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2022
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THE AMERICAN COLLEGE OF GASTROENTEROLOGY
Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

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.
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.

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

**Week 33 – August 18, 2022**

Update on the Acute-on-Chronic Liver Failure Clinical Guidelines
Faculty: Jasmohan S. Bajaj, MD, MS, FACC
Thursday, DATE at Noon Eastern and **NEW! 8pm Eastern!**

**Week 34 – August 25, 2022**

Update on the Management of Anticoagulants and Antiplatelets Guidelines
Faculty: Neena S. Abraham, MD, MSc (Epid), FACC
Moderator: Bryan G. Sauer, MD, MSc (Clin Res), FACC
Thursday, DATE at Noon Eastern and **NEW! 8pm Eastern!**

Visit [gi.org/ACGVGR](http://gi.org/ACGVGR) to Register
Disclosures

Lisa L. Strate, MD, MPH, FACG
No relevant financial relationships

Neil H. Stollman, MD, FACG
No relevant financial relationships
Diverticular Disease in 2022: Where Are We Now?

Lisa L. Strate, MD, MPH, FACG
Professor of Medicine
University of Washington School of Medicine

Outline

• Epidemiology of diverticular disease
• Acute diverticulitis
• Recurrent diverticulitis
• Smoldering diverticulitis
• Chronic symptoms with diverticulosis
  • Post-diverticulitis irritable bowel syndrome (IBS)
  • Symptomatic uncomplicated diverticular disease (SUDD)
  • Segmental colitis associated with diverticular disease (SCAD)
Diverticulitis – An Uncommon Complication of a Common Disease

60% of Americans by age 60
< 5% with diverticulosis

No diverticulosis → Diverticulosis → Diverticulitis

1M outpatient or ED visits per year
300,000 hospital admissions
$5.5 B

Peery, et al Gastroenterol 2018

Complicated Diverticulitis is Uncommon

12% with diverticulitis

80% of complications occur during first episode

Bharucha et al Am J Gastroenterol 2015; 110:1589
Daniels L et BJS 2017;104:52

Uncomplicated diverticulitis rarely evolves
Case 1 - Diverticulitis

- 37 male without a significant medical history presents with LLQ pain
  - WBC 13
  - Afebrile
  - CT scan with sigmoid colon thickening with fat stranding consistent with uncomplicated diverticulitis

Antibiotics or Not?

Antibiotics Do Not Hasten Recovery or Reduce Acute Complications

*Multicenter RCT (AVOD trial) of CT confirmed uncomplicated diverticulitis*

<table>
<thead>
<tr>
<th></th>
<th>No Antibiotics (n=309)</th>
<th>Antibiotics (n=316)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abscess</td>
<td>6 (1.9%)</td>
<td>3 (1.0%)</td>
</tr>
<tr>
<td>Recurrence</td>
<td>47 (16.2%)</td>
<td>46 (15.8%)</td>
</tr>
</tbody>
</table>

a Abdominal pain  
b Temperature   
c Abdominal tenderness

More Data on Safety of Withholding Antibiotics: DIABLO Trial

528 patients with CT confirmed diverticulitis randomized to Amox Clavulanic acid vs No antibiotics

Long-term Outcomes – No Difference in Recurrence or Complications

24 month follow up of 528 patients in DIABLO trial

<table>
<thead>
<tr>
<th></th>
<th>No Antibiotics N=262</th>
<th>Antibiotics n=266</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent diverticulitis</td>
<td>15.4%</td>
<td>14.9%</td>
<td>0.89</td>
</tr>
<tr>
<td>Complicated diverticulitis</td>
<td>4.8%</td>
<td>3.3%</td>
<td>0.40</td>
</tr>
</tbody>
</table>
Possibly Higher Elective Surgery without Antibiotics

<table>
<thead>
<tr>
<th></th>
<th>No Antibiotics</th>
<th>Antibiotics</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sigmoid resection</td>
<td>9% (n=262)</td>
<td>5% (n=266)</td>
<td></td>
</tr>
<tr>
<td>Elective surgery</td>
<td>7.7% (n=17)</td>
<td>4.2% (n=10)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

- Indications for surgery in No Antibiotic Group more often obstruction, ongoing diverticulitis and recurrent diverticulitis.
- 6 patients in the No Antibiotic Group were censored when enrolled in a trial regarding surgical treatment

*Peery A Am J Gastroenterol 2018*

Non-antibiotic Treatment Successful for Outpatients- DINAMO Study

- 480 patients mild diverticulitis
- 238 Amox-Clavulanic Acid
- 242 No antibiotic

No Differences in:
- Hospitalization rates
- ED re-visits
- Poor pain control
Current Antibiotic Guidelines- Selective Use

• AGA, ASCRS and ACP recommend

Selective use in healthy, immunocompetent patients with uncomplicated diverticulitis

*(conditional recommendation, low quality evidence)*

Stollman et al. Gastroenterology 2015;149
Qaseem et al. Annals Int Med 2022;175

Choice of Outpatient Antibiotic- Amox-Clavulanic Acid Over Metronidazole+ Fluoroquinolone

*Amoxicillin-clavulanic acid versus metronidazole + fluoroquinolone
Using nationwide administrative databases*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Difference</th>
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<tbody>
<tr>
<td>1-year risk of hospital admission</td>
<td>same</td>
</tr>
<tr>
<td>1-year risk of surgery</td>
<td>same</td>
</tr>
<tr>
<td>1-year risk of C difficile colitis</td>
<td>Higher with fluoroquinolone</td>
</tr>
<tr>
<td>3-year risk of elective surgery</td>
<td>same</td>
</tr>
</tbody>
</table>

Gaber et al Annals of Int Med 2021
Practical Approach in Low Risk Patients

- CT scan if first episode or severe/atypical presentation
- Discuss antibiotic vs no antibiotic options (patient preference!)
- If antibiotics:
  - 4-7 day course & then reassess
  - Amoxicillin-clavulanic acid if possible
- Clear liquid diet 1-2 days, advance as tolerated
- Antispasmodic and acetaminophen for pain
- Close follow up (~ 2 days) if no antibiotic given

High Risk Patients – Treat with Antibiotics

- Immunocompromised
- Significantly elevated WBC (>15 cells/L), CRP (>140mg/L)
- Long segment of inflammation on CT (~ 10cm)
- Signs of sepsis
- Frail or elderly
- Significant comorbidity (ASA class 3 or 4)
- History of smoldering/refractory diverticulitis
- No reliable follow up

Broersen LHA, et al BMJ Open Gastroenterol 2017;4
Rottier SJ, et al Surg Infect (Larchmt) 2019
Van Dijk ST, et al Int J Colorectal dis 2017;32
Case 1 – Diverticulitis Follow up

37M with diverticulitis recovers uneventfully with conservative therapy. He is asymptomatic and specifically denies rectal bleeding. He has no family history of colon polyps or cancer.

Colonoscopy or Not?

Risk of Colon Cancer Following Diverticulitis

- All guidelines recommend colonoscopy after complicated diverticulitis
- Conflicting guidelines regarding uncomplicated disease.
- AGA recommends colonoscopy if high-quality exam not done within 1 year

Peery AF BMJ 2021
Case 1 Continued

Patient returns to clinic 3 years later.

• 3 recurrences all similar to his prior episode
• CT scan done for 2 episodes finding sigmoid diverticulitis
• All episodes resolve promptly with antibiotics
• Concerned regarding possibility of more serious future events
• Curious about ways to prevent episodes

How to manage patients with recurrent, uncomplicated diverticulitis?

Recurrent Diverticulitis is Common

- Diverticulitis All cases: 8% at 1 year 1st recurrence, 20% at 1 year 2nd recurrence, 25% at 1 year 3rd recurrence
- Diverticulitis With Abscess Non-operative rx: 14% at 1 year 1st recurrence, 20% at 5 years

Risk increases with each episode
Recurrence higher in complicated dz; 57% within 1st year

Bharucha et al Am J Gastroenterol 2015; 110:1589
Aquina et al BJS 2019;106: 467
Most Complications Occur During First Episode

Prospective single center study of 934 patients over 11 year period

Ritz et al Surgery 2011;149:606

Evolving Mechanisms & Prevention

Strate, Morris Gastroenterol 2019; 156
Pharmacological Prevention of Recurrent Diverticulitis

<table>
<thead>
<tr>
<th>Benefit</th>
<th>5-ASA</th>
<th>Rifaximin</th>
<th>Probiotics</th>
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</thead>
<tbody>
<tr>
<td>No benefit</td>
<td>?</td>
<td>?</td>
<td></td>
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<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>5-ASA</th>
<th>Rifaximin</th>
<th>Probiotics</th>
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<tbody>
<tr>
<td>6 RCTs Meta-analyses</td>
<td></td>
<td>Small unblinded trial rifaximin vs fiber</td>
<td>Small randomized trial</td>
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</table>

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>5-ASA</th>
<th>Rifaximin</th>
<th>Probiotics</th>
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<tbody>
<tr>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
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<table>
<thead>
<tr>
<th>Recommendation</th>
<th>5-ASA</th>
<th>Rifaximin</th>
<th>Probiotics</th>
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</thead>
<tbody>
<tr>
<td>Don’t use</td>
<td>Don’t use</td>
<td>Don’t use</td>
<td></td>
</tr>
</tbody>
</table>

Strate, Peery, Neumann Gastroenterol 2015; Stollman et al Gastroenterol 2015

Surgery vs. Conservative Treatment
Recurrent Diverticulitis (DIRECT Trial)

- 27 centers in the Netherlands with follow up to 6 months
- 107 patients randomized to elective resection vs. conservative treatment

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic resection (n=53)</th>
<th>Conservative (n=56)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of life (GiQli)</td>
<td>114</td>
<td>110</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serious Adverse Events</td>
<td>10</td>
<td>12 “unbearable complaints”</td>
<td></td>
</tr>
<tr>
<td>Recurrences</td>
<td>0</td>
<td>7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Van de Wall, Lancet Gastrohep 2017;2
Recurrence Reduced, Not Eliminated After Surgery

![Risk of Recurrence Graph]

Thornblade et al, Ann Surg 2019

ASCRS 2014 Guideline

“The decision to recommend elective sigmoid colectomy after recovery from uncomplicated acute diverticulitis should be individualized.”

Feingold et al Dis Colon Rectum 2014;57:284

AGA 2015 Guideline

“The AGA suggests against elective colonic resection in patients with an initial episode of acute uncomplicated diverticulitis. The decision to perform elective prophylactic colonic resection in this setting should be individualized” (Conditional recommendation, very-low quality of evidence)

Stollman et al Gastroenterol 2015; 149:1944
### Framework for Considering Surgery for Recurrent Diverticulitis

<table>
<thead>
<tr>
<th>For</th>
<th>Against</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoldering diverticulitis</td>
<td>Fewer than 3 episodes of diverticulitis</td>
</tr>
<tr>
<td>Frequent and/or severe attacks</td>
<td>Episodes resolve readily with treatment</td>
</tr>
<tr>
<td>Significant impact on quality of life</td>
<td>Infrequent episodes</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>Functional symptoms; no inflammation</td>
</tr>
<tr>
<td>Patient preference</td>
<td>Diverticulitis in multiple locations</td>
</tr>
<tr>
<td>Diverticulitis events in same location</td>
<td>Poor surgical risk</td>
</tr>
</tbody>
</table>

*Regenbogen et al JAMA Surgery 2014
Feingold et al Dis Col Rectum 2014*

### What Else Can be Done to Prevent Recurrent Diverticulitis?

[Diagram showing the progression from Diverticulitis to Recurrent Diverticulitis]
**Diet, Lifestyle & Risk of Diverticulitis**

*Adjusted Relative Risk*


---

**Adherence to Low-Risk Factors Reduces Risk**

Low Risk Factors:
- BMI 18-25
- Red meat < 4/week
- ≥ 23 g fiber / day
- Exercise 2 h/week
- No smoking

Account for 50% of population attributable risk

*Liu PH, et al, Am J Gastroenterol 2017*
Nuts, Corn, Popcorn: NO Increased Risk of Diverticulitis

Comparison of high to low quartile of intake
In cohort of 51,000 men followed for 20+ years

* Adjusted for age, period, dietary fat, red meat, calories, fiber, nuts/corn, NSAIDs, activity


Not all Risk Factors are Modifiable – Genetics Plays a Role

Danish nationwide patient and twin registries 1977-2011
10,400 index siblings and 923 twins with diverticular disease

50% of liability to diverticular disease due to genetic factors

Strate, et al. Gastroenterol 2013
Case 1 - Is Back Again

Patient comes back to clinic 2 months later

- His symptoms have not resolved despite 2 courses of antibiotics.
- CT scan shows persistent sigmoid diverticulitis
- Fecal calprotectin is 234

How to diagnose and treat smoldering diverticulitis?

Case 1 – Flexible Sigmoidoscopy

- Bowel wall edema
- Patchy erythema without erosion in the sigmoid colon
Smoldering Diverticulitis

• Diverticulitis refractory to treatment or recurring shortly after stopping therapy
• Often in patients with multiple prior recurrences
• Much more likely to require surgery
  • 50% unexpected abscess at the time of surgery
  • 90% improve after surgery


Diagnosis and Treatment of Smoldering Diverticulitis

• Diagnosis:
  • Repeat CT scan
  • Consider (gentle) flexible sigmoidoscopy
  • Consider fecal calprotectin
• Treatment:
  • Re-treatment with another type of antibiotic
  • Consider admission for IV antibiotics in severe cases
  • Low threshold for surgery referral
Case 2

54F with a history of uncomplicated diverticulitis a year ago is referred for ongoing left-sided abdominal pain
- Normal CT scan
- Colonoscopy normal except diverticulosis
- Labs normal including CRP

Post-Diverticulitis Functional Bowel Disease

Retrospective study of 1100 cases of diverticulitis and 1100 controls without a prior diagnosis of functional bowel disease followed for average of 6 years

IBS:
Adjusted HR 4.7 (95% CI, 1.6-14)
23 cases
4 controls

Functional GI Diagnosis:
Adjusted HR 2.4 (95% CI, 1.6-3.6)
95 cases
51 controls

Symptomatic Uncomplicated Diverticular Disease (SUDD)

- Persistent abdominal symptoms attributed to diverticula in the absence of macroscopic colitis or diverticulitis
- Term coined in the early 1990s
- Greater interest in Europe than US
- Variably applies to those with /without prior diverticulitis

Spiller RC Dig Dis. 2012;30:64

### IBS vs Diverticular Disease

<table>
<thead>
<tr>
<th></th>
<th>IBS</th>
<th>Diverticular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td>Young</td>
<td>Older</td>
</tr>
<tr>
<td></td>
<td>Female &gt;&gt; Male</td>
<td>Female = Male</td>
</tr>
<tr>
<td><strong>Colon structural changes</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Prevalence of symptoms</strong></td>
<td>100%</td>
<td>15% of diverticulosis pts</td>
</tr>
<tr>
<td><strong>Rome criteria</strong></td>
<td>100%</td>
<td>15%</td>
</tr>
<tr>
<td><strong>Pain pattern</strong></td>
<td>Frequent recurrences, short-lived</td>
<td>Long remissions, prolonged (&gt;24hrs)</td>
</tr>
<tr>
<td><strong>Pain location</strong></td>
<td>Diffuse</td>
<td>Left lower quadrant</td>
</tr>
<tr>
<td><strong>Bowel alteration</strong></td>
<td>Diarrhea &amp; constipation</td>
<td>Diarrhea &gt; constipation</td>
</tr>
<tr>
<td><strong>Fecal calprotectin</strong></td>
<td>Normal</td>
<td>Elevated</td>
</tr>
</tbody>
</table>

Spiller RDig Dis 2012;30:64-69
Tursi A J Clin Gastroenterol 2014
## Treatment of SUDD

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>Fiber</th>
<th>5-ASA</th>
<th>Rifaximin</th>
<th>Probiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small studies; often combined with other therapy</td>
<td>One small Randomized Trial</td>
<td>Often in combination with fiber or probiotics</td>
<td>Few small randomized trials</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>Fiber</th>
<th>5-ASA</th>
<th>Rifaximin</th>
<th>Probiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td></td>
</tr>
</tbody>
</table>

**In general, treat like IBS**


---

### Case 3

59F with a history of recurrent diverticulitis presents with 2 months of diarrhea now bloody, frequent stools and abdominal cramping.

- C diff and stool culture negative
- CT with long segment of sigmoid thickening
- Does not respond to a course of antibiotics

*Is this diverticulitis, IBD or SCAD?*
IBD vs. SCAD

Similarities
• Endoscopic findings
• Histology findings
• Treatment

Differences
• Older age of onset in SCAD
• SCAD spares rectum
• Lower relapse rate

Clinical and pathological findings are not pathognomonic


Classic Endoscopic Findings

Patchy erythema
Accentuated on the crests of folds
“Crescentic fold disease”

Case 3 Endoscopic Findings

Initial flexible sigmoidoscopy
Flexible sigmoidoscopy for persistent symptoms

Natural History of SCAD – Most Cases evolve to IBD

• Literature (case series or case reports)
  - 30% progresses to IBD or require surgery
• My experience
  • A rare disorder
  • Most patients are eventually diagnosed with IBD and respond to IBD therapy (biologic)
• Treat like IBD

Rampton, Colorectal Disease 2001
**Take Home Points**

- **Diverticulitis**
  - Avoid antibiotics in select healthy, immunocompetent patients
  - Avoid fluoroquinolone + metronidazole if possible

- **Recurrence**
  - Emphasize diet and lifestyle changes
  - After informed discussion, refer select patients to surgery

- **Smoldering diverticulitis**
  - Important to recognize / diagnose
  - Re-treatment with antibiotics
  - Low threshold for surgery

---

**Take Home Points**

- **Functional symptoms in patients with diverticulosis**
  - IBS is very common following diverticulitis
  - SUDD is difficult to distinguish from IBS

- **Segmental Colitis Associated with Diverticular Disease**
  - Very rare presentation
  - Difficult to distinguish from IBD
  - Not the same as smoldering diverticulitis
  - Treat like IBD
Questions and Answers

Lisa L. Strate, MD, MPH, FACG

Neil H. Stollman, MD, FACG

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