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2022
ACG'S ENDOSCOPY SCHOOL & SOUTHERN REGIONAL POSTGRADUATE COURSE
DECEMBER 2-4, 2022
GRAND HYATT
NASHVILLE, TENNESSEE
Register online: meetings.gi.org

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2023
ACG HEPATOLOGY SCHOOL & WESTERN
REGIONAL POSTGRADUATE COURSE
JANUARY 27-29, 2023 | CAESARS PALACE LAS VEGAS, NEVADA
Register online: meetings.gi.org

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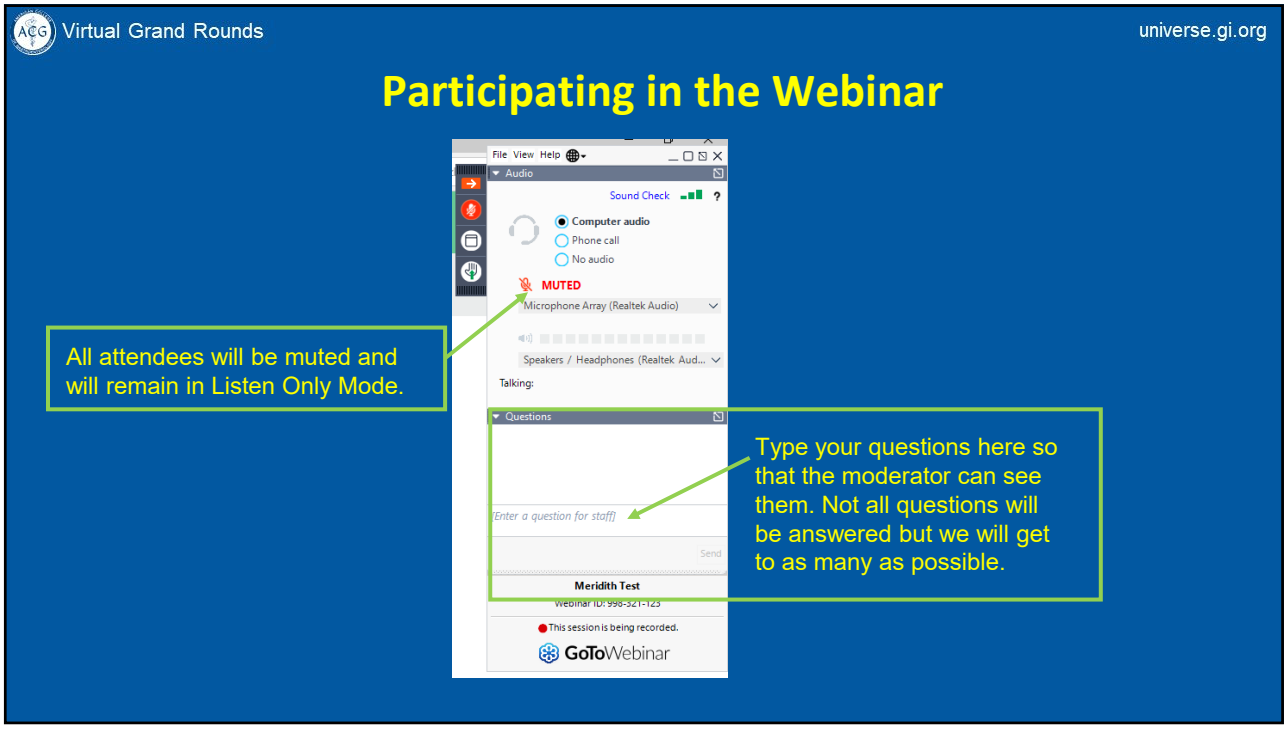
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How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2023 for this activity.

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MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.
THESE ANSWERS WILL BE REVIEWED.

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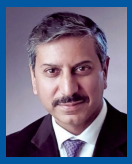
ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 45 – Thursday, November 10, 2022
GI Diseases and Endoscopy in Pregnancy and Postpartum Period: The ACG Pregnancy Monograph
Faculty: Sunanda V. Kane, MD, MSPH, FACG; Vivek Kaul, MD, FACG; and Shivangi T. Kothari, MD, FACG
At Noon Eastern and NEW! **8pm Eastern!**



Week 46 –Thursday, November 17, 2022
COVID-19 Vaccine Update
Faculty: Freddy Caldera, DO
Moderator: Daniel J. Pambianco, MD, FACG
At Noon Eastern and NEW! **8pm Eastern!**

There will be no ACG Virtual Grand Rounds November 24th

Visit **gi.org/ACGVGR** to Register

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ACG'S ENDOSCOPY SCHOOL & SOUTHERN REGIONAL POSTGRADUATE COURSE

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Disclosures

Kathy P. Bull-Henry, MD, MBA, FACG
Dr. Bull-Henry has no relevant financial relationships with ineligible companies.

John R. Saltzman, MD, FACG
Dr. Saltzman has no relevant financial relationships with ineligible companies.

All treatments described are Off Label

**All of the relevant financial relationships listed for these individuals have been mitigated*

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Obscure Bleeding: Are There Options After Endoscopy?

Kathy Bull-Henry, MD, FACG
Medical Director, JHBMC Endoscopy Unit
Johns Hopkins Bayview Medical Center
Baltimore, Maryland

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Learning Objective

- Evaluate testing and management strategies when endoscopy doesn't reveal the source of bleeding

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Obscure GI Bleeding

- Unidentified origin after upper and lower GI evaluation
- Most bleeding sources are in the small bowel

Am J Gastroenterol 2015;110:1265

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Table 2

Common causes		Rare causes
Under age 40 years	**Over age 40 years**	**Henoch–Schoenlein purpura**
Inflammatory bowel disease	Angioectasia	Small bowel varices and/or portal hypertensive enteropathy
Dieulafoy's lesions	Dieulafoy's lesions	Amyloidosis
Neoplasia	Neoplasia	Blue rubber bleb nevus syndrome
Meckel's diverticulum	NSAID ulcers	Pseudoxanthoma elasticum
Polyposis syndromes		Osler–Weber–Rendu syndrome
		Kaposi's sarcoma with AIDS
		Plummer–Vinson syndrome
		Ehlers–Danlos syndrome
		Inherited polyposis syndromes (FAP, Peutz–Jeghers)
		Malignant atrophic papulosis
		Hematobilia
		Aorto-enteric fistula
		Hemosuccus entericus

FAP, familial adenomatous polyposis; NSAID, nonsteroidal anti-inflammatory drug.

ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding

Gerson, Lauren B; Fidler, Jeff L; Cave, David R; Leighton, Jonathan A

Official journal of the American College of Gastroenterology | ACG110(9):1265-1287, September 2015.

doi: 10.1038/ajg.2015.246

Causes of small bowel bleeding

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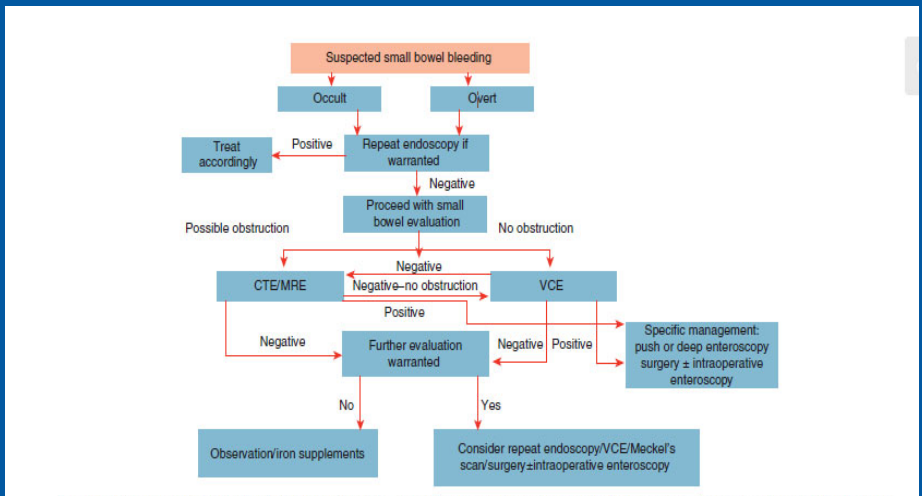

Figure 1. Algorithm for suspected small bowel bleeding. CTE, computed tomographic enterography; MRE, magnetic resonance enterography; VCE, video capsule endoscopy.

Am J Gastroenterol 2015;110:1265–1287

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Outcomes after Endoscopic Therapy

- Rebleeding rates from vascular lesions ranges from 20-46%
- Risk factors for recurrent bleeding
  - Number of vascular lesions
  - Age over 65 years
  - Presence of lesions in the jejunum
  - Presence of aortic stenosis (Heyde's syndrome)
  - Left ventricular assist devices
  - Chronic renal failure
  - Usage of anticoagulant medications
  - Need for transfusion

Samaha E. Am J Gast 2012;107:240-6
Shinozaki S, Clin Gastro Hepatol 2010;8:151-8
Fan G et al. J Dig Dis 2013;14:113-6
Arakawa D et al. GIE 2009;69:866-74
Koh S et al. World J Gastro 2013;19:1632-8

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Nonendoscopic Therapy

Supportive

Oral Iron Supplementation

- Ferrous sulfate, ferrous gluconate, ferrous fumarate, ferric maltol, and iron polysaccharide.
- Most contain 60 to 70 mg of elemental iron, of which only 25% is absorbed.
- The most effective oral iron regimen dosing is every 48 h
- Side effects include nausea, dyspepsia, constipation, diarrhea, dark or melenic stools, and pill esophagitis

IV Iron Supplementation

- Iron sucrose, ferric carboxymaltose, ferric gluconate, low molecular weight iron dextran, iron isomaltoside, and ferumoxytol
- Iron sucrose and ferric carboxymaltose most commonly used
  - Ferric carboxymaltose can be given in 750 mg doses for a full treatment course in 1–2 doses
  - Iron sucrose is given in 200 mg doses, requiring 5 doses for a full course

Westrich D. Curr Gastroenterol Rep 2021;23:12

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Nonendoscopic Treatment Options

- Hemostatic Treatment
  - Stop bleeding
- Prophylactic Treatment
  - Prevent rebleeding
- Rescue Treatment
  - When other modalities have failed

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Hemostatic Therapy

- Selective embolization by angiography
  - Used in actively bleeding lesions
  - Hemostatic effectiveness 80-90%
  - Selectively catharize vessel feeding the avm
  - Inject embolizing agent- biodegradable sponge, microcoils
  - Complex procedure
  - Complication rate 5-9%
    - 2% are severe
    - Hematoma, hematomas, bowel infarction, arterial dissection, thrombosis, and pseudoaneurysms

Sakai E. World J Gastroenterol 2019;25:2549

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Prophylactic Therapy
Pharmacologic Therapy

- Hormonal therapy
  - Estrogen +/- progesterone
- Somatostatin analogs
  - Octreotide
- Antiangiogenics
  - Thalidomide
  - Lenalidomide
  - Bevacizumab

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

- Twenty-two studies, 831 patients with ADs:
  - 14 papers reporting the efficacy of endoscopic therapy for ADs in 623 patients,
  - 2 case – control studies involving hormonal therapy for 63 subjects,
  - 4 studies reporting outcomes with somatostatin analogs in 72 patients,
  - 2 papers reporting outcomes with AVR in 73 patients.
  - No studies involving diagnostic or provocative angiography met the inclusion criteria

Am J Gastro 2014;109:474

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Prophylactic Therapy
Hormonal Therapy

- Hormonal therapy- Estrogen +/- progesterone
- Unknown mechanism, increases the number of circulating activated platelets thereby shortening the bleeding time
  - Based on two case – control studies with 63 pts
  - (2001): Re-bleeding occurred in 13/33 of the treated group and 16/35 in the placebo arm (P = 0.6).
  - (1992): Rebleeding occurred in 15/30 in treated group vs 15/34 in controls
  - Hormonal therapy was not effective for bleeding cessation

Am J Gastro 2014;109:474
Gastro 2001;121:1073
J Clin Gastroenterol 1992;15:99

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Prophylactic Therapy
Somatostatin Analogs- Octreotide

- Somatostatin analogs- Octreotide
  - Mechanisms:
    - Inhibition angiogenesis by inhibiting vascular epithelial growth factor
    - Decreased duodenal and splanchnic blood flow
    - Increased vascular resistance
    - Enhanced platelet aggregation
    - Reduced portal and mesenteric blood flow via inhibition of vasodilator peptides
  - (2007) 32 pts Octreotide 50 mcg 12h SQ and 38 pts placebo
  - Rebleeding lower in octreotide pts 23% vs 48% in placebo pts.
  - 1-yr and 2-yr rebleeding free rates were higher in the octreotide pts 77% and 68% vs placebo group 55% and 36%
  - 4 studies, 72 pts
  - The pooled odds ratio was 14.5 (95 % CI: 5.9 – 36) for bleeding cessation
  - Octreotide was effective for bleeding reduction

Am J Gastro 2014;109:474
Am J Gastro 2007;102:254
Gastrointest Endoscopy Clin N Am 2017;27:51

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Prophylactic Therapy
Antiangiogenics

- Thalidomide
  - Thalidomide inhibits vascular endothelial growth factor (VEGF) to decrease angiogenesis
  - (2011) randomized pts to 100 mg of thalidomide vs. iron therapy for 4 months, demonstrated decreased re-bleeding rates and transfusions
    - Thalidomide reduced transfusion dependent patients (11% vs 48%); Reduced re-hospitalizations due to bleeding (39% vs 100%)
    - 71% of the thalidomide group reported side effects-fatigue and somnolence
  - (2012) treated 12 refractory GIAD patients and demonstrated an increase in hemoglobin values (6.5 g/dl to 12.1 g/dl) after 4 months in 9/12 patients
  - Thalidomide effective for bleeding reduction but has significant side effects

Gastro 2011;41:1629
Rev Esp Enferm Dig 2012;104:69

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Prophylactic Therapy
Antiangiogenics

- Lenalidomide
  - Thalidomide analog
  - Developed in the 1990s to achieve improved potency in the absence of significant side effects.
  - Inhibits vascular endothelial growth factor (VEGF) to decrease angiogenesis
  - Retrospective case series, 5 pts with VWD and bleeding AD, Decrease blood transfusion
  - Needs more studies
- Bevacizumab
  - Avastin- Monoclonal antibody against vascular endothelial growth factor
  - Strong antiangiogenic activity and a favorable side-effect profile

Haemophilia 2018;24:278
World J Gastro 2007;13:5979

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Rescue Therapy

- Radiological, endoscopic and pharmacological treatments
- Surgery
  - Last resort; Discrete lesions
  - Intraoperative enteroscopy guided resection
    - 47 consecutive patients with IOE via an enterotomy: A bleeding source was identified on IOE in 73% of all cases.
  - Angiography guided resection
    - Case report: Methylene blue injection via a super-selective angiographic microcatheter followed by focused enterectomy

J Gastrointest Surg 2012;16:2177
Gastrointest Endosc 2005;61:826
World J Emerg Surg 2014;9:17

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Aortic Stenosis and Heyde's Syndrome

- Relationship between severe aortic stenosis and angiodysplasia
- Destruction of von Willebrand factor when passing through a stenosed aortic valve (acquired von Willebrand syndrome)
- Chronic hypoxia from aortic stenosis
  - Leads to sympathetic induced vasodilation and smooth muscle relaxation, which in turn leads to formation of angioectasias and subsequent bleeding
- Review 2021: 46 Case reports, 55 pts with AS,
  - 43 underwent AVR, and 12 received transcatheter AVR.
  - Two patients had recurrent gastrointestinal bleeding.
- AVR may be effective treatment for Heyde's

Oxford Medical Case Reports, 2019;2:85–87
Chin Med Sci J. 2021;36:307
Am J Gastroenterol 2014 ; 109 : 474 – 83

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LVAD Patients

- Octreotide
  - Dosing: 50 to 100 µg subcutaneous (SQ) twice daily (BID) or octreotide long-acting release (LAR) 20 to 30 mg intramuscularly (IM) monthly.
  - 26 LVAD Pts, Octreotide reduced bleeding episodes (Juricek, 2018)
    - LAR pre-treatment episodes was 3 ± 2.4 per year vs 0.7 ± 1.3 per year post treatment.
    - 43% of the cohort was free of further bleeding episodes in follow-up
  - Side effects include diarrhea, abdominal pain, nausea, vomiting, gallstone formation, glucose abnormalities, pruritis, hypothyroidism, headaches and dizziness
  - First line therapy
- Thalidomide
  - Dosing: 50 mg of thalidomide was used daily or twice daily with up titration to 100 mg twice daily with bleeding episodes
  - 17 LVAD pts, Single center, Retrospective review, Thalidomide reduced GI bleeding episodes (Namdaran, 2019)
    - Pretreatment was 4.6 episodes per year vs 0.4 episodes per year.
    - Reduced blood transfusions from 36.1 to 0.9 units per year.
    - High adverse event rate; ranging from 58-71%. The more common adverse events encountered were dizziness, neuropathy, fatigue, constipation, transaminitis, and somnolence

Curr Probl Cardiol 2021;46:1
The Journal of Heart and Lung Transplantation 2018;37:1035
World J Gastroenterol 2020 May 28; 26(20): 2550-2558

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LVAD Patients

- Bevacizumab
  - Humanized monoclonal antibody against VEGF, in lowering the rate of GI bleeding in refractory cases
  - 5 LVAD pts, reduced blood transfusions and hospitalizations
  - Annual decreases in blood product usage from 45.8 to 6.0 units, reduced hospitalizations per year from 5.6 to 1.7 and an annual reduction in endoscopy from 10.6 to 2.3 procedures.
  - Well tolerated without side effects in the study participants
- Danazol
  - Androgen-like steroid
  - Decreases GIB by inhibiting endothelial permeability
  - Danazol has demonstrated effectiveness in patients with LVAD and refractory GIB requiring multiple procedures
    - Decreased hospitalizations and reduced blood transfusions
- ACEi/ARB
  - May reduce GI bleeding
  - 131 LVAD pts, 31 patients that did not receive an ACEi/ARB, 48% had a GI bleeding vs 24% of those that received an ACEi/ARB
  - Mechanism mainly centers around the downregulation of TGF-β
  - Needs further studies

World J Gastroenterol 2020 May 28; 26(20): 2550-2558

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Take Home Points

- Endoscopic therapy
  - Treatment of gastrointestinal bleeding in patients with angiodysplasias is clinically challenging
  - Initial endoscopic therapy is effective, but the pooled recurrence bleeding rate was 36% over 22 months.
  - Re-bleeding increased to 45% when studies included only small-bowel Ads
- Iron supplementation
- Medical Therapy
  - Hormonal therapy is not effective
  - Octreotide therapy is effective
  - Antiangiogenic therapy shows promise
  - Evaluate for prothrombotic conditions before considering treatment with pharmacologic therapy
  - The risk for thromboembolic events and potential benefits of decreased GI bleeding should be carefully weighed before using these drugs

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Take Home Points

- LVAD patients
  - Thalidomide, Danazol, Octreotide reduce recurrent GI bleeding
  - Bevacizumab promising
- Aortic Stenosis (Heyde's Syndrome)
  - Aortic Valve Replacement may reduce recurrent GI bleeding

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Thank you

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Questions?

Kathy P. Bull-Henry, MD, MBA, FACG

John R. Saltzman, MD, FACG

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