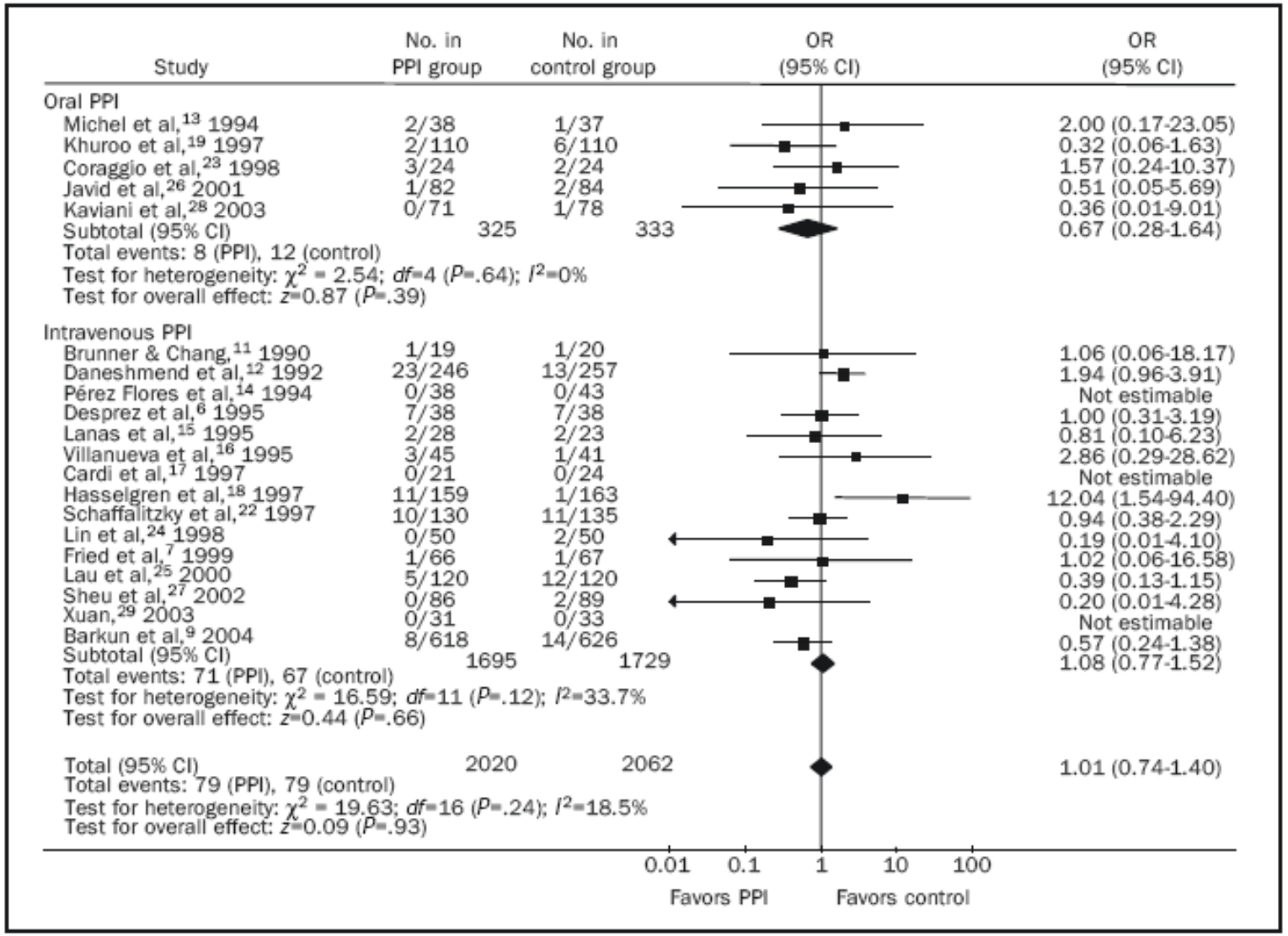
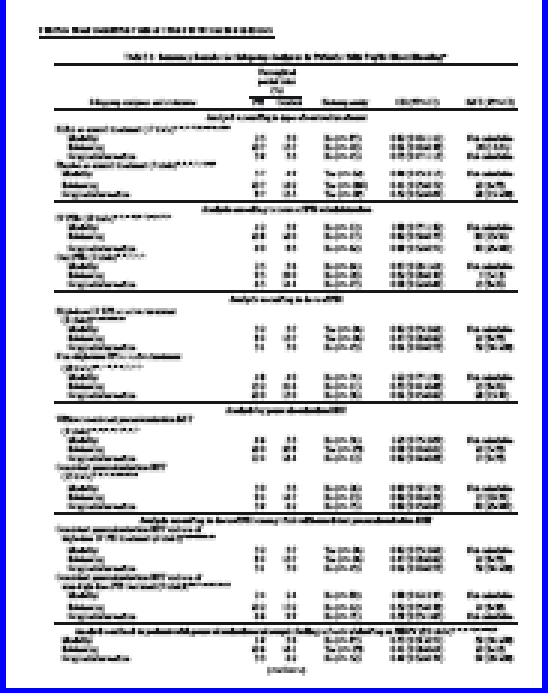
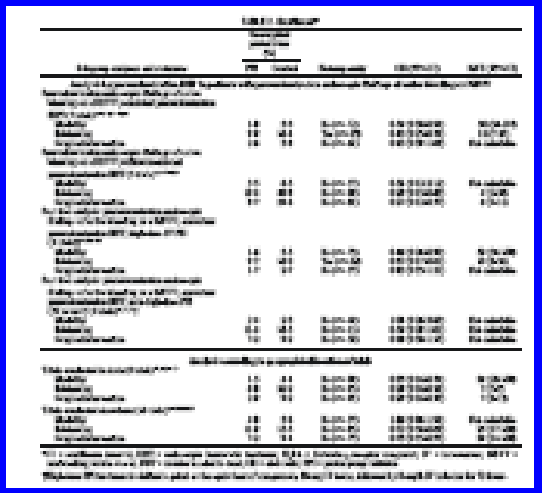


FIGURE 2. Forest plot of the odds ratios (ORs) and 95% confidence intervals (CIs) of individual trials and pooled data for mortality; subgroup analysis according to route of proton pump inhibitor (PPI) administration.

Mortality

Mayo Clin Proc. 2007;82(3):286-296





Multiple subgroup analysis were done……

TABLE 2. **Summary Results for Subgroup Analyses in Patients With Peptic Ulcer Bleeding***

Subgroup analyses and outcomes	Unweighted pooled rates (%)		Heterogeneity	OR (95% CI)	NNT (95% CI)
	PPI	Control			
Analysis according to route of PPI administration					
IV PPIs (19 trials)[6-12,14-18,20-22,24,25,27,29]					
Mortality	4.2	3.9	No (P=.12)	1.08 (0.77-1.52)	Not calculable
Rebleeding	10.8	16.0	No (P=.17)	0.62 (0.50-0.75)	20 (13-34)
Surgical intervention	6.0	8.3	No (P=.62)	0.69 (0.52-0.91)	50 (25-100)
Oral PPIs (5 trials)[13,19,23,26,28]					
Mortality	2.5	3.6	No (P=.64)	0.67 (0.28-1.64)	Not calculable
Rebleeding	9.5	24.0	No (P=.20)	0.32 (0.20-0.50)	7 (5-12)
Surgical intervention	6.5	14.4	No (P=.47)	0.38 (0.22-0.66)	13 (8-25)

TABLE 2. **Summary Results for Subgroup Analyses in Patients With Peptic Ulcer Bleeding***

Subgroup analyses and outcomes	Unweighted pooled rates (%)		Heterogeneity	OR (95% CI)	NNT (95% CI)
	PPI	Control			
Analysis confined to patients with prerandomization endoscopic findings of active bleeding or NBVV (12 trials)[9-11,16-19,21,24-26,28]					
Mortality	1.9	3.6	No (P=.87)	0.53 (0.31-0.91)	50 (34-100)
Rebleeding	10.6	18.1	Yes (P=.03)	0.41 (0.26-0.64)	10 (6-20)
Surgical intervention	3.3	6.2	No (P=.52)	0.49 (0.32-0.74)	34 (20-100)

TABLE 2. **Summary Results for Subgroup Analyses in Patients With Peptic Ulcer Bleeding***

Subgroup analyses and outcomes	Unweighted pooled rates (%) PPI	Control	Heterogeneity	OR (95% CI)	NNT (95% CI)
Analysis according to geographical location of trials					
Trials conducted in Asia (8 trials)[19,21,24-29]					
Mortality	1.5	4.4	No (P=.99)	0.35 (0.16-0.74)	34 (20-100)
Rebleeding	6.8	22.2	No (P=.95)	0.24 (0.16-0.36)	7 (5-9)
Surgical intervention	2.9	9.2	No (P=.91)	0.29 (0.16-0.53)	7 (6-13)
Trials conducted elsewhere (16 trials)[6-18,20,22,23]					
Mortality	4.8	3.6	No (P=.37)	1.36 (0.94-1.96)	Not calculable
Rebleeding	11.9	15.5	No (P=.85)	0.72 (0.58-0.89)	25 (17-100)
Surgical intervention	7.2	9.4	No (P=.77)	0.73 (0.55-0.95)	34 (14-100)

*CI = confidence interval; EHT = endoscopic hemostatic treatment; H_2RA = histamine$_2$-receptor antagonist; IV = intravenous; NBVV = nonbleeding visible vessel; NNT = number needed to treat; OR = odds ratio; PPI = proton pump inhibitor.

†High-dose PPI treatment is defined a priori as the equivalent of omeprazole, 80-mg IV bolus, followed by 8-mg/h IV infusion for 72 hours.

Metanalysis done for consensus guidelines preparation

31 RCTs (24)
Total 5792

PPI treatment with or without endoscopic therapy compared with placebo or H2RA

1)Main outcome:

Rebleeding: OR 0.45 (95%CI 0.36, 0.57)

2) Secondary outcome:

Surgery: OR 0.56 (95%CI 0.45, 0.70)

Mortality: OR 0.90 (95%CI 0.67, 1.19)

Ann Intern Med. 2010;152:101-113.

Online appendix table 2

PPI's Summary

- There is no definitive improvement in mortality overall
  - Probably a benefit in those with high risk lesions
  - Demonstrating mortality benefit would be a very high standard
- PPI s seem to consistently decrease need for transfusion and need for operation
- The effects of oral PPI **versus** IV PPIs have not been directly compared (enough) – similar outcomes appear to be expected given the current data
- PPI's seem to work better with a bolus followed by continuous infusion
- Timing of EGD should not be influenced by administration of PPI
- PPIs are not likely to be harmful (in the short run)

- **Statement A8**
- *Preendoscopic PPI therapy may be considered to downstage the endoscopic lesion and decrease the need for endoscopic intervention but should not delay endoscopy.*
- (Agree, 94% [Vote: a, 32%; b, 38%; c, 24%; d, 3%; e,3%]. Grade: Moderate, 1b, “do it”)

- My assessment: PPIs are helpful, probably not harmful

- What to do about aspirin in patients with UGI bleeding ?

- Gastroenterologist/lawyer from the podium
  - “I can stop most GI bleeds.”
  - “I can’t stop most MIs”

Statement E3

In patients who receive low-dose ASA and develop acute ulcer bleeding, ASA therapy should be restarted as soon as the risk for cardiovascular complication is thought to outweigh the risk for bleeding.

(Agree, 100% [Vote: a, 70%; b, 30%]. Grade: Moderate,1b, “do it”)

Annals of Internal Medicine | ARTICLE

Continuation of Low-Dose Aspirin Therapy in Peptic Ulcer Bleeding

A Randomized Trial

Joseph J.Y. Sung, MD, PhD; James Y.W. Lau, MD; Jessica Y.L. Ching, MPH; Justin C.Y. Wu, MD; Yuk T. Lee, MD; Philip W.Y. Chiu, MD; Vincent K.S. Leung, MD; Vincent W.S. Wong, MD; and Francis K.L. Chan, MD

Background: It is uncertain whether aspirin therapy should be continued after endoscopic hemostatic therapy in patients who develop peptic ulcer bleeding while receiving low-dose aspirin.

Objective: To test that continuing aspirin therapy with proton-pump inhibitors after endoscopic control of ulcer bleeding was not inferior to stopping aspirin therapy, in terms of recurrent ulcer bleeding in adults with cardiovascular or cerebrovascular diseases.

Design: A parallel randomized, placebo-controlled noninferiority trial, in which both patients and clinicians were blinded to treatment assignment, was conducted from 2003 to 2006 by using computer-generated numbers in concealed envelopes. (ClinicalTrials.gov registration number: NCT00153725)

Setting: A tertiary endoscopy center.

Patients: Low-dose aspirin recipients with peptic ulcer bleeding.

Intervention: 78 patients received aspirin, 80 mg/d, and 78 received placebo for 8 weeks immediately after endoscopic therapy. All patients received a 72-hour infusion of pantoprazole followed by oral pantoprazole. All patients completed follow-up.

Measurements: The primary end point was recurrent ulcer bleeding within 30 days confirmed by endoscopy. Secondary end points were all-cause and specific-cause mortality in 8 weeks.

Results: 156 patients were included in an intention-to-treat analysis. Three patients withdrew from the trial before finishing follow-up. Recurrent ulcer bleeding within 30 days was 10.3% in the aspirin group and 5.4% in the placebo group (difference, 4.9 percentage points [95% CI, −3.6 to 13.4 percentage points]). Patients who received aspirin had lower all-cause mortality rates than patients who received placebo (1.3% vs. 12.9%; difference, 11.6 percentage points [CI, 3.7 to 19.5 percentage points]). Patients in the aspirin group had lower mortality rates attributable to cardiovascular, cerebrovascular, or gastrointestinal complications than patients in the placebo group (1.3% vs. 10.3%; difference, 9 percentage points [CI, 1.7 to 16.3 percentage points]).

Limitations: The sample size is relatively small, and only low-dose aspirin, 80 mg, was used. Two patients with recurrent bleeding in the placebo group did not have further endoscopy.

Conclusion: Among low-dose aspirin recipients who had peptic ulcer bleeding, continuous aspirin therapy may increase the risk for recurrent bleeding but potentially reduces mortality rates. Larger trials are needed to confirm these findings.

Primary Funding Source: Institute of Digestive Disease, Chinese University of Hong Kong.

Ann Intern Med. 2010;152:1-9. www.annals.org

For author affiliations, see end of text.

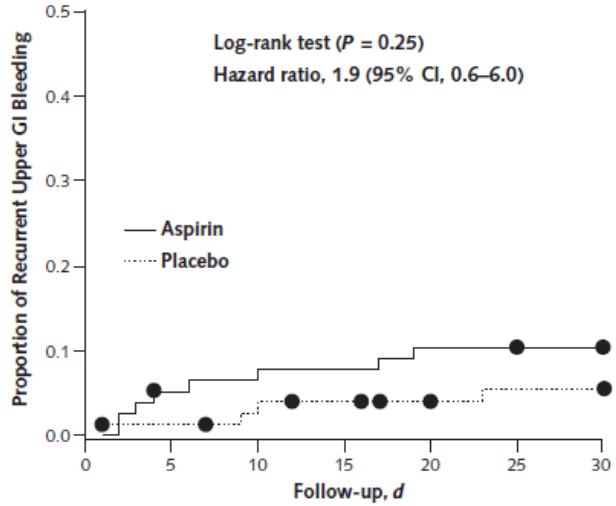
This article was published at www.annals.org on 1 December 2009.

- RCT among persons with ulcer related bleeding requiring endoscopic treatment
- All had been on ASA prophylaxis for documented CVD or cerebrovascular disease
- All got PPI and HP testing and treatment

- ASA 85 mg vs placebo

ASA group
More bleeding 10% vs 5% at 2 months
Less dying 1% vs 12% at 2 months

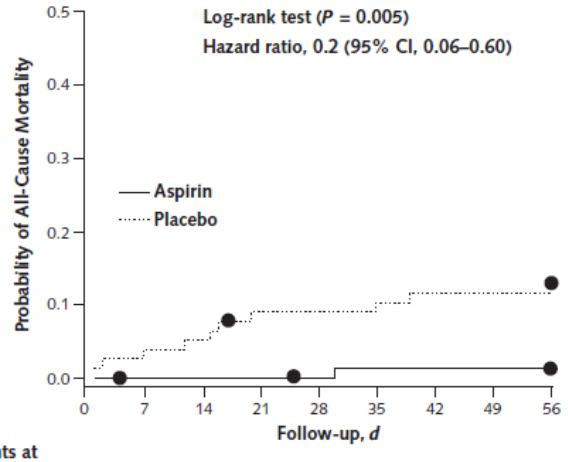
Figure 2. Kaplan–Meier estimates of the incidence of confirmed recurrent upper GI bleeding within 30 days.



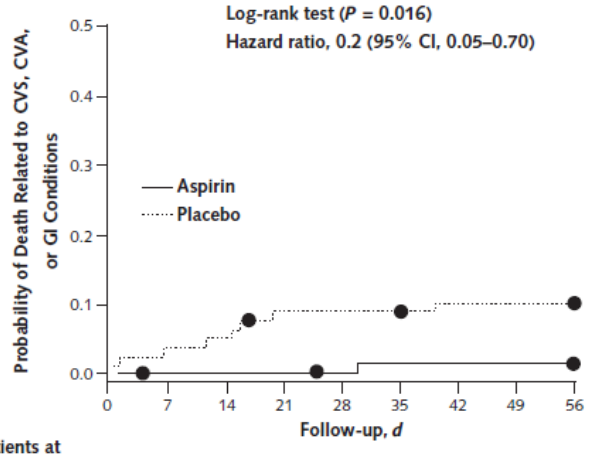
Patients at risk, n							
Aspirin	78	73	71	71	69	68	67
Placebo	78	75	72	71	68	67	67

Solid circles indicate censoring. GI = gastrointestinal.

Figure 3. Kaplan–Meier estimates of the incidence of mortality within 8 weeks.



Patients at risk, n									
Aspirin	78	77	77	77	76	75	75	75	75
Placebo	78	75	74	70	70	69	68	68	67



Patients at risk, n									
Aspirin	78	77	77	77	76	75	75	75	75
Placebo	78	75	74	70	70	69	68	68	67

Solid circles indicate censoring. CVA = cerebrovascular; CVS = cardiovascular; GI = gastrointestinal.

Statement E3

In patients who receive low-dose ASA and develop acute ulcer bleeding, ASA therapy should be restarted as soon as the risk for cardiovascular complication is thought to outweigh the risk for bleeding.

(Agree, 100% [Vote: a, 70%; b, 30%]. Grade: Moderate,1b, “do it”)

My assessment: I agree with this – especially since an RCT published after the guideline supports this

- **Statement A5**
- *In patients receiving anticoagulants, correction of coagulopathy is recommended but should not delay endoscopy.*
- (Agree, 97% [Vote: a, 38%; b, 44%; c, 15%; d, 3%]. Grade: Low, 2c, “probably do it”)

Ann Intern Med. 2010;152:101-113.

Antithrombotics in bleeding

- Weak indication (Primary prophylaxis of afib etc.) : hold or reverse anticoagulation
- Among those with a strong indication for anticoagulation
    - bare metal stents in first several weeks or drug eluting stents for 12 months
    - Mitral valve, PE, Acute coronary syndrome etc.
  - Restart aspirin once bleeding is controlled
  - Hold the antithrombotics and non aspirin antiplatelet agents until bleeding is controlled (usually < 24 hours)
  - Reverse the antithrombotics if bleeding is not controlled and patient is in shock/may go to OR

This is what I emphasize to the Surgery housestaff and GI Fellows

- **Diagnose Upper GI bleeding**
- **Triage according to risk**
- **Stabilize patient : Start Resuscitation**
- **Call GI and Surgery early**
- **Initiate empiric therapy**

Virtually immediately (minutes) the job of internist/ hospitalist with input from GI

- Decide about timing of endoscopy
- Make diagnosis
- Treat underlying condition

Hours: the job of GI and surgery


ROAN MOUNTAIN FIRE Dept.
FIRE WORK SALES

- Endoscopy in acute upper GI bleeding

- Timing
- Preparation
- Interventions

Statement B3

- *Early endoscopy (within 24 hours of presentation) is recommended for most patients with acute upper gastrointestinal bleeding.*
- (Agree, 100% [Vote: a, 85%; b, 12%; c, 3%]. Grade: Moderate, 1b, “do it”)

Ann Intern Med. 2010;152:101-113.

3 RCTs		Total 528	Urgent endoscopy (1-12 hours) compared with later endoscopy (>12 h to 48 h) 1) Main outcome: Rebleeding: OR 0.71 (95%CI 0.28, 1.81) 2) Secondary outcomes Surgery: OR 1.16 (95%CI 0.39, 3.51) Mortality: OR 0.70 (95%CI 0.14, 3.57) Comments: A recommendation of "do it" because early endoscopy (<24 hours) was adopted based on previously noted improvements in secondary outcome measures (15), however without the need for a more urgent timing of the endoscopy. It was noted that endoscopy may need to be delayed or deferred in selected high-risk patients (e.g., very elevated INR, active acute coronary syndrome, suspected perforation (38))
Bjorkman 2004 (75)	• EGD within 6 h • EGD within 48 h	47 46	
Lin 1996 (84)	• EGD < 12 h • EGD > 12 h	162 163	
Lee 1999 (85)	• Urgent endoscopy ≤1-2 h in emergency • Elective endoscopy ≤1-2 days of admission	56 54	

- No proven mortality benefit from "very early" (1-12 hours) vs early < 24 hours

- Some observational data to suggest benefit from "after hours" vs "no after hours" endoscopy availability

Ann Intern Med. 2010;152:101-113.

Preparing for endoscopy

- GI patients usually need to be NPO…..
- if they can eat…..why are they in the hospital ?
- Note: Gastroenterologist's and Insurance company views only

- *Promotility agents should not be used routinely before endoscopy to increase the diagnostic yield.*
- (Agree, 82% [Vote: a, 35%; b, 35%; c, 12%; d, 6%;e, 3%; f, 9%]. Grade: Moderate, 2b, “probably don’t do it”)

Ann Intern Med. 2010;152:101-113.

- “A meta-analysis (21) of 3 trials that evaluated erythromycin (60–62), comprising 316 patients, and 2 abstracts that evaluated metoclopramide (63, 64) found that use of a prokinetic agent significantly reduced the need for repeated endoscopy (odds ratio [OR], 0.51 [95% CI, 0.30 to 0.88]) in patients suspected of having blood in their stomach, compared with placebo or no treatment (**Appendix Table2).”**

Ann Intern Med. 2010;152:101-113.

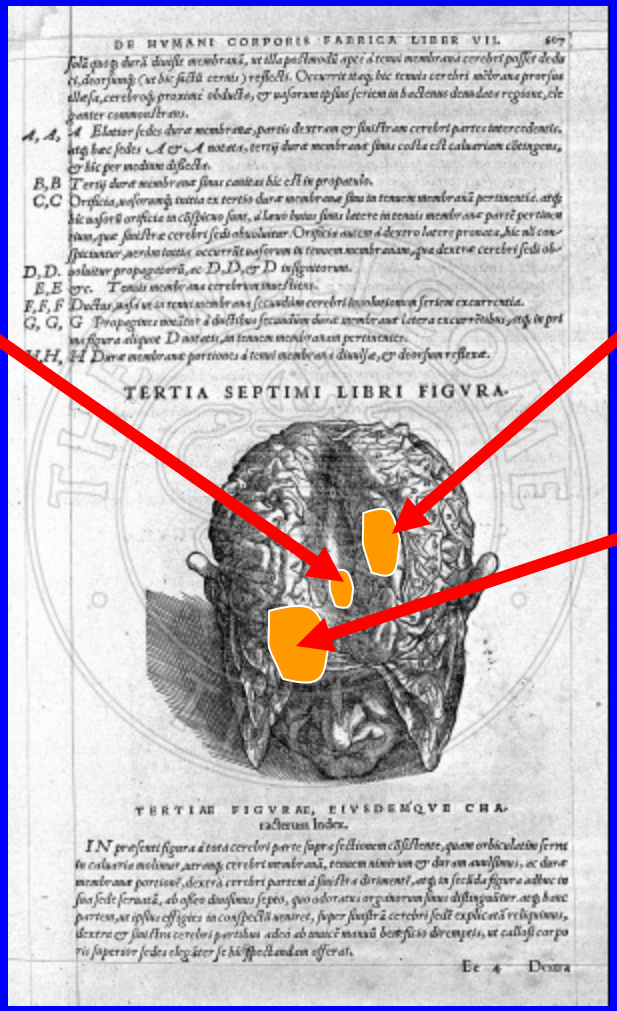
- *Promotility agents should not be used routinely before endoscopy to increase the diagnostic yield.* (Agree, 82% [Vote: a, 35%; b, 35%; c, 12%; d, 6%;e, 3%; f, 9%]. Grade: Moderate, 2b, “probably don’t do it”)
- The data cited by the guideline document is consistently positive
  - 3/3 RCTs, double blinded etc
  - The guideline writers fail to make a case why not to use promotility agents routinely
  - There possible risks to IV erythromycin but these were unapparent in the trials

Ann Intern Med. 2010;152:101-113.

- Sometimes guideline voting does not follow the data presented

Neuroanatomy for Endoscopists

1. The “remember to breath” center



2. The “don’t let them put something down my throat” center

3. The “don’t let them put something in my rectum” center

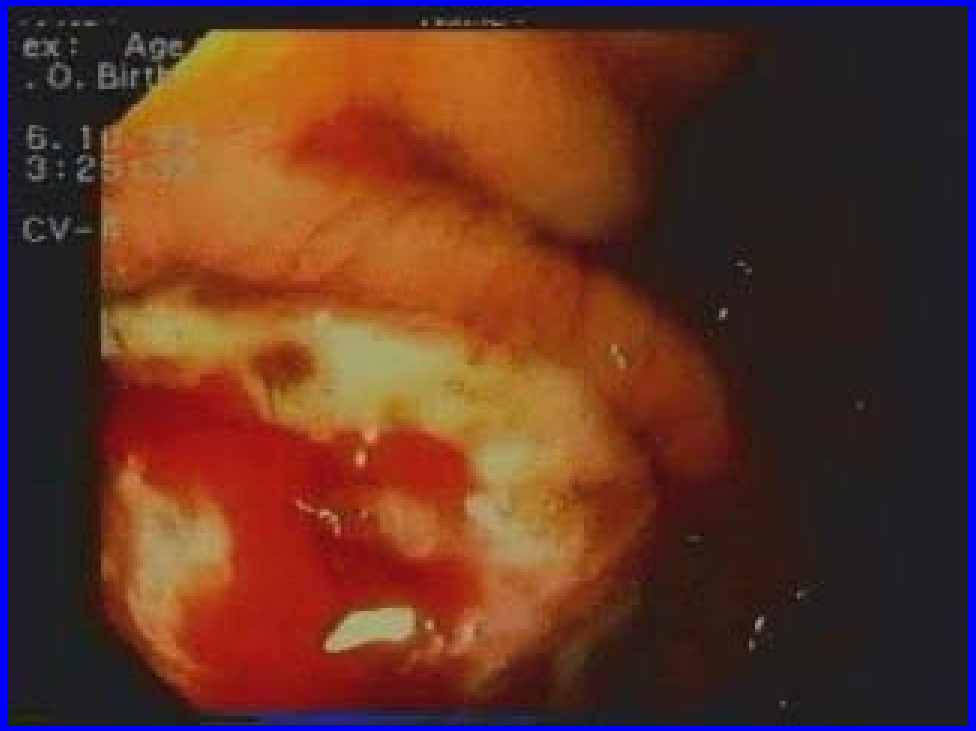
Goal of conscious sedation: knock out #2 and #3 while not bothering #1

Endotracheal tubes

- Protect airway
  - "Elective intubation is better than emergent intubation"
  - Setting
    - Massive bleeding (hematemesis)
    - Decreased mental status
  - Allows for more aggressive conscious/deep sedation
  - Allows for more definitive endoscopic therapy in patients with massive bleeding ("gourmet endoscopy")

- ASGE Guidelines "Patients with ongoing, significant hematemesis or those who may not be able to protect their airway for any reason and are at risk for aspiration should be considered for endotracheal intubation before undergoing endoscopy."

- Now that we are doing endoscopy what do we do when we get there ?



Prognostic information from endoscopy "Stigmata of recent hemorrhage" (SRH)

- High risk

Spurting vessel	Attempt treatment
Oozing vessel	Attempt treatment
Adherent clot	Attempt treatment
Dark spot	Observe ?
Clean Base	Send home ?

- Low Risk

- B5. A finding of a clot in an ulcer bed warrants targeted irrigation in an attempt at dislodgement, with appropriate treatment of the underlying lesion.†
- B7. Endoscopic hemostatic therapy is indicated for patients with high-risk stigmata (active bleeding or a visible vessel in an ulcer bed).*
- B8. Epinephrine injection alone provides suboptimal efficacy and should be used in combination with another method.†

- B9. No single method of endoscopic thermal coaptive therapy is superior to another.*
- B10. Clips, thermocoagulation, or sclerosant injection should be used in patients with high-risk lesions, alone or in combination with epinephrine injection.†
- B11. Routine second-look endoscopy is not recommended.†
- B12. A second attempt at endoscopic therapy is generally recommended in cases of rebleeding.*

“Endoscopic therapy for patients with UGIB caused by PUD has been studied in randomized, controlled trials.

Laser therapy; monopolar electrocautery ; bipolar electrocautery; heat probe; epinephrine injection; and epinephrine injection with additives, such as the sclerosants ethanolamine and polidocanol,

are all effective when compared with no therapy or sham therapy.”

ASGE guideline: the role of endoscopy in acute non-variceal upper-GI hemorrhage 2004

“Numerous prospective randomized studies of endoscopic treatment methods have been performed.

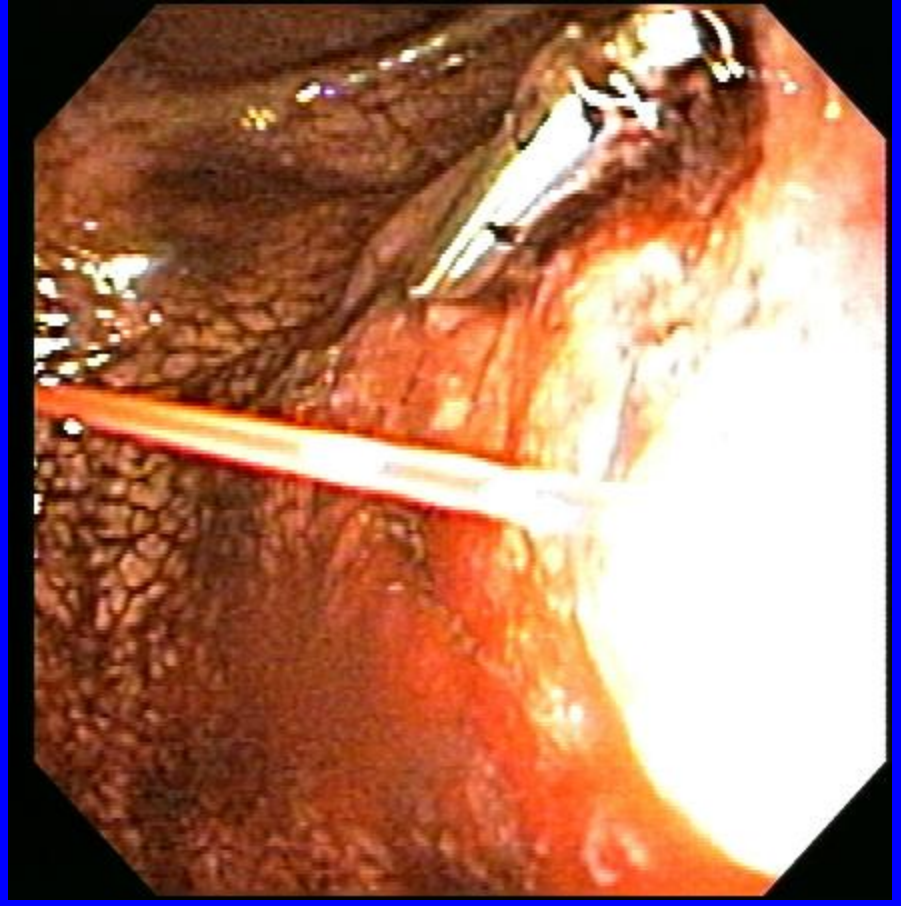
No single modality has been shown to be superior for treating UGIB caused by PUD.

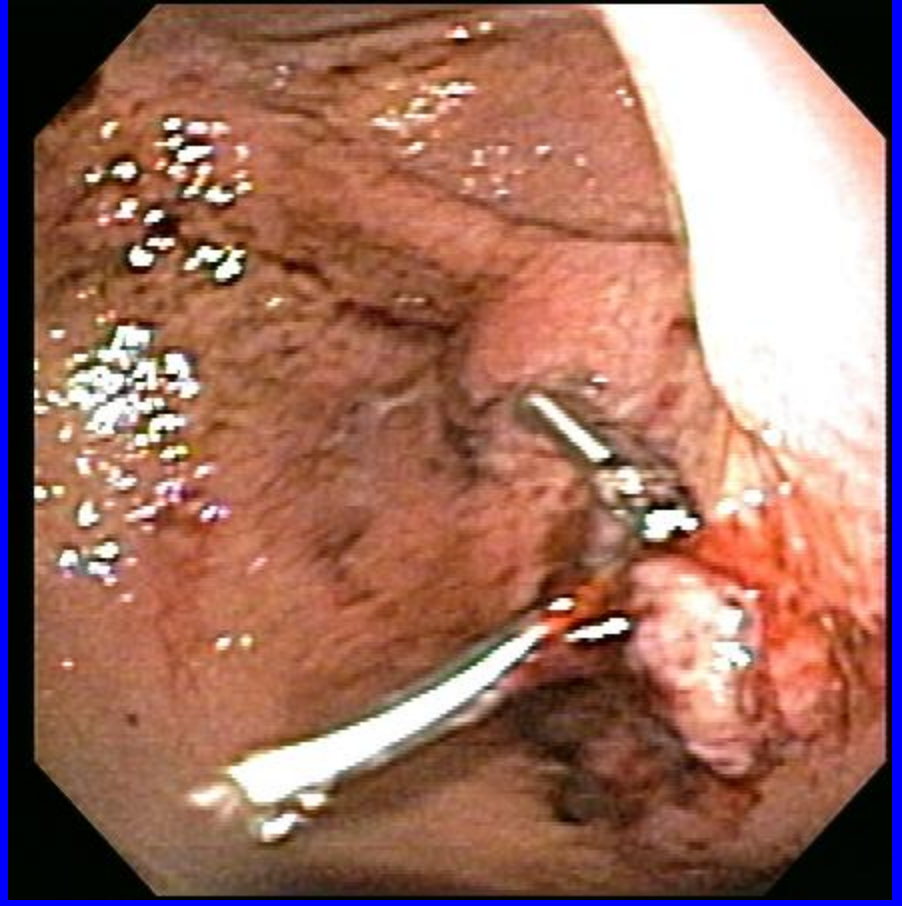
For epinephrine injection, the addition of a second modality (combination therapy) reduces further bleeding, the need for surgery, and mortality.

Operator experience plays a significant role in modality choice and in achieving hemostasis.”

Pick one or two modalities – use them a lot.

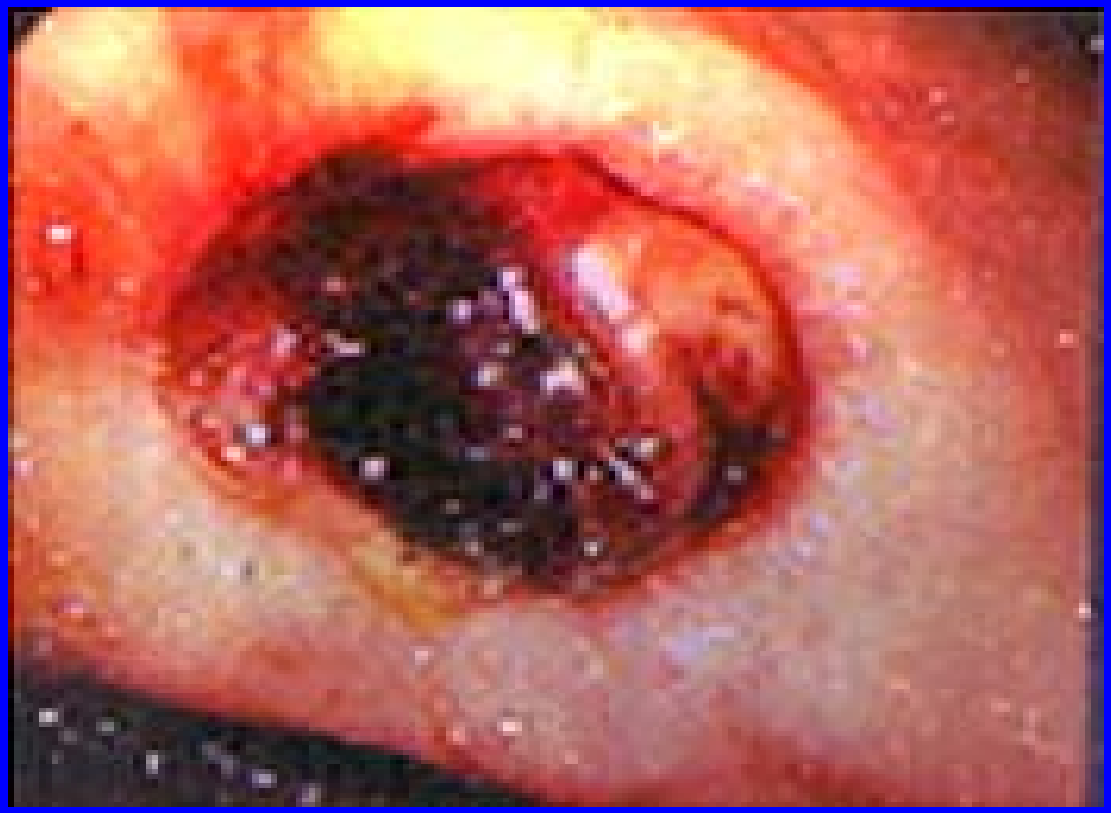
ASGE guideline: the role of endoscopy in acute non-variceal upper-GI hemorrhage 2004





In 2008 most would agree that endoscopically placed clips also should be included in the list of modalities effective in treating ulcer bleeding

Adherent clots: amorphous red clots attached to an ulcer base which did not wash away with vigorous irrigation



What should we do when we see an adherent clot ?

- John Tarpley
  - "Don't poke a skunk"
- Dennis Jensen (UCLA)
  - Shave off the clot from (currently) non bleeding lesions and treat

Table 3. Outcomes After Randomization by Treatment Group

	Medical treatment	Endoscopic treatment	*P* value
Patients	17	15	
Rebleeding before discharge	6 (35.3%)	0	0.011
Further endoscopic treatment	4 (23.5%)	0	0.045
Units RBCs transfused[a]	2.3 ± 0.9	1.0 ± 1.0	0.35
Hospital days, median	4	4	0.33
ICU days, median	1	1	0.44
Ulcer surgery, 30 days	2 (11.8%)	1 (6.7%)	0.62
Mortality, 30 days	1 (5.9%)	1 (6.7%)	0.93

[a]Expressed as mean ± SEM.

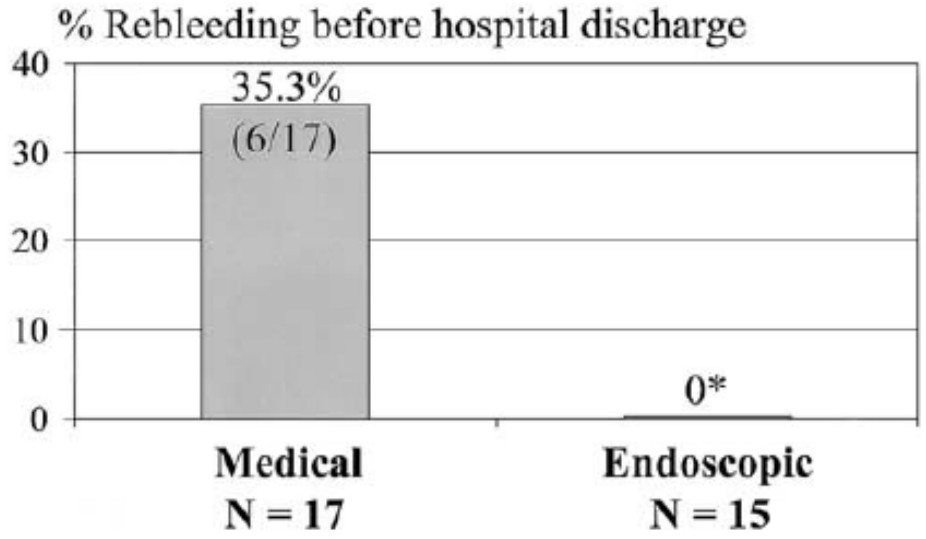
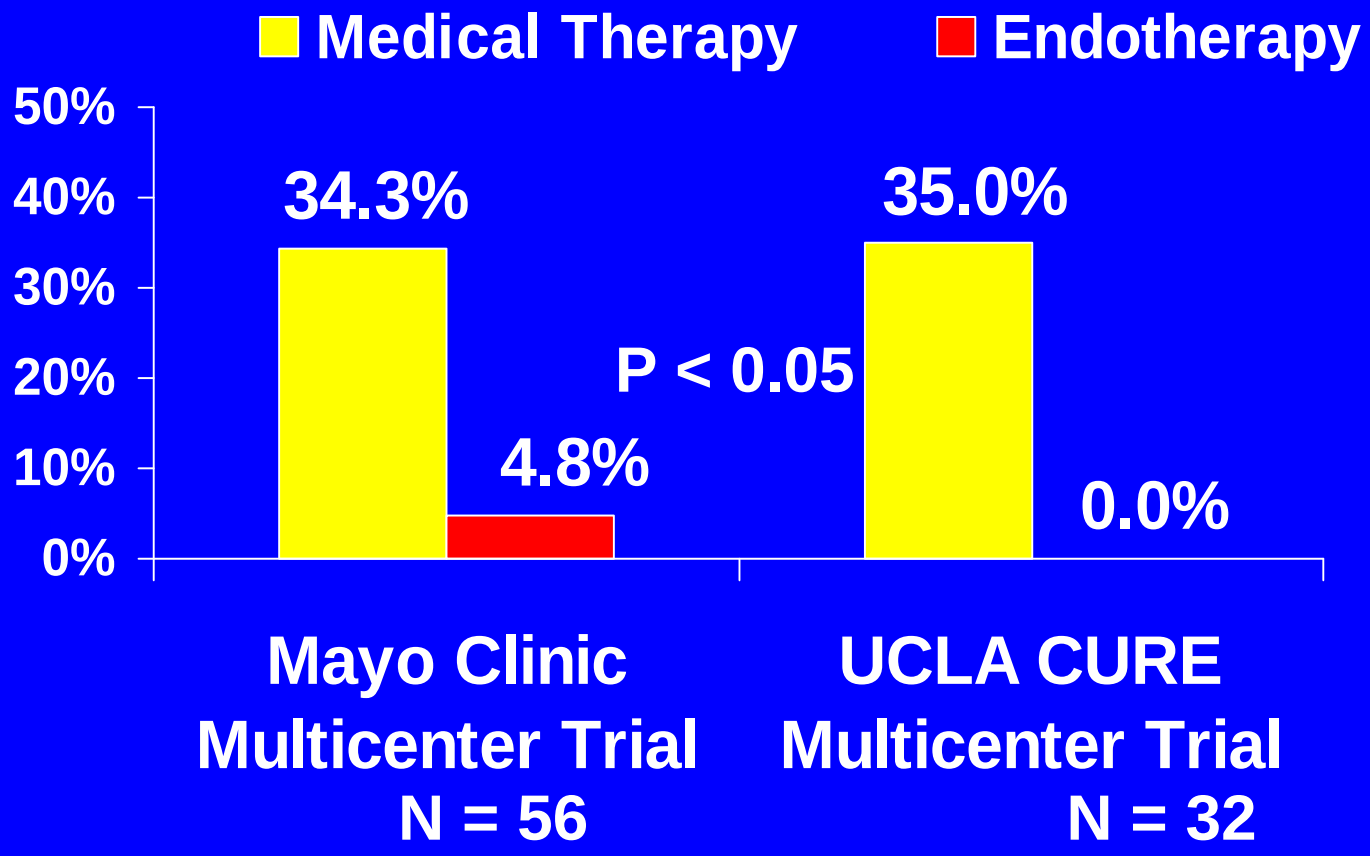


Figure 1. The recurrence of ulcer hemorrhage following randomization to medical vs. endoscopic therapy, up to the time of hospital discharge for patients with nonbleeding adherent clots. *Indicates a significant difference ($P = 0.011$).

This RCT influences us to be more aggressive in Nonbleeding lesions with stigmata of recent hemorrhage

Gastro:Jensen:2002

Rebleeding Rates in RCT's of Treatment of Adherent Clots



- Limitation of procedural RCTs

- Are our endoscopies (endoscopists) like endoscopies (endoscopists) from UCLA or Mayo?

Routine Repeat Endoscopy?

- Review of 6 randomized trials
  - No reduction in risk of rebleeding
  - Increased number of procedures
  - Possibly increase risk from unnecessary retreatment

Romagnuolo J. Can J Gastroenterol 18(6): 401 2004

Endoscopy vs. Surgery for Recurrent Bleeding

- 100 patients with rebleeding after endoscopic control randomized to repeat endoscopy (n=48) or direct surgery (n=44)
- 13 (23%) patients in endoscopy group had salvage surgery compared to 100% in the surgery arm
  - NNT (repeat scope) to prevent one operation < 2
- Overall similar outcomes (mortality, length of hospital stay, number of blood transfusions)
- Complications higher with direct surgery (16 vs. 7, p=0.03)
- Analysis of endoscopy failures: ulcers> 2cm, hypotension at randomization

Lau N Engl J Med 1999;340:751

Role of radiology

- Angiography
  - must be bleeding rapidly (1-3 cc/minute)
  - ~ 4-6 units per day
  - may guide surgery
  - may replace surgery
    - infusion
    - Embolization
- CT Angiography: appearing more often in the literature
- Usually coordinated by GI or Surgery

Role of nuclear medicine: Tagged cell scan

- Hypothetically < 1 unit per day
- Early (15 minute) scan is most useful
- Early scans done at Vanderbilt
- Not usually done at VA
- Not utilized by VA GI service very often
- REQUIRED by VUMC angiographers prior to angio attempt : “facilitates selective angiography”

Lower GI bleeding

- Self limited in > 80% cases
- Most common
  - Diverticular disease
  - AVMs
- Less common
  - Colitis (Inflammatory or infectious)
  - Tumors
  - Hemorhoids
  - Miscellaneous ulcers
  - Ischemia

Lower GI Bleed - Overview

- Hematochezia
- Pattern
  - Single, painless, massive : diverticular
  - Recurrent, painless: AVMs
  - Pain, fever: colitis
  - Rectal pain: tear, hemorrhoidal
  - Massive with shock: could be upper GI bleed with rapid transit

Lower GI bleed : Overview

- Evaluate and triage according to risk
  - (Similar to UGI Bleed)
  - Age, comorbid conditions, hemodynamics
- Stabilize : replace volume
- Call GI and Surgery Consultants early

Endoscopic evaluation of lower GI bleed with hemodynamic compromise

- EGD
  - rule out upper bleed
  - (bonus: preclude surgical confusion and plausible deniability)

- Colonoscopy:
  - Sometimes: limited lower exam without prep
    - Can we regionalize the bleeding (i.e. left colon with blood/ proximal colon without blood)
  - “Rapid purge” and definitive lower exam
  - Golytely when stabilized

URGENT COLONOSCOPY FOR THE DIAGNOSIS AND TREATMENT OF SEVERE DIVERTICULAR HEMORRHAGE

DENNIS M. JENSEN, M.D., GUSTAVO A. MACHICADO, M.D., ROME JUTABHA, M.D., AND THOMAS O.G. KOVACS, M.D.

Not an RCT

"We treated it when we saw it"

TABLE 3. OUTCOME OF TREATMENT FOR DIVERTICULAR HEMORRHAGE.

VARIABLE	MEDICAL AND SURGICAL TREATMENT (N=17)	MEDICAL AND COLONOSCOPIC TREATMENT (N=10)	P VALUE
Endoscopic hemostasis — no. (%)	0	10 (100)	0.001
Additional bleeding — no. (%)*	9 (53)	0	0.005
Severe bleeding — no. (%)†	6 (35)	0	0.03
Emergency hemicolectomy — no. (%)	6 (35)	0	0.03
Median time to discharge after colonoscopy — days	5	2	<0.001
Complications — no. (%)	2 (12)‡	0	0.26
Late bleeding — no. (%)	0	0	1.0
Follow-up — mo			
Median	36	30	
Range	24–54	18–49	

*Additional bleeding was defined as self-limited or recurrent hematochezia that occurred after purging of the colon and colonoscopy and that required no more than an additional 2 units of packed red cells.

†Severe bleeding was defined as continued or recurrent hematochezia that required at least 3 units of packed red cells.

‡One patient had pneumonia, and one had a wound infection.

PEG solution was either orally (in the case of 67 percent of patients) or by nasogastric tube (in the case of 33 percent) to rid the colon of clots, stool, and blood.

The procedure usually required 5 to 6 liters of purge and three to four hours before the colon was clean.

Urgent colonoscopy was defined as colonoscopy performed at the bedside 6 to 12 hours after hospitalization or the diagnosis of hematochezia and within 1 hour after clearance of stool, blood, and clots, as documented by a physician.

The New England Journal of Medicine

URGENT COLONOSCOPY FOR THE DIAGNOSIS AND TREATMENT OF SEVERE DIVERTICULAR HEMORRHAGE

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Not an RCT
"We treated it when we saw it"
10/27 times

NNC&T to prevent one operation was about 3

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Randomized Trial of Urgent vs. Elective Colonoscopy in Patients Hospitalized With Lower GI Bleeding

Laine et al. *Am J Gastroenterol* 2010; 105:2636–2641;

85 patients with shock and BRBPR
EGD then randomization to urgent (< 12 H) or routine colonoscopy

15% had UGI source

Among those with lower GI source no difference in outcomes

- **Need for operation**
- **Hospital days, volume of transfusion, costs**

Endoscopy in acute lower GI bleeding

- More purely diagnostic that in UGI bleed
- Identify level of bleeding
  - examination of ileum if possible
- Therapeutic:
  - AVM cautery/injection
  - Diverticular bleed (Only at UCLA ?)
- Will typically need rapid colon prep after EGD

- A major role of the physician will be to parse Clinical Practice Guidelines to most effectively use the available resources to a patient with individual risk factors and preferences.

Smalley	Guideline authors		
A. Resuscitation, risk assessment, and preendoscopy management			
Y			A1. Immediately evaluate and initiate appropriate resuscitation.*
			A2. Prognostic scales are recommended for early stratification of patients into low- and categories for rebleeding and mortality.†
no	Y		A3. Consider placement of a nasogastric tube in selected patients because the findings prognostic value.*
Y			A4. Blood transfusions should be administered to a patient with a hemoglobin level 70
			A5. In patients receiving anticoagulants, correction of coagulopathy is recommended b not delay endoscopy.
maybe	Y		A6. Promotility agents should not be used routinely before endoscopy to increase the d yield.
Y			A7. Selected patients with acute ulcer bleeding who are at low risk for rebleeding on th clinical and endoscopic criteria may be discharged promptly after endoscopy.†
			A8. Preendoscopic PPI therapy may be considered to downstage the endoscopic lesion decrease the need for endoscopic intervention but should not delay endoscopy.†
B. Endoscopic management			
Y			B1. Develop institution-specific protocols for multidisciplinary management.* Include a an endoscopist trained in endoscopic hemostasis.*
			B2. Have available on an urgent basis support staff trained to assist in endoscopy.*
< 6 hours	Y		B3. Early endoscopy (within 24 hours of presentation) is recommended for most patien acute upper gastrointestinal bleeding.†
Y			B4. Endoscopic hemostatic therapy is not indicated for patients with low-risk stigmata (based ulcer or a nonprotuberant pigmented dot in an ulcer bed).*
			B5. A finding of a clot in an ulcer bed warrants targeted irrigation in an attempt at dislo with appropriate treatment of the underlying lesion.†

Smalley	Guideline authors	
B. Endoscopic management		
remove clot	Y	B6. The role of endoscopic therapy for ulcers with adherent clots is controversial. En considered, although intensive PPI therapy alone may be sufficient.†
	Y	B7. Endoscopic hemostatic therapy is indicated for patients with high-risk stigmata (a an ulcer bed).*
	Y	B8. Epinephrine injection alone provides suboptimal efficacy and should be used in c method.†
	Y	B9. No single method of endoscopic thermal coaptive therapy is superior to another.
	Y	B10. Clips, thermocoagulation, or sclerosant injection should be used in patients with combination with epinephrine injection.†
	Y	B11. Routine second-look endoscopy is not recommended.†
	Y	B12. A second attempt at endoscopic therapy is generally recommended in cases of r
		C. Pharmacologic management
	Y	C1. Histamine-2 receptor antagonists are not recommended for patients with acute u
Maybe Until patients can take po	Y	C2. Somatostatin and octreotide are not routinely recommended for patients with ac
	Y	C3. An intravenous bolus followed by continuous-infusion PPI therapy should be used mortality in patients with high-risk stigmata who have undergone successful endosco
	Y	C4. Patients should be discharged with a prescription for a single daily-dose oral PPI f underlying etiology.
		D. Nonendoscopic and nonpharmacologic in-hospital management
	Y	D1. Patients at low risk after endoscopy can be fed within 24 hours.*
	Y	D2. Most patients who have undergone endoscopic hemostasis for high-risk stigmata 72 hours thereafter.

Smalley	Guideline authors	
B. Endoscopic management		
		D. Nonendoscopic and nonpharmacologic in-hospital management
	Y	D1. Patients at low risk after endoscopy can be fed within 24 hours.*
	Y	D2. Most patients who have undergone endoscopic hemostasis for high-risk stigmata 72 hours thereafter.
	Y	D3. Seek surgical consultation for patients for whom endoscopic therapy has failed.*
	Y	D4. Where available, percutaneous embolization can be considered as an alternative endoscopic therapy has failed.
	Y	D5. Patients with bleeding peptic ulcers should be tested for H. pylori and receive era with confirmation of eradication.†
Maybe	Y	D6. Negative H. pylori diagnostic tests obtained in the acute setting should be repeat
		E. Postdischarge, ASA, and NSAIDs
would not use COX-II	Y	E1. In patients with previous ulcer bleeding who require an NSAID, it should be recogn traditional NSAID plus PPI or a COX-2 inhibitor alone is still associated with a clinically bleeding.
would not use COX-II	Y	E2. In patients with previous ulcer bleeding who require an NSAID, the combination o recommended to reduce the risk for recurrent bleeding from that of COX-2 inhibitors
	Y	E3. In patients who receive low-dose ASA and develop acute ulcer bleeding, ASA thera the risk for cardiovascular complication is thought to outweigh the risk for bleeding.
	Y	E4. In patients with previous ulcer bleeding who require cardiovascular prophylaxis, it clopidogrel alone has a higher risk for rebleeding than ASA combined with a PPI.