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Original Article

Comparing the Real-World Effectiveness of High- Versus Low-Volume Split Colonoscopy Preparations: An Experience Through the British Columbia Colon Cancer Screening Program

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Abstract

Background: The British Columbia Colon Screening Program (BCCSP) is a population-based colon cancer screening program. In December 2018, physicians in Vancouver, Canada agreed to switch from a low-volume split preparation to a high-volume polyethylene glycol preparation after a meta-analysis of studies suggested superiority of the higher volume preparation in achieving adequate bowel cleansing and improving adenoma detection rates.

Aims: To compare the quality of bowel preparation and neoplasia detection rates using a high-volume split preparation (HVSP) versus a low-volume split preparation (LVSP) in patients undergoing colonoscopy in the BCCSP.

Methods: A retrospective review of patients undergoing colonoscopy through the BCCSP at St. Paul's Hospital from July 2017 to November 2018 and December 2018 to November 2019 was conducted. Inclusion criteria included age 50 to 74 and patients undergoing colonoscopy through the BCCSP. Variables collected included patient demographics and bowel preparation quality. Rates of bowel preparation and neoplasia detection were analyzed using chi-squared test.

Results: A total of 1453 colonoscopies were included, 877 in the LVSP group and 576 in the HVSP group. No statistically significant difference was noted between rates of inadequate bowel preparation (LVSP 3.6% versus HVSP 2.8%; $P = 0.364$). Greater rates of excellent (48.4% versus 40.1%; $P = 0.002$) and optimal (90.1% versus 86.5%; $P = 0.041$) bowel preparation were achieved with HVSP. The overall adenoma detection rate was similar between the two groups (LVSP 53.1% versus HVSP 54.0%; $P = 0.074$). LVSP demonstrated higher overall sessile serrated lesion detection rate (9.5% versus 5.6%; $P = 0.007$).

Conclusions: Compared to LVSP, HVSP was associated with an increase in excellent and optimal bowel preparations, but without an improvement in overall neoplasia detection.

Keywords: *Bowel preparation; Colonoscopy; Colon cancer screening*

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Introduction

Colorectal cancer (CRC) is the second most common cause of cancer death in Canadian men and the third in women (1). Every year, approximately 3000 people in British Columbia are diagnosed with colon cancer and 94% of these cases are in individuals aged 50 years or older (2). The risks of developing colon cancer are likely modifiable by factors such as diet, exercise and avoidance of smoking and alcohol consumption, but the cornerstones of its prevention is screening and detection of adenomatous polyps (3). Colon cancer screening has been effective in reducing incidence, morbidity and mortality from colon cancer (4,5). The Canadian Task Force on Preventative Health has recommended screening with either a fecal occult blood test every 2 years or flexible sigmoidoscopy every 10 years in individuals 50 to 74 years of age (6).

Bowel preparation is one of the quality indicators for colonoscopy (7,8). A poorly prepared colon interferes with the detection of adenomas (9,10). Therefore, an adequate bowel preparation is critical to view the colon for adenomas and to minimize the requirement for repeated procedures secondary to suboptimal visualization (8,11). Many commercially available bowel preparation regimens exist, each with its marketed advantages (12–14). While split dosing is known to yield more favourable bowel cleansing than day-before dosing (12,15), there has not been an established consensus guideline in British Columbia or in Canada as to which bowel preparation should be used. In 2015, a study looking at split-dose bowel preparation reported the potential superiority of high volume achieving better quality bowel preparation compared to low-volume split dosing (15), but a more recent meta-analysis of 17 randomized controlled trials has shown equal efficacy of the two contrasting bowel preparations (16). Yet, in addition to these discrepancies in the literature, the evidence for its real-world applicability and effectiveness is lacking.

The British Columbia Colon Screening Program (BCCSP) performs approximately 20,000 colonoscopies annually on individuals with an abnormal fecal immunochemical test (FIT), a personal history of neoplastic polyps or a high-risk family history of CRC. BCCSP patients who live in the Vancouver area receive standardized bowel cleansing instructions from a centralized, trained staff. In December 2018, physicians agreed to change the bowel preparation regimen for the program colonoscopies from low-volume split-dose bowel preparation to a 4L polyethylene glycol (PEG)-based split bowel preparation. The aim of this study was to compare the quality of bowel preparation and neoplasia detection rates between high-volume (4 L) split preparation (HVSP) regimen versus low-volume (≤2 L) split preparations (LVSP) in BCCSP patients undergoing colonoscopy at St. Paul's Hospital in Vancouver, BC.

METHODS

A retrospective chart review and data analysis of patients referred by the BCCSP to St. Paul's Hospital for a screening-related colonoscopy between July 2017 to November 2019 were conducted. This study was approved by the University of British Columbia (UBC) Ethics Review Board as a quality improvement study.

Study Population, Setting and Design

To reflect on the impact of the proposed provincial-wide change in bowel regimen in December 2018, we included all HVSP colonoscopies starting December 2018 to November 2019 and compared it to all LVSP colonoscopies between December 2017 and November 2018 for patients undergoing a colonoscopy through the BCCSP. BCCSP participants are men and women between 50 and 74 years of age. Colonoscopy is recommended if the biennial FIT is ≥10 ng/g (NS-Plus, Alere, Japan), if an individual has a personal history of neoplastic polyp removal or if an individual has a first degree relative diagnosed with CRC at less than 60 years of age or two or more first degree relatives diagnosed at any age. Patients undergoing colonoscopy receive standardized bowel preparation instructions from trained staff. This includes verbal and written instructions as well as access to educational videos. The study was aimed to be powered (85% with an alpha of 0.05) to detect halving of poor bowel preparation rates with an initial assumption of these rates to be between 5% and 7% at our institution. This would have required approximately 750 to 1000 patients in each arm (or 1500 to 2000 patients total) and we aimed to include patients 1 year pre- and post-policy implementation.

Procedures were split into two groups: HVSP and LVSP. Each bowel preparation was instructed to be taken in a split-dose fashion. HVSP was defined as 4 L of PEG-based solution split into day before and day of procedure ingestion. LVSP was defined as a composite of two commercially available bowel preparations that required ≤2 L split into day before and day of procedure ingestion (MoviPrep and Pico-Salax). All colonoscopies were performed in hospital at a large tertiary centre by 11 academic gastroenterologists who completed the reports directly—no trainees were involved.

Electronic medical records of procedure reports, nursing records and pathology reports were gathered to collect clinical variables including: patient demographics, bowel preparation quality, withdrawal time, pathologic findings and their location.

The primary outcome measure was bowel preparation quality between HVSP and LVSP and the secondary outcome measure was neoplasia detection rate between HVSP and LVSP.

Bowel Preparation and Neoplasia Detection Rate

Bowel quality was determined based on the modified Aronchick preparation scale used widely in British Columbia. This scale

utilizes the following definitions: (i) Excellent: Small amount of clear liquid with clear mucosa seen, more than 95% mucosa seen; (ii) Good: Small amount of turbid fluid without feces not interfering with examination, more than 90% mucosa seen; (iii) Fair: Moderate amount of stool that can be cleared with suctioning permitting adequate evaluation of entire colonic mucosa, more than 90% mucosa seen; (iv) Poor: Poor preparation quality but examination completed, enough feces or turbid fluid to prevent a reliable examination and less than 90% mucosa seen; and (v) Incomplete: Poor preparation quality hinders full examination including cecum intubation (17). We used the following definitions to further characterize bowel preparations: optimal (excellent or good), suboptimal (fair, poor or incomplete), adequate (excellent, good or fair) and inadequate (poor or incomplete).

The adenoma detection rate (ADR) was calculated as a percentage of patients in each group who had at least one adenoma. Non-advanced adenoma was defined as tubular adenoma <1 cm. Advanced adenoma was defined as tubular adenoma ≥1 cm, villous adenoma and tubulovillous adenoma. Sessile serrated lesions were not counted toward the ADR, as recommended by the American Society for Gastrointestinal Endoscopy (8). Proximal adenoma was defined as an adenoma located proximal to the splenic flexure including the cecum, ascending colon and transverse colon. If more than one adenoma was present, the most advanced was used for analysis. The rates of adenomas were then compared. Prevalence was defined as the number of pathological findings divided by the number of patients in each of HVSP and LVSP groups.

Statistical Analysis

Categorical variables including rate of bowel preparation qualities, ADR and sessile serrated lesion detection rate (SSDR) were analyzed using chi-squared test using GraphPad Prism; P <0.05 was considered to be statistically significant. Continuous variables including age and withdrawal time were analyzed using Student's t-test using GraphPad Prism; P <0.05 was considered to be statistically significant.

RESULTS

A total of 1453 colonoscopies were included; 576 in the HVSP group between December 2018 and November 2019, and 877 in the LVSP group between July 2017 and November 2018. Forty-seven colonoscopies were excluded due to missing data (n = 37) or using an unconventional preparation such as those exceeding a volume of 4 L (n = 8) or ingested over a span of greater than 24 h (n = 2) (Figure 1). Baseline characteristics between the two groups were similar (Table 1). No significant differences were observed between the two groups with respect to age, gender and withdrawal time. The number of HVSP that were being performed even prior to the BCCSP policy change, and vice versa with LVSP being utilized after the policy change were initially underestimated. This posed a challenge to meet our target sample sizes by the study conclusion date (November 2019). As such, the pre-policy change date had to be extended back by 5 months (July 2017 from December 2017) in an attempt to ensure we came close to having 750 patients in each

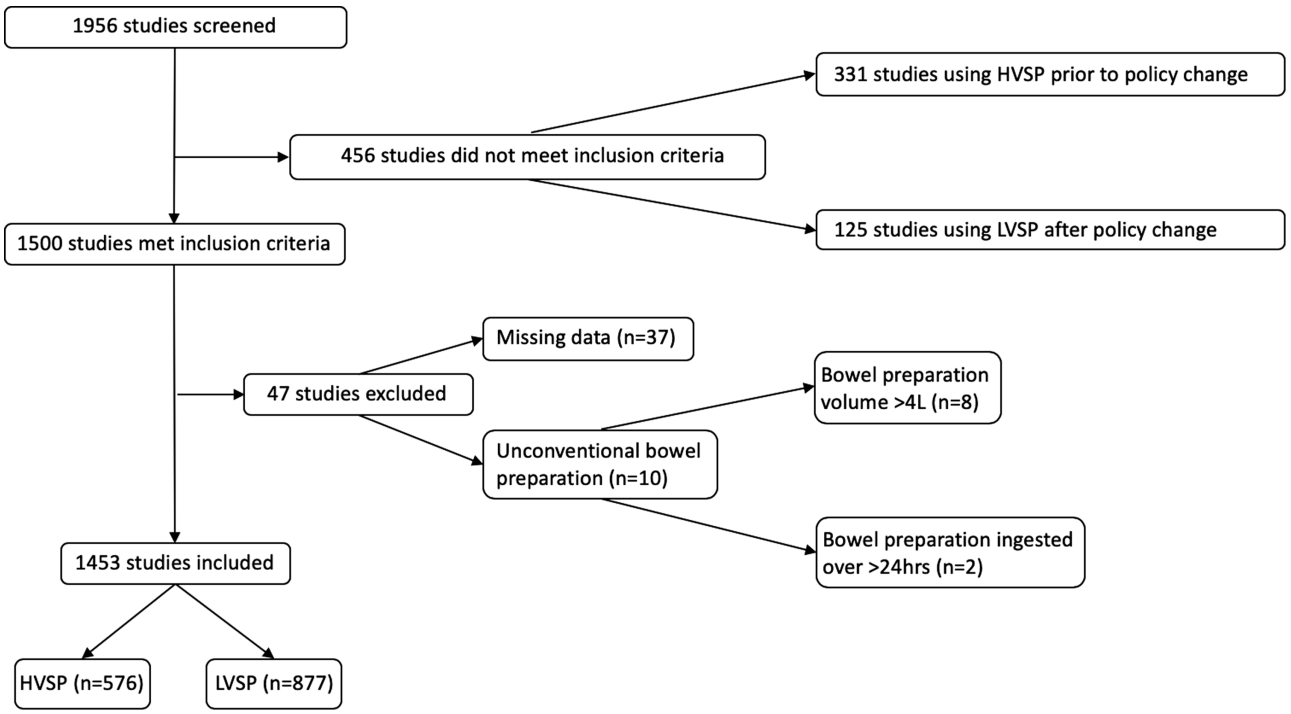

Figure 1. Flow chart of colonoscopies screened and analyzed.

arm and 1500 patients total to ensure the study was not grossly underpowered.

Bowel Preparation quality

There was no statistical difference between the rate of poor bowel preparation in the HVSP group and the LVSP group (1.6% versus 2.5%; P = 0.222) (Table 2). Comparison between individual preparation qualities graded as fair or good and the number of incomplete examinations also did not yield a significant difference between the two groups. However, the HVSP group showed a higher rate of excellent quality bowel preparation (48.4% versus 40.4%; P = 0.002) and optimal (excellent and good) bowel preparation (90.1% versus 86.5%; P = 0.041 as well as a reduced number of suboptimal (fair, poor and incomplete) preparations (9.9% versus 13.45%; P = 0.041) in comparison to the LVSP cohort. There were similar rates of adequate (97.2% versus 96.4%; P = 0.364) and inadequate (2.8% versus 3.6%; P = 0.364) bowel preparations. No significant difference was noted with respect to the rate of recommendation for repeat bowel preparation and colonoscopy (2.8% versus 3.4%; P = 0.494).

Table 1. Baseline characteristics

	HVSP	LVSP	*P*-value
	N = 576	*N* = 877	
Age (±SD)	63.2 ± 6.8	63.8 ± 7.1	0.110
Withdrawal time (min)	8.39 ± 2.5	8.62 ± 2.9	0.138
Gender (% female)	50.5	47.0	0.186

HVSP, High-volume split preparation; LVSP, Low-volume split preparation.

Neoplasia Detection Rate

No significant difference was noted in the ADR between HVSP and LVSP (54.0% versus 53.1%; P = 0.074) (Table 3). A higher rate of proximal adenoma detection was noted in the HVSP group (37.2% versus 29.0%; P = 0.001). LVSP yielded a higher SSDR (9.5% versus 5.6%; P = 0.007) and greater number of proximal SSDR (8.0% versus 3.0%; P < 0.001) compared to HVSP.

Pathological Findings

HVSP was associated with having a higher number of large (>=1 cm) tubular adenomas being detected compared to LVSP (14.4% versus 10.5%; P = 0.025) (Table 4). Between the two

Table 2. Bowel preparation quality between HVSP and LVSP

	HVSP	LVSP	*P*-value	Interpretation
	N = 576 (%)	*N* = 877 (%)		
Excellent quality preparation	279 (48.4)	354 (40.1)	0.002	Favours HVSP
Good quality preparation	240 (41.7)	405 (46.2)	0.090	NSSD
Fair quality preparation	41 (7.1)	86 (9.8)	0.058	NSSD
Poor quality preparation	9 (1.6)	22 (2.5)	0.222	NSSD
Incomplete examination	7 (1.2)	10 (1.1)	0.897	NSSD
Optimal quality preparation	519 (90.1)	759 (86.5)	0.041	Favours HVSP
Suboptimal quality preparation	57 (9.9)	118 (13.5)	0.041	Favours HVSP
Adequate quality preparation	560 (97.2)	845 (96.4)	0.364	NSSD
Inadequate quality preparation	16 (2.8)	32 (3.6)	0.364	NSSD
Repeat bowel preparation required	16 (2.8)	30 (3.4)	0.494	NSSD

HVSP, High-volume split preparation; LVSP, Low-volume split preparation; NSSD, No statistically significant difference.

Table 3. Neoplasia detection rate between HVSP and LVSP

	HVSP	LVSP	*P*-value	Interpretation
	N = 576 (%)	*N* = 877 (%)		
Adenoma detection rate	279 (54.0)	383 (53.1)	0.074	NSSD
Proximal adenoma detection rate	214 (37.2)	254 (29.0)	0.001	Favours HVSP
Sessile serrated lesion detection rate	32 (5.6)	83 (9.5)	0.007	Favours LVSP
Proximal sessile serrated lesion detection rate	17 (3.0)	70 (8.0)	<0.001	Favours LVSP

HVSP, High-volume split preparation; LVSP, Low-volume split preparation; NSSD, No statistically significant difference.

Table 4. Comparison of the prevalence of pathological findings between HVSP and LVSP

Findings	HVSP	LVSP	*P*-value	Interpretation
	N = 576 (%)	*N* = 877 (%)		
Normal/incomplete exam	218 (37.8)	332 (37.9)	0.997	NSSD
Non-advanced adenoma				
<1 cm tubular adenoma	173 (30.0)	244 (27.8)	0.831	NSSD
Advanced adenoma	102 (17.7)	132 (15.1)	0.178	NSSD favours
≥1 cm tubular adenoma	83 (14.4)	92 (10.5)	0.025	HVSP
Villous adenoma	1 (0.2)	6 (0.7)	0.169	NSSD
Tubulovillous adenoma	18 (3.1)	34 (3.9)	0.450	NSSD
Sessile serrated lesion	32 (5.6)	83 (9.5)	0.007	Favours LVSP
Hyperplastic polyp	47 (8.2)	79 (9.0)	0.574	NSSD
Adenocarcinoma	4 (0.7)	7 (0.8)	0.823	NSSD

HVSP, High-volume split preparation; LVSP, Low-volume split preparation; NSSD, No statistically significant difference.

cohorts, no individual differences were noted in their detection rate of hyperplastic polyps, tubular adenomas <1 cm, villous adenomas, tubulovillous adenomas or adenocarcinomas. The rate of advanced adenoma as a group (tubular adenoma ≥ 1 cm, villous adenoma and tubulovillous adenoma) was similar in both HVSP and LVSP. The most common pathological finding was tubular adenoma <1 cm in both groups (30.0% in HVSP and 27.8% in LVSP). Tubular adenomas ≥1 cm were the most common advanced adenoma finding in HVSP and LVSP (17.7% and 15.1%, respectively).

Discussion

We report our experience in the outcomes of a screening colonoscopy by universally switching over to a large volume split bowel preparation and comparing with low-volume split bowel preparations used previously. Prior to our study, one meta-analysis has shown that higher volume preparations may potentially be superior in producing a high-quality bowel preparation (15), but lower volume preparations have been preferred in many settings due to its better patient tolerability (16). It is known that while there is no established single best bowel preparation, current guidelines suggest choosing a split regimen bowel preparation based on patient's medical history, medications and prior procedure history (14,18). Our study shares the real-world effectiveness of routinely endorsing a high-volume over a low-volume split bowel preparation prior to colonoscopy.

The transition to universally utilizing a large volume split bowel preparation did not result in a statistically significant decrease in poor bowel preparation rates. However, it did increase the rate of excellent bowel preparations and reduced the rate of suboptimal preparations defined as fair, poor or incomplete. Two observational studies also support our finding and noted LVSP in association with increased suboptimal preparations (19,20). This appears to favour the HVSP over the LVSP in patients who are more likely to have suboptimal bowel preparation, such as those who are male, elderly, have elevated body mass index, use opioids or tricyclic antidepressants or have a history of diabetes, constipation and/or cirrhosis (12,19,21,22). In addition, the HVSP may be preferable in those who have historically demonstrated poor bowel cleansing with LVSP. The overall rate of poor bowel preparation at our centre (3.4%) was well under the recommended rate of less than 10% to 15% proposed by gastrointestinal endoscopy societies (8,23). When comparing the proportion of bowel preparation grades between the two groups, HVSP appears to confer an advantage over LVSP by upgrading more of the suboptimal ratings to become optimal, and good ratings to become excellent.

Despite the increase in excellent quality preparations and the reduction of suboptimal preparations, HVSP failed to yield a higher ADR. In other words, the increase in overall bowel quality did not appear to have a clinical impact in raising ADR. Indeed, our findings are similar to studies comparing the ADR between high versus low-volume split preparations (16). This, however, does not take into account the high miss rates of adenomas known to arise from suboptimal bowel preparations which are later discovered in the repeat colonoscopy (24). Perhaps because there were similar rates of inadequate exams between the two groups, we also did not find a significant difference in the rate of recommendation for repeated bowel preparation and colonoscopy.

While a meta-analysis of comparative studies noted no difference between rates of right-sided and proximal adenoma detection with improved bowel preparation quality (25)—as this is the segment of the bowel that often harbours sessile serrated lesions which may be difficult to visualize (26)—we observed an increase in proximal ADR favouring HVSP. Our result is similar to repeat colonoscopy studies noting an

increase in right-sided ADR with improved bowel preparation (27,28), suggesting that HVSP does have a clinical impact on improving detection of proximal adenomas that may be missed on an initial colonoscopy with LVSP. Our observed ADR was well above the recommended rate of 25% or greater in those undergoing a screening colonoscopy (8) as expected in an enriched cohort containing predominantly FIT positive patients.

With the improved overall bowel preparation quality with HVSP, we anticipated an increase in the SSDR as these lesions are flat and challenging to identify endoscopically (25,29). However, we observed the opposite—our study noted a higher overall rate of sessile serrated lesions and detection of proximal sessile serrated lesions in the LVSP cohort compared to the HVSP cohort. The paradoxical phenomena of increased overall SSDR and proximal SSDR despite less optimal bowel cleansing were also observed by Siddiki et al. (19) and we highlight two important factors that also closely matched their explanation. Firstly, the improved bowel cleansing with the HVSP likely washed away the mucous cap that is a tell-tale sign of an underlying sessile serrated lesion, making it more difficult to identify. Secondly, we hypothesize that endoscopists tend to irrigate and evaluate the bowel mucosa more closely in cases of suboptimal more so than optimal bowel preparations, which may have led to higher SSDR. In fact, other studies have reported an unexpected decrease in ADR (30,31) and SSDR (30) with excellent bowel preparation compared to its counterparts, suggesting that endoscopists may spend less time looking for adenomas when assessing a bowel with superb cleansing. This bias likely allowed additional sessile serrated lesions to be discovered in the LVSP cohort, especially in the proximal colon. This also denotes the importance of endoscopists to maintain vigilance in finding these lesions even with ideal bowel preparations and reveals the room for improvement among colonoscopists in recognizing sessile serrated lesions. Although there is no consensus target for SSDR (8), the rates of SSDR in our study were slightly lower than rates observed in the aforementioned study (5.6% versus 7.9% in HVSP and 9.5% versus 11.9% in LVSP) (19).

A meta-analysis of 27 studies looking at screening colonoscopies concluded that while poor preparations decrease advanced ADR, suboptimal preparations do not (25). This highlights the diminishing returns of bowel preparation quality with respect to detecting advanced adenomas. Although we observed increased detection of one particular advanced adenoma (tubular adenoma ≥1 cm) in the HVSP group, our overall advanced ADR remained similar between the two groups with comparable rates of poor bowel preparation. In contrast to our study, their analyses also revealed a negative impact on non-advanced ADR with suboptimal bowel preparation. It is important to note, however, that these were indirect comparisons as our study did not evaluate ADRs with respect to each bowel preparation qualities.

The limitation of our study includes the inherent limitations of a retrospective study and the colonoscopists not being blinded to the bowel preparation. In addition, as the two bowel preparations were used in different time periods, we were unable to control for differences in colonoscopy performance, which may have evolved between the two study periods. The 11 academic gastroenterologists performing the colonoscopies remained the same. Our study did not use other validated bowel preparation quality scores that may offer more details on individual bowel segments such as the Boston (32) and Ottawa Bowel Preparation Scale (33). However, the clinical simplicity of the Aronchick scale is more applicable in real life, which was the aim of this study. We do not have data on patient tolerability of their respective bowel preparation as it was beyond the scope of this study. Finally, we did not have other patient characteristics such as medications, co-morbid medical illnesses, lifestyle factors and indication for colonoscopy that can affect adequacy of bowel preparation and prevalence of colon neoplasia. The main strength of our study lies in its generalizability and that our data reproduced findings in other studies comparing HVSP and LVSP (19,20). All provinces and the Yukon territory have implemented or announced colon screening programs which will lead to similar large cohorts undergoing colonoscopy to follow-up a positive FIT. Given the lack of consensus and conflicting publications comparing high- and low-volume bowel preparations, our results may be useful to these other jurisdictions when deciding on standardized bowel preparations for their programs.

Although a statistically significant reduction in poor bowel preparation quality or an improvement in ADR was not observed, at our centre we have received informal colonoscopist feedback indicating that the HVSP is preferred as it improves the overall rate of excellent and optimal bowel preparation quality and do not feel that it is appropriate to go back to its low-volume counterparts. However, this study has identified a need for adopting a more informative bowel preparation reporting scale and continuing colonoscopist education regarding recognition of sessile serrated lesions.

Conclusions

In comparison to the LVSP, the high-volume PEG-based split bowel preparation was associated with increased proportion of excellent and optimal bowel preparations and raised proximal ADR. However, this was also in association with decreased sessile serrated lesion detection and no improvement in overall neoplasia detection. Educational initiatives to improve sessile serrated lesion detection among program colonoscopists are needed.

Conflict of interest: The authors declare no conflict of interest.

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