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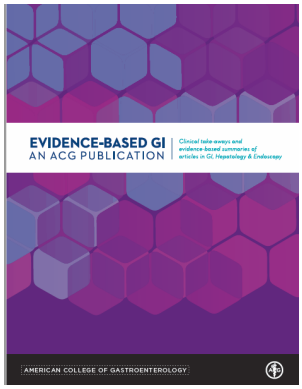

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CRC SCREENING

Free Online Program Improves Adenoma Detection Rate and Decreases Post-Colonoscopy Colorectal Cancer

Jeffrey Lee, MD, MPH
Associate Editor

Jeffrey Lee, MD, MPH

Research Scientist and Attending Gastroenterologist, Kaiser Permanente San Francisco Medical Center, San Francisco, CA

This article reviews Corley DA, Jensen CD, Lee JK, et al. Impact of a Scalable Training Program on the Quality of Colonoscopy Performance and Risk of Post-Colonoscopy Colorectal Cancer. [Published ahead of print April 22, 2023]. Gastrointest Endosc. doi: 10.1016/j.gie.2023.04.2073 .

Correspondence to Jeffrey Lee, MD, MPH. Associate Editor. Email: EBGI@gi.org

STRUCTURED ABSTRACT

Question: Is a 30-minute, interactive, online educational program about quality of colonoscopy associated with an increased adenoma detection rate (ADR) and decreased risk of post-colonoscopy colorectal cancer (CRC)?

Design: Retrospective cohort study with endoscopists serving as their own controls, pre- and post-online education.

Setting: Kaiser Permanente Northern California endoscopy centers (n =21).

Study Population: All gastroenterologists practicing at Kaiser Permanente Northern California sites in 2014, who completed ≥ 100 colonoscopies/year with ≥25 screening exams/year during the 3-year period before and after online training (n = 86).

Intervention/Exposure: Completion of 30-minute, interactive, online training about quality of colonoscopy during a 3-month training period in

2014. Using behavior-change theory, research on evidence-based interventions, and identified drivers of ADR variability, the training program reviewed optimal colonoscopy exam techniques, identification of flat adenomas, and social incentives for normalizing a quality-focused culture. The online training program is available for free at https://deliveryscience-appliedresearch.kaiserpermanente.org/specialty-research-networks/gastroenterology-hepatology.

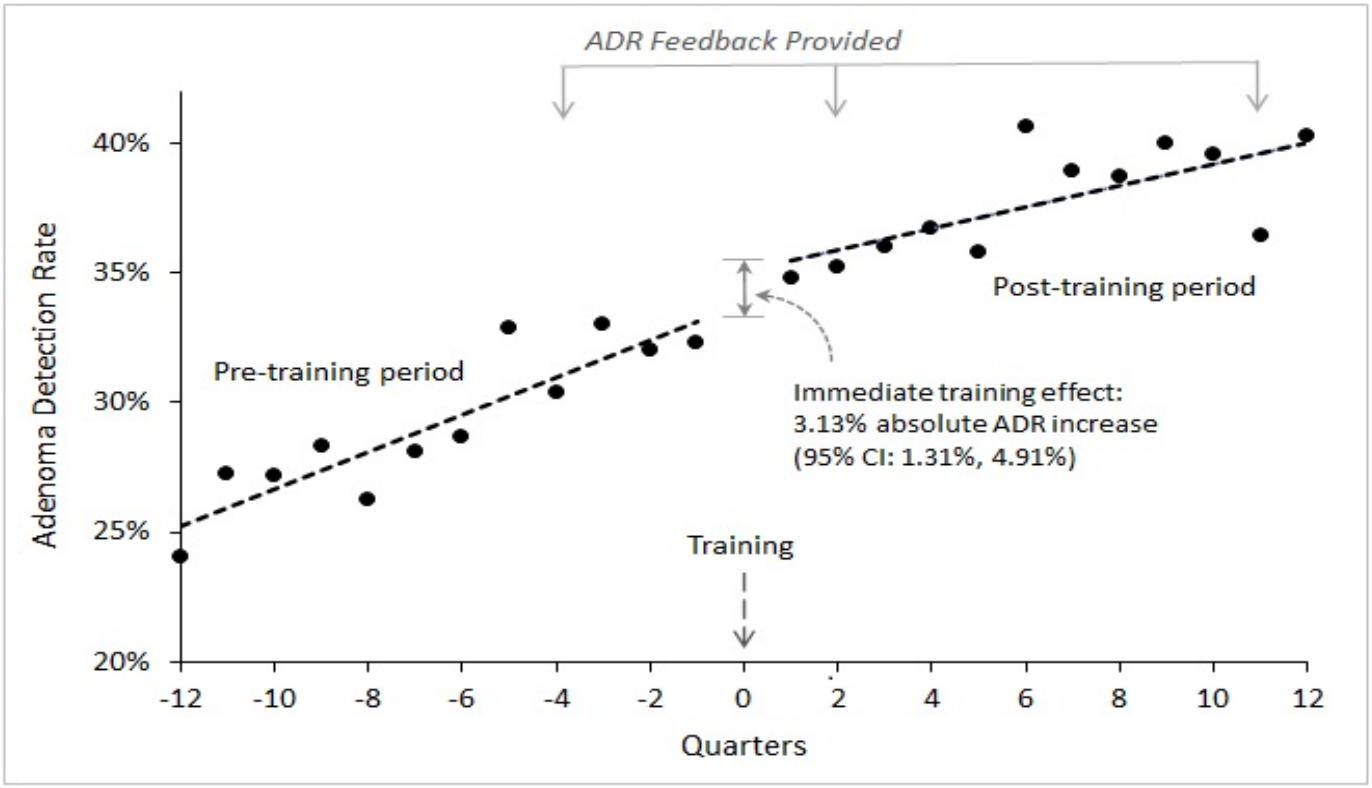
Outcome: The primary outcome was change in individual endoscopist's ADR derived from average-risk screening colonoscopies during the 3-year post-training period compared to 3-year pre-training period. The secondary outcome was association between endoscopists' ADR and their patients' risk of post-colonoscopy CRC.

Data analysis: Interrupted time series analysis, adjusted for temporal trends in ADR. Cox proportional hazards regression used to assess association between ADR and risk of post-colonoscopy CRC to produce adjusted hazards ratio (aHR).

Funding: National Cancer Institute.

Results: Among 86 study endoscopists, 133,225 colonoscopies were performed in the pre-training period with 23.8% performed for CRC screening (n=31,643), and 146,786 colonoscopies performed during the post-training period with 19.4% performed for CRC screening (n=28,408). Patient characteristics were similar in pre- and post-training period: median age = 63; 51% female; 61-63% White; and body mass index (BMI)=27.3.

Median ADR rose from 29.2% (interquartile range [IQR]: 22.8%-35.1%) in the pre-training period to 35.5% (IQR: 31.3%-44.5%) in the post-training period. In the initial 3-month period following training, mean ADR increased by 3.13%. This increase was greatest for endoscopists whose pre-training ADR was below the group's median ADR of 29.2% (Figure 1). Each 1% increase in ADR was associated with a 4% decrease in their patients' risk of post-colonoscopy CRC (aHR = 0.96; 95% confidence interval: 0.93-0.99).



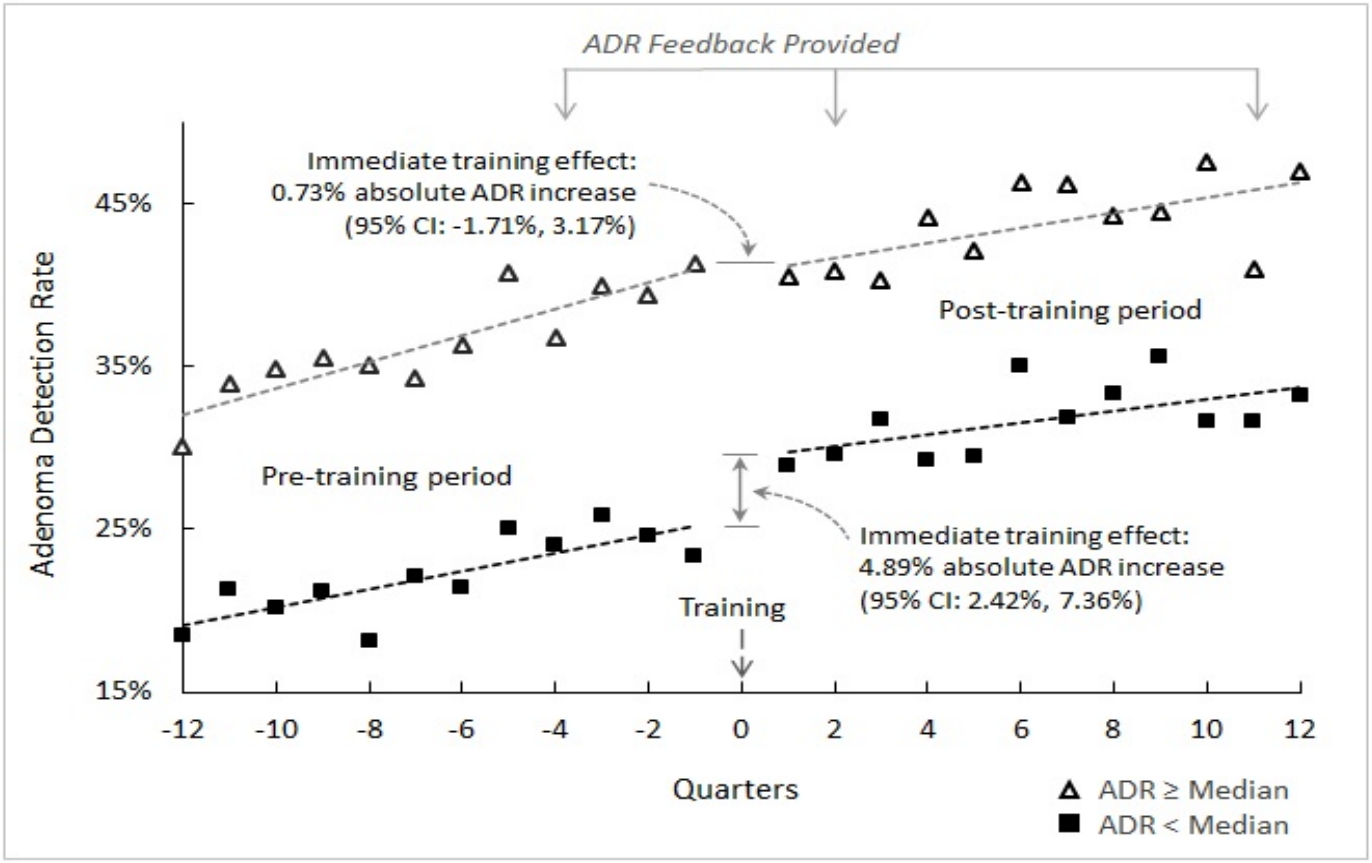


Figure 1. Endoscopist adenoma detection rate pre– and post-training.

ADR, adenoma detection rate; CI, confidence interval.

COMMENTARY

Why Is This Important?

The beneficial effect of colonoscopy on reducing CRC incidence and mortality is largely derived from early detection and removal of adenomas.[1] Studies have consistently shown the magnitude of this benefit varies based on the quality of the colonoscopy examination, particularly the ability to detect adenomas.[2,3] To improve colonoscopy quality, multiple guidelines recommend physician ADR benchmarks of ≥25%.[4] Despite its widespread adoption as a key colonoscopy quality measure in clinical practice, there are still significant variation in ADR among endoscopists.[2,3] As such, numerous interventions have been developed to enhance ADR including increased emphasis on withdrawal times to 9 minutes, recommending a second look or retroflexing in the right colon, and use of distal attachment and artificial intelligence devices.[5] While many of these interventions have shown to improve ADR, they can be costly, difficult to implement, or require additional in-person training. Thus, this study addresses an important gap in implementation by developing a 30-minute online training program aimed to improve ADR while being freely available for all endoscopists. Importantly, this easily scalable intervention was shown to improve ADR among endoscopists from the study while also reducing the risk of post-colonoscopy CRC.

Key Study Findings

A freely available 30-minute online training program was associated with a mean absolute increase in physician ADR of 3.1%. The effect was more pronounced among endoscopists who had ADRs below the median pre-training ADR of 29.2% compared to those above the median. (i.e., 4.9% increase versus 0.7% increase, respectively). Post-training, each 1% absolute increase in ADR among endoscopists was associated with a 4% decrease in their patients' PCCRC risk.

Caution

The main limitation of this study is that it was not a randomized controlled trial; however, the study used a pre- and post-training design that allowed endoscopists to serve as their own control and the interrupted time series analysis controlled for temporal trends in

ADRs. Another limitation is that this study took place in a setting where ADR feedback was provided annually.

My Practice

In our large medical group consisting of over 160 gastroenterologists across 21 medical centers, screening and overall ADRs along with other quality metrics (e.g., cecal intubation rate, etc.) are provided annually to all gastroenterologists to facilitate self-assessment and performance improvement. In addition to measuring ADR, our organization has provided the 30-minute online training program to all gastroenterologists and has required it for all new hires.

In my personal practice, I use several tools and techniques that are highlighted in this online training program to optimize adenoma detection. First, it is critical to use a high-definition colonoscope with image enhancement (e.g., narrow band imaging) capabilities to help detect and evaluate subtle lesions. Second, it is important to understand all the subtle features of flat polyps and have mindset for detecting flat polyps since these lesions are often missed. Third, I maximize mucosal exposure by working the folds (i.e., deflecting the tip of the colonoscope into the inner-haustral valley and exposing the proximal sides of each haustral folds), cleaning and suctioning any stool debris, and distending the lumen adequately. Fourth, I perform 2 or 3 passes in the right colon since adenomas are often missed in this location. Lastly, when available, I often use a distal attachment device such as a clear translucent cap to help expose the proximal sides of each haustral fold and improve mucosal exposure.

For Future Research

A randomized trial evaluating this online training program in a different setting would improve the generalizability of this study's findings. In addition, testing whether this freely available online training program can improve proximal serrated detection rates, which has been shown to be variable among endoscopists and is associated with PCCRC, should be performed.

Conflict of Interest

Dr. Lee was a co-author and investigator of this study.

Note: The authors of the article published in *GIE* are active on social media. Tag the to discuss their work and this EBGI summary!

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EVIDENCE-BASED GI
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Screening Colonoscopy in the Elderly Population—Is Less Better?

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Philip N. Okafor, MD, MPH
Associate Editor

This summary reviews El Halabi J, Burke C, Hariri E, et al. Frequency of use and outcomes in individuals older than 75 years. JAMA Intern Med 2023; 183:519-19.

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STRUCTURED ABSTRACT

Question: When performing screening colonoscopy in individuals >75 years old, what is the frequency that life expectancy is <10 years and frequency of adverse events within 10-days of colonoscopy?

Design: This was a retrospective cross-sectional study using screening colonoscopy data between January 2009 and January 2022.

Setting: Cleveland Clinic in Ohio and Florida.

Participants: Asymptomatic individuals >75 years old who underwent colonoscopy for indication of screening. Patients with incomplete colonoscopy data, history of inflammatory bowel disease or colorectal cancer (CRC), or history of colonoscopy within past 5 years were excluded.

Intervention/Exposure: Screening colonoscopy complete to the cecum with an adequate bowel preparation.

Outcomes: The primary outcome was percentage of screening

colonoscopies performed in individuals with <10 years life expectancy. Secondary outcomes were frequency of adverse events, defined as emergency visit or hospital admission, within 10-days of colonoscopy, and colonoscopy findings defined as normal, non-advanced polyps only (adenoma/hyperplastic polyp <10 mm) only, or advanced neoplasia (any adenoma ≥1 cm, villous adenoma, serrated adenoma, or CRC).

Data Analysis: Procedure details, colonoscopy and pathology findings were extracted using an internally validated natural language processing algorithm. Comorbidity-adjusted life expectancy at time of colonoscopy was estimated based on patients' age and comorbidities from the Charlson comorbidity index using a standardized tool. Chart review was performed for each identified adverse event to assess likelihood of association between colonoscopy and adverse event using American Society for Gastrointestinal Endoscopy methodology.

Funding: None.

Results: In the cohort of 7,067 individuals undergoing screening colonoscopy, demographic data included 56% women, 77% White, and median age as 78 (interquartile range: 77-79) with 81.7% (n=5,775) between 76-80 years old, 14.4% (n=1,021) between 81-85 years old, and 3.8% (n=271) over 85 years old. The percentage of colonoscopies performed in individuals with life expectancy <10 years was 30% in the 76–80 year old cohort, 71% in the 81-85 year old cohort, and 100% in the >85 year old cohort (Table 1). Adverse event rate (hospitalization or emergency visit) was 13.6 per 1,000 patients, and individuals with life expectancy <10 years had approximately double the rate of adverse events as individuals with life expectancy ≥10 years. Prevalence of advanced neoplasia was 5.4% in 76–80 year olds, 6.2% in 81–85 year olds, and 9.5% in >85 year olds.

COMMENTARY

Why Is This Important?

Care that has a greater potential for harm than benefit is increasingly recognized in the United States and forms the basis of the American Board of Internal Medicine's "Choosing Wisely" campaign[1]. Overtreatment occurs when there is little evidence of a clinically meaningful net benefit from an intervention. As it pertains to CRC screening,

Outcome (%)	Normal Colonoscopy	Non-advanced polyps only	Advanced Neoplasia
Age 76-80 with ≥ 10 year life expectancy (n=4,042)	47.5%	48.6%	3.9%
Age 76-80 with <10 year life expectancy (n =1,733)	74.5%	16.5%	9.0%
Age 81-85 with ≥ 10 year life expectancy (n = 296)	33.8%	62.7%	3.5%
Age 81-85 with < 10 year life expectancy (n = 725)	67.9%	25.0%	7.1%
Age > 85 with < 10 year life expectancy (n = 271)[1]	66.4%	24.0%	9.6%

Table 1. Prevalence of advanced neoplasia, stratified by life expectancy < or ≥ years.

[1]No patients >85-years old had a comorbidity-adjusted life expectancy of >10 years.

the 2021 United States Preventative Services Task Force recommendations for CRC screening in patients older than age 75 years come with a Grade C recommendation. This means that the selective recommendation of colonoscopies to individuals is based on professional judgment and patient preferences. Inadvertently, this may lead to indication creep which occurs when providers apply recommendations that may be appropriate for high-risk patients to all their patients[2]. Overscreening for CRC in patients older than 75 years is associated with physical and financial costs while often providing little benefit. This study by El Halabi et al provides supporting evidence of the low benefit and higher risk associated with most screening colonoscopies in patients older than 75 years, in a single health system in the United States.

Key Study Findings

The authors show a very low rate (0.2%) of invasive colorectal adenocarcinoma in the cohort of patients screened at an age over 75 years. Among patients with invasive colorectal adenocarcinoma and a life expectancy <10 years, only 1 of 9 received treatment for the malignancy.

They also observed a higher adverse event rate at 10 days which increased with age, especially among patients older than 85 years, suggesting that the risk of screening this group of patients was much higher than any

derived benefit.

Caution

One limitation of this study is that it comes from a single health system which may limit secondary generalizability. In addition, in spite of the reports of lower advanced adenoma rates in their cohort, the study does not include data on colon polyp surveillance. It also does not compare outcomes between patients undergoing their first screening colonscopy vs those with a previous negative screening colonoscopy. The latter point is important to highlight as some studies have shown that colonoscopies in 76–80 year-olds do seem to reduce mortality due to CRC and the incidence of CRC, but only in patients who are "healthy," meaning no prior myocardial infarction/stroke or no combination of diabetes, hypertension, elevated cholesterol, or coronary artery disease. The benefit was highest if no screening colonoscopies had been done prior to age 75.[3]

My Practice

The bulk of screening colonsocopies in my institution come from open access referrals. As a result, I see septuagenarians and octogenarians with significant comobididites still being referred for screening colonsocopies. To limit this, I try to document in the endoscopy report when further screening is not recommended, especially in patients 75 years and older, particularly if they have a high comorbidity burden. It is important to highlight: (1) the importance of estimating a patient's life expectancy when making the decision to recommend screening colonoscopy in patients >75 years, and (2) the availability of online tools that allow a quick estimation of life expectancy that can be used in the decision-making process, including but not limited to ePrognosis.

For Future Research

Calderwood et al showed that up to 58% of older adults with less than 5-year life expectancy were recommended to return for future surveillance colonscopy[4]. This highlights that patient selection is the most important factor when recommending screening or surveillance colonoscopies in older adults. In addition, per the 2022 US Multi-Society Task Force recommendations, individuals with no prior screening colonoscopy who are 76-84 years and have a life expectancy of 5-10 years may be appropriate for offering screening colonoscopy based on

patients' preferences[5]. As such, intervention studies that assess the impact of provider education tools for estimating patient comorbidity burden and subsequent life expectancy on the decision to recommend screening colonoscopy in patients >75 years are needed to help reduce overscreening.

Conflict of Interest

Dr. Okafor reports no potential conflicts of interest.

Note: The authors of the article published in JAMA Internal Medicine are active on social media. Tag them to discuss their work and this EBGI summary.

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EVIDENCE-BASED GI
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Cephalosporins and Ciprofloxacin Still Appropriate First-Line Treatment for Spontaneous Bacterial Peritonitis

Dr Philip Schoenfeld
Editor-in-Chief

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Chief (Emeritus), Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI.

LIVER

This article reviews Yim HJ, Kim TH, Suh SJ, et al. Response-Guided Therapy with Cefotaxime, Ceftriaxone, or Ciprofloxacin for Spontaneous Bacterial Peritonitis: A Validation Study of 2021 AASLD Practice Guideline for SBP. Am J Gastroenterol 2023; 118: 654-63.

Correspondence to Philip Schoenfeld, MD, MSEd, MSc. Editor-in-Chief. Email: EBGI@gi.org

STRUCTURED ABSTRACT

Question: Are standard American Association for the Study of Liver Disease (AASLD) guideline-recommended antibiotics, cefotoxime, ceftriaxone, and ciprofloxacin, still effective for the treatment of spontaneous bacterial peritonitis (SBP) despite the rise in multidrug resistant organisms?

Design: Multicenter, unblinded randomized controlled trial (RCT).

Setting: Nine tertiary hospitals in South Korea between 2007-2018.

Patients: Included patients were: (a) age 16-75 years old; (c) clinical diagnosis of cirrhosis with ascites; and (c) ascitic polymorphonuclear (PMN) cell count $\geq$ 250/mm^3. Multiple exclusion criteria were used to exclude patients with secondary peritonitis as cause of elevated PMN count.

Interventions/Exposure: Two grams of Cefotaxime intravenously (IV) every 8 hours vs ceftriaxone 2 grams IV every 24 hours vs 200 mg

ciprofloxacin IV every 12 hours for 5 days with 1:1:1 randomization.

Repeat paracentesis was performed 48 hours after starting antibiotics. If ascitic PMN count had not decreased by >25%, then the patient was switched to broader-spectrum antibiotics. Twenty percent albumin could be infused at admission and at 48 hours after admission to prevent acute kidney injury at the discretion of the investigator.

Outcome: The primary endpoint was resolution of SBP at 120 hours (5 days) defined by: a decrease in ascitic PMN cell count < 250/mm^3; normalized leukocytosis in peripheral blood count; no bacterial growth in blood or ascitic fluid cultures; and resolution of any symptoms/signs of SBP, including abdominal pain and fever.

Data Analysis: Intention-to-treat (ITT) analysis for patients who received at least 1 dose of antibiotic and per-protocol (PP) analysis for patients who completed assigned antibiotic course were performed. Categorical variables were compared using chi-square test or Fisher exact test, as appropriate, and continuous variables were assessed with analysis of variance (ANOVA).

Funding: Korea Healthcare Technology R&D Project, Ministry of Health and Welfare, Republic of Korea, and a research grant from Korea University.

Results: Among 261 randomized patients, mean age was 56 years (51-63); 76% male; etiology of cirrhosis was 43% alcohol, 40% chronic hepatitis B infection, 11% chronic hepatitis C infection; mean Child-Pugh score 10 (9-12) and mean MELD score was 20 (16-24). For the primary endpoint, there was no significant difference in resolution of SBP at 120 hours for cefotaxime vs ceftriaxone vs ciprofloxacin, respectively: 67.8% vs 77.0% vs 73.6% (P= 0.39) in the ITT analysis. Per-protocol analysis results were 80.6% vs 85.5% vs 85.9%, respectively (P= 0.65) (Figure 1). After the 48-hour paracentesis, broad spectrum antibiotics were started because PMN count had not decreased by at least 25% in a minority of patients initially treated with cefotaxime vs ceftriaxone vs ciprofloxacin, respectively (10.3% vs 5.7% vs 12.6% [P= 0.21]). *Escherichia coli* was the most frequently isolated bacteria in culture (34.1%) and 21.4% of these isolates were resistant to third-generation cephalosporins. There were no significant differences in other secondary outcomes.

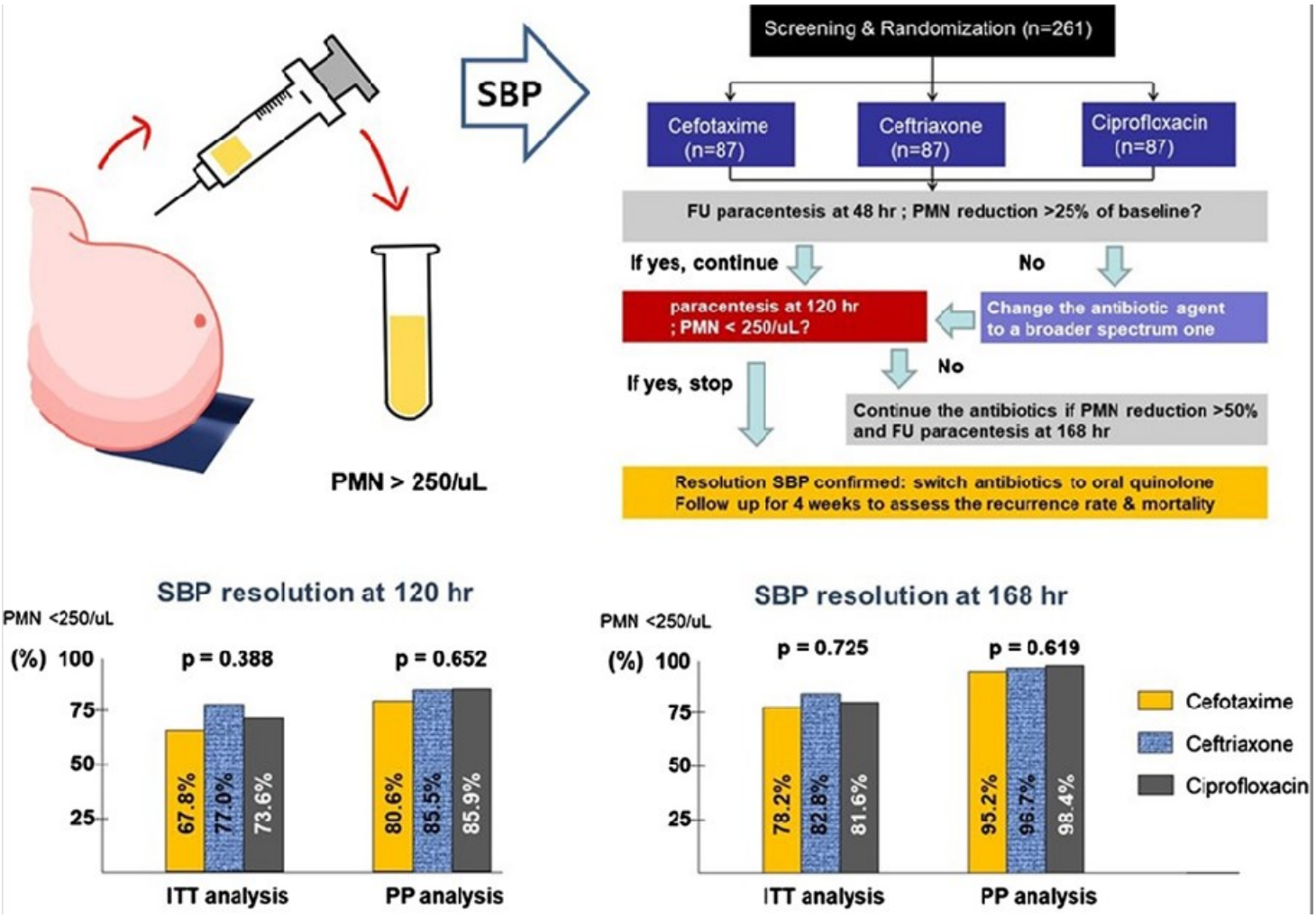

Figure 1. Visual abstract
FU, follow-up; ITT, intention-to-treat; PMN, polymorphonuclear; PP, per-protocol; SBP, spontaneous bacterial peritonitis.

COMMENTARY

Why Is This Important?

The 2021 AASLD guidelines[1] recommend that SBP should initially be treated with a third-generation cephalosporin, such as ceftriaxone, followed by repeat paracentesis in 48 hours. If ascitic PMN count has not decreased by 25%, then broader-spectrum antibiotics, such as piperacillin/tazobactam plus carbopenams, can be initiated.

SBP resolution rates of 90% had previously been reported with third-generation cephalosporins, but lower rates have been reported recently due to multi-drug resistant species of *E. coli* and *Klebsiella pneumoniae*. This has led to more routine use of broader-spectrum antibiotics, like piperacillin/tazobactam, as first-line treatment. However, increased use of these antibiotics may represent poor

antibiotic stewardship and lead to more antimicrobial resistance.[2]

This RCT is an important contribution because it validates current AASLD guidelines. The investigators should be commended for their excellent study design and diligence to address this important issue.

Key Study Findings

There was no significant difference in resolution of SBP at 120 hours for cefotaxime vs ceftriaxone vs ciprofloxacin, respectively: 67.8% vs 77.0% vs 73.6% (P= 0.39) in the ITT analysis.

Per-protocol analysis results were 80.6% vs 85.5% vs 85.9%, respectively (P= 0.65).

Caution

This is a South Korean study which took 11 years to enroll the study population. Unknown factors may confound the results and minimize its applicability to US settings. However, unless your setting has substantially higher rates of third generation cephalosporin-resistant *E. coli* and *Klebsiella* spp these results should apply to your SBP patients.

My Practice

Although I'm a general gastroenterologist, I treat SBP patients frequently on our inpatient service. Usually, our internal medicine staff have already started a patient on antibiotics before I see the patient. They usually prescribe broad-spectrum antibiotics, such as piperacillin-tazobactam— which the AASLD guideline recommends avoiding as first-line therapy and saving for patients that are likely to have multidrug-resistant (MDR) organisms.

I'm reassured by the 85% SBP resolution rates reported with ceftriaxone in this trial, which reinforces my current teaching to house staff to start ceftriaxone as first-line treatment for SBP, unless the patient was recently hospitalized and is at higher risk for MDR organisms. This represents good antibiotic stewardship. I will check with my infectious disease colleagues and our infection control teams to assess the frequency of MDR *E. coli* and *Klebsiella sp.* in our setting. If it's substantially higher than 20%, then I may reassess my practice after consultation with my hepatology and infectious disease colleagues. This study is also a good reminder to follow AASLD

guidelines[1] to repeat paracentesis at 48 hours and confirm that patients are responding to antibiotic therapy with at least 25% decrease in PMN count.

For Future Research

Better tools, including molecular diagnostic tools, are needed to quickly identify MDR organisms and guide selection of appropriate antibiotic therapy.[1]

Conflict of Interest

Dr. Schoenfeld reports no conflicts of interest.

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Joint AGA-ACG Clinical Practice Guideline on Chronic Idiopathic Constipation Treatments: Parsing Benefits and Risks

GUIDELINE

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This article reviews Chang L, Chey WD, Imdad A, et al. AGA-ACG Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation. Am J Gastroenterol 2023; 118(6):936-954. doi: 10.14309/ajg.0000000000002227

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STRUCTURED ABSTRACT

Question: Which therapies are superior to placebo for chronic idiopathic constipation (CIC)?

Design: Evidence-based guidelines using GRADE methodology and Evidence-to-Decision (EtD) frameworks to assess benefits, risks, and costs, among other factors.

Patients: Patients diagnosed with CIC, although individual trials used different definitions of CIC.

Interventions/Exposure: Fiber supplements (psyllium, methylcellulose, bran, and inulin), osmotic or surfactant laxatives (polyethylene glycol [PEG], magnesium oxide, lactulose, docusate), stimulant laxatives (bisacodyl, senna, sodium picosulfate), secretagogues (lubiprostone, linaclotide, plecanatide), serotonin agonists (prucalopride). Active interventions could be compared versus placebo, no intervention or standard of

care. Studies comparing different CIC therapies without a placebo arm were excluded.

Outcome: Complete spontaneous bowel movements (CSBMs) per week, spontaneous bowel movements (SBMs) per week, responder rate (defined as $\geq$ 3 CSBMs per week and an increase from baseline of 1 CSBM per week), diarrhea (adverse event) leading to discontinuation of treatment, serious adverse events, global relief, and quality of life. CSBMs per week, SBMs per week, and adverse events leading to discontinuation of medication were chosen as critical outcomes.

Data Analysis: Meta-analysis was performed using ReviewManager software (RevMan; Cochrane Collaboration, Copenhagen, Denmark) and the Cochrane Risk of Bias tool assessed risk of biased results based on use of concealment of allocation, blinding, incomplete outcome data reporting, selective reporting, and other potential biases. GRADEpro software (McMaster University and Evidence Prime, Hamilton, ON, Canada) was used to facilitate the assessment of study design, risk of bias, imprecision, and other factors to assess certainty of evidence, which refers to the likelihood that the estimated treatment effect from meta-analysis reflects the true effect of the medication. EtD frameworks then facilitate decision-making on whether or not to provide a strong recommendation (i.e., most patients should receive the treatment) or conditional recommendation for use (i.e., different choices will be appropriate for individual patients based on their preferences and values).

Funding: None

Results: Among over the counter (OTC) agents, PEG was the only therapy to receive a strong recommendation for chronic use (Table 1). Bisacodyl/sodium picosulfate received a strong recommendation for short-term (< 4 weeks) use or as rescue therapy. Based on low or very low-quality evidence, other OTC agents, including fiber supplements—specifically psyllium—senna, magnesium oxide, and lactulose were suggested for use (i.e, conditional recommendation: different choices will be appropriate for individual patients consistent with his/her values and preferences.) Among prescription agents, linaclotide, plecanatide, and prucalopride were all strongly recommended for use after unsuccessful trials of OTC agents, based on moderate certainty of evidence about treatment effect

and risk of adverse events. Lubiprostone was suggested based on low certainty of evidence. No assessment of surfactant laxatives/stool softeners was provided.

Superior to Placebo with Strong Recommendation	Strength of Recommendation[1]	Certainty of Evidence[2]
Polyethylene Glycol	Strong	Moderate
Superior to Placebo and Use After Failing OTC Agents		
Linaclotide	Strong	Moderate
Plecanatide	Strong	Moderate
Prucalopride	Strong	Moderate

Table 1. Strongly recommended CIC therapies.
[1]Strong Recommendation: Most patients should receive the intervention.
[2]Moderate Certainty of Evidence: Moderately confident that the true effect lies close to that of the estimated effect from meta-analysis.
CIC, chronic idiopathic constipation; OTC, over the counter.

COMMENTARY

Why Is This important?

CIC is one of the most common disorders treated by gastroenterologists, but CIC guidelines from the ACG and AGA have not been updated since 2013-14.[1-2]. For the first time, magnesium oxide and prucalopride randomized control trial (RCT) data is included, and the authors emphasize that prescription therapies should only be used after OTC agents. While I agree with this approach, many CIC patients are dissatisfied with their current treatment and cycle through multiple OTC treatments before getting prescription medications and experiencing adequate symptom improvement. Utilizing these guideline recommendations, we should recognize this cycle and prescribe therapies proven to be effective, and I commend the authors for the huge effort required to produce this well-designed guideline.

Key Study Findings

PEG is superior to placebo and strongly recommended for treatment of CIC based on moderate quality evidence. Linaclotide, plecanatide, and prucalopride are all superior to placebo and strongly recommended

for treatment of CIC after OTC treatments fail based on moderate quality of evidence. Fiber supplementation, senna, and magnesium oxide were conditionally suggested for treatment of CIC based on low or very low-quality evidence.

Caution

The GRADE methodology and EtD frameworks provide transparency about how recommendations were made, although most of these data are in the supplemental information and require careful review to understand how the authors parsed benefits, risks, and costs of different therapies. Thus, the authors' subjective opinions do influence choice of critical outcomes, assessments about the strength of recommendations, and certainty of evidence.

The Methods section states that docusate, a stool softener or surfactant laxative, will be evaluated, but no recommendations or literature review is presented. Prior guidelines[3] identified small RCTs with methodologic limitations of docusate, which reported no superiority to placebo and inferiority to psyllium.

My Practice

While OTC agents, including fiber supplementation, PEG, and stimulant laxatives, should be an initial therapy for CIC, the vast majority of my patients have already tried and failed some combination of OTC agents along with diet modification prior to my evaluation. We should always remember to ask patients about what they have tried and failed in the past, focus on initiating prescription therapies, and avoid combination of OTCs in supra-therapeutic doses in these patients. Shared decision-making is also crucial. It's unhelpful to prescribe an agent that the patient cannot afford. However, if the patient has commercial insurance or Medicare Part D, then at least one effective prescription agent is usually available without prior authorization. Patient co-pays also can be minimized with coupons available online. I usually start with linaclotide or plecanatide in CIC patients who have failed to get adequate relief with PEG or other OTC agents.

Remember the basics: perform a digital rectal exam and assess for pelvic floor dysfunction based on inappropriate ascent of the pelvic floor when the patient does a Valsalva maneuver. When I suspect pelvic floor dysfunction, especially

in women who have had complicated vaginal deliveries and have failed multiple CIC therapies, I'll order anorectal manometry and defecography.

Finally, I will combine therapies in severe CIC patients, but it may be even more important to set appropriate expectations. Near-total resolution of symptoms is not the expected goal. We proactively educate our patients that getting several complete spontaneous bowel movements per week is success and to expect occasional loose stools when starting potent therapies.

For Future Research

Comparative RCTs are needed to clarify superiority amongst therapies. Properly designed RCTs of stool softeners, including docusate sodium and docusate calcium, are needed to clarify if these agents actually improve stool frequency or consistency.

Conflict of Interest

Dr. Schoenfeld reports serving on advisory boards, consultant and speakers bureau for Ironwood Pharmaceuticals, AbbVie Pharmaceuticals, and Ardelyx Pharmaceuticals, and serving as an advisory board member for Takeda Pharmaceuticals and Salix Pharmaceuticals within the past 3 years.

Note: The authors of the article published in *The American Journal of Gastroenterology* are active on social media. Tag them to discuss their work and this EBGI summary.

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