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AGA SECTION

Optimizing Adequacy of Bowel Cleansing for Colonoscopy: Recommendations From the US Multi-Society Task Force on Colorectal Cancer

David A. Johnson,[1] Alan N. Barkun,[2] Larry B. Cohen,[3] Jason A. Dominitz,[4] Tonya Kaltenbach,[5] Myriam Martel,[2] Douglas J. Robertson,[6,7] C. Richard Boland,[8] Frances M. Giardello,[9] David A. Lieberman,[10] Theodore R. Levin,[11] and Douglas K. Rex[12]

[1]*Eastern VA Medical School, Norfolk, Virginia;* [2]*McGill University Health Center, McGill University, Montreal, Canada;* [3]*Icahn School of Medicine at Mount Sinai, New York, New York;* [4]*VA Puget Sound Health Care System and University of Washington, Seattle, Washington;* [5]*Veterans Affairs Palo Alto, Stanford University School of Medicine, Palo Alto, California;* [6]*VA Medical Center;* [7]*Geisel School of Medicine at Dartmouth, White River Junction, Vermont;* [8]*Baylor University Medical Center, Dallas, Texas;* [9]*Johns Hopkins University School of Medicine, Baltimore, Maryland;* [10]*Oregon Health and Science University, Portland, Oregon;* [11]*Kaiser Permanente Medical Center, Walnut Creek, California;* [12]*Indiana University School of Medicine, Indianapolis, Indiana*

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Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the United States.[1] Colonoscopy can prevent CRC by the detection and removal of precancerous lesions. In addition to CRC screening and surveillance, colonoscopy is used widely for the diagnostic evaluation of symptoms and other positive CRC screening tests. Regardless of indication, the success of colonoscopy is linked closely to the adequacy of preprocedure bowel cleansing.

Unfortunately, up to 20%–25% of all colonoscopies are reported to have an inadequate bowel preparation.[2,3] The reasons for this range from patient-related variables such as compliance with preparation instructions and a variety of medical conditions that make bowel cleansing more difficult to unit-specific factors (eg, extended wait times after scheduling of colonoscopy).[4] Adverse consequences of ineffective bowel preparation include lower adenoma detection rates, longer procedural time, lower cecal intubation rates, increased electrocautery risk, and shorter intervals between examinations.[3,5–7]

Bowel preparation formulations intended for precolonoscopy cleansing are assessed based on their efficacy, safety, and tolerability. Lack of specific organ toxicity is considered to be a prerequisite for bowel preparations. Between cleansing efficacy and tolerability, however, the consequences of inadequate cleansing suggest that efficacy should be a higher priority than tolerability. Consequently, the choice of a bowel cleansing regimen should be based on cleansing efficacy first and patient tolerability second. However, efficacy and tolerability are closely interrelated. For example, a cleansing agent that is poorly tolerated and thus not fully ingested may not achieve an adequate cleansing.

The goals of this consensus document are to provide expert, evidence-based recommendations for clinicians to optimize colonoscopy preparation quality and patient safety. Recommendations are provided using the Grades of Recommendation Assessment, Development and Evaluation (GRADE) scoring system, which weighs the strength of the recommendation and the quality of the evidence.[8]

Methods

Search Strategy

Computerized medical literature searches were conducted from January 1980 (first year of approval of polyethylene glycol–electrolyte lavage solution [PEG-ELS]–based preparation by the Food and Drug Administration [FDA]) up to August 2013 using MEDLINE, PubMed EMBASE, Scopus, CENTRAL, and ISI Web of knowledge. We used a highly sensitive search strategy to identify reports of randomized controlled trials[9] with a combination of medical subject headings adapted to each database and text words related to colonoscopy and gastrointestinal agents, bowel preparation, generic name, and brand name. The complete search terms are available in Appendix A. Recursive searches and cross-referencing also were performed using a "similar articles" function; hand searches of articles were identified after an initial search. We included all fully published adult human studies in English or French.

A systematic review of published articles and abstracts presented at national meetings was performed to collect and select the evidence. A meta-analysis and consensus agreement were used to analyze the evidence. Expert

Abbreviations used in this paper: **ADR, adenoma detection rate; CI, confidence interval; CRC, colorectal cancer; FDA, Food and Drug Administration; ITT, intention-to-treat; NaP, sodium phosphate; NDA, New Drug Application; OR, odds ratio; OSS, oral sulfate solution; OTC, over-the-counter; PEG-ELS, polyethylene glycol–electrolyte lavage solution; PICO, sodium picosulfate; USMSTF, US Multi-Society Task Force.**

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consensus was used to formulate the recommendations. The GRADE system was used to rate the strength of the recommendations. The guideline was reviewed by committees of and approved by the governing boards of the member societies of the Multi-Society Task Force on Colorectal Cancer (American College of Gastroenterology, American Gastroenterological Association, and American Society of Gastrointestinal Endoscopy).

Effect of Inadequate Preparation on Polyp/Adenoma Detection and Recommended Follow-up Intervals

Recommendations

1. Preliminary assessment of preparation quality should be made in the rectosigmoid colon, and if the indication is screening or surveillance and the preparation clearly is inadequate to allow polyp detection greater than 5 mm, the procedure should be either terminated and rescheduled or an attempt should be made at additional bowel cleansing strategies that can be delivered without cancelling the procedure that day (***Strong recommendation, low-quality evidence***)
2. If the colonoscopy is complete to cecum, and the preparation ultimately is deemed inadequate, then the examination should be repeated, generally with a more aggressive preparation regimen, within 1 year; intervals shorter than 1 year are indicated when advanced neoplasia is detected and there is inadequate preparation (***Strong recommendation, low-quality evidence***)
3. If the preparation is deemed adequate and the colonoscopy is completed then the guideline recommendations for screening or surveillance should be followed (***Strong recommendation, high-quality evidence***)

Inadequate colonic preparation is associated with reduced adenoma detection rates (ADRs). A large prospective European study of 5832 patients enrolled in 21 centers across 11 countries examined the association of preparation quality and polyp identification during colonoscopy performed for a range of common indications. High-quality preparation was associated with identification of polyps of all sizes (odds ratio [OR], 1.73; 95% confidence interval [CI], 1.28–2.36), and with polyps greater than 10 mm in size (OR, 1.72; 95% CI, 1.11–2.67).[2] An analysis of a national endoscopic database examined the association of preparation quality and polyp identification in 93,004 colonoscopies.[3] Colon preparation (as entered by the endoscopist at the time of the procedure) was dichotomized into adequate (excellent, good, and fair/adequate) and inadequate (fair, inadequate, and poor). In adjusted models, adequate preparation was predictive of detection of all polyps (OR, 1.21; 95% CI, 1.16–1.25), but not polyps greater than 9 mm and/or suspected cancer (OR, 1.5; 95% CI, 0.98–1.11). Similarly, a single-center study based at a US Veterans Affairs Medical Center examined preparation quality and ADRs in 8800 colonoscopies performed between 2001 and 2010.[10] When comparing those examinations with an inadequate/poor preparation (n = 829) with those with an adequate preparation (n = 5162), overall polyp detection was reduced (OR, 0.66; 95% CI, 0.56–0.83).

Two retrospective single-center studies examined the association of preparation quality and adenoma miss rates when the preparation was considered inadequate and the examination was repeated within a short interval.[11,12] Miss rates were the total adenomas found on the second examination divided by the total adenomas found on both examinations. In 1 study[11] there were 12,787 colonoscopies with 3047 (24%) suboptimal preparations (fair or poor). Repeat colonoscopy within 3 years in 216 individuals who achieved adequate preparation showed an overall adenoma miss rate of 42%, and a miss rate of 27% for lesions 10 mm or larger in size. The other study identified 373 average-risk screening patients with poor or inadequate preparation.[12] Repeat colonoscopy in 133 patients (77% achieved excellent or good preparation) showed a 47% overall adenoma miss rate.

A single prospective Korean study evaluated 277 individuals after a complete colonoscopy and then a per-protocol repeat "tandem" colonoscopy within 3 months of the initial examination.[13] The patient adenoma miss rate increased as baseline preparation quality decreased on the Aronchick scale. In the 19 patients with poor preparation the adenoma and advanced adenoma miss rates were 47% and 37%, respectively, compared with 21% and 9% in those with excellent preparation ($P = .024$).

Surveys report that in the setting of a poor preparation, endoscopists' recommendations for follow-up evaluation vary and err on shorter return intervals.[14,15] In 1 study 65 board-certified gastroenterologists and 13 gastroenterology fellows[14] were shown images of preparations of "excellent to intermediate quality." With a "nearly perfect" preparation, a 10-year interval generally was recommended for a normal screening colonoscopy. However, recommendations were quite variable for the lower-quality preparations, ranging from more than 5 years to an immediate repeat procedure. A survey of gastroenterologists (n = 116) preparing for board certification found that 83% would recommend follow-up evaluation in 3 years or less for 1–2 small adenomas and a suboptimal preparation.[15]

Several studies have examined actual recommendations for follow-up evaluation within the framework of clinical practice. One study abstracted charts from 152 physicians in 55 North Carolina practices on 125 consecutive persons in each practice.[16] Preparation quality was not reported in 32% of the examinations. Bowel preparations rated less than excellent were associated with more aggressive surveillance for those found with no polyps or small and/or

medium adenomas. A prospective single-center study of 296 patients showed that when endoscopists encountered a poor preparation they recommended follow-up intervals that more often were nonadherent with guidelines (34% nonadherent vs 20% adherent; $P = .01$).[17] A prospective study estimated that for each 1% of bowel preparations deemed inadequate and requiring repeat colonoscopy at a shortened interval, the costs of delivering colonoscopy overall were increased by 1%.[5] These substantial adverse effects of inadequate preparation are the rationale for establishing a target for rates of adequate preparation (see later).

Dosing and Timing of Colon Cleansing Regimens

Recommendations

1. Use of a split-dose bowel cleansing regimen is strongly recommended for elective colonoscopy (***Strong recommendation, high-quality evidence***)
2. A same-day regimen is an acceptable alternative to split dosing, especially for patients undergoing an afternoon examination (***Strong recommendation, high-quality evidence***)
3. The second dose of split preparation ideally should begin 4–6 hours before the time of colonoscopy with completion of the last dose at least 2 hours before the procedure time (***Strong recommendation, moderate-quality evidence***)

Split-Dose Regimens

When preparation agents are administered entirely the day before colonoscopy, chyme from the small intestine enters the colon and accumulates, producing a film that coats the proximal colon and impairs detection of flat lesions. The length of time between the last dose of preparation and the initiation of colonoscopy correlates with the quality of the proximal colon cleansing.[18–20] In 1 study the chance of good or excellent preparation of the right colon decreased by up to 10% for each additional hour between the end of ingesting the preparation and the start of the colonoscopy.[20]

"Splitting" implies that roughly half of the bowel cleansing dose is given on the day of the colonoscopy. Overwhelmingly consistent data show superior efficacy with a split dose compared with the traditional regimen of administering the preparation the day before the procedure.[18,21–24] Split dosing leads to higher ADRs.[25,26] Four guidelines have endorsed split dosing of preparations for colonoscopy.[27–30]

Same-Day Regimens

Same-day bowel cleansing is an effective alternative to split dosing for patients with an afternoon colonoscopy.[31–34] In a large, single-blind, prospective study, same-day preparation provided better mucosal cleansing, less sleep disturbance, better tolerance, less impact on activities of daily living, and greater patient preference scores compared with split dosing.[35]

Obstacles to Split and Same-Day Regimens

Anecdotally, anesthesia providers sometimes oppose split and same-day dosing because of concern for aspiration risk. An evidenced-based guideline from the American Society of Anesthesiologists, however, states that ingestion of clear liquids until 2 hours before sedation does not affect residual gastric volume.[36] Furthermore, 2 endoscopic studies found that ingestion of bowel cleansing agents on the day of colonoscopy did not affect residual gastric volumes, indicating that the rate of gastric emptying of bowel preparations is similar to other clear liquids.[37,38] Preoperative dehydration may be a greater safety concern than drinking clear liquids before anesthesia.

A second objection to split dosing is that patients scheduled for early morning procedures may be unwilling to get up during the night to take the second dose of laxatives. Acceptance of and compliance with split-dose bowel preparation is high and should not pose a deterrent to prescribing split-dose preparations for colonoscopy.[39,40] The risk of fecal incontinence during transit to the endoscopy center is increased only minimally with split dosing.[40]

Diet During Bowel Cleansing

Recommendation

1. By using a split-dose bowel cleansing regimen, diet recommendations can include either low-residue or full liquids until the evening on the day before colonoscopy (***Weak recommendation, moderate-quality evidence***)

Traditionally, patients are instructed to ingest only clear liquids the day before colonoscopy. Recent randomized trials report that a liberalized diet the day before colonoscopy is associated with better tolerance of the preparation and comparable or better bowel cleansing.[41–48] The diet regimens in these trials were variable and included a regular diet until 6 PM, regular breakfast, low-residue breakfast, lunch and snack, a soft diet, and a semiliquid diet (heterogeneity: $P = .008$; $I = 62\%$). With this degree of heterogeneity we are reluctant to recommend a regular diet the day before colonoscopy. Accordingly, a low-residue diet for part or all of the day before colonoscopy can be considered for patients without other identifiable preprocedural risks for inadequate colon preparation. Pending additional study, colonoscopists carefully should evaluate any compromise in efficacy if dietary flexibility is allowed.

Usefulness of Patient Education and Navigators for Optimizing Preparation Results

Recommendations

1. Health care professionals should provide both oral and written patient education instructions for all components of the colonoscopy preparation and emphasize the importance of compliance (***Strong recommendation, moderate-quality evidence***)
2. The physician performing the colonoscopy should ensure that appropriate support and process measures are in place for patients to achieve adequate colonoscopy preparation quality (***Strong recommendation, low-quality evidence***)

A patient education program administered by health care professionals increases patient compliance, improves quality, and decreases repeat examinations and costs.[49] The use of both verbal and written instructions, compared with written instructions only, is an independent predictor of adequate bowel preparation quality. Educational tools such as booklets, information leaflets, animations, and visual aids should be standardized and validated,[50,51] and should be effective across a range of health literacy and education levels.[4,52] The use of a novel patient educational booklet on precolonoscopy preparation resulted in better bowel preparation quality scores than those achieved using conventional instructions (OR, 3.7; 95% CI, 2.3–5.8).[53]

Trained patient navigators help guide patients through the colonoscopy process. They provide education to patients, address barriers to colonoscopy, review bowel preparation protocols and appointments, and ensure that patients have an escort for appointments. Patient navigators for urban minorities in open-access referral systems resulted in an increase for screening colonoscopy completion rates.[54,55] In safety-net hospitals the costs of navigation are offset by increased screening compliance and navigation is cost effective.[56] Barriers to successful navigation included incomplete contact information, language problems, and insurance lapses. The impact of the sex, ethnicity, and professional status of the patient navigator needs additional evaluation.

Rating the Quality of Bowel Preparation During Colonoscopy

Recommendations

1. Adequacy of bowel preparation should be assessed after all appropriate efforts to clear residual debris have been completed (***Strong recommendation, low-quality evidence***)
2. Measurement of the rate of adequate colon cleansing should be conducted routinely (***Strong recommendation, moderate-quality evidence***)
3. Adequate preparation, defined as cleansing that allows a recommendation of a screening or surveillance interval appropriate to the findings of the examination, should be achieved in 85% or more of all examinations on a per-physician basis (***Strong recommendation, low-quality evidence***)

Reporting the quality of the bowel preparation is a required element of the colonoscopy report.[57,58] In clinical trials cleansing quality often is estimated using scales that downgrade quality for retained fluid. In clinical practice, however, retained fluid and much of the semisolid debris in the colon can be removed by intraprocedural cleansing. Because the capacity to conduct effective mucosal inspection is established after intraprocedural cleansing, the preparation quality in clinical practice should be assessed only after appropriate intraprocedural washing and suctioning has been completed. For this reason, the use of a validated bowel preparation scale that includes scoring retained fluid (eg, Aronchick, Ottawa) is not recommended. The US Multi-Society Task Force (USMSTF) considers the operational definition of an adequate preparation is one in which the colonoscopist can and does recommend a follow-up screening or surveillance interval for the next colonoscopy that is appropriate for the examination findings. Unfortunately, the scores in validated scales that correspond to the point at which the preparation meets the USMSTF operational definition of an adequate preparation (ability to follow the recommended screening or surveillance interval) generally are uncertain. In clinical practice clinicians often use an imprecisely defined 4-point scale of excellent, good, fair, and poor. In this scheme, excellent and good are widely viewed as adequate, but some research indicates that many fair preparations in clinical practice also are adequate.[10] The USMSTF previously recommended that clinicians could consider the preparation adequate if after suctioning and washing the mucosa during the procedure it was deemed adequate for the detection of lesions greater than 5 mm in size.[59] This concept is not part of a validated bowel preparation scale but it does reflect current concepts about the sizes of colorectal lesions that are clinically most important to detect.[60] Additional research is needed to develop validated scales for scoring bowel cleansing that do not consider retained fluid and include defined points that correspond to adequate preparation. Currently, the Boston Bowel Preparation scale comes closest to meeting these criteria because it does not consider retained fluid and a Boston Bowel Preparation Scale score of 5 or higher was associated with only a 2% rate of recommending shortened follow-up intervals.[61] A detailed review of bowel preparation scales is shown in Appendix B.

Whichever scale is used in practice, we recommend that the method for defining an adequate preparation should include whether the colonoscopist recommends the

expected screening or surveillance intervals based on the colonoscopy findings, and that the ability to detect lesions greater than 5 mm in size throughout the colon is a clinically relevant test of adequacy and appropriateness to follow screening and surveillance intervals. Furthermore, endoscopists are encouraged to submit procedure reports into a data registry that benchmarks performance and quality measures against minimally accepted national thresholds and mean levels of performance among peers. If the rate of adequate bowel preparation for an endoscopist is below the USMSTF recommended benchmark of 85%, an improvement initiative should be undertaken. High rates of inadequate preparations can reflect low patient compliance, failure to adjust preparation regimens for medical predictors of inadequate preparation, or signal that processes and policies of the endoscopy unit need revision.

FDA-Approved Preparations

Recommendations

1. Selection of a bowel-cleansing regimen should take into consideration the patient's medical history, medications, and, when available, the adequacy of bowel preparation reported from prior colonoscopies (***Strong recommendation, moderate-quality evidence***)
2. A split-dose regimen of 4 L PEG-ELS provides high-quality bowel cleansing (***Strong recommendation, high-quality evidence***)
3. In healthy nonconstipated individuals, a 4-L PEG-ELS formulation produces a bowel-cleansing quality that is not superior to a lower-volume PEG formulation (***Strong recommendation, high-quality evidence***)

Polyethylene glycol–electrolyte lavage solution (PEG-ELS)–based cleansing agents are available in 4 L (considered large or high volume) or as 2 L plus an adjunct (considered low volume). Sodium phosphate (NaP) solution (Fleet Phospho-Soda and Fleet EZ-PREP; C.B. Fleet Co, Lynchburg, VA) is a hyperosmotic cleansing agent that was withdrawn from the US over-the-counter (OTC) market in December 2008 because of concern regarding phosphate-induced renal disease.[62] A prescription tablet formulation of NaP (OsmoPrep; Salix Pharmaceuticals, Raleigh, NC) remains available, although a boxed warning about the risk of acute phosphate nephropathy has been added to the label.[62] Recently approved low-volume agents include oral sulfate solution (OSS) (SUPREP; Braintree Laboratories, Braintree, MA), sodium picosulfate/magnesium citrate (Prepopik; Ferring Pharmaceuticals, Inc, Parsippany, NJ), and a combination of PEG-ELS and OSS (SUCLEAR; Braintree Laboratories).

Polyethylene Glycol–Electrolyte Lavage Solution

Reduced-volume, FDA-approved PEG-ELS formulations were developed to improve tolerance. One of these preparations (2-L PEG-ELS with bisacodyl, HalfLytely; Braintree Laboratories), recently was removed from the market. Another 2-L PEG-ELS product contains supplemental ascorbate and sodium sulfate (MoviPrep; Salix Pharmaceuticals).

Several 4-L PEG-ELS–based preparations have been approved by the FDA, including Colyte (Alaven Pharmaceuticals, Marietta, GA), Gavilyte (Gavis Pharmaceuticals, Somerset, NJ), Golytely (Braintree Laboratories), and Nulytely (Braintree Laboratories), which is sulfate free.

High-volume PEG-ELS ($\geq$3 L) was compared with low-volume PEG-ELS ($<$3 L) in 28 trials yielding 7208 intention-to-treat (ITT) patients (3456 high-volume PEG-ELS; 3752 low-volume PEG-ELS).[18,63–89] Twenty-one trials included analyzable bowel-cleanliness outcomes.[64–72,74–76,79,81–86,88,89] High-volume PEG-ELS did not show a significant increase in bowel cleanliness (OR, 1.03; 95% CI, 0.80–1.32).

Eight trials included a PEG-ELS split dose in which 2 L were administered the day before and 2 L were administered the day of the procedure compared with a PEG-ELS nonsplit regimen regardless of dosage, yielding 1990 ITT patients (846 PEG-ELS split [2 L + 2 L] dose; 1144 PEG nonsplit).[18,46,66,81,84,85,90,91] Six trials were analyzable, resulting in significantly increased cleanliness for the PEG-ELS split-dose regimen (2 L + 2 L) compared with the PEG-ELS nonsplit dose (OR, 4.38; 95% CI, 1.88–10.21).[46,66,81,84,85,90]

Because they are iso-osmotic, PEG-ELS regimens often are considered preferred regimens in patients who are less likely to tolerate fluid shifts, including patients with renal insufficiency, congestive heart failure, and advanced liver disease.

Oral Sulfate Solution

Two trials evaluated OSS.[92,93] One trial compared OSS in a split-dose regimen with 4 L PEG-ELS taken the day before and found more successful preparations with OSS (98.4% vs 89.6%; $P < .04$, per-protocol data).[93] The second trial compared OSS with PEG-ELS 2 L plus ascorbate. Both OSS and 2 L PEG-ELS plus ascorbate were more effective when given in split doses, and the FDA approved OSS for split-dose administration only.[92] The combined results of 923 ITT patients (462 OSS, 461 PEG) found that OSS did not increase bowel cleanliness (OR, 1.12; 95% CI, 0.77–1.62).[92,93]

Sodium Picosulfate

Sodium picosulfate (PICO), a stimulant laxative often combined with a magnesium salt, recently was introduced to the US market after considerable experience in Canada, Europe, and Australia. Eleven trials compared PICO vs PEG-ELS and yielded 3097 ITT patients (1385 PICO, 1715 PEG-ELS).[77,94–103] The PICO preparations were combined either with magnesium oxide or magnesium citrate. Ten trials included analyzable cleanliness data comparing PICO with PEG-ELS.[94–103] The PICO formulation did not show a significant increase in efficacy compared with PEG-ELS (OR, 0.92; 95% CI, 0.63–1.36).

Eight trials compared PICO with NaP, yielding 1792 ITT patients (966 PICO, 826 NaP).[77,97,104–109] Three trials included analyzable cleanliness data, PICO was not superior

to NaP (OR, 0.60; 95% CI, 0.22–1.65).[97,106,107] Only 1 trial compared the PICO split-dose regimen vs PICO the day before or the same day including 250 ITT patients (127 split, 123 not split).[110] PICO split-dose compared with PICO day-before or same-day regimen had a significantly higher proportion of bowel cleanliness (OR, 3.54; 95% CI, 1.95–6.45).

Sodium Phosphate

Oral NaP use for bowel preparation has decreased because of the rare occurrence of renal damage from tubular deposition of calcium phosphate.[111,112] Potential risk factors for NaP-induced nephropathy include the following: female sex, pre-existing renal insufficiency, inadequate hydration during bowel preparation, reduced time interval between the 2 doses of sodium phosphate (<12 h), hypertension, older age, and certain medications (diuretics, nonsteroidal anti-inflammatory drugs, and renin-angiotensin inhibitors).[113]

Forty-eight trials were included in a comparison of NaP vs PEG-ELS, yielding 11,368 ITT patients (5529 PEG vs 5839 NaP).[75–77,97,108,114–157] Thirty-three trials included analyzable bowel-cleanliness outcomes.[75,76,97,108,114,115,117,119,121,124,126,127,129–133,136,137,139–141,143,145,146,148,150–156] The use of NaP did not show an increase in bowel cleanliness (OR, 1.02; 95% CI, 0.77–1.36) but was associated with better willingness to repeat the regimen (OR, 2.61; 95% CI, 1.48–4.59). Comparisons of NaP with OSS and PICO were discussed previously.

Three trials[144,158,159] were included in the comparison of the NaP split-dose regimen with NaP the day before the procedure or the same day for a total of 598 ITT patients (355 split vs 243 nonsplit).[144,158,159] Two trials[158,159] included analyzable data and showed better cleansing with split-dose regimens (OR, 2.35; 95% CI, 1.27–4.34).[158,159]

Although NaP is effective and well tolerated by most patients, the risk of adverse events makes it unsuitable as a first-line agent. Furthermore, NaP is not recommended in patients with renal insufficiency (creatinine clearance, < 60 mL/min/1.73 m^2), pre-existing electrolyte disturbances, congestive heart failure (New York Heart Association class III or IV or ejection fraction < 50%), cirrhosis, or ascites. Caution should be used in prescribing NaP to patients who are elderly, hypertensive, or taking angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs, or diuretics.

OTC Non–FDA-Approved Preparations

Recommendations

1. The OTC bowel cleansing agents have variable efficacy that ranges from adequate to superior, depending on the agent, dose, timing of administration, and whether it is used alone or in combination; regardless of the agent, the efficacy and tolerability are enhanced with a split-dose regimen (***Strong recommendation, moderate-quality evidence***)
2. Although the OTC purgatives generally are safe, caution is required when using these agents in certain populations; for example, magnesium-based preparations (both OTC and FDA-approved formulations) should be avoided in patients with chronic kidney disease (***Weak recommendation, very low quality evidence***)

The use of OTC products for bowel cleansing before colonoscopy is deemed to be safe for use by the public without advice from a health care professional. The efficacy and safety of these products for specific indications may be unproven because the FDA's oversight of OTC products generally is conducted by therapeutic class rather than for individual drugs. Consequently, an OTC product may have little or no supporting evidence or comparative data showing either efficacy or safety relative to other available products. Products marketed specifically for colonoscopy bowel preparation must be evaluated in randomized trials to assess their efficacy and safety and then must receive approval via a New Drug Application (NDA) from the FDA. Such products are available only by prescription. For a purgative agent to be marketed without an approved NDA it must meet the requirements for OTC agents as set forth in the Laxative Monograph (Unpublished data). The FDA specifically recognized only 2 bowel cleansing kits,[160] and any kit with different components would require an approved NDA and/or further amendment to the monograph (highly unlikely). These cleaning kits are as follows: magnesium citrate oral solution, bisacodyl tablets, and bisacodyl suppositories; and magnesium citrate oral solution, phenolphthalein, and sodium bicarbonate–sodium bitartrate suppositories.

These OTC medications or combinations can be recommended by physicians as part of a bowel-cleansing regimen in preparing patients for surgery or for preparing the colon for x-ray or endoscopic examination.

The following section reviews available data on several OTC agents that have been used for bowel cleansing before colonoscopy.

PEG-3350 Powder

PEG-3350 powder, an OTC laxative marketed for constipation, is available as an 8.3-oz bottle (238 g). When used for a precolonoscopy bowel preparation, the contents of 1 bottle often are mixed with 64 ounces of Gatorade (PepsiCo, Chicago, IL) to create a 2-L PEG formulation. In some instances, clinicians prescribe bisacodyl tablets or magnesium citrate in conjunction with the PEG-3350 powder. Five randomized controlled trials (total, 1556 patients) have compared PEG-3350 powder, either alone or combined with an adjunct, with commercially available 4 L PEG-ELS.[69,73,80,84,161]

In 1 study, satisfactory colon cleansing was less frequent with PEG-3350 powder than with 4 L PEG-ELS (68% vs 83%; $P = .018$).[69] In the remaining 4 studies, including 1 study that used 306 g rather than 238 g, the proportion of patients having an adequate bowel preparation was comparable with PEG-3350 powder and 4 L PEG-ELS.[29–31] Tolerability based on taste and overall experience was better with PEG-3350

powder than with 4 L PEG-ELS in 4 studies,[73,80,84,161] and no difference in tolerability was observed in 1 series.[69]

Adverse events with PEG-3350 overall are rare. Although hyponatremia is a potential risk when using a hypotonic lavage solution such as PEG powder, no statistical differences in serum electrolyte levels were observed in 3 studies that compared PEG powder vs 4 L PEG-ELS.[80,84,161] Reports of hyponatremia have occurred when administered the evening before, but not with split-dose regimens.[162] Widespread use of PEG-3350 for bowel preparation seems to have been remarkably safe, but additional evaluation of safety and is warranted and desirable.

Magnesium Citrate

Magnesium citrate, a widely used agent in the United States, was evaluated in 4 randomized trials, including 2 trials that combined it with either PEG-ELS or NaP solution.[81,163–165] Magnesium citrate (300 mL × 3) was superior to NaP solution (45 mL × 2), producing good or excellent quality cleansing in 94% and 97% of patients in the right and left colon, respectively ($P < .001$).[165] A transient increase in serum magnesium level may be observed, but has not been reported to cause clinical adverse events in healthy persons. The use of magnesium-based preparations in patients with chronic kidney disease should be avoided because of possible magnesium toxicity.[166,167] A PEG-ELS–based regimen is preferred in such cases.

Other OTC Products

Senna was studied in 4 randomized controlled trials, either alone (3 trials) or combined with 2 L PEG-ELS (1 trial), comparing it with either high- or low-volume PEG-ELS.[71,168–170] High-dose senna (24 tablets of 12 mg each) was as effective as 4 L PEG-ELS in 2 studies, although patients receiving senna experienced significantly more cramps and abdominal pain.[168,170] Low-dose senna (3–12 tablets) has been combined with 2 L PEG-ELS to increase its cleansing effect.[71,169] In 2 randomized trials that compared bisacodyl (30–40 mg) with NaP solution, bisacodyl achieved significantly lower rates of satisfactory bowel cleansing.[171,149] Patient tolerability for bisacodyl and NaP solution was comparable with the exception of nausea, which was more common with NaP.

Adjuncts to Colon Cleansing Before Colonoscopy

Recommendation

1. The routine use of adjunctive agents for bowel cleansing before colonoscopy is not recommended (***Weak recommendation, moderate-quality evidence***)

Numerous adjunctive agents, intended to enhance purgation and/or visualization of the mucosa, have been investigated for precolonoscopy cleansing of the mucosa. These have included simethicone, flavored electrolyte solutions (eg, Gatorade), prokinetics, spasmolytics, bisacodyl, senna, olive oil, and probiotics. None consistently have shown improved efficacy, safety, or tolerability of the bowel preparation. Currently, the routine use of adjunctive agents for colonic cleansing before colonoscopy is not recommended, but the agents may be useful in select circumstances, at the discretion of the prescribing physician.

Simethicone is the best-studied adjunctive agent for bowel cleansing. In a meta-analysis of 7 randomized trials comparing colonoscopy bowel purgative with or without the addition of simethicone, the overall efficacy of colon preparation was comparable (OR, 2.06; 95% CI, 0.56–7.53; $P = .27$), despite a notable reduction in the presence of intraluminal bubbles (OR, 39.3; 95% CI, 11.4–135.9; $P \leq .01$) in the group receiving simethicone.[172] The dosage of simethicone varied between studies, ranging from 120 to 240 mg, or 45 mL of a 30% solution.[76,172–174]

In randomized trials, prokinetics such as metoclopramide, domperidone, cisapride, and tegaserod have not improved patient tolerability or quality of the bowel preparation.[175–178] Mosapride and itopride, 2 motility-enhancing agents currently in clinical development, improved preprocedure tolerability with significant reductions in nausea, vomiting, bloating, and abdominal pain,[177] and improved efficacy in patients receiving split-dose preparations.[178] Alverine citrate added as a spasmolytic adjunct produced no increase in preparation quality or tolerance when compared with NaP alone in a randomized trial of 147 patients.[179] Senna and bisacodyl have been used as adjuncts to low-volume PEG-ELS–based agents with improved tolerability,[68] although the quality of the bowel preparation was not as effective compared with standard-volume solutions.[71,74,161]

Ascorbate was studied in a randomized trial comparing 2 low-volume PEG-ELS preparations. PEG-ELS citrate-simethicone with bisacodyl and PEG ascorbate showed similar tolerability, safety, acceptability, and compliance.[180] Another randomized study of 107 patients showed better colon cleansing with 2 L PEG-ELS ascorbate compared with PEG-ELS with bisacodyl.[181] When combined with Gatorade, PEG,[80] or PEG-3350 powder,[84] these formulations have shown adequate bowel cleansing but inconsistent satisfaction across studies.[80,84] Olive oil followed by low-volume PEG-ELS improved cleansing quality in the right colon, but had no impact in the left colon compared with 4 L PEG-ELS.[63] The use of menthol candy lozenges recently was shown to increase palatability and improve ingestion of PEG-ELS.[182] A 2-week course of a probiotic containing *Bacillus subtilis* and *Streptococcus faecium* before NaP in constipated patients improved cleansing compared with placebo, but had no effect in patients with normal defecation.[183]

Differences in Patient Preference/ Willingness to Repeat Comparisons

Recommendations

1. Split-dose bowel cleansing is associated with greater willingness to repeat regimen compared with the day before regimen (***Strong recommendation, high-quality evidence***)

2. The use of low-volume bowel cleansing agents is associated with greater willingness to undergo a repeat colonoscopy (***Strong recommendation, high-quality evidence***)

Meta-analysis data from 5 randomized blinded trials showed better patient satisfaction and adherence with fewer preparation discontinuations (OR, 0.52; 95% CI, 02.8–0.98; $P = .04$) with a split-dose regimen.[21] Split-dose PEG-ELS significantly increased the number of adequate bowel preparations (OR, 3.7; 95% CI, 2.79–491; $P < .01$). No difference in compliance was observed in randomized patients scheduled for early morning colonoscopy who underwent day-before vs split-dose 4 L PEG-ELS; and adverse symptoms such as nausea, vomiting, and bloating were more frequent in the single-dose group.[184]

In trials of high-volume PEG-ELS (≥3 L) compared with low-volume PEG-ELS (<3 L), willingness to repeat bowel cleansing regimen was lower in the high-volume group (OR, 0.34; 95% CI, 0.18–0.64)[63,66,69,70,78,79,81,83,85] and higher for the split-dose group (OR, 1.76; 95% CI, 1.06–2.91; $P = .03$).[39] For OSS, willingness to repeat was not reported in any of the studies.[92,93] Willingness to repeat the same preparation was higher with split-dose PICO than with PEG-ELS (OR, 8.77; 95% CI, 3.28–23.43)[97,106,107,185] and was not reported in the 1 trial comparing a PICO split-dose regimen vs a PICO day-before or same-day regimen.[110] In the studies comparing PEG-3350 powder with PEG-ELS, willingness to repeat was higher with PEG-3350 powder.[69,84]

A prospective study examined new symptoms after colonoscopy in 247 previously asymptomatic people[186] who completed a standardized interview at 7 and 30 days after colonoscopy. Bloating or abdominal pain occurred in 34% in the week after and in 6% between days 7 and 30. On multivariate analysis, women (OR, 1.78, 95% CI, 1.21–2.62) and longer procedure duration (20–29 min: OR, 1.06; 95% CI, 0.64–1.75; 30–39 min: OR, 1.77; 95% CI, 1.03–3.05; ≥40 min: OR, 2.63; 95% CI, 1.49–4.63) were associated with minor complications. Most symptomatic subjects (94%) lost 2 or fewer days from normal activities for the colonoscopy itself, preparation, or recovery.

Selection of Bowel Preparation in Specific Populations

Recommendations

1. There is insufficient evidence to recommend specific bowel preparation regimens for elderly persons; however, we recommend that NaP preparations be avoided in this population (***Strong recommendation, low-quality evidence***)
2. There is insufficient evidence to recommend specific bowel preparation regimens for children and adolescents undergoing colonoscopy; however, we recommend that NaP preparations should not be used in children younger than age 12 or in those with risk factors for complications from this medication (***Strong recommendation, very low quality evidence***)
3. NaP should be avoided in patients with known or suspected inflammatory bowel disease (***Weak recommendation, very low quality evidence***)
4. Additional bowel purgatives should be considered in patients with risk factors for inadequate preparation (eg, patients with a prior inadequate preparation, history of constipation, use of opioids or other constipating medications, prior colon resection, diabetes mellitus, or spinal cord injury) (***Weak recommendation, low-quality evidence***) A detailed discussion of patient factors that predict inadequate preparation is presented in Appendix C
5. Low-volume preparations or extended time delivery for high-volume preparations are recommended for patients after bariatric surgery (***Weak recommendation, very low quality evidence***)
6. Tap water enemas should be used to prepare the colon for sigmoidoscopy in pregnant women (***Strong recommendation, very low quality evidence***)
7. There is insufficient evidence to recommend specific regimens for persons with a history of spinal cord injury; additional bowel purgatives should be considered (***Weak recommendation, very low quality evidence***)

Subgroups of individuals may benefit from tailoring the bowel preparation regimen because of concerns about tolerability, effectiveness, or adverse events related to the preparation.

Advanced Age

Although advanced age is a predictor of suboptimal bowel preparation, overall tolerance of the bowel preparation is similar between octogenarians and younger patients undergoing colonoscopy.[187,188] In 2 trials of 72 and 116 elderly patients, respectively, randomized to receive either NaP or PEG-ELS, there was no significant difference in tolerability or quality of the bowel cleansing.[116,189] There were, however, more electrolyte abnormalities in the NaP group in 1 study,[189] and associated serious electrolyte abnormalities have been reported in the elderly.[190,191] Hypokalemia was associated with use of PEG-ELS in elderly patients.[192] A large population-based retrospective study of 50,660 individuals older than age 65 who underwent outpatient colonoscopy in Ontario reported that serious events, including nonelective hospitalization, emergency department visit, or death within 7 days of colonoscopy were similar between those receiving PEG-ELS or PICO (28 per 1000 procedures for each group).[193]

Pediatrics

Selection of bowel preparation regimens for pediatric patients should be individualized according to the patient's age, clinical state, and anticipated willingness or ability to comply with the specific medications.[194] Maintenance of adequate hydration during colonoscopy preparation is important, especially in children.[195] Few controlled trials of bowel preparation regimens have been performed in pediatric patients, although many regimens have been described.[196] Inpatient administration is sometimes required.

Ingestion of clear liquids for 24 hours along with the administration of a normal saline enema (10 mL/kg) usually is sufficient for infants with normal or frequent bowel movements.[194,197] Older children typically can undergo bowel preparation with intestinal lavage or laxatives and enemas.[196,198] In a study of children aged 1.5–19 years, metoclopramide followed by PEG-ELS at a dose of 40 mL/kg/h resulted in clear stool after 2.6 hours, although nausea, emesis, and distension were common.[199] Of note, 11 of the 20 children in this study had nasogastric administration of the lavage because of the unpleasant taste. In a randomized study comparing 3 regimens (PEG-ELS vs magnesium citrate with sennosides [eg, X-Prep, senna dry extract] vs bisacodyl tablets plus an enema), the PEG-ELS solution resulted in the highest-quality colon cleansing but was least well tolerated.[200] Another purgative option used in children is PEG-3350 administered at a dose of 1.5 g/kg/d for 4 days before the procedure, with a clear liquid diet on the fourth day (sometimes in combination with an enema).[201,202] Other regimens using PEG-3350, including a 1-day preparation, also have been effective, although there are no controlled trials using this agent in children.[203,204]

In a randomized trial comparing a combined preparation of PICO, magnesium oxide, and citric acid with PEG-ELS in children, the combined preparation was better tolerated with similar cleansing effectiveness.[205] Another randomized study comparing PICO with magnesium citrate with bisacodyl tablets in addition to phosphate enemas found that the oral PICO regimen was superior to the bisacodyl regimen.[206]

Sodium phosphate is associated with improved tolerability and less discomfort in children compared with PEG-ELS[207,208] or magnesium citrate with enemas.[209] The bowel cleansing effectiveness of NaP was superior to PEG in 1 study[207] and similar in another study.[208] In a randomized study comparing a prepackaged diet kit including magnesium citrate and bisacodyl laxatives with NaP, the 2 regimens had comparable tolerability, although the quality of cleansing was superior with the magnesium citrate regimen.[210] The Israeli Society of Pediatric Gastroenterology and Nutrition reviewed the evidence of adverse events with oral NaP and recommended that NaP should not be used in children younger than 12 years of age, children with any type of kidney disease, children treated with medications that affect renal function, children with significant comorbidities (eg, liver disease, hypertension, hypoparathyroidism, diabetes, and heart disease), children at high risk for dehydration or electrolyte imbalance, and children with ileus or suspected severe colitis.[211] The Israeli Society of Pediatric Gastroenterology and Nutrition has 6 recommended products as colon cleansing agents for children: PEG-ELS, NaP (for ages $\geq$ 12 y), PICO, PEG-3350, bisacodyl, and enemas.

Inflammatory Bowel Disease

The use of NaP-containing bowel preparations can be associated with the development of superficial mucosal abnormalities that may resemble features of early inflammatory bowel disease.[97,212–219] In a prospective study of 730 patients without known inflammatory bowel disease, mucosal lesions resulting from NaP were reported in 3.3%.[217] In a prospective, randomized, single-blinded trial in 634 patients, Lawrance et al[97] reported that preparation-induced mucosal inflammation was 10-fold greater with NaP ($P = .03$) and PICO ($P = .03$) compared with PEG. In another prospective, randomized, single-blinded trial in 97 patients, aphthoid-like mucosal lesions were reported in 2.3% of patients receiving PEG compared with 24.5% of patients who received NaP solution.[216] Although these mucosal changes may mimic the changes of Crohn's disease, the histologic appearance is distinctive and permits differentiation from idiopathic inflammatory bowel disease.[214,220]

After Bariatric Surgery

There currently is no published clinical trial evidence to recommend specific regimens for persons with a history of prior bariatric surgery. Patients with restrictive gastric surgery should be counseled to use low-volume preparations, or if high-volume preparations are used the timelines for ingestion need to be extended. In addition, patients should be advised to consume sugar-free drinks and liquid foods to avoid symptoms related to dumping from the high sugar content.[221]

Pregnancy

Colonoscopy rarely is indicated during pregnancy. If necessary, it should be deferred until the second trimester whenever possible and always should have a strong indication with a careful assessment of risk vs benefit.[222] Therefore, the safety and efficacy of bowel preparations have not been well studied in this group. The US FDA has assigned categories of risk for use of medications during pregnancy (http://www.drugs.com/pregnancy-categories.html). Both PEG-ELS and NaP solutions are category C medications. Low doses of PEG-ELS were reported to be safe in a study of 225 pregnant patients who were treated for constipation.[223] Antenatal failure of bone growth and mineralization was reported in a case of a mother who repeatedly had taken phosphate enemas during pregnancy.[224] The American Gastroenterological Association recommends that NaP should be avoided[225] whereas the American Society of Gastrointestinal Endoscopy states that NaP preparations should be used with caution owing to possible fluid and electrolyte abnormalities.[222] One survey

found that only 12.9% of obstetricians previously have or would prescribe PEG-ELS to a pregnant patient compared with 53.8% of gastroenterologists ($P < .001$).[226] In contrast, 29.1% of obstetricians vs 7.7% of the surveyed gastroenterologists previously have or would prescribe an oral NaP preparation in a pregnant patient. Although PEG-ELS is considered a low-risk option, tap water enemas are recommended by the American Gastroenterological Association for lower endoscopy because full colonoscopy rarely is indicated during pregnancy.[225]

Salvage Options for Inadequate Preparation

There is insufficient evidence to recommend a single salvage strategy for those patients encountered with a poor preparation that precludes effective completion of the colonoscopy. The following options can be considered in such cases:

Recommendations

1. Large-volume enemas can be attempted for patients who, presenting on the day of colonoscopy, report brown effluent despite compliance with the prescribed colon-cleansing regimen (***Weak recommendation, very low quality evidence***)
2. Through-the-scope enema with completion colonoscopy on the same day can be considered, especially for those patients who receive propofol sedation (***Weak recommendation, very low quality evidence***)
3. Waking the patient entirely from sedation and continuing with further oral ingestion of cathartic with same-day or next-day colonoscopy has been associated with better outcomes than delayed colonoscopy (***Weak recommendation, low-quality evidence***)

Although multiple studies have addressed risk factors for inadequate preparation, only a single study examined such factors for a second examination. In 235 patients who underwent a second colonoscopy specifically because of inadequate preparation, the second examination failed again because of inadequate preparation in 54 of those 235 patients (23%).[227] Next-day colonoscopy (relative to any other timing) was associated with a reduced risk of repeat failure (OR, 0.31; 95% CI, 0.1–0.92). Recognizing individuals likely to have a poor preparation at the time of arrival to the endoscopy suite might allow for salvage efforts before sedation. One study found that those reporting brown liquid or solid effluent had a 54% chance of having a fair or poor preparation.[228] In such cases, further preparation with large-volume enemas or additional oral preparation could be considered.

Two studies describe the use of a through-the-scope enema technique as a salvage regimen during colonoscopy.[229,230] In each study, the patients are recovered from propofol sedation and then permitted to use the bathroom to evacuate residual fluid. The earlier of the 2 studies describes application of the technique in 21 adults (mean age, 66 y) found to have inadequate preparation.[230] After passing the colonoscope as proximally as possible, either a phosphate enema (133 mL/19 g) followed by a bisacodyl enema (37 mL/10 mg) (10 cases) or 2 bisacodyl enemas (11 cases) were instilled into the colon through the accessory channel of the colonoscope. The investigators reported success (colon "well prepared") in all cases. The other study evaluated 26 adults (median age, 59 y) in whom the Aronchick scale was used to assess the quality of the preparation in the rectosigmoid region.[227] For those determined to have poor or inadequate preparation, a rescue enema (polyethylene glycol solution/500 mL) was instilled at the level of the hepatic flexure via the biopsy channel. By using this technique, 96% (25 of 26) were cleansed successfully (excellent or good). In each case the colonoscopy was completed successfully.

Finally, Ibanez et al[231] reported on 51 adult patients (mean age, 61.5 y) with a previously failed outpatient colonoscopy as a result of inadequate preparation in whom they then tried an intensive bowel-cleansing strategy before the second procedure. The Boston Bowel Preparation Scale was applied at the time of the initial colonoscopy and those with a score of 0 or 1 on any segment were deemed inadequate. The bowel regimen in these cases included a low-fiber diet for 72 hours followed by a liquid diet on the day before the procedure. On the evening of the procedure, 10 mg of bisacodyl was administered along with 1.5 L of PEG-ELS. A second 1.5-L dose of PEG-ELS was administered on the day of the colonoscopy. By using this approach, 90% (46 of 51) had an adequate preparation as assessed by the Boston Bowel Preparation Scale (ie, $\geq$2 each segment).

Overall, the data on management of patients with inadequate preparation are limited. A variety of measures that use additional oral purgatives or enemas are likely to be effective. Supplemental measures aimed at effective colonoscopy and acted on as soon as deemed safe are likely to result in fewer patients being lost to follow-up evaluation. Patients who present to the endoscopy unit with persistent brown effluent are at increased risk of inadequate preparation and may warrant more oral laxatives or enemas before any attempt at colonoscopy.

Summary

Ineffective bowel cleansing for colonoscopy results in missed precancerous lesions and increased costs related to early repeat procedures. Efficacy and tolerability of bowel preparations are important and related goals, but efficacy is of primary importance because of the substantial consequences of inadequate cleansing. Adequate bowel preparation implies that the colonoscopist will recommend a screening or surveillance interval consistent with the findings of the examination and current screening and surveillance guidelines. The rate of adequate bowel cleansing should be at least 85%, and higher whenever possible. Awareness of medical factors that increase the risk of

inadequate preparation and nonmedical factors that predict poor compliance with instructions can direct physicians to the use of more efficacious or aggressive preparation regimens or more extensive education (including navigation), respectively. Some patients who present with inadequate preparation can have their procedures salvaged by additional cleansing on the day of the procedure. Bowel preparation quality should be judged after intraprocedural efforts to enhance cleansing quality have been completed.

Appendix A

Key Word Searches for USMSTF Document

("Patient Compliance" [medical subject headings (MeSH)] OR "Appointments and Schedules" [MeSH] OR "patient satisfaction" [MeSH] OR "Patient Acceptance of Health Care" [MeSH] OR complian* [ti] OR accept* [ti] OR adheren* [ti] OR satisfaction* [ti]) (educat* [ti] OR comprehension [tiab] OR understanding [tiab] OR "Educational Status" [MeSH] OR "Health Education" [MeSH] OR "Patient Education as Topic" [MeSH] OR "education" [sh]) ("colonoscopy" [MeSH] OR sigmoidoscop* [tiab] OR proctosigmoidoscop* [tiab] OR "gastrointestinal endoscopy" [tiab] OR colonoscop* [tiab]) ("Laxatives" [MeSH] OR "Laxatives" [Pharmacological Action] OR laxative* [tiab] OR "Cathartics" [MeSH] OR "Cathartics" [Pharmacological Action] OR "therapeutic irrigation" [MeSH] OR preparat* [tiab] OR clean* [tiab] OR cathartic* [tiab] OR "Polyethylene Glycols" [MeSH] OR "polyethylene glycol" [tiab] OR "magnesium citrate" [tw] OR "Sodium phosphate" [tw] OR "Sodium picosulphate" [tw] OR "magnesium oxide" [tw] OR "citric acid" [tw] OR Golytely [tw] OR Nulytely [tw] OR Glycolax [tw] OR Trilyte [tw] OR Colyte [tw] OR HalfLytely [tw] OR Moviprep [tw] OR Miralax [tw] OR Clenz-lyte [tw] OR PEG-3350 [tw] OR Gavilax [tw] OR Gavilyte [tw] OR PegLyte [tw] OR Clearlax [tw] OR Purelax [tw] OR Lax-lyte [tw] OR Dulcolax [tw] OR GlycoPrep [tw] OR Visicol [tw] OR Fleet [tw] OR Osmoprep [tw] OR Pico-salax [tw] OR Purg-odan [tw] OR Citro-Mag [tw] OR PicoPrep [tw] OR Bi-Peglyte [tw]) ("food, formulated" [MeSH] OR "diet" [MeSH] OR "electrolytes" [MeSH] OR "fasting" [MeSH] OR "diet therapy" [sh] OR "dietary fiber" [MeSH] OR diets [ti] OR dietary [ti] OR diet [ti] OR formulat* [ti]).

Appendix B

Bowel Preparation Quality Scales

Bowel preparation quality has been described using a variety of approaches, typically categorizing the quality as excellent, good, fair, or poor. However, these terms lack standardized definitions. Automated processes for quantification of the quality of a bowel preparation are under development, but are not ready for clinical application.[232] For a bowel preparation scale to be of clinical value, it should be both valid and reliable.[233] Validity refers to measuring what is intended to be measured, as determined by experts. Reliability refers to the reproducibility, such as between different observers examining the same information.[28]

Numerous bowel preparation quality scales have been reported, but few have undergone a formal assessment of validity. The Aronchick scale (Table 1) describes the percentage of fluid or stool that covers the bowel surface and has κ intraclass correlation coefficients ranging from very good (0.79) for the cecum to poor (0.31) for the distal colon.[234] Given that there are no reliability data and the scale downgrades quality for retained fluid, this scale is not recommended for clinical practice.

The Ottawa scale assesses cleanliness and fluid volume separately.[233] Cleanliness for the right, mid-, and rectosigmoid segments are scored separately with scores of 0–4 for each segment. A summary score is reported for overall cleanliness (Figure 1). Additionally, the quantity of fluid is scored from 0 (perfect) to 2 (large) and this is added to the cleanliness value with a maximum total of 14 (solid stool throughout with lots of fluid). In the validation study, the Ottawa scale was found to have a significantly higher Pearson correlation coefficient than the Aronchick scale (0.89 vs 0.62; $P < .001$). Furthermore, the κ statistic and intraclass correlation coefficient was significantly higher (0.94 vs 0.77; $P < .001$).[233] Because the scale reports the quality of the preparation before washing and suctioning, the Ottawa scale is not recommended for clinical practice.

The Boston Bowel Preparation Scale was developed specifically for application during withdrawal of the colonoscope, after all bowel cleansing has been completed.[235] The Boston Bowel Preparation Scale involves assigning each of 3 regions of the colon (right, transverse, and left) a score from 0 to 3 (Table 2). Each segment score is summed for a total Boston Bowel Preparation Scale score ranging from 0 to 9 (with 9 corresponding to a perfectly clean colon and 0 corresponding to a nonprepped colon). If the procedure is aborted because of an inadequate preparation, then the proximal segments are assigned a score of 0. A priori, the developers recommended that a score of less than 5 corresponds to an inadequate bowel preparation. The scale developers have published 4 endoscopic images depicting examples of preparations corresponding to scores of 0–3. Furthermore, a 15-minute training video was developed and is available on the Internet (https://www.cori.org/bbps/login.php). In the validation study, the weighted κ statistic for intra-observer agreement for the total Boston Bowel Preparation Scale score was 0.77, and the intraclass correlation coefficient for interobserver agreement was 0.74.[235] Construct validity also was tested, comparing the Boston Bowel Preparation Scale score with a traditional scoring

Table 1. Aronchick Bowel Preparation Scale

Excellent: small volume of clear liquid or >95% of surface seen
Good: large volume of clear liquid covering 5%–25% of the surface but >90% of the surface seen
Fair: some semisolid stool that could be suctioned or washed away but >90% of the surface seen
Poor: semisolid stool that could not be suctioned or washed away and <90% of the surface seen
Inadequate: re-preparation needed

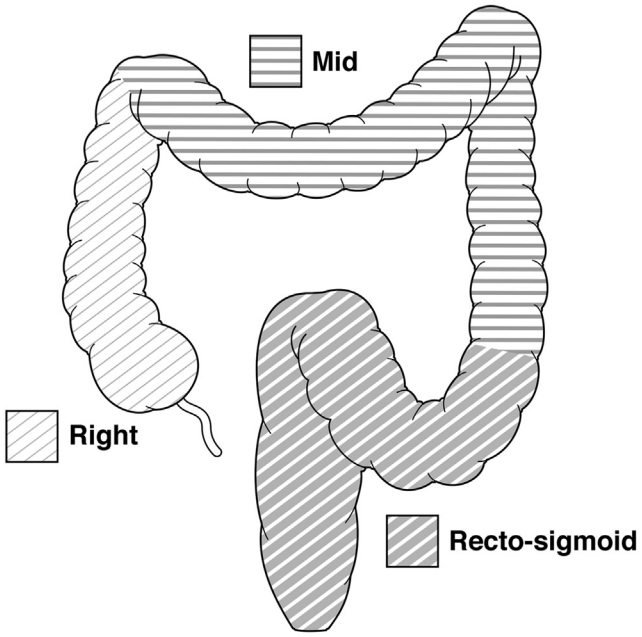

Figure 1. Ottawa scale. The Ottawa bowel preparation quality scale use guide. (1) Part A of the scale is applied to each colon segment: right colon (*Right*), midcolon (*Mid*), and the rectosigmoid colon (*Recto-Sigmoid*). (2) The fluid quantity is a global value for the entire colon. (3) The score is calculated by adding the ratings of 0–4 for each colon segment and the fluid quantity rating of 0–2. (4) The scale has a range from 0 (perfect) to 14 (solid stool in each colon segment and lots of fluid; ie, a completely unprepared colon). (5) Before using the scale in a study or audit, observers need to perform a calibration exercise.

system (excellent, good, fair, poor, or unsatisfactory), the perception of inadequate bowel preparation, the polyp detection rate, and the insertion and withdrawal times from 633 screening colonoscopies. There was a significant decreasing trend in the mean Boston Bowel Preparation Scale score assigned to each category using the traditional system (P for trend $< .001$). The polyp detection rate was 40%. For patients with a Boston Bowel Preparation Scale score of 5 or greater the polyp detection rate was 40%, compared with 24% for those with a score of less than 5 ($P < .02$), and a repeat colonoscopy owing to inadequate preparation was recommended only 2% of the time, compared with 73% of the time for those with a score of less than 5 ($P < .001$). Furthermore, the total Boston Bowel Preparation Scale scores were correlated inversely with both insertion and withdrawal times. In a follow-up validation study, the intraclass correlation coefficient was 0.91 and the intrarater reliability was substantial (weighted κ, 0.78).[236] The Boston Bowel Preparation Scale was used prospectively by 12 attending gastroenterologists in 983 screening colonoscopies and showed an association between higher Boston Bowel Preparation Scale scores and polyp detection in the right and left colon, although no association was found for the transverse colon.[236] The Boston Bowel Preparation Scale has the best data for a validated scoring system.

Table 2. Boston Bowel Preparation Scale

0: Unprepared colon segment with mucosa not seen because of solid stool that cannot be cleared
1: Portion of mucosa of the colon segment seen, but other areas of the colon segment are not well seen because of staining, residual stool, and/or opaque liquid
2: Minor amount of residual staining, small fragments of stool, and/or opaque liquid, but mucosa of colon segment is seen well
3: Entire mucosa of colon segment seen well, with no residual staining, small fragments of stool, or opaque liquid

Appendix C

Risk Factors for Inadequate Preparation

We identified 16 reports (15 observational studies[2,4,61,228,237–247] and 1 trial[248]) that identified patient-related variables associated with a poor-quality bowel cleansing. Observational studies that used only univariate analysis (n = 5) were not considered further.[237,238,242,247,248] Assessment of bowel preparation in most studies relied on Aronchick-like scales that had either 4 or 5 categories, which then were dichotomized to adequate (excellent/good) or inadequate (fair/poor) preparations. In total, the 10 observational studies using multivariate analysis evaluated 25,376 participants and on average preparation was deemed inadequate 23.8% of the time (range, 10.3%–33%).

Regarding basic demographics, age and sex were evaluated in all 10 studies. Older age[61,241,243,245] and male sex[61,243,244] occasionally were associated with inadequate preparation. Higher body mass index was associated with inadequate preparation in 2 of the 7 studies in which it was recorded.[61,239] Four studies reported a significant association of inadequate preparation with inpatient relative to outpatient status.[2,239,243,244]

Past medical and surgical history also are important predictors of preparation quality. Those with a more complicated past medical history either measured as a composite score or by the number of medications used are more difficult to prepare adequately. For example, in a large (n = 5832) multicenter study performed in Europe and Canada, those with an American Society of Anesthesiologists status of class III through class V were significantly less likely to accomplish a high-quality preparation relative to American Society of Anesthesiologists class I patients (OR, 0.51; 95% CI, 0.32–0.73).[2] Nguyen and Wieland[245] retrospectively analyzed reports of 300 screening colonoscopy patients and found that patients with 8 or more prescriptions were significantly more likely to have a poor colonoscopy preparation (OR, 6.52; 95% CI, 5.12–8.56). Neurologic conditions associated with poor mobility such as stroke and Parkinson's disease[61,228,239,244] also frequently were associated with inadequate preparation. A history of prior gastrointestinal surgical resection[61,240,245] also was found to be associated with poorer preparation quality. Certain drugs such as tricyclic antidepressants[239,244] and

narcotics[239] occasionally were seen as a risk factor for poor preparation.

Diabetes mellitus is associated with a higher proportion of patients with inadequate bowel preparation at the time of colonoscopy.[248,249] In a small trial (n = 99) using a 6-L PEG-ELS preparation, nondiabetic patients had preparations rated as good or better in 97% of cases relative to 62% of cases in diabetic patients.[248] In 1 small study of 54 nondiabetic and 45 diabetic patients undergoing outpatient colonoscopy after ingesting 6 L of PEG, blinded review documented a superior bowel preparation in the nondiabetic group.[248] One small study randomized 198 diabetic patients undergoing colonoscopy to receive either 4 L of PEG with 10 oz of magnesium citrate or the same preparation with an additional dose of magnesium citrate on the day before the usual preparation.[249] A good preparation was reported in 70% receiving the additional magnesium citrate compared with 54% receiving the usual preparation ($P = .02$).

Segmental colonic resection is associated with lower-quality bowel preparation. In 1 prospective study, bowel preparation was rated as unsatisfactory significantly more often in those with prior bowel resection (60.9%) than in controls (43.5%; $P = .02$).[250] Unsatisfactory preparation was observed in 64.0% of patients with a prior gastric resection and in 59.7% of patients with a prior colonic resection, despite the administration of 4 L PEG-ELS on the morning of the colonoscopy. In a prospective study of 362 patients undergoing colonoscopy, prior history of colorectal resection was associated with an increased rate of inadequate bowel preparation (OR, 7.5; 95% CI, 3.4–17.6).[240]

Persons with spinal cord injury have neurogenic bowel dysfunction[251] that may reduce the effectiveness of traditional bowel purgative regimens. In a randomized study comparing 4 L PEG-ELS, oral NaP (90 mL in divided doses), and a combination of both (doses not specified) in 36 patients with spinal cord injury, a difference was found in bowel preparation quality between groups, with at least 73% of bowel preparations rated as "unacceptable."[252] In 1 case series, spinal cord injury patients undergoing colonoscopy were given an extended bowel preparation consisting of a clear liquid diet and 20 oz of magnesium citrate on day 1, 4 L of PEG-ELS on day 2, followed by NaP/biphosphate enemas (as needed to facilitate evacuation), and additional NaP/biphosphate enemas on day 3 (the day of colonoscopy) until the return was clear of fecal matter.[253] All 18 patients were reported to have an acceptable bowel preparation, with 4 patients requiring nasogastric tube placement to complete the preparation.

The objective of studies determining risk factors for inadequate preparation is the potential to develop a reliable predictive model to identify individuals who would benefit from a tailored approach to the preparation. Recently, a single group of investigators developed such a predictive model in a large (n = 2811) prospective study performed in the outpatient setting across 18 medical centers.[61] In multivariate analysis, many of the factors highlighted earlier were confirmed as risk factors including the following: older age (OR, 1.10; 95% CI, 1.00–1.02); male sex (OR, 1.2; 95% CI, 1.02–1.15); increased body mass index (OR, 1.1; 95% CI, 1.03–1.1), Parkinson's disease (OR, 3.2; 95% CI, 1.2–9.3), and prior colorectal surgery (OR, 1.6; 95% CI, 1.2–2.2). However, when using a split-dose regimen, the model had only modest predictive ability (area under the receiver operating characteristic curve, 0.63) in the validation set.

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Reprint requests
Address requests for reprints to: David A. Johnson, MD, Eastern VA Medical School, Norfolk, Virginia. e-mail: dajevms@aol.com; fax: (757) 466-9082.

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Conflicts of interest
These authors disclose the following: David Johnson has served as a consultant and clinical investigator for Epigenomics, as a consultant for Given Imaging, and as a clinical investigator for Exact Sciences; A. Barkun has served as a consultant for Olympus, Inc, and Pendopharm, Inc, and has received clinical research support from Boston Scientific and Cook; L. B. Cohen has served as a consultant and on the speaker's bureau and received research support from Salix, and as a consultant for Braintree; T. Kaltenbach has been a research grant recipient and consultant for Olympus America, Inc, D. J. Robertson has served as a consultant for Given Imaging; D. A. Lieberman has served on the scientific advisory boards for Exact Sciences, Given Imaging, and Roche, and as a consultant for MOTUS; and D. K. Rex has received research support and served as a consultant for Braintree Laboratories and Ferring Pharmaceuticals, Given Imaging, and Olympus America Corp, has served as a consultant for Epigenomics and Exact Sciences, and has served on the speaker's bureau for Boston Scientific, Inc. The remaining authors disclose no conflicts.