# 1 Bowel preparation and quality of colonoscopy

*Franco Radaelli*

Colorectal cancer (CRC) is recognized as a significant health problem in both developed and developing countries and a major cause of cancer-related morbidity and mortality across the globe.[1] It represents the third most common cancer worldwide and the second most common cause of cancer death, accounting for an estimated 1.8 million new cancer diagnoses and >880,000 deaths in 2018.[2] Due to its slow progression from detectable precancerous lesions and to the much better prognosis of patients diagnosed at early stages, the potential for reducing the burden of the disease by early detection is significant. Organized screening programs are being implemented worldwide, and they have been shown to reduce the CRC-associated mortality, although their effectiveness is jeopardized by a multitude of factors, including the limitations of test performance, lack of accessibility, and suboptimal screening compliance.[3, 4]

Though several options are available as alternatives to colonoscopy for CRC screening, it maintains a pivotal role in any screening program, because the reduction of incidence and mortality of CRC eventually depend on the removal of colorectal neoplastic lesions by endoscopic polypectomy.[5-10] The effectiveness of colonoscopy in CRC prevention mostly depends on the quality of the examination (*i.e.*, the accuracy in detection colorectal neoplasia) and on patient adherence to the procedure itself, which are both largely affected by bowel preparation.[11] Thus, optimizing bowel preparation in terms of efficacy and acceptance plays a key role in increasing the effectiveness of colonoscopy in CRC prevention (**FIGURE 1.1**).

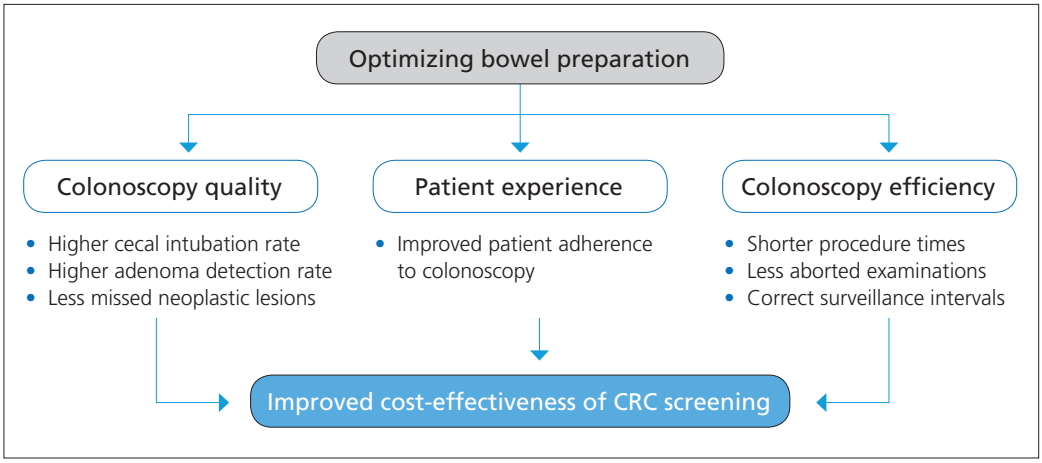



**FIGURE 1.1** Bowel preparation and the cost-effectiveness of colonoscopy in colorectal cancer (CRC) screening.

## Bowel preparation and diagnostic yield of colonoscopy

While colonoscopy is considered the "gold standard" for detection of CRC and its precursors, the effectiveness of colonoscopy in CRC protection is suboptimal.[12, 13] Post-colonoscopy interval cancers (namely, a cancer diagnosed before the recommended surveillance interval) occur, especially in the right colon, and they account for approximately 3.4-9% of all cases of CRC.[14] There are several possible reasons that can explain the occurrence of interval cancers, including biological variation in tumor growth rates and incomplete polyp resection. However, most of them arise from neoplastic lesions that are missed during the examination.[15-18] A recent meta-analysis of 43 studies and more than 15,000 tandem colonoscopies reported a miss rate of 26% for adenomas, 9% for advanced adenomas, and 27% for serrated lesions. The miss rate is particularly high for proximal advanced adenomas (14%) and flat adenomas (34%).

Inadequate colon cleansing, which prevents a meticulous inspection of the mucosa, largely contributes to the risk of missing lesions. This has been elegantly demonstrated in a prospective, observational study evaluating the miss rates of adenomas according to the scores of bowel cleansing, evaluated through the Boston Bowel Preparation Scale (BBPS). The study included 438 male subjects undergoing two different colonoscopy examinations within 60 days by a different blinded endoscopist. The proportion of miss rates of adenomas >5 mm in the first examination was comparable for segments with BBPS scores of 2 (good bowel preparation) versus those with BBPS scores of 3 (excellent bowel preparation). However, the miss rate of adenomas >5 mm in segments with BBPS scores of 1 (fair bowel preparation) was three times higher than in those with BBPS scores of 2 or 3, suggesting that the pursuit of higher levels of bowel prep is crucial to optimize adenoma detection.[19] Another prospective study from the same group aimed at evaluating the detection rate of sessile serrated lesions (SSLs) according to different levels of bowel preparation quality, demonstrated a two-fold higher detection rate of right-sided SSLs in patients with BBPS scores of 3 than scores of 2. This study confirms the need for the highest levels of bowel prep to correctly identify flat lesions with neoplastic potential.[20]

Several studies have also demonstrated a strict association between the quality of colon cleansing and the adenoma detection rate (ADR, namely the number of patients found with at least one pre-cancerous adenomatous polyp divided by the overall number of patients undergoing screening colonoscopy), which is widely accepted as the most robust quality metric of colonoscopy due to its strict association with the risk of post-colonoscopy interval cancer and CRC-related mortality.[21, 22] Kaminski *et al.*[23] further reinforced the importance of the ADR as a quality measure. They showed that the increased of ADR resulted in a 37% and 49% reduced risk of incidence of interval CRC and cancer death, respectively.[23] In a large observational Italian study including 75,569 screening subjects undergoing colonoscopy for positive fecal immunochemical test, inadequate bowel preparation reduced the ADR by 35%.[24] A recent meta-analysis, including 21 studies summarizing 247,277 colonoscopies regarding overall detection of colonic lesions and 10 studies summarizing 122,958 colonoscopies regarding advanced lesions, demonstrated that with inadequate bowel preparation, the chance of detecting early and advanced polyps drops by 44% and 23%, respectively. With

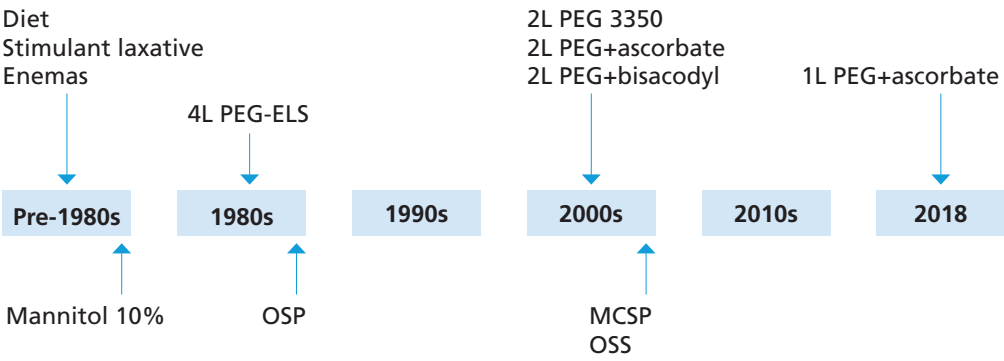
suboptimal preparation, detection of early lesions is reduced by 20%, and advanced lesions also tend to be detected less frequently.[25] According to these data, optimizing colon cleansing is crucial to maximize the visualization of mucosal lesions and the ADR and, ultimately, the colonoscopy effectiveness in CRC prevention.

## Bowel preparation and patient attitude toward colonoscopy

While screening has been demonstrated to reduce the incidence and mortality for CRC and screening programs have been implemented in various countries, the participation rate remains disappointingly low and compliance with colonoscopy referral is suboptimal.[26] Several factors have been posited as responsible for the low adherence to CRC screening and poor colonoscopy compliance, including lack of physician recommendation, gaps in knowledge about screening, organizational problems, and obstacles arising from socioeconomic status.[27-30] Among them, patient barriers to colonoscopy figure prominently. Many patients feel embarrassed to undergo the procedure and have misconceptions about the procedure-related discomfort and risk, overestimating the likelihood of experiencing pain during the procedure and perceiving the procedure as too invasive. They are also reluctant to prepare for a colonoscopy, considering bowel preparation as the most burdensome aspect of the procedure, sometimes even worse than the examination itself. From a patient perspective, bowel preparation is undoubtedly a major reason why a significant proportion of the population avoids colonoscopy.[31]

The role of bowel preparation in the patients' attitude toward colonoscopy has been recently evaluated in a survey conducted in five European Union countries – France, Germany, Italy, Spain, and the United Kingdom – among 2,500 subjects who had never had a colonoscopy (colonoscopy-naïve respondents) and 500 subjects who had had a colonoscopy in the last five years (colonoscopy-experienced respondents). Forty-seven percent of colonoscopy-experienced respondents believed that the bowel preparation had been the "worst part" of the process, while only 26% of colonoscopy-naïve respondents expected it to be. These data confirm that bowel preparation really represents a negative experience for many patients who have undergone the procedure, but also indicate that colonoscopy-naïve respondents may be underestimating the discomfort of bowel preparation. A contributing factor to this underestimation may be that colonoscopy-naïve respondents tended to misjudge the volume of bowel preparation fluid needed. Indeed, among colonoscopy-naïve respondents, 67% thought that 1 L of bowel preparation fluid or less needed to be drunk whereas, historically, 2 L or more of bowel preparation fluid has been required.[32]

The large volume of fluids to be taken within a short period of time, along with the unpleasant taste of the purgative solution, undoubtedly represents the most problematic aspect of bowel preparation. This is supported by several studies confirming that low-volume bowel preparations are better tolerated than high-volume ones.[33, 34] This factor also explains why in the last decade, low-volume bowel cleansing agents have increasingly replaced high-volume bowel preparation in the marketplace, and why new-generation, very-low-volume preparations are likely to gain increasing acceptance in the near future (**FIGURE 1.2**). However, the burden of bowel preparation may also be associated with other factors not necessarily related to the cleansing agent; these aspects may affect pre-procedural quality of life, such as dietary restrictions, im-




PEG: polyethylene glycol; ELS: electolyte lavage solution; OSP: oral sodium phosphate; OSS: oral sulfate solution (trisulfate); MCS: mMagnesium citrate with sodium picosulfate.

**FIGURE 1.2** The history of colon cleansing agents.

portant adjustments in work or social schedule, and sleep disturbances.[35] Thus, optimizing the tolerability of bowel preparation and, in turn, patient adherence to colonoscopy is a complex process in which the choice of the most appropriate cleansing agent, administration regimen (split- or single-dose regimens versus day-before regimen) and diet (low-fiber versus clear liquid diet) before colonoscopy play a key role, as highlighted in the subsequent chapters.

## Bowel preparation and efficiency of colonoscopy

Inadequate bowel preparation has detrimental effects not only on the quality of colonoscopy, but also on its efficiency. It represents the most unfavorable predictor for aborted or incomplete examinations that need to be rescheduled,[36-38] prolonged procedure time,[39, 40] and shortened surveillance intervals.[41, 42] Surveys have reported that in the setting of a poor preparation, endoscopists' recommendations for follow-up evaluation vary and err on shorter return intervals. In one study, 65 board-certified gastroenterologists and 13 gastroenterology fellows were shown images of preparations of "excellent to intermediate quality." With a "nearly perfect" preparation, a 10-year interval was generally 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[41]. A survey of 116 gastroenterologists 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.[42]

All the above-mentioned factors increase health care costs and reduce the efficiency of colonoscopy. Cost analysis has indicated that imperfect bowel preparation resulted in a 12% and 22% increase in costs of colonoscopy at university and public hospitals, respectively.[43] Based on these considerations, optimizing bowel preparation is crucial for reducing colonoscopy costs in clinical practice and improving its cost effectiveness for CRC screening.[44]

## REFERENCES


1. Vermeer N, Snijders H, Holman F, *et al.* Colorectal cancer screening: systematic review of screen-related morbidity and mortality. Cancer Treat Rev 2017;54:87-98.
2. Bray F, Ferlay J, Soerjomataram I, *et al.* Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
3. Kuipers EJ, Grady WM, Lieberman D, *et al.* Colorectal cancer. Nat Rev Dis Primers 2015;1:15065.
4. Kuipers EJ, Rösch T, Bretthauer M. Colorectal cancer screening – optimizing current strategies and new directions. Nat Rev Clin Oncol 2013;10:130-42.
5. Zauber AG, Winawer SJ, O'Brien MJ, *et al.* Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012;366:687-96.
6. Winawer SJ, Zauber AG, Ho MN, *et al.* Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 1993;329:1977-81.
7. Pox CP, Altenhofen L, Brenner H, *et al.* Efficacy of a Nationwide Screening Colonoscopy Program for Colorectal Cancer. Gastroenterology 2012;142:1460-7.e2.
8. Kahi CJ, Imperiale TF, Juliar BE, *et al.* Effect of screening colonoscopy on colorectal cancer incidence and mortality. Clin Gastroenterol Hepatol 2009;7:770-5.
9. Brenner H, Chang-Claude J, Jansen L, *et al.* Reduced risk of colorectal cancer up to 10 years after screening, surveillance, or diagnostic colonoscopy. Gastroenterology 2014;146:709-17.
10. Baxter NN, Goldwasser MA, Paszat LF, *et al.* Association of colonoscopy and death from colorectal cancer. Ann Intern Med 2009;150:1-8.
11. Hewett DG, Kahi CJ, Rex DK. Efficacy and effectiveness of colonoscopy: how do we bridge the gap? Gastrointest Endosc Clin N Am 2010;20:673-84.
12. Brenner H, Chang-Claude J, Seiler CM, *et al.* Protection from colorectal cancer after colonoscopy: a population-based, case-control study. Ann Intern Med 2011;154:22-30.
13. Baxter NN, Warren JL, Barrett MJ, *et al.* Association between colonoscopy and colorectal cancer mortality in a US cohort according to site of cancer and colonoscopist specialty. J Clin Oncol 2012;30:2664-9.
14. Reumkens A, Rondagh EJ, Bakker CM, *et al.* Post-Colonoscopy Complications: A Systematic Review, Time Trends, and Meta-Analysis of Population-Based Studies. Am J Gastroenterol 2016;111:1092-101.
15. le Clercq CM, Bouwens MW, Rondagh EJ, *et al.* Postcolonoscopy colorectal cancers are preventable: a population-based study. Gut 2014;63:957-63.
16. Anderson R, Burr NE, Valori R. Causes of Post-Colonoscopy Colorectal Cancers Based on World Endoscopy Organization System of Analysis. Gastroenterology 2020;158:1287-99.
17. Pohl H, Robertson DJ. Colorectal cancers detected after colonoscopy frequently result from missed lesions. Clin Gastroenterol Hepatol 2010;8:858-64.
18. Baxter NN, Sutradhar R, Forbes SS, *et al.* Analysis of administrative data finds endoscopist quality measures associated with postcolonoscopy colorectal cancer. Gastroenterology 2011;140:65-72.
19. Clark BT, Protiva P, Nagar A, *et al.* Quantification of adequate bowel preparation for screening or surveillance colonoscopy in men. Gastroenterology 2016;150:396-405.
20. Clark BT, Laine L. High-quality bowel preparation is required for detection of sessile serrated polyps. Clin Gastroenterol Hepatol 2016;14:1155-62.
21. Kaminski MF, Regula J, Kraszewska E, *et al.* Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med 2010;362:1795-803.
22. Corley DA, Jensen CD, Marks AR, *et al.* Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med 2014;370:1298-306.
23. Kaminski MF, Wieszczy P, Rupinski M, *et al.* Increased rate of adenoma detection associates with reduced risk of colorectal cancer and death. Gastroenterology 2017;153:98-105.
24. Zorzi M, Senore C, Da Re F, *et al.* Quality of colonoscopy in an organised colorectal cancer screening programme with immunochemical faecal occult blood test: the EQuIPE study (Evaluating Quality Indicators of the Performance of Endoscopy). Gut 2015;64:1389-96.

25. Zhao S, Wang S, Pan P, *et al.* Magnitude, risk factors, and factors associated with adenoma miss rate of tandem colonoscopy: A systematic review and meta-analysis. Gastroenterology 2019;156:1661-74.
26. Senore C, Basu P, Anttila A, *et al.* Performance of colorectal cancer screening in the European Union Member States: data from the second European screening report. Gut 2019;68:1232-44.
27. Hassan C, Kaminski MF, Repici A. How to Ensure Patient Adherence to Colorectal Cancer Screening and Surveillance in Your Practice. Gastroenterology 2018;155:252-7.
28. Wools A, Dapper EA, de Leeuw JRJ. Colorectal cancer screening participation: a systematic review. Eur J Public Health 2016;26:158-68.
29. Honein-AbouHaidar GN, Kastner M, Vuong V, *et al.* Systematic Review and Meta-study Synthesis of Qualitative Studies Evaluating Facilitators and Barriers to Participation in Colorectal Cancer Screening. Cancer Epidemiol Biomarkers Prev 2016;25:907-17.
30. Klabunde CN, Vernon SW, Nadel MR, *et al.* Barriers to colorectal cancer screening: a comparison of reports from primary care physicians and average-risk adults. Med Care 2005;43:939-44.
31. McLachlan SA, Clements A, Austoker J. Patients' experiences and reported barriers to colonoscopy in the screening context--a systematic review of the literature. Patient Educ Couns 2012;86:137-46.
32. Amlani B, Radaelli F, Bhandari P. A survey on colonoscopy shows poor understanding of its protective value and widespread misconceptions across Europe. PLoS One 2020;15:e0233490.
33. Xie Q, Chen L, Zhao F, *et al.* A meta-analysis of randomized controlled trials of low-volume polyethylene glycol plus ascorbic acid versus standard-volume polyethylene glycol solution as bowel preparations for colonoscopy. PLoS One 2014;9:e99092.
34. Spadaccini M, Frazzoni L, Vanella G, *et al.* Efficacy and Tolerability of High- vs Low-Volume Split-Dose Bowel Cleansing Regimens for Colonoscopy: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol 2020;18:1454-65.e14.
35. Sharara AI, El Reda ZD, Harb AH, *et al.* The burden of bowel preparations in patients undergoing elective colonoscopy. United European Gastroenterol J 2016;4:314-8.
36. Hsu CM, Lin WP, Su MY *et al.* Factors that influence cecal intubation rate during colonoscopy in deeply sedated patients. J Gastroenterol Hepatol 2012;27:76-80.
37. Radaelli F, Meucci G, Sgroi G *et al.* Technical performance of colonoscopy: the key role of sedation/analgesia and other quality indicators. Am J Gastroenterol 2008;103:1122-30.
38. Aslinia F, Uradomo L, Steele A, *et al.* Quality assessment of colonoscopic cecal intubation: an analysis of 6 years of continuous practice at a university hospital. Am J Gastroenterol 2006;101:721-31.
39. Froehlich F, Wietlisbach V, Gonvers JJ, *et al.* Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. Gastrointest Endosc 2005;61:378-84.
40. Burke CA, Church JM. Enhancing the quality of colonoscopy: the importance of bowel purgatives. Gastrointest Endosc 2007;66:565-73.
41. Ben-Horin S, Bar-Meir S, Avidan B. The impact of colon cleanliness assessment on endoscopists' recommendations for follow-up colonoscopy. Am J Gastroenterol 2007;102:2680-5.
42. Saini SD, Nayak RS, Kuhn L, *et al.* Why don't gastroenterologists follow colon polyp surveillance guidelines? Results of a national survey. J Clin Gastroenterol 2009;43:554-8.
43. Rex DK, Imperiale TF, Latinovich DR, *et al.* Impact of bowel preparation on efficiency and cost of colonoscopy. Am J Gastroenterol 2002;97:1696-700.
44. Kingsley J, Karanth S, Revere FL, *et al.* Cost effectiveness of screening colonoscopy depends on adequate bowel preparation rates - a modeling study. PLoS One 2016;11:e0167452.

# 2 Assessing the adequacy of bowel preparation: the bowel preparation quality scales

*Alida Andrealli*

Adequate bowel preparation is essential to ensure sufficient visualization of the colonic mucosa and to optimize lesion detection. However, in up to 25% of colonoscopies, preparation may be inadequate,[1, 2] and this is correlated with lower detection of polyps and adenomas.[3] Practical guidelines recommend that at least 85-90% of screening colonoscopies should be rated as having "adequate" or better bowel cleansing and that bowel preparation quality should be documented at the time of the examination.[4, 5] Adequate preparation carries the important implication that the recommended interval before the next colonoscopy will be consistent with guidelines. On the other hand, poor bowel preparation prolongs the cecal intubation time and withdrawal time, reduces polyp detection, and implies that the colonoscopy is repeated at shorter interval than what is usually recommended.[5]

As terms such as "adequate", "inadequate", "poor", "good", or "excellent" are subjective and do not have standardized definitions in clinical practice, several scales to assess more formally bowel cleanliness have been published over the past years (**TABLE 2.I**). Essential attributes of a bowel preparation quality scale include reliability and validity. *Reliability* refers to the degree to which an instrument yields reproducible results for the same investigator (intra-rater reliability) or among different investigators (inter-rater reliability). *Validity* indicates how well the scale is able to measure what it is designed to assess; it may be evaluated by comparison with the results of other established and accepted scales used for the same purpose in the same test population.[6] However, only a few of the existing bowel preparation scales have been formally validated to guide clinical management, and data on direct head-to-head comparisons of the performance and simplicity of the different scales are scant.[7]

## Bowel Preparation Scales

### Aronchick Scale

In 1999, the Aronchick Scale (AS) was the first bowel preparation quality scale to be evaluated for reliability.[8] This scale characterizes the percentage of the total colonic mucosal surface covered by fluid or stool and is performed before washing or suctioning (**TABLE 2.I**). Although the AS was a significant step forward to a standardized approach, it has some limitations. First, it requires the user to make quantitative assessments of the percentage of visible bowel mucosa, an approach that may lack of interobserver reliability. Second, the cleansing score is based on a global assessment of the entire colon, without scoring individual segments.[8] Athough some studies have demonstrated that inter-rater reliability is high for the cecum and the total colon, but low for the distal colon and the ascending colon segments.[8]

**TABLE 2.1** Different bowel preparation quality scales, modified from Kastenberg *et al.*[3]

| Bowel preparation scale | Score | Description | Characteristics |
|---|---|---|---|
| aronchick Scale | **1** (excellent) | Small volume of liquid; >95% of mucosa seen | Before washing/suctioning<br>Global colon rating<br>No cut-off (adeqaute/ inadequate) |
| | **2** (good) | Clear fluid covering 5-25% of mucosa, >90% of mucosa seen | |
| | **3** (fair) | Not removable semisolid stool, >90% of mucosa seen | |
| | **4** (poor) | Not removable semisolid stool, <90% of mucosa seen | |
| | **5** (inadequate) | Repetition needed | |
| Ottawa Bowel Preparation Scale | **0** (excellent) | Mucosal clearly visible, with no stool and no fluid/fluid clear | Before washing/suctioning<br>Rating by colon segment<br>No cut-off (adequate/ inadequate)<br>Total score: adding score for each segments and fluid score (0-2) for the whole colon |
| | **1** (good) | Some turbid fluid/stool, mucosa visible without suctioning/washing | |
| | **2** (fair) | Some turbid fluid/stool, mucosa visible with suctioning/washing | |
| | **3** (poor) | Stool obscuring mucosa, reasonable view with suctioning/washing | |
| | **4** (inadequate) | Stool obscuring mucosa | |
| Ottawa Bowel Preparation Scale (total colon fluid) | **0** | Small amount of fluid | Before washing/suctioning<br>Global colon rating |
| | **1** | Moderate amount of fluid | |
| | **2** | Large amount of fluid | |
| Boston Bowel Preparation Scale | **0** (inadequate) | Solid stool, mucosa not visible | After washing/suctioning<br>Segments separately rated<br>Total score: adding scores for each segments<br>Optimal cut-off ≥6 globally and ≥2 per segment |
| | **1** (poor) | Part of mucosa seen, but other areas not well seen because of not washable stool | |
| | **2** (good) | Minor amount of residue, mucosa well seen | |
| | **3** (excellent) | Entire mucosa well seen | |
| Harefield Cleansing Scale | **0** | Irremovable stools | After washing/suctioning<br>Segments separately rated<br>Total score: adding scores for each segments |
| | **1** | Semisolid, partially removable stools | |
| | **2** | Semi-solid/liquid fully removable stools | |
| | **3** | Clear liquid | |
| | **4** | Colon empty and clean | |
| Chicago Bowel Preparation Scale | **0** | Irremovable stools (>15% of mucosa not seen) | Before and after washing/ suctioning<br>Segments separately rated<br>Total score: adding scores for each segments<br>No cut-off (adeqaute/ inadequate) |
| | **5** | Part of mucosa seen after cleaning (up to 15% not seen) | |
| | **10** | Minor residue after cleaning (mucosa well seen) | |
| | **11** | Entire mucosa well seen after washing | |
| | **12** | Entire mucosa well seen before washing | |
| Chicago Bowel Preparation Scale (total colon fluid) | **0** | Little fluid (<50 mL) | Before washing/suctioning<br>No cut-off (adeqaute/ inadequate)<br>Not incorporated into total score |
| | **1** | Minimal fluid (51-150 mL) | |
| | **2** | Moderate fluid (151-300 mL) | |
| | **3** | Large amount (>300 mL) | |