Thieme

Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2019

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MAIN RECOMMENDATIONS

ESGE recommends a low fiber diet on the day preceding colonoscopy.
Strong recommendation, moderate quality evidence.
ESGE recommends the use of enhanced instructions for bowel preparation.
Strong recommendation, moderate quality evidence.
ESGE suggests adding oral simethicone to bowel preparation.
Weak recommendation, moderate quality evidence.
ESGE recommends split-dose bowel preparation for elective colonoscopy.
Strong recommendation, high quality evidence.
ESGE recommends, for patients undergoing afternoon

colonoscopy, a same-day bowel preparation as an acceptable alternative to split dosing.
Strong recommendation, high quality evidence.
ESGE recommends to start the last dose of bowel preparation within 5 hours of colonoscopy, and to complete it at least 2 hours before the beginning of the procedure.
Strong recommendation, moderate quality evidence.

ESGE recommends the use of high volume or low volume PEG-based regimens as well as that of non-PEG-based agents that have been clinically validated for routine bowel preparation. In patients at risk for hydroelectrolyte disturbances, the choice of laxative should be individualized.
Strong recommendation, moderate quality evidence.

SOURCE AND SCOPE

This Guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE). It provides practical advice on the different aspects of bowel preparation for colonoscopy. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was adopted to define the strength of recommendations and the quality of evidence.

Introduction

Inadequate bowel preparation has a detrimental effect on all aspects of the colonoscopy procedure and, especially, on its accuracy. It has been associated with significantly lower rates of detection of adenomas and advanced adenomas in two recent meta-analyses [1,2]. A subsequent prospective observational study with repeat colonoscopy performed by a blinded endoscopist revealed a threefold higher miss rate for adenomas ≥5 mm in size when bowel cleansing was inadequate [3]. Inadequate bowel preparation is also one of the most unfavorable predictors for cecal intubation failure [4–6] and unsatisfactory patient experience [7]. In addition it results in shorter colonoscopy surveillance intervals [8,9], longer hospital stays, and increased healthcare costs [10,11] and may render screening colonoscopy cost-ineffective [12]. For these reasons, a ≥90% minimum standard for adequate bowel preparation (assessed using validated scales) has been recently recommended by the Quality Committee of the European Society of Gastrointestinal Endoscopy (ESGE) [13].

Since the publication of the ESGE Guideline on bowel preparation in 2013 [14], additional evidence has been published on the efficacy and safety of different aspects of bowel preparation, including diet, timing, and type of laxative, as well as patient information and specific scenarios. The main aim of this update is to incorporate such new evidence into the clinical recommendations to be adopted in routine and specific scenarios.

Methods

The Guideline Committee chairs worked with subgroup leaders (C.H., J.E, J.-M.D., C.S., F.R.) to identify pertinent systematic search terms that included "colon," "rectum," "bowel preparation," "diet," "laxative," "colonoscopy," and "endoscopy." Searches were performed (at least) on Medline (via PubMed) and the Cochrane Central Register of Controlled Trials from after 2013 (date of the previous ESGE guideline [14]) up to December 2018. Evidence tables were generated for each key question (**Appendix 1s**, online-only Supplementary Material), summarizing the level of evidence from the available studies. For important outcomes, articles were individually assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to grade the evidence levels and recommendation strengths (see **Appendix 2s**) [15]. The role of bowel preparation as a metric of the quality of colonoscopy was excluded as this had already been addressed in the ESGE Quality Improvement Initiative [13]. The evidence tables are presented in **Appendix 3s**.

The subgroups developed draft proposals that were presented to the entire group for general discussion during a meeting held in January 2019 in Munich. Further details on the development methodology of ESGE guidelines have been reported elsewhere [16]. In March 2019, a draft prepared by the task force leaders was sent to all group members. After the agreement of

ABBREVIATIONS

ADR	adenoma detection rate
CI	confidence interval
ESGE	European Society of Gastrointestinal Endoscopy
GI	gastrointestinal
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HR	hazard ratio
IBD	inflammatory bowel disease
LGIB	lower gastrointestinal bleeding
MCSP	magnesium citrate plus sodium picosulfate
OSP	oral sodium phosphate
OSS	oral sulfate solution
OR	odds ratio
PEG	polyethylene glycol
RCT	randomized controlled trial
RR	relative risk

all group members had been obtained, the manuscript was sent for further comments to the ESGE national societies and individual members. After this it was submitted to the journal *Endoscopy* for publication.

This Guideline was issued in 2019 and will be considered for update in 2024. Any interim updates will be noted on the ESGE website: http://www.esge.com/esge-guidelines.html.

Diet, and patient information

RECOMMENDATION

ESGE recommends a low fiber diet on the day preceding colonoscopy.

Strong recommendation, moderate quality evidence.

Diet restriction, either a clear liquid diet or a low residue diet, has traditionally been recommended before colonoscopy but adherence is low. In a real-life prospective study (789 patients), the proportion of patients actually following a low residue diet for 2 days before colonoscopy was 44.2% and a high residue diet was independently associated with inadequate bowel preparation [17]. In trials, adherence to a low residue diet was 90.4% (874 of 967 patients randomized to a low residue diet) [18–23]. Two meta-analyses [24, 25] have compared a low residue diet vs. a clear liquid diet on the day before colonoscopy, with the same laxative in both arms. In the included trials, a diet was usually considered to be low residue when the total fiber intake was <10 g/day. Most of the randomized controlled trials (RCTs) used the terms low residue/low fiber interchangeably and few of them specified the amount of fiber in their regimen. Examples of foods allowed in a low residue diet included some fresh peeled and pitted fruits and cooked vegetables (e.g., apples, carrots), cheese, meat, fish, and white bread, while wholegrain bread, muesli, brown rice were not allowed together with some fruits and vegetables (e.g., orange, mushroom). Some trials used prepackaged low fiber or fiber-free food while in others instructions were given to the participants on preparation of their food.

The first meta-analysis (9 RCTs, 1686 participants) found that, compared with a clear liquid diet, a low residue diet was associated with a higher willingness to repeat bowel preparation (odds ratio [OR] 1.86, 95% confidence interval [CI] 1.34–2.59; $P<0.01$) and better tolerability (OR 1.92, 95%CI 1.36–2.70; $P<0.01$) [24]. No differences between groups were found in terms of adequate bowel preparation (OR 1.21, 95%CI 0.64–2.28; $P=0.58$) or adverse effects (OR 0.88, 95%CI 0.58–1.35; $P=0.57$).

The most recent meta-analysis (12 RCTs, 3674 participants) grouped patients taking a low residue diet (8 RCTs) or a regular diet (4 RCTs) and compared them to patients taking a clear liquid diet [25]. The low residue diet was provided until breakfast (n=1), lunch (n=3), or dinner (n=4), depending on study protocol. Compared with a clear liquid diet, the low residue/regular diet was associated with higher willingness to repeat the procedure (relative risk [RR] 1.08, 95%CI 1.01–1.16), better tolerability (RR 1.04, 95%CI 1.01–1.08), and more frequent consumption of a targeted amount of the bowel laxative (RR 1.04, 95%CI 1.01–1.08). No differences between groups were found in terms of adequate bowel preparation for the whole meta-analysis (RR 1.00, 95%CI 0.97–1.04) as well as for subgroup analyses of high quality trials (5 RCTs, 1649 patients), split/morning preparations (5 RCTs, 1431 patients), or single-dose preparation (4 RCTs, 1528 patients). No differences between groups were found in terms of adenoma detection rate (ADR) (3 RCTs, 1228 participants) or adverse events except for more hunger in the clear liquid diet arm (RR 1.93, 95%CI 1.13–3.3).

A third meta-analysis (7 RCTs, 1590 participants) had similar inclusion criteria except that it did not restrict inclusion to studies with an identical purgative in both arms [26]. Compared with a clear liquid diet, a low residue diet was associated with higher willingness to repeat the procedure (RR 1.17, 95%CI 1.09–1.26) and better tolerance (RR 1.06, 95%CI 1.02–1.11). No differences between groups were found in terms of adequate bowel preparation (RR 1.01, 95%CI 0.91–1.13), adverse events, and compliance with diet (RR 0.97, 95%CI 0.87–1.08).

A further four recent RCTs have also shown that patient satisfaction, ease of preparation, and willingness to repeat an identical preparation were higher with a low residue diet vs. a clear liquid diet in all trials that analyzed those outcomes (3, 2, and 1 RCTs, respectively); and the proportions of patients with adequate bowel preparation (3 RCTs) were similar or higher with a low residue diet vs. a clear liquid diet (**Table 1s**, **Appendix 3s**, online-only Supplementary Material) [18, 19, 27, 28]. Recently, a possible additional effect of multiple-day vs. single-day low residue diet among participants receiving a split-dose bowel preparation has been excluded in a randomized trial [29].

Three RCTs assessed the effect of different liquids for bowel preparation with polyethylene glycol (PEG) [30–32]. One of these used dilution of PEG powder in Coca Cola Zero instead of water [30], and in another orange juice was kept in the mouth for a few seconds just before drinking the bowel preparation solution [32]. Various parameters were improved, including palatability of the bowel preparation (in both RCTs), speed of bowel preparation intake, bowel cleanliness, willingness to repeat the same preparation, and adverse events (mainly nausea) (in one RCT each). The third RCT found that the addition of 1 L of pineapple juice after bowel preparation intake had little effect (better proximal colon cleanliness but not in the whole colon) [31]. Polyp and adenoma detection rates were not modified by these interventions.

Gum chewing was tested in three RCTs that used different protocols of gum chewing [33–35]. One of them used a purgative rarely employed for bowel preparation and reported below-standard cecal intubation rates [33]. The other two RCTs reported higher patient satisfaction and willingness to repeat the same bowel preparation, more complete and faster bowel preparation intake, and less abdominal discomfort (one RCT each) but no improvement in bowel cleansing [34, 35].

RECOMMENDATION
ESGE recommends the use of enhanced instructions for bowel preparation.
Strong recommendation, moderate quality evidence.

A meta-analysis (8 RCTs, 3795 patients) found that, compared with patients receiving regular instructions before colonoscopy, those who received enhanced instructions had better bowel cleanliness (OR 2.35, 95 %CI 1.65 – 3.35; $P<0.001$), a higher cecal intubation rate (OR 2.77, 95 %CI 1.73 – 4.42; $P<0.001$) and more willingness to repeat the preparation (OR 1.91, 95 %CI 1.20 – 3.04; $P=0.006$), but a similar polyp detection rate [36]. Enhanced instructions consisted of visual aids, a social media app, telephone or short message service (SMS), and smartphone applications. Improvements were observed with 2 L as well as 4 L PEG and with split-dose as well as single-dose regimens, and with a delay between enhanced instructions and colonoscopy of 1 week or less as well as with a delay of more than 1 week. Adverse events were similar in both groups.

These data were confirmed in three more recent RCTs that used a phone call, a series of SMSs or a video as enhanced instructions for bowel preparation: compared to regular instructions, these improved bowel cleansing and ADR (three RCTs), and cecal intubation rate, and patient satisfaction (one RCT each) [37 – 39] (**Table 2s**). Interestingly, in the study that used SMSs, each patient received a total of 15 nonpersonalized messages and 89 % of them reported that they would use SMS guidance again for their next colonoscopy. Finally, an RCT (283 patients) that used different types of bowel preparation found that sending a video before colonoscopy improved bowel cleanliness with low volume bowel preparations (2 L PEG glycol/ascorbate or sodium picosulfate/magnesium citrate) but not with 4 L PEG [40].

Adjunctive drugs

RECOMMENDATION
ESGE does not suggest the routine use of prokinetic agents for bowel preparation.
Weak recommendation, low quality evidence.

RCTs that compared identical bowel preparation regimens with vs. without prokinetics are summarized in **Table 3s**.

The effect of 24 – 96 µg lubiprostone, a chloride channel-2 activator increasing intestinal secretion and transit, has been assessed in three RCTs; all of them used single-dose bowel preparation [41 – 43]. The three RCTs reported better bowel cleansing with lubiprostone but the difference was significant in only one study [41]; this was the largest study and the only one to use low dose (2 L) PEG. These results need to be confirmed by other studies using split regimens.

Itopride (200 mg) improved bowel cleanliness in an RCT that used split-dose bowel preparation, with similar ADRs and adverse event rates between groups [44]. Finally, mosapride, a drug that is not as widely available as other prokinetics, has been tested in two RCTs with a single-dose bowel preparation; bowel cleansing was better in one study, in the left colon only [45].

Prokinetics have also been used in attempts to reduce the dose of purgative but the data do not allow conclusions to be drawn [46, 47].

RECOMMENDATION
ESGE suggests adding oral simethicone to bowel preparation.
Weak recommendation, moderate quality evidence.

A meta-analysis published in 2011 (7 RCTs, 714 patients) concluded that the amount of bubbles was less frequently unacceptable in patients who had received oral simethicone vs. those who had not, but no difference in colon cleanliness was found and the diagnostic yield was not reported [48].

Since then, four RCTs (see **Table 4s**) have compared identical bowel preparation regimens with vs. without oral simethicone; they found that oral simethicone decreases the amount of bubbles (four RCTs), improves bowel cleanliness (three RCTs), and also the ADR (two RCTs). Adverse events were analyzed in only three RCTs; two found that they were less frequent with vs. without simethicone. A meta-analysis assessed these four RCTs (1536 patients); in a subgroup analysis it found that oral simethicone increases the ADR (OR 1.23, 95 %CI 1.04 – 1.47, $P=0.02$) [49]. Of note, the doses of simethicone used in these four RCTs were higher than those used in previous RCTs (400 – 1200 mg vs. < 400 mg in 6 of 7 RCTs included in the 2011 meta-analysis) [48]. No other antifoaming agent has been recently studied for colonoscopy.

Another meta-analysis is difficult to interpret as it included studies using different purgatives in the arm with vs. without simethicone [50].

Various professional societies, including ESGE, as well as endoscope manufacturers, have warned against the use of simethicone through the auxiliary water channel during endoscopy [51, 52]. If it is used during endoscopy, simethicone should be injected via the biopsy rather than the auxiliary water channel of the endoscope, at the lowest effective concentration. Simethicone residues could contribute to the formation of biofilms and the biopsy channel is brushed during reprocessing while the auxiliary water channel is not.

RECOMMENDATION
ESGE recommends against the routine use of enemas for bowel preparation.
Strong recommendation, moderate quality evidence.

An RCT found that adding an enema to standard bowel preparation did not improve bowel cleansing and decreased the acceptability of bowel preparation [53]. Another RCT found that a 5-day regimen of oral nutritional supplements plus enema did not provide adequate bowel cleansing [54].

Timing

RECOMMENDATION

ESGE recommends split-dose bowel preparation for elective colonoscopy.

Strong recommendation, high quality evidence.

A meta-analysis (47 RCTs, 13 478 patients) found that split-dose regimens, regardless of the type and dose of the cleansing agent, provided excellent/good colon cleansing more frequently than day-before bowel preparation (OR 2.51, 95 %CI 1.86 – 3.39). This result was confirmed in subanalyses restricted to PEG (OR 2.60, 95 %CI 1.46 – 4.63), sodium phosphate (OR 9.34, 95 %CI 2.12 – 41.11), and picosulfate (OR 3.54, 95 %CI 1.95 – 6.45). Moreover, split dosing was associated with a higher proportion of patients willing to repeat the preparation (OR 1.90, 95 %CI 1.05 – 3.46) [55].

Seven subsequent RCTs comparing identical cleansing agents (sodium picosulfate, three studies [56 – 58]; high volume PEG, two studies [59, 60]; low volume PEG, two studies [61, 62]) further confirmed the superiority of split dosing over a day-before regimen in terms of colon cleansing [56 – 62] and patient tolerability [59 – 61] (**Table 5s**).

Concerning the detection of neoplastic lesions, the above-mentioned meta-analysis [55] included two small trials that reported on this outcome, and no difference was found. Two further RCTs were specifically designed and adequately powered to compare split-dose vs. single-dose regimens regarding the detection of neoplastic lesions. In one RCT that included 690 patients undergoing screening colonoscopy after positive fecal immunochemical testing, split-dose vs. day-before bowel preparation with 2 L PEG/ascorbate resulted in a higher detection rate of adenomas (primary study endpoint; 53.0 % vs. 40.9 %; RR 1.22, 95 %CI 1.03 – 1.46; number needed to treat [NNT] = 9) and of advanced adenomas (26.4 % vs. 20.0 %; RR 1.35, 95 %CI 1.06 – 1.73; NNT = 16) [62]. The other RCT compared split-dose 2 L PEG/ascorbate vs. a day-before regimen of sodium picosulfate/magnesium citrate; the split regimen was associated with a trend towards a higher polyp detection rate (primary endpoint; 51.5 % vs. 44.0 %, $P = 0.14$), and a significantly higher detection rate of right-sided polyps (28.0 % vs. 16.6 %, $P = 0.007$) and adenomas (21.0 % vs. 11.9 %, $P = 0.015$) [63]. Moreover, large observational studies confirmed that split dosing led to higher polyp and/or adenoma detection rates compared with single-dose regimens [64 – 66].

RECOMMENDATION

ESGE recommends, for patients undergoing afternoon colonoscopy, a same-day bowel preparation as an acceptable alternative to split dosing.

Strong recommendation, high quality evidence.

Two meta-analyses (11 and 14 RCTs) compared split-dose with same-day bowel preparation and showed similar results regarding the quality of bowel preparation, patient willingness to repeat it, and the overall tolerability [67, 68], albeit patients taking the same-day regimen reported less bloating (OR 0.68, 95 %CI 0.40 – 0.94) [67] and better sleep quality (OR 0.44, 95 %CI 0.24 – 0.82) [68]. The ADR was similar for the two regimens [67]. It is noteworthy that most patients included in these studies were scheduled in afternoon colonoscopy slots.

Three RCTs compared same-day vs. split regimens for morning colonoscopy only, using an identical PEG bowel preparation [69 – 71]. The same-day regimen was associated with a significantly lower quality of bowel preparation in one study [69], whereas the other two studies reported similar efficacy in bowel cleansing but lower patient tolerability and compliance [70, 71], and lower willingness to repeat the same preparation in the future [70]. Overall, these data favor split-dose over same-day regimens for morning colonoscopy (**Table 6s**).

RECOMMENDATION

ESGE recommends to start the last dose of bowel preparation within 5 hours of colonoscopy, and to complete it at least 2 hours before the beginning of the procedure.

Strong recommendation, moderate quality evidence.

Observational studies have shown an inverse correlation between the degree of mucosal cleanliness and the interval between the last dose of bowel preparation and the start of colonoscopy [72, 73]; an interval of 3 – 5 hours resulted in the best preparation quality scores throughout the colon [73]. A meta-regression analysis of 29 RCTs comparing split vs. day-before regimens showed that the clinical gain of the split-dose regimen was highest within 3 hours from last dose intake, progressively decreased after 4 to 5 hours, and became statistically not significant at 5 hours [74].

Some clinicians, mainly anesthesiologists, are concerned about the risk of pulmonary aspiration of residual gastric fluid when a second dose of bowel preparation is given close to the time of endoscopy.

However, a systematic review, including 28 RCTs, 2 controlled trials, and 10 observational studies (22 936 patients) did not show any association between shorter “nothing per mouth” intervals prior to colonoscopy and pulmonary aspiration risk [75].

In addition, several endoscopic studies demonstrated that the residual gastric volumes in patients who had a split-dose regimen were similar to [76 – 79] or even lower [80] than those

obtained by more prolonged fasting after a day-before regimen. This supports the notion that bowel preparation regimens should be regulated in the same way as clear liquids. Thus, it is reasonable and safe to recommend 2 hours as the minimum interval between the intake of last dose of preparation and the colonoscopy, in line with the American Society of Anesthesiologists' recommendation for clear liquids (e.g., water, fruit juice without pulp, carbonated beverages, clear tea, and black coffee) before elective procedures requiring sedation/analgesia or anesthesia [81].

Laxatives

RECOMMENDATION

ESGE recommends the use of high volume or low volume PEG-based regimens as well as that of non-PEG-based agents that have been clinically validated for routine bowel preparation. In patients at risk for hydroelectrolyte disturbances, the choice of laxative should be individualized.

Strong recommendation, moderate quality evidence.

Data on the efficacy and safety of laxatives formally validated in a clinical setting are provided in ▶ **Table 1**.

High volume PEG

Efficacy

In a recent meta-analysis, split-dose high volume (≥3 L) appeared to be superior to split-dose low volume PEG (6 studies; 1305 patients; OR 1.89, 95 %CI 1.01 – 3.46) [82]. This confirmed a previous meta-analysis [83] showing the superiority of split-dose high volume PEG vs. other alternatives (9 studies; 2477 patients; OR 3.46, 95 %CI 2.45 – 4.89) including low volume PEG with different adjuvants and sodium phosphate, regardless of the adoption of the split regimen. After the meta-analyses were published, several trials compared high volume PEG vs. low volume PEG or non-PEG split regimens as detailed in each of the sections below. Overall, such trials showed an equivalence or superiority of the high volume vs. low volume PEG or non-PEG regimens in terms of efficacy, while confirming the worse tolerability of the high volume PEG regimens.

Safety

High volume osmotically balanced solutions containing PEG and electrolytes are intended to impair the intestinal absorption of water and sodium. This is achieved by maintaining isosmosis of the bowel lumen content. Studies have not demonstrated significant alterations in vital or biochemical parameters (e.g., sodium, potassium, chloride, bicarbonates) linked to these formulations. This accounts for the high safety and few contraindications associated with these products, which are also considered safe in the setting of renal failure, pre-existing electrolyte imbalance, or in those who cannot tolerate sodium loads (e.g., patients with cirrhosis) [84, 85].

Low volume PEG plus adjuvants

Efficacy

1 2 L PEG plus ascorbate (▶ Table 1, Table 7s)

In order to reduce the volume of PEG solutions, with the aim of improving tolerability, a formulation of 2 L PEG with the adjunct of osmotically active ascorbic acid has been introduced. One meta-analysis [86], including 11 RCTs comparing 2 L PEG plus ascorbate vs. 4-L PEG preparations for elective colonoscopies, has shown a noninferior efficacy for bowel cleansing (OR 1.08, 95 %CI 0.98 – 1.28) but a significantly better compliance for 2 L PEG plus ascorbate (OR 2.23, 95 %CI 1.67 – 2.98), with reduced nausea and vomiting. Initial reports questioned the ability of the product to provide a satisfactory cleansing in the right colon [87], but more recent RCTs have reported a similar efficacy of colon cleansing also in this clinically important segment [88 – 91].

Four additional trials published after the abovementioned meta-analysis have compared 2 L PEG plus ascorbate vs. 4 L PEG [60, 89, 92, 93]. One of these included only afternoon colonoscopies [92] and demonstrated a trend for the 4 L PEG to provide better colon cleansing than 2 L PEG plus ascorbate (both administered in a same-day regimen), but no difference was noticed in overall cleansing adequacy and patient satisfaction (despite higher bloating in the PEG plus ascorbate regimen). In the other three published RCTs [60, 89, 93] comparing split-dose 2 L PEG plus ascorbate with split-dose 4 L PEG, successful cleansing was very high (between 92.1 % [60] and 97.5 % [89]) and not different between the two products (two studies also demonstrated similarly high ADRs [89, 93]); moreover, differently from previous studies, no difference was demonstrated in the adequacy of right colon cleansing. As previously demonstrated, 2 L PEG plus ascorbate solutions were associated with higher tolerability and willingness to repeat the regimen.

Four RCTs have compared 2 L PEG plus ascorbate vs. magnesium citrate plus sodium picosulfate (MCSP) [94 – 97]. The most recent of these [95], with both preparations in split-dose regimens, demonstrated similarly high overall cleansing success (93.5 % vs. 93.8 %, $P = 0.72$; including successful cleansing of the right colon), polyp detection rates, and ADRs, along with a higher rate of adverse events (mainly nausea) in the PEG plus ascorbate group and a higher willingness to repeat the regimen in the MCSP group (83.4 % vs. 92.1, $P = 0.001$). Another RCT involving 973 patients [96] and comparing 2 L PEG plus ascorbate vs. MCSP and vs. 4 L PEG found no difference in bowel cleansing between products, provided they were used in split-dose regimens, but MCSP (OR = 8.39 [95 %CI 5.74 – 12.27]) and 2 L PEG ascorbate (OR = 1.69 [95 %CI 1.21 – 2.35]) were better tolerated than 4 L PEG.

After the abovementioned meta-analysis had been published, two RCTs compared 2 L PEG plus ascorbate vs. oral sodium phosphate (OSP) [98, 99]. In one [98], the two products were equivalent in cleansing efficacy, but PEG plus ascorbate was associated with less vomiting and more complaining about the volume and inability to complete the regimen. In the other RCT [99], in contrast, 2 L PEG plus ascorbate was associated with higher efficacy of bowel cleansing (93.4 % vs. 22.8 %,

▶ **Table 1** Summary data on efficacy and safety of validated laxatives for routine bowel preparation.

Agent	Efficacy (split/same-day regimen)	Safety
High volume polyethylene glycol (PEG)	Noninferior or superior to low volume PEG or non-PEG regimens	Not recommended in: ▪ Patients with congestive cardiac failure (NYHA class III or IV).
Low volume PEG plus adjuvants		
▪ 2 L PEG + ascorbate	Noninferior to high volume PEG and non-PEG regimens	Not recommended in patients with: ▪ Severe renal insufficiency (creatinine clearance < 30 mL/min); ▪ Congestive heart failure (NYHA III or IV); ▪ Phenylketonuria; or ▪ Glucose-6-phosphate dehydrogenase deficiency.
▪ 2 L PEG + citrate	Noninferior to high volume PEG or 2 L PEG + ascorbate	Not recommended in patients with: ▪ Severe renal insufficiency (creatinine clearance < 30 mL/min): ▪ Congestive heart failure (NYHA III or IV) ▪ Unstable angina; or ▪ Acute myocardial infarction. No long-term data available. Limited post-marketing data available.
▪ 1 L PEG + ascorbate	Noninferior to 2 L PEG + ascorbate, oral sulfate solution (OSS), and magnesium citrate plus picosulphate (MCSP). No comparison with high volume PEG.	Not recommended in patients with: ▪ Severe renal insufficiency (creatinine clearance < 30 mL /min); ▪ Congestive heart failure (NYHA III or IV); ▪ Phenylketonuria; or ▪ Glucose-6-phosphate dehydrogenase deficiency. Adequate hydration must be maintained. Limited post-marketing data available.
▪ 2 L PEG + bisacodyl	Noninferior to high volume PEG or 2 L PEG + ascorbate	Occasional reports of ischemic colitis with high dose bisacodyl. Not recommended in: ▪ Patients with congestive cardiac failure (NYHA class III or IV).
Magnesium citrate plus picosulphate (MCSP)	Noninferior to high volume PEG or 2 L PEG + ascorbate	Not recommended in patients with: ▪ Congestive heart disease; ▪ Hypermagnesemia; or ▪ Severe kidney insufficiency. Not recommended in patients at risk for: ▪ Hypermagnesemia; or ▪ Rhabdomyolysis.
Trisulfate (magnesium sulfate, sodium sulfate, and potassium sulfate), also called oral sulfate solution (OSS)	Noninferior to high volume PEG, 2 L PEG ascorbate Superior to MCSP in a single RCT	Not recommended in patients with: ▪ Severe renal insufficiency (creatinine clearance < 30 mL/min); ▪ Congestive heart failure; or ▪ Ascites.

NYHA, New York Heart Association; RCT, randomized controlled trial.

P < 0.001; also in the right colon), significantly higher willingness to repeat bowel preparation (88.4 % vs. 78.1 %, P < 0.001), and fewer electrolyte disturbances; however in this last trial PEG plus ascorbate was administered in split-dose fashion, while OSP was administered as a day-before bowel preparation.

2 2 L PEG plus citrate (▶ Table 1)

More recently, a new formulation of 2 L PEG plus citrate and simethicone has become available. When this solution has been compared (in RCTs) with 4 L PEG, there was no difference in adequate bowel cleansing (73.6 % vs. 72.3 %, 95 %CI difference −7.5 to 10.1), safety, and compliance, but gastrointestinal tolerability was better for the low volume solution (25.4 % vs. 37.0 %, P < 0.01) and acceptability was higher (93.9 % vs. 82.2 %, P < 0.001) [100]. Moreover, when compared with 2 L PEG plus ascorbate, bowel cleansing (78.3 % vs. 74.3 %, P = 0.37), safety (including electrolyte measurement), acceptability (81.4 % vs. 80.8 %, P = 0.74), compliance, and willingness to repeat the same preparation were equivalent [101]. In both studies, the rates of adequate colon preparation were higher for all the products when administered according to the split-dose modality. Adenoma and polyp detection rates were not evaluated.

3 1 L PEG plus ascorbate (▶ Table 1)

A new 1 L PEG solution with a higher ascorbate concentration has been evaluated against MCSP, oral sulfate solution (OSS), and 2 L PEG plus ascorbate in three RCTs. These included patients aged between 18 and 85, with blinded central readers evaluating primary endpoints using validated scales.

Compared with MCSP, with both products taken in a day-before fashion [102], 1 L PEG plus ascorbate demonstrated nonin-

ferior overall cleansing (62.0% vs. 53.8%; $P=0.04$) and high quality cleansing in the right colon (4.4% vs. 1.2%; $P=0.03$) in the intention-to-treat analysis (and superiority in the per-protocol analysis), along with noninferior polyp and adenoma detection rates. Tolerability and adherence were high (but the latter was higher with MCSP), despite a higher rate of mild adverse events in the 1l PEG plus ascorbate group (17.0% vs. 10.0%; $P=0.03$).

When compared with OSS in a split-dose schedule [103] 1L PEG plus ascorbate was noninferior in terms of successful bowel cleansing (85.1% vs. 85.0%; $P=0.53$) and high quality cleansing of the right colon (35.9% vs. 29.3%; $P=0.06$). No difference was demonstrated in polyp and adenoma detection rates, adherence, overall tolerability and safety.

Finally, when 1L PEG plus ascorbate in split-dose and same-day fashion was compared with split-dose 2L PEG plus ascorbate [104], noninferiority of 1L PEG plus ascorbate in both regimens was established in the intention-to-treat analysis. Furthermore, superiority was demonstrated in the per-protocol analysis of overall success of split-dose 1L PEG plus ascorbate (97.3% vs. 92.2%; $P=0.01$) and of high quality right colon cleansing for both split-dose and same-day 1L PEG plus ascorbate regimens vs. 2L PEG plus ascorbate. Polyp and adenoma detection rates were also noninferior. Adherence, tolerability, and safety (including blood and urinary values) were comparable between arms, despite a higher rate of vomiting in the same-day regimen arm compared with the split-dose 2L PEG ascorbate regimen (6.3% vs. 1.1%, $P=0.002$).

4 2L PEG plus bisacodyl (▶ Table 1, Table 8s)

One meta-analysis [105] of 6 RCTs found that, compared with 4L PEG, 2L PEG plus bisacodyl (10–20 mg) provided similar bowel cleansing with no difference in abdominal pain, but was associated with less nausea, vomiting, and bloating.

After this meta-analysis was published, seven RCTs evaluated the addition of bisacodyl to PEG [88, 106–111] compared with 4L PEG and 2L PEG plus ascorbate. Two RCTs further evaluated whether the addition of bisacodyl could lower the required volume of PEG plus ascorbate to 1L [88, 111], using 2L PEG plus ascorbate as comparator. Three RCTs [106, 107, 109] evaluated the addition of bisacodyl to PEG plus citrate plus simethicone.

All these trials, except one [106], demonstrated no substantial difference in overall colon cleansing, but improved tolerability only in RCTs using higher volumes of PEG as comparator. No difference was demonstrated in head-to-head comparison of split-dose 2L PEG plus ascorbate with split-dose 2L PEG plus bisacodyl [108]).

Safety

Solutions containing aspartame and ascorbate (such as 2L and 1L PEG plus ascorbate solutions) are contraindicated in patients with phenylketonuria or glucose-6-phosphate dehydrogenase deficiency [112]. These products are not recommended in patients with renal insufficiency and creatinine clearance <30 mL/min and in patients with New York Heart Association (NYHA) III or IV congestive heart failure. A high rate of hypernatremia has been observed following the administration of 1L PEG plus ascorbate, primarily due to the sodium content of the product. For this reason, additional clear liquids are recommended. Hyponatremia cases have been described with 2L PEG ascorbate; this prompted caution in patients at risk of electrolyte disturbances.

In solutions where PEG is associated with citrate and simethicone, caution is suggested if the products are administered in patients with creatinine clearance <30 mL/min, NYHA III or IV congestive heart failure, unstable angina, or acute myocardial infarction. In the case of symptoms of electrolyte disturbances or in an at-risk patient, laboratory evaluation of electrolytes and renal function must be considered before and after the regimen. As these are low volume hyperosmotic formulations, attention must be paid to encourage the intake of additional liquids to prevent dehydration and electrolyte imbalance.

Even though specific or statistically significantly different adverse events have not been reported in the bisacodyl arms of the aforementioned RCTs, cases of ischemic colitis have been reported following the intake of >5 mg bisacodyl [113–115].

Magnesium citrate with sodium picosulfate (MCSP) (▶ Table 1, Table 9s)

Efficacy

Magnesium citrate with sodium picosulfate was compared with PEG and with OSP in two meta-analyses [116, 117], including 6 and 13 studies, respectively. In the study by Tan & Tjandra [116], MCSP provided satisfactory colon cleansing in a similar proportion of patients compared with PEG, with less frequent adverse events. However OSP produced better colon cleansing than MCSP. In the study by Lieshout et al. [117], which included only RCTs in which colon cleansing was rated according to a validated scale, MCSP provided a slightly better quality of bowel cleansing compared with PEG (RR 1.06, 95%CI 1.02–1.11); this was lost however when MCSP was compared with 4L PEG only. Moreover, MCSP was better tolerated than PEG, with a higher capability of completing the preparation.

In the most up-to-date meta-analysis [118], including 25 RCTs comparing MCSP with PEG (but with different regimens), no difference was found in colon cleansing, polyp detection rate, and ADR. However adverse events were less frequent in the MCSP group (RR 0.78, 95%CI 0.66–0.93; i.e. nausea, vomiting, bloating, but not dizziness), and a higher proportion of patients were likely to complete the MCSP regimen (RR 1.08, 95%CI 1.04–1.13) and willing to repeat the same regimen (RR 1.44, 95% CI, 1.25–1.67).

Since the most up-to-date meta-analysis, four RCTs [94–97] have been published that included comparisons between split-dose MCSP vs. split-dose 2L PEG plus ascorbate (with/without 10 mg bisacodyl); these demonstrated overall high rates of adequate preparation without significant differences between the two regimens. One recent RCT [119] compared 4L PEG vs. MCSP in a primary screening setting, including 13 497 patients. Adequate bowel preparation was more frequent in the PEG than in the MCSP group (86.4% vs. 79.0%; $P<0.001$). However, a split regimen was not systematically recommended for either product.

Safety

Because of hyperosmolarity and magnesium content, solutions containing MCSP are contraindicated in patients with congestive heart disease, hypermagnesemia, rhabdomyolisis, gastrointestinal ulcerations, and severe impairment of renal function, which can lead to magnesium accumulation. In a retrospective population-based study, using administrative data and enrolling >65-year-old patients, compared with PEG, MCSP was associated with an increased risk of hospital admission due to hyponatremia [120]. In a post hoc analysis of two RCTs investigating MCSP regimens (excluding patients with basal renal insufficiency), 10 % of patients had slightly above normal magnesium levels, but this produced no clinically significant effect on monitored cardiac conduction, including in those patients with mild-to-moderate renal impairment [121]. There have been reports of acute gastric and esophageal injury caused by undissolved or poorly dissolved MCSP powder [122].

Oral sulfate solution (OSS) (trisulfate; ▸ Table 1)

Efficacy

Recently, a formulation of magnesium sulfate, sodium sulfate, and potassium sulfate (also called oral sulfate solution [OSS] or trisulfate) has become available in Europe.

This preparation was compared with 4 L PEG in three RCTs [123 – 125]. Overall, these trials showed the noninferiority of split OSS versus split high volume PEG in terms of efficacy, a high OSS safety, and better tolerability. In addition, three RCTs compared OSS with 2 L PEG plus ascorbate and showed similarly high efficacy when both regimens were used in split or same-day regimens [126 – 128].

OSS has also been compared with MCSP in one RCT [129], using the two products in split-dose fashion, and demonstrated better cleansing success in the OSS group.

Safety

OSS is contraindicated in patients with congestive heart disease, ascites, and severe renal insufficiency (glomerular filtration rate < 30 mL/min). Data are scarce regarding OSS in the setting of renal insufficiency and liver failure. Clinically significant electrolyte disturbances and kidney injury or significant creatinine elevation have not been reported to date [130]. However real-life clinical experience with these solutions is limited and prudence is mandatory. Because of the potential risk of hydroelectrolytic disturbances, laboratory evaluation of electrolytes and renal function may be appropriate before and after the procedure in at-risk patients. Adequate hydration must be encouraged in all patients.

These solutions may also cause transient elevation of uric acid levels, which must be considered in patients affected with hyperuricemia or gout.

Laxatives in elderly people

There is insufficient evidence to recommend a specific product for elderly people. Osmotically balanced PEG solutions are theoretically the safest, and are preferred in these patients [153]. However high volume products are thought to be particularly poorly tolerated in elderly patients. Even if compliance may be increased with specific measures, the most relevant being the adoption of a split-dose regimen, future research must focus on the safety profile of low volume regimens in the elderly population.

Two RCTs specifically enrolled elderly patients. In one study [60] comparing 2 L PEG ascorbate with 4 L PEG and enrolling more than 200 patients aged > 65 years with normal renal function and electrolytes, no increases in adverse events were found (but no laboratory evaluation was done after the regimen), along with comparable cleansing efficacy and higher willingness to repeat the regimen. One RCT [125] randomized almost 200 patients, aged between 65 and 75 and without systemic co-morbidities, to receive OSS or 4 L PEG both in a split-dose fashion. No differences in frequency of acute kidney injury or significant electrolyte changes were found, along with very high and not different cleansing success between the two groups and significantly higher willingness to repeat the OSS regimen.

RCTs of 1 L PEG ascorbate against OSS [103], MCSP [102], and 2 L PEG ascorbate [104] included a proportion of patients aged between 65 – 85 years without systemic co-morbidities, but safety outcomes were not specifically reported for these subgroups.

At-risk patients and laxatives

Even if all cleansing regimens are associated with the risk of dehydration and potential electrolyte imbalances (even caused only by vomiting), hyperosmotic preparations may further increase these risks in at-risk populations, such as patients with chronic renal insufficiency, congestive heart failure, or liver failure with ascites. Although the majority of RCTs exclude such patients, PEG solutions with osmotically balanced electrolytes are often selected, on account of their safety profiles, for patients in these categories [154].

Only retrospective cohorts have found relative safety of PEG in patients with impaired renal function compared to other formulations (e. g. vs. OSP [155]). In one retrospective cohort, patients with glomerular filtration rate < 60 mL /min ingested either 4 L PEG or 2 L PEG ascorbate solutions [156]. No statistically significant change in electrolytes or blood urea nitrogen or increase in creatinine was found after intake of either preparation. Comparing the regimens, a transient > 30 % increase in creatinine levels was found in 7.5 % of 4 L PEG patients and in 11.5 % of 2 L PEG plus ascorbate patients; this was not statistically significantly different [156].

Patients with creatinine clearance > 30 mL/min have generally been included in RCTs evaluating PEG plus ascorbate solutions. Further data are needed to recommend a specific regimen in this setting.

Oral sodium phosphate (OSP)

RECOMMENDATION
ESGE recommends against the routine use of oral sodium phosphate for bowel preparation.
Strong recommendation, low quality evidence.

Safety

The most feared adverse event following oral sodium phosphate (OSP) intake is kidney injury. The largest report of kidney injury (21 patients) described the development of acute renal failure within a few weeks after colonoscopy; this modestly improved over time and required renal replacement therapy in four of the patients [131]. A meta-analysis of 7 controlled studies (12 168 patients) that compared the effect of OSP vs. another bowel preparation on kidney function found no statistically significant association between OSP and kidney injury [132]. However, these studies were usually not powered to detect rare serious complications and their tight control of inclusion criteria tended to exclude individuals at risk for complication development. Moreover, between January 2006 and December 2007, 171 cases of renal failure were reported to the United States Food and Drug Administration (FDA) following the use of OSP and 10 following the use of PEG [131]. A retrospective, population-based national analysis in Iceland estimated that the risk of biopsy-proven acute phosphate nephropathy is approximately 1 per 1000 OSP doses sold [131]. Another severe complication of OSP for bowel preparation consists of acute disruption of electrolyte homeostasis, including hyperphosphatemia, hypocalcemia, hypokalemia, and hyper- or hyponatremia. The spectrum of clinical presentation varies from mild symptoms related to hypocalcemia to death [131].

Generally accepted contraindications specific to OSP for bowel preparation include the following as absolute contraindications: pregnancy, age <18 years, stage 3–5 chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m^2), inability to maintain adequate fluid intake, pre-existing electrolyte disturbances, ascites, symptomatic congestive heart failure, and recent (within <6 months) symptomatic ischemic heart disease (unstable angina or myocardial infarction). Relative contraindications include active inflammatory bowel disease, parathyroidectomy, and delayed bowel transit [133–137]. In addition, recognized risk factors for acute phosphate nephropathy following the use of OSP include age >55 years, hypovolemia, baseline kidney disease, bowel obstruction, or active colitis, as well as intake of drugs that affect renal perfusion or function such as diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers and, possibly, nonsteroidal anti-inflammatory drugs [133–137].

Care should be taken in individuals with presumably normal renal function because unrecognized chronic kidney disease may affect a large proportion of older individuals (up to 23%–36% of people aged 65 years or older) [138, 139].

Strategies recommended to prevent acute phosphate nephropathy include: avoidance of OSP in high risk patients; screening for unrecognized chronic kidney disease and electrolyte imbalances; avoiding dehydration before, during, and after OSP administration; minimizing the dose of OSP; and maintaining a minimum of 12 hours between the administration of the two OSP doses [140]. It is the prescribers' responsibility to ensure that the patient understands the importance of maintaining an adequate fluid intake [134]. Renal function should be checked as close to the colonoscopy appointment as practically possible, but in any case within 3 months.

Efficacy (**Table 10s**)

Overall, seven meta-analyses, published over an 18-year period (1998–2016), have compared oral sodium phosphate with PEG [116, 141–146]. In the latest meta-analysis including only RCTs comparing OSP and PEG [146], the two regimens demonstrated no difference in the rate of adequate preparation (7 studies, 1128 patients for efficacy assessment), but better scores for OSP when only studies using the Ottawa Bowel Preparation scale were considered. With the OSP regimen, compliance was higher as well as acceptability, with better taste and with less nausea, vomiting, and abdominal pain, and with no statistically significant difference in post-procedural electrolyte imbalance and creatinine levels between the two regimens.

Since the latest meta-analyses, one RCT [147] has been published that compares OSP tablets vs. 4 L PEG, both prescribed in split-dose fashion in a selected population without contraindications and severe co-morbidities. The trial showed no difference in colon cleansing efficacy, in polyp detection rate, or in the rate of any adverse events; compliance to the regimen was slightly in favor of OSP tablets, and ingestion was considered significantly easier in that group. Thus, if OSP is used, 90 mL solution or 32 tablets each containing 1.5 g sodium phosphate, both in a split-dose regimen, is to be preferred [148–152].

Specific categories of patients

Patients with constipation

RECOMMENDATION
ESGE does not suggest any specific bowel preparation in patients with constipation.
Weak recommendation, low quality evidence.

Chronic constipation has been identified as one of the risk factors for inadequate bowel preparation. Despite the low quality of the evidence, additional bowel purgatives are often considered in patients with chronic constipation who are about to undergo colonoscopy. Since 2013, only five studies have specifically addressed special regimens for constipated patients. However, these few studies are heterogeneous, comparing different bowel preparations, volumes, timings, and adjunctive treatments. There is neither any meta-analysis nor multicenter RCT.

One well-designed RCT in 400 patients with chronic constipation compared 2 L PEG plus citrate plus simethicone plus 2-day bisacodyl vs. 4 L PEG and showed no significant differences

between groups [157]. Another RCT that included constipated and nonconstipated patients [158] compared four different regimens: OSP vs. OSP plus bisacodyl vs. PEG 4 L vs. PEG 2 L plus bisacodyl. The authors reported no statistically significant differences between groups, but when analyzing only constipated patients (n = 65), they found that 45 mL OSP plus 20 mg bisacodyl was significantly superior to the 4-L PEG preparation (95 % of patients had satisfactory colon cleansing vs. 66 %, respectively; $P = 0.03$). One nonrandomized study including 372 patients, of whom 65 had constipation, compared 4 L PEG vs. 2 L PEG plus ascorbate, both in split dose [159]. Based on the Aronchick scale for quality of bowel preparation, the authors did not find statistically significant differences between groups, either in constipated or nonconstipated patients. However, several methodological issues were not clarified. Another nonrandomized Turkish study [160] in 227 patients with constipation (constipation not clearly defined) evaluated the addition of a 200-mL enema to standard preparation with sennoside. They compared three groups: enema before preparation, enema after preparation, and standard preparation (no enema). They did not find overall differences between groups. However, in constipated women, enema before preparation was superior to the other regimens.

In conclusion, evidence is still lacking that would allow recommendation of a special regimen or supplemental treatment for bowel preparation in patients with chronic constipation. Low volume PEG and OSP seem to be better tolerated than 4 L PEG with no differences regarding efficacy. Despite good results regarding OSP preparations in terms of tolerance, compliance, efficacy, and safety profile in one study, these results are irrelevant in our setting given that the use of OSP is not recommended by current guidelines because of its safety profile [14, 161]. There is no additional evidence to recommend using bisacodyl or enemas as complementary measures in bowel preparation. In special cases, such as cystic fibrosis, more intensive regimens have been suggested [162], but additional evidence is needed.

Patients with inflammatory bowel disease (IBD)

RECOMMENDATION

ESGE recommends high volume or low volume PEG-based bowel preparation in patients with inflammatory bowel disease (IBD).

Strong recommendation, high quality evidence.

Colon cleansing in inflammatory bowel diseases is critically important both for disease assessment and detection of dysplasia. Recently the promotion of chromoendoscopy in international guidelines has made high quality bowel preparation even more crucial [163]. Patients with IBD bear a heavy burden from colonoscopy for disease assessment and surveillance [164]. One in eight patients may experience a disease flare in the weeks following colonoscopy that may relate to the bowel preparation [165]. In an RCT of patients without colitis, sodium phosphate- or sodium picosulfate-based preparations resulted in a 10-fold increase in mucosal inflammation compared to PEG-based bowel preparation [166]. An observational study of 730 patients noted a 3.3 % rate of erosions or other inflammatory lesions in patients without IBD or without current nonsteroidal anti-inflammatory drug (NSAID) use, that was related to sodium phosphate-based bowel preparation [167].

Limited comparative data are available for bowel preparation efficacy and tolerability in colitis. A recent 2017 meta-analysis identified four fully published comparative studies [168]; no more studies were identified after further searches. One study from the 1980s compared the use of bowel preparation regimens that would not be acceptable in contemporary practice (castor oil vs. high dose senna) [169], and one examined the use of addition of simethicone to PEG-based preparation to reduce bubbling [170]. Two further studies looked at high volume vs. low volume PEG plus adjuvant (ascorbic acid or bisacodyl) preparation [171, 172]. Combining the latter two studies, which compared low volume PEG (≤ 2 L) plus adjuvant vs. high volume PEG (> 3 L), no significant difference in bowel cleansing was observed (OR 1.19, 0.52 – 2.71), though low volume regimes appeared more acceptable to patients (OR for willingness to repeat 5.11, 1.31 – 20.00). In an analysis restricted to split-dose high volume PEG vs. split-dose low volume PEG plus adjuvant, there was no difference in preparation quality (OR 0.84, 0.37 – 1.92). A Japanese RCT, presented as an abstract, that compared low volume PEG plus ascorbic acid vs. large volume PEG alone in patients with ulcerative colitis and Crohn's disease, found similar results in terms of similar or better cleansing with PEG plus adjuvant, and better patient acceptability (author contacted for full results) [173]. Only low volume 2 L PEG-based bowel preparations have been validated in this setting. Data for very low volume (< 2 L) PEG-based bowel preparation with adjuvants are awaited.

Current consensus guidelines recommend chromoendoscopy with targeted biopsies for IBD surveillance [161]. No study has yet focused on which preparation regimes are optimal for chromoendoscopy; however a recent case series noted that having a clear liquid diet for 24 hours pre-procedure led to a higher probability that preparation would be good enough to allow chromoendoscopy (OR 0.11, 95 %CI 0.01 – 0.85; $P < .034$) [174].

Pregnant/lactating patients

RECOMMENDATION

ESGE found insufficient evidence to determine for or against the use of specific regimens in pregnant/breastfeeding women. However, if colonoscopy is strongly indicated, PEG regimens may be considered, with tapwater enemas preferred for sigmoidoscopy.

Insufficient evidence to determine net benefits or risks.

Colonoscopy appears feasible and relatively safe in pregnancy when strongly indicated [175]. The use of PEG in pregnancy has not been extensively studied and it is unknown whether it can cause fetal harm; when used for treating constipation dur-

ing pregnancy, it is considered relatively safe. Because full colonoscopy is rarely indicated during pregnancy, tapwater enemas are recommended as bowel preparation for sigmoidoscopy.

No reported series allows any evaluation of the role of bowel preparation during lactation. If bowel preparation is strictly recommended, interrupting breastfeeding during and after bowel preparation may be an option.

Acute lower gastrointestinal bleeding (LGIB)

RECOMMENDATION

ESGE recommends PEG regimens for bowel preparation if urgent colonoscopy is scheduled for lower gastrointestinal bleeding (LGIB).

Strong recommendation, moderate quality evidence.

Preparation of the colon in the setting of acute lower GI bleeding facilitates endoscopic visualization, diagnosis, and treatment, and may reduce the risk of bowel perforation. Preparation for colonoscopy should include 4 – 6 L of a PEG solution or the equivalent, administered over 3 – 4 hours until the rectal effluent is clear [176 – 178]. The use of lower volume or alternative colon preparation solutions in the setting of LGIB has not been specifically addressed, but preliminary data seem encouraging [179].

Many patients with acute LGIB are unable to tolerate rapid colon preparation and thus a nasogastric tube can be placed to facilitate this process as long as the risk of aspiration is low. Aspiration precautions should be used particularly in older and debilitated patients. In addition, administration of a prokinetic/antiemetic agent immediately prior to initiating the colon preparation may reduce nausea and facilitate gastric emptying. Unprepped sigmoidoscopy/colonoscopy in the setting of acute LGIB is not recommended since cecal intubation rates and diagnostic yields are low, and poor visualization may increase the risk of perforation [176, 177].

Inadequate bowel preparation: management, inpatients, and risk factors

Management of inadequate bowel preparation

RECOMMENDATION

ESGE recommends early repetition of colonoscopy within 1 year in the case of inadequate bowel preparation, unless clinically contraindicated.

Strong recommendation, moderate level of evidence.

Same-day or next-day colonoscopy after additional preparation – with either laxative or enema – may be suggested. The next regimen of bowel preparation should be individualized according to the possible reasons for failure.

Weak recommendation, very low level of evidence.

Possible regimens for repeated colonoscopy

As already reported in the Introduction, patients with an inadequate cleansing must repeat the colonoscopy because of a high risk of clinically relevant lesions having been missed. The evidence on the efficacy of a next-day or same-day colonoscopy, after additional bowel preparation, compared with a later colonoscopy is limited and conflicting. In a single-center series of 235 patients with inadequate preparation, next-day colonoscopy vs. non-next-day rescheduled colonoscopy was associated with a reduced risk of secondary failure (OR 0.31, 95 %CI 0.1 – 0.92) [180]. This was not confirmed in a larger single-center series of 397 patients with inadequate procedure as recurrent failure was observed in 30 % of the next-day group and 23.5 % of the non-next-day group ($P = 0.48$) [181]. However, in a retrospective study on 3047 procedures with inadequate cleansing, patients advised to have next-day colonoscopy were more likely to adhere to the repeat colonoscopy recommendation [182].

In a single-center prospective nonrandomized study, 87 patients with inadequate preparation after an initial 4 L PEG received either an additional 2 L PEG on the same day or a 4 L PEG plus bisacodyl 1 week later after 3 days of a low residue diet, with no difference found between the two regimens [183]. In an observational study, 60 patients with inadequate preparation received a same-day repeat colonoscopy after receiving an additional laxative of 250 mL of senna alkaloids with 1.5 L of water [184]; the repeat colonoscopy reached the cecum in 83 % of patients.

A recent randomized trial showed the superiority of a high volume PEG-based regimen over a low volume PEG when associated with an intensive regimen of preparation [185].

Direct enema or irrigation

Direct administration of laxative enemas through the colonoscope into the right colon via the biopsy channel (133 mL/19 g phosphate enema plus 37 mL/10 mg bisacodyl enema, 10 patients; two 37 mL/10 mg bisacodyl enemas, 11 patients) was reported to be effective in 21 patients with inadequate preparation after low volume PEG and bisacodyl preparation [186]. In a similar study, 26 patients with inadequate preparation after low volume PEG received 500 mL PEG into the right colon via the colonoscope biopsy channel. Overall, preparation was successful in 25 patients [187].

On the other hand, a randomized trial compared 1 L PEG enema administered through the colonoscope to the additional oral ingestion of 2 L PEG in 125 patients with inadequate preparation. An appropriate preparation was obtained in 35 out of 66 (53 %) in the enema group vs. 53 out of 67 (81 %) in the oral group, with respective Boston Bowel Preparation Scale scores of 6.3 vs. 7.4 ($P < 0.001$) [188].

In a single-center study, 42 patients with inadequate preparation were randomized to receive either pump irrigation with a 650 mL/min flow rate (Jetprep; Herzliya, Israel) or syringe irrigation with 30 – 50-mL aliquots. Pump irrigation was superior in improving per-procedure preparation with a significant difference in the right colon [189].

Other approaches

Surveys showed that additional ingestion of the same or a different preparation, additional instillation through the colonoscope, and additional enema are useful, as are rescheduled subsequent colonoscopy with the same or different preparation, or the same preparation but with better observance of diet [190–193].

Careful assessment of the primary reason for failure of the previous preparation, such as vomiting, poor adherence, and risk factors for inadequate cleansing, is recommended before prescribing a new regimen.

Bowel preparation in inpatients

RECOMMENDATION

ESGE recommends specific verbal or written instructions to patients and to clinic staff caring for hospitalized patients, to improve the quality of bowel preparation.
Strong recommendation, moderate quality evidence.

One recent systematic review and meta-analysis [194] summarized the evidence from eight RCTs and nine observational cohort studies (**Table 11s**). In this systematic review, included studies were arbitrarily classified according to the intervention used for improving bowel cleanliness as: (a) education of patients and/or personnel regarding bowel preparation; (b) modification of preparation regimen; and (c) other interventions. Colon cleansing that was adequate (or an equivalent measure calculated from the available data) was achieved in 67 % (95 % CI [60–75]%) of patients overall; in 77 % (62–91)% of the intervention group in the studies assessing the impact of educational interventions vs. 50 % (32–68)% of the controls; in 71 % (60–81)% of the participants with various preparation regimens; and in 55 % (22–87)% in the single study examining the administration of bowel preparation through esophagogastroduodenoscopy. The heterogeneity of the various cathartics used and the variation in timing of their administration, and the existence of only a single study in the third intervention group precluded meta-analysis of study results for intervention categories (b) and (c).

Regarding the effect of specific educational intervention, patients in the intervention arms received either brief counselling and written instructions or an educational booklet [195, 196], while in three studies [197–199] leaflets, lectures, and/or presentations were used to educate personnel involved in patients' preparation. Finally, in one study [200], both personnel and patients were educated. Among these studies the OR (95 %CI) of achieving adequate colon cleansing was 3.49 (1.67–7.28) in the intervention group compared to the standard practice group. Inconsistences in the reporting of ADR, adverse events, tolerance, and willingness of patients to repeat the preparation preclude conclusions on the value of the interventions for these outcomes.

There is evidence that the rate of inadequate bowel preparation in inpatients undergoing colonoscopy is high, although several interventions have been implemented to address the problem. There is moderate evidence that educational interventions provided to patients and health care personnel may improve colon cleansing.

Risk factors for inadequate bowel cleansing

RECOMMENDATION

ESGE found insufficient data to recommend the use of specific predictive models for inadequate bowel preparation in clinical practice.

Inadequate colon preparation has been reported in up to 18 %–35 % of patients undergoing colonoscopy [201, 202]. Overall, 5 RCTs, 20 prospective and 12 retrospective observational studies, as well one case-control and one study of unknown design attempted to identify predictors of preparation failure (**Table 12s**) using multivariate analysis. Moreover, two recent meta-analyses including 67 and 24 studies with more than 75 000 and almost 50 000 participants, respectively, evaluated independent risk factors identified in the literature up to 2016 [201, 202]. The authors acknowledged the limitations of their analyses because of the high heterogeneity for all outcomes and because of the mix of RCTs and various types of non-interventional studies. Patients' baseline characteristics (increasing age and male gender), clinical conditions (constipation, diabetes mellitus, hypertension, cirrhosis, stroke, and dementia), and medication use (narcotics and tricyclic antidepressants) were identified as predictors of colonoscopy preparation failure in both meta-analyses. On the other hand, both meta-analyses failed to identify previous abdominal surgery as a predictor, while there were inconsistent results regarding body mass index (BMI) and history of colon preparation failure (**Appendix 4s**).

Identification of risk factors for poor bowel cleansing would have the potential benefit of selecting patients who need more intensive bowel preparation. Thus, three models have been developed so far using these factors to correctly predict adequate colon cleansing [203–205]. Hassan et al. built their model on patient-related risk factors identified in a multicenter prospective study of 2811 consecutive patients who underwent colonoscopy. The model was established in the exploratory group (randomly half of the included population) and validated in the rest of the participants; the area under the curve of the logistic regression model for predicting adequate bowel preparation was 0.63 [203]. A total of 1331 colonoscopies were included in the development cohort of a Dutch study that identified American Society of Anesthesiologists (ASA) score ≥ 3, use of tricyclic antidepressants or opioids, diabetes, constipation, previous abdominal and/or pelvic surgery, history of inadequate bowel preparation, and hospitalization as independent predictors for inadequate bowel preparation. These factors were included in the prediction model with a discriminative ability indicated by an area under the curve of 0.77 in the validation cohort [205]. Finally, another model was developed using data from 667 consecutive Spanish outpatients. Antidepressant use, co-morbidity, constipation, and abdominal/pelvic surgery were included in

the model as independent predictors for inadequate cleansing. The model showed an area under the curve of 0.70 in a validation cohort that included 409 individuals [204]. So far, none of these predictive models have been tested in other than their validation cohort populations, and no study has attempted to apply a different regimen to patients presenting with risk factors for inadequate colon cleanliness.

There is moderate quality evidence that patients' epidemiological and clinical characteristics may predict colonoscopy preparation failure. However, no predictive model has been applied in clinical practice, so far.

Disclaimers

The legal disclaimer for ESGE Guidelines [16] applies to this Guideline.

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Competing interests

R. Benamouzig has provided consultancy to Alfasigma. R. Bisschops has received speaker's fees from Norgine (1 January 2017 to present); he is Co-Editor of *Endoscopy*. E. Dekker is Co-Editor of *Endoscopy*. M. Dinis-Ribeiro is Co-Editor-in-Chief of *Endoscopy*. J. East received a speaker fee from Falk (January 2018); his department received support from Boston Scientific (March 2018 to March 2019). I. Gralnek declares consultancy, MAB, and share ownership in Motus GI (2014 to present). C. Hassan provides consultancy to Norgine; his department receives support from Alfasigma. R. Jover has received travel grants from Norgine (2015 to 2019); he has provided advisory services to Norgine (2015 to 2019), Alfasigma (2017 to 2018), GI Supply (2018 to 2019), and CPP Pharmaceuticals (2019); his department has received research grants from MSD (2010 to 2019). M.F. Kaminski has provided speaking and teaching services to Olympus, Alfasigma, and Norgine (2017 to present) and Fujinon (2018 to present), consultancy to Olympus (2017 to present), and advisory services to Alfasigma (2017 to present). M. Pellisé has received consultancy fees from Norgine Iberia (2012 to 2017, 2019 to present), and speaker's fees from Casen Recordati (2018) and Olympus (2017); her department has been loaned equipment from Fujifilm (2017 to present); she is on the *Endoscopy* Board. F. Radaelli has received consultancy fees from Norgine (January 2018 to December 2018). C. Spada has received consultancy fees from Norgina and Alfasigma (2016 to 2019). J.E. van Hooft has received lecture fees from Medtronics (2014 to 2015) and Cook Medical (2019), and consultancy fees from Boston Scientific (2014 to 2017); her department has received research grants from Cook Medical (2014 to 2018) and Abbott (2014 to 2017). H. Awadie, M. Bretthauer, J.-M. Dumonceau, M. Ferlitsch, L. Frazzoni, L. Fuccio, C. Mangas-Sanjuan, K. Triantafyllou, and G. Vanella have no competing interests.

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