Run While You Can:

ELUSIVE GI BLEEDING FROM A GASTROENTEROLOGIST'S PERSPECTIVE

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NCSG
North Carolina Society of Gastroenterology Annual Meeting 2020

- No Disclosures
- Talk will include off-label use of medications

Goals

- Understand the reasons why elusive GIB is becoming increasingly common
- Recognize different phenotypes of elusive GIB
- Understand management options for these challenging pts

Run, Run While You Can

- Published rates: 5 – 10% of GI Bleeds arise from the SB
  - Vascular lesions dominate in older pts
  - Younger patients bleed more from inflammatory or neoplastic pathology
- An emerging epidemic is upon us
  - Aging population
  - Enhanced ability to keep pt's with ESRD, CHF, VHD and cirrhosis alive
  - Increasing use of A/C and an increasing variety of these agents
  - Other sources are going away:
    - Ubiquity of PPI's and increased HP testing → decreased risk of PUD
    - Increased CRC screening → decreasing rates of colon neoplasm

What Is a Gastroenterologist to Do?

Phenotype 1: Mild and Indolent

- IDA without overt bleeding or with rare sporadic melena
- Elderly
- Associated conditions (VHD, PAD, ESRD, Cirrhosis) are common
- A/C is common
- Often maintained with iron supplementation
- Not overly symptomatic
- Evaluation frequently unremarkable
- Can transition to Phenotype 2

Example:

- SW is an 84 yo W first noted to be anemic 5 years ago. At that time, EGD and colonoscopy did not reveal a source of bleeding.
- She has a history of Afib and CKD.
- She was on warfarin for several years but this was stopped 10 months ago
- Hgb has ranged from 8.7 – 10.4 over the past 2 years since she started iron supplementation with PO daily and periodic IV infusions

Management for Phenotype 1: Feathers and Finger-Crossing

- "Speak softly to the bear and try not to show fear"
- Endoscopy primarily for diagnostic purposes as pt is already at a reasonable end point for therapy
  - Recent EGD / Colonoscopy to exclude neoplasm
  - VCE reasonable to exclude dominant source in the SB
    - AVMs do not need to be chased if pt remains clinically stable
- Maintain iron supplementation
- Monitor Hgb
- Keep away from A/C if possible
- End Goal: Hgb stability, Avoid PRBCs / admissions

Phenotype 2: Moderate and Demanding

- Intermittent melena
- Elderly
- Associated conditions (VHD, PAD, ESRD, Cirrhosis) are common
- A/C is very common
- Hgb nadirs low enough to require periodic PRBC transfusion
- Periodically admitted with symptomatic anemia
- Can transition back to Phenotype 1

Example:

- DP is a 73 yo M with 18 months of intermittent melena and anemia since being started on rivaroxaban for Afib.
- He has a history of CKD and a recent echocardiogram showed moderate AS.
- He has been admitted twice for symptomatic anemia with weakness and his Hgb nadir has been in the 6's.
- He has undergone 2 EGD's, 1 colonoscopy and 1 VCE over this period and the only notable findings have been scattered angioectasias in the small bowel
- He is on IV iron infusions but still requiring PRBCs every 6 weeks

Management for Phenotype 2: Lather, Rinse, Repeat

- "FIGHT BACK if a bear attacks you"
- 1) Endoscopic Interventions (Losing Battle or Path to Victory?):
  - Repeat colonoscopy if not done recently or any associated symptoms
  - Push Enteroscopy higher yield than standard EGD
  - VCE should be pursued if the above are non-diagnostic
    - + for something other than angioectasia → DAE
    - + for angioectasia and symptoms persist / progress → DAE
    - Negative and symptoms progress → +/- DAE (depending on pt factors / risk)
  - If + findings on prior interventions, Push Enteroscopy / VCE / DAE can be repeated prn
  - If initial endoscopic evaluations for anemia were negative, repeat interventions will be low yield
- 2) Medical Interventions ("use rocks, sticks, binoculars or any object that may be available to you"):
  - Iron Supplementation
  - Stop A/C if possible (or change agent)
  - Encourage Epo if ESRD or advanced CKD
  - Somatostatin Analogs
  - Thalidomide
  - Hormonal Therapy
  - Bevacizumab, Aminocaproic or Transexamic Acids
- End Goal: decrease PRBC requirements, limit admissions, ideally convert to Phenotype 1

A Losing Battle?

ORIGINAL ARTICLE

Is Endoscopic Therapy Effective for Angioectasia in Obscure Gastrointestinal Bleeding?

A Systematic Review of the Literature

Joseph Romagnuolo, MD, MSc, FACG, FASGE, Andrew S. Brock, MD,† and Nathaniel Ranney, MD†*

- 24 articles (490 patients) who received endoscopic therapy for angioectasias
- 6 articles (130 patients) describing the natural history of angiectasias ('89 - '10)

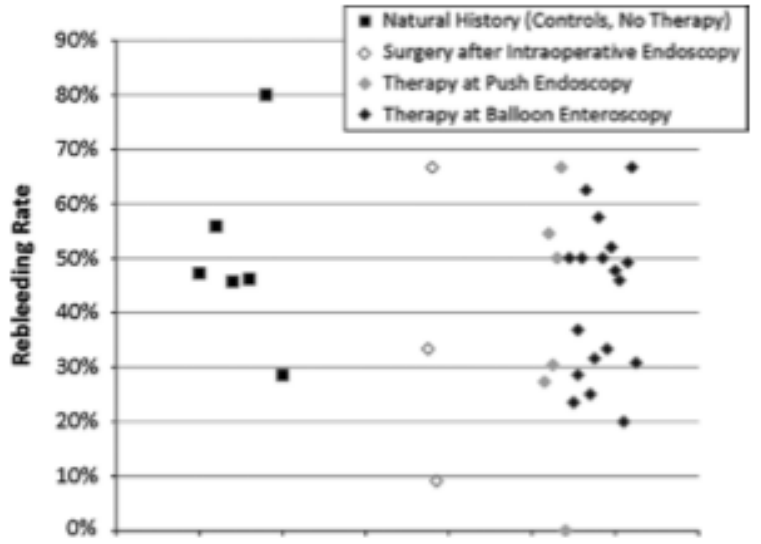

FIGURE 1. Scatter plot of the rebleed rates from the natural history [no treatment (left)] studies, the rebleed rates after endoscopic therapy at various types of endoscopy access (right), and the rebleed rates after surgical therapy after intraoperative endoscopy localization (middle).

Tx'd pts: 209/490 (**42.7%;** 95% CI, 38%-47%) rebled

Controls: 64/130 (**49.2%**; 95% CI, 40%-58%) rebled

NNT: 15-16

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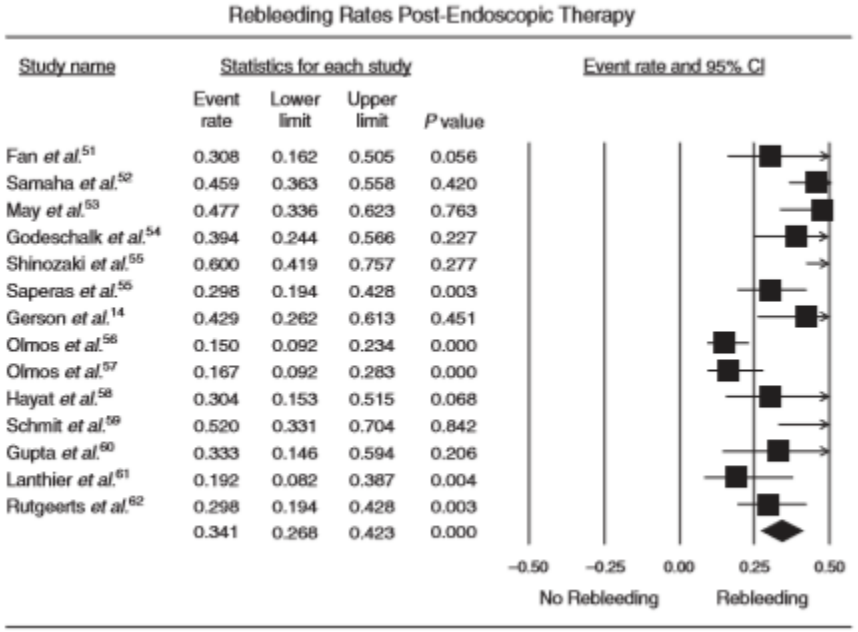
REVIEW

Management of Gastrointestinal Angiodysplastic Lesions (GIADs): A Systematic Review and Meta-Analysis

Christian S. Jackson, MD, FACG[1] and Lauren B. Gerson, MD, MSc, FACG, FASGE, AGAF[2]



Pooled recurrence rate in all studies = 34% with [22 mo] f/u

Pooled recurrence rate with AVMs confined to SB = 45% with [26 mo] f/u

American Journal of Gastroenterology.

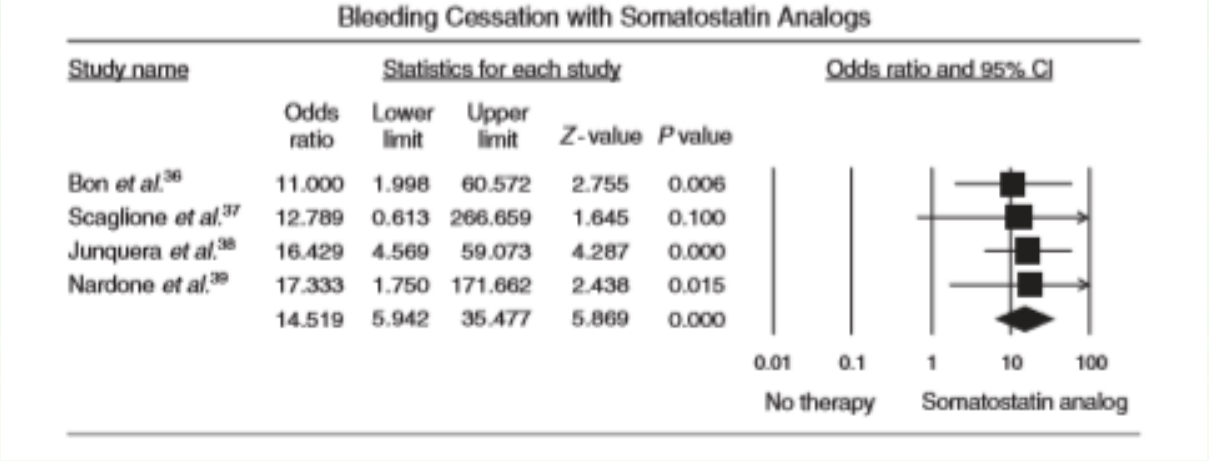
Path to Victory?

- Germany: 50 pts who had DBE for OGIB (88% of exams had AVMs)
  - [55 months] of f/u: [Hgb]: 7.6 vs 11; pts needing PRBCs: 60% vs 16%
- US: 61 pts underwent SE for OGIB
  - [f/u] = 25 mos: overt bleeding: 62% → 26%; [Hgb]: 10.6 → 12.6
  - Units of PRBCs decreased by 4 U / pt
- Japan: 43 pts had 69 DBE's with AVM tx
  - overt re-bleeding seen in 16 pts (37%)
    - More likely in those with multiple rather than singular AVMs
  - 12 of these 16 pts (75%) had repeat DBE with AVM tx
    - Frequency of re-bleeding after 1st yr of f/u decreased to 0.12/yr vs 0.52/yr in those not re-scoped
    - Median 3 additional procedures (range 2-6)

May A. Endoscopy 2011
Williamson JB. Gastrointest Endosc. 2012
Shonozaki S. Gastrointest Endosc. 2014

Medical Therapy: Rocks, Sticks and Binoculars…

- Somatostatin Analogs:



Pooled OR for bleeding cessation = 14.5

Reduction in [#] of PRBC units after 1 year of tx = 0.55

- Thalidomide:
  - 28 pts on 100 mg PO daily vs 27 controls on iron for 4 months then followed for 1 year
    - 1° outcome (decrease in bleeding episodes by ≥ 50%): 71.4% in Tx grp vs 3.7% in controls
- Hormonal Therapy:
  - Meta-Analysis of 2 studies (< 100 pts): pooled OR = 1
- Case Reports for a variety of other agents

Jackson C. Am J. Gastroenterol 2014
Ge ZZ. Gastro 2011

Medical Therapy: Alter the A/C

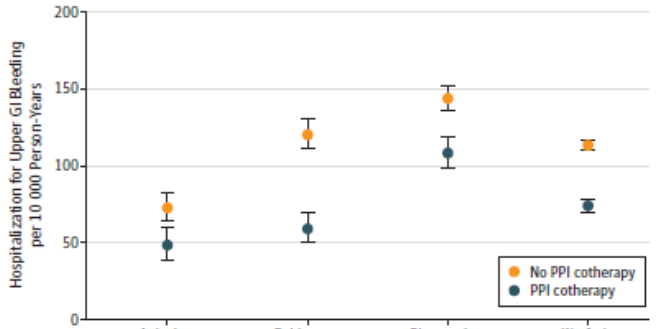
JAMA | Original Investigation

Association of Oral Anticoagulants and Proton Pump Inhibitor Cotherapy With Hospitalization for Upper Gastrointestinal Tract Bleeding

Wayne A. Ray, PhD; Cecilia P. Chung, MD, MPH; Katherine T. Murray, MD; Walter E. Smalley, MD, MPH; James R. Daugherty, MS; William D. Dupont, PhD; C. Michael Stein, MB, ChB

Adjusted incidence of hospitalization for UGIB was significantly higher for rivaroxaban than apixiban, dabigatran and warfarin

Figure 1. Adjusted Incidence of Hospitalization for Upper Gastrointestinal (GI) Tract Bleeding by Individual Oral Anticoagulants[a]



	Apixaban	Dabigatran	Rivaroxaban	Warfarin
RD (95% CI)	-24 (-38 to -11)	-61 (-75 to -47)	-36 (-49 to -22)	-39 (-44 to -34)
IRR (95% CI)	0.66 (0.52 to 0.85)	0.49 (0.41 to 0.59)	0.75 (0.68 to 0.84)	0.65 (0.62 to 0.69)

IRR indicates incidence rate ratio; PPI, proton pump inhibitor; RD, rate difference per 10 000 person-years. Error bars indicate 95% CIs.

[a] Adjusted for all covariates listed in eTable 3 in Supplement 1.

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SYSTEMATIC REVIEWS AND META-ANALYSES

Siddharth Singh, Section Editor

Risk of Gastrointestinal Bleeding in Patients Taking Non–Vitamin K Antagonist Oral Anticoagulants: A Systematic Review and Meta-analysis

Corey S. Miller,[*,a] Alastair Dorreen,[‡,a] Myriam Martel,[§] Thao Huynh,[‖] and Alan N. Barkun[§,¶]

*Internal Medicine Residency Training Program, Department of Medicine, §Department of Epidemiology and Biostatistics and Occupational Health, ‖Division of Cardiology, ¶Division of Gastroenterology, McGill University Health Center, McGill University, Montreal, Canada, ‡Division of Gastroenterology, Dalhousie University, Halifax, Nova Scotia, Canada

Overall no difference in bleeding risk between NOACs and conventional A/C but dabigatran (2% vs 1.4%) and rivaroxaban (1.7% vs 1.3%) were both associated with significantly increased OR of bleeding compared to conventional A/C

No such association for apixiban or edoxaban

Phenotype 3: Fast and Furious

- Intermittent melena or hematochezia
- Younger
- Associated conditions (VHD, ESRD, Cirrhosis) are less common
- A/C is uncommon
- Go from "0 to 60": brown stool and normal Hgb → Hgb of 5 and hematochezia
- Admitted when the bleeding events occur

Example:

- AH is a 34 yo W with Crohn's disease that has been in remission on 6-MP for more than 10 years who has been admitted twice for red hematochezia associated with 5 – 6 gram drops in Hgb
- She is otherwise healthy and returned to an asymptomatic baseline between episodes
- She has not had prior surgery for Crohn's.
- She has undergone CTA, EGD x 1, colonoscopy x2 and VCE x 2 with the only finding being blood without a clear source in the mid small bowel on one of the 2 VCE's

Management for Phenotype 3: If At First You Don't Succeed…

- Aggressive multi-modality approach performed as close to the bleeding event as possible
- Bleeding Protocol CT Scan
  - Ideally followed by VIR / A-gram if +
- Push Enteroscopy if nothing else available
- Colonoscopy if hematochezia, no recent exam or other symptoms
- VCE
  - Early and often
- DAE
  - Ideally directed by VCE or CT findings
- …Try, Try Again: may require multiple cycles if source is a vascular lesion
- End Goal: Find and treat the source of bleeding

VCE: Timing

- UMass Study spanning 2008-2010
  - 260 VCE done for OGIB
  - Dx Yield in Inpts vs Outpts 66% vs 53% (P 0.054)
  - VCE w/in 3d of admission
    - Active bleeding or AVM seen in 44%
    - Subsequent Tx intervention in 19%
  - VCE done > 3d after admission
    - Active Bleeding or AVM seen in 28%
    - Subsequent Tx intervention in 7%
  - Outpt VCE
    - Active Bleeding or AVM seen in 26%
    - Subsequent Tx intervention in 10%

Singh A GIE 2013

Conclusions

- Elusive bleeding is becoming more problematic
- Assess the Bleeding Phenotype: Mild and Indolent, Moderate and Demanding, Fast and Furious
- Recognize the goals of therapy
  - M/I: Hgb maintenance, avoid PRBCs / admissions
  - M/D: decrease PRBC requirements / admissions, ideally convert to M/I
  - F/F: find and treat the source
- Endoscopy has a role but also has limits
- Interventions often need to be repeated
- Medical therapy has a role but there is no ideal agent or strategy
- Enlist the help of colleagues: Surgery, VIR, Heme

Knowledge Check Questions

- 1) What are the rates of re-bleeding following endoscopic ablation of small bowel angioectasias?
  - A) 10%
  - B) 20%
  - C) 40%
  - D) 60%

- 2) All of the following have a potential role in the management of elusive GI bleeding ***except***?
  - A) octreotide
  - B) switching from apixaban to rivaroxaban
  - C) thalidomide
  - D) device-assisted enteroscopy