Tzu Chi Medical Journal 2018; 30(3): 127-34

Review Article

Increase your adenoma detection rate without using fancy adjunct tools

*Yu-Hsi Hsieh[a,b], Felix W. Leung[c,d]**

[a]Division of Gastroenterology, Department of Medicine, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chiayi, Taiwan, [b]School of Medicine, Tzu Chi University, Hualien, Taiwan, [c]Sepulveda Ambulatory Care Center, Veterans Affairs Greater Los Angeles Healthcare System, North Hill, CA, USA, [d]Division of Gastroenterology, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Abstract

The correlation between a low adenoma detection rate (ADR) and interval cancers (ICs) has made ADR one of the most important quality indicators for colonoscopy. Data from nation-wide colorectal cancer (CRC) screening programs showed that there is room for improvement in ADR in order to reduce ICs in Taiwan. Measures with and without adjunct tools have been shown to have the potential to increase ADR, with the latter being more convenient to apply without additional cost. Optimal withdrawal techniques coupled with sufficient withdrawal time, training endoscopists with emphasis on recognition of subtle characteristics of flat lesions, dynamic position changes during the withdrawal phase, removing small polyps found during insertion, and retroflexion in the right colon have all been associated with increased ADR. In particular, water exchange (WE), which is characterized using water in lieu of air and suction removal of infused water during insertion, appears to meet the needs of colonoscopy patients in Taiwan. Analyses of both primary and secondary outcome variables of recently published studies have consistently shown that WE yields higher ADR than traditional air insufflation, even in propofol-sedated patients. Colonoscopists participating in the nationwide CRC screening program in Taiwan should consider applying one or more of the above measures to improve ADR and hopefully reduce ICs.

Keywords: *Adenoma detection rate, Colonoscopy, Interval cancer, Water exchange*

Received : 09-Jan-2018
Revised : 24-Feb-2018
Accepted : 28-Mar-2018

Introduction

The incidence of colorectal cancer (CRC) in Taiwan is among the highest in the world – 43 cases/100,000 individuals in 2015. The Taiwanese Nationwide CRC Screening Program has been in place since 2004, offering biennial fecal immunochemical testing (FIT) to average-risk individuals of 50–69 years old, followed by colonoscopy for those who test positive. However, interval cancers (ICs) which are linked to a low adenoma detection rate (ADR) still occur after colonoscopy in Taiwan [1] as in Western countries [2]. The ADR, which is defined as the proportion of patients with at least one adenoma, has emerged as one of the most important quality measures for colonoscopy. Each 1.0% increase in ADR is associated with a 3.0% decrease in the risk of ICs [2].

Various techniques to increase ADR have been reported. They can be categorized as measures with and without adjunct tools [3]. The former include the Third Eye Retroscope, the Full Spectrum Endoscopy system, cap-assisted colonoscopy, Endorings, and Endocuff, to name a few [3,4]. An American Society of Gastrointestinal Endoscopy technology report in 2015 concluded that the data supporting the efficacy of these tools in enhancing ADR were not sufficiently robust and more studies are needed [5]. Moreover, these tools are not universally available to all endoscopists, and when available, result in additional costs. Methods which do not require adjunct tools include adequate withdrawal time and techniques, training to recognize subtle polyps, right colon retroflexion, and dynamic position changes [3,4]. Endoscopists can apply these methods anytime, anywhere without additional costs, although there is a learning curve for new techniques such as right colon retroflexion and water exchange (WE).

WE is a recent modification of water immersion (WI), distinguished by the timing of suction removal of the water infused to guide the advancement of the colonoscope during insertion (WE) or during withdrawal (WI). The distinction between the two methods is important. A systematic review [6] and a meta-analysis [7] of randomized controlled trials (RCTs) comparing air insufflation (AI) with either WI or WE suggested that WE produced greater reduction of insertion pain than WI and potentially yielded a higher ADR than AI. Subsequently published studies on head-to-head comparison of AI, WI, and WE using either real-time insertion pain scores [8,9] or

**Address for correspondence:*
Dr. Felix W. Leung,
Sepulveda Ambulatory Care Center, Veterans Affairs Greater Los Angeles Healthcare System, 16111 Plummer Street, North Hill, CA, USA.
E-mail: felix.leung@va.gov

Access this article online

Quick Response Code:

Website: www.tcmjmed.com

DOI: 10.4103/tcmj.tcmj_86_18

How to cite this article: Hsieh YH, Leung FW. Increase your adenoma detection rate without using fancy adjunct tools. Tzu Chi Med J 2018;30:127-34.

ADR [10,11] as primary outcomes confirmed these hypotheses. This article intends to review recent advances in measures without adjunct tools to increase ADR, with special emphasis on WE.

How adenomas could be missed

A considerable proportion of polyps and adenomas are missed in colonoscopy, at rates estimated between 20% and 25% in most back-to-back colonoscopy studies [12]. The multiple factors reported to be responsible for missing polyps fall into two broad categories, endoscopist-dependent and nonendoscopist-dependent factors. The endoscopist can be a more powerful factor than the age and gender of patients in predicting ADR [13], which varies widely from 2.5-fold to 8-fold among endoscopists [14]. Potentially modifiable endoscopist-dependent factors accounting for missed adenomas include insufficient withdrawal time for meticulous mucosal inspection [15], suboptimal withdrawal techniques [16], and lack of training to identify subtle lesions [17]. The nonendoscopist-dependent factors include the relative difficulty of visualizing polyps at the proximal side of the haustral folds or near the anal verge [18,19], the presence of flat lesions that are difficult to identify with the naked eye [20], and poor bowel preparation that obscures polyps [21]. Surface visualization with standard 140° and 170° colonoscopes is approximately 87%–92% in a clean colon, which illustrates the limitation of older versions of standard colonoscopes to adequately visualize the entire mucosa [22].

Adenoma detection rate in Taiwan

Taiwanese patients have a slightly lower ADR than westerners (14.7% vs. 20.7%) [23]. In a study involving 29,969 individuals who underwent complete colonoscopy after a positive FIT in the Taiwanese Nationwide CRC Screening Program, the overall ADR was 39.5%. Among the participating hospitals, 5.4% had ADRs <15%, 77.5% had ADRs between 15 and 30%, and 17.1% had ADRs >30% [1]. The current recommendation for ADR as a quality indicator in Western countries calls for an ADR of ≥30% in male patients and ≥20% in female patients [24]; these figures are supposed to be higher in FIT-positive patients. The mean ADR in Taiwanese FIT-positive individuals [1] was lower than the rates of 44.8% in Italy (FIT-based) [25] and 46.5% in the United Kingdom (g uaiac-based) [26].

Withdrawal time and technique

An important quality improvement measure to maximize ADR is taking adequate time for inspection during colonoscope withdrawal. A mean withdrawal time >6 min was associated with a higher ADR [15]. In another study, an increase of withdrawal time beyond 10 min did not further increase ADR [27]. Therefore, a minimal standard of 6 min and a targeted standard of 10 min for withdrawal should be used. The withdrawal time alone, however, was not enough to ensure a quality examination, as mandating longer inspection times was unsuccessful in significantly improving ADR [28], and little correlation with ADR was seen with withdrawal times within a limited range of 6–11 min [29]. The possible explanation could be that withdrawal techniques were more important than withdrawal time.

Adequate withdrawal techniques, including looking behind every fold, cleaning debris, and adequate distention, were shown to correlate with a higher ADR [30], and a lower miss rate [16]. Rather than solely focusing on prolonging the withdrawal time, meticulously applying withdrawal techniques invariably required a withdrawal time of >6–10 min.

Training to recognize the subtle appearance of flat polyps

What we see depends mainly on what we look for [31]. Although the presence of flat adenomas and carcinomas has long been established by Japanese endoscopists, Western endoscopists have only recently recognized their presence. In an early telltale study, a pair of Japanese and American endoscopists separately performed an equal number of colonoscopies in American patients during the same period. Flat adenomas were indeed present and detectable, but only when they were actively searched for by endoscopists trained in the detection of flat lesions [17].

Recent studies showed that training of endoscopists could enhance ADR [32,33]. The intervention consisted of two didactic sessions of ~1–2 h each. These sessions reviewed the importance of ADR and techniques and methods to increase ADR. Multiple image and video examples with special focus on recognition of subtle characteristics of flat lesions (color, friability, vascular changes, and wall deformity) were utilized to provide examples. The ADR in the trained group increased from 36% to 47%, while those in the control group remained unchanged. Follow-up study showed the gain in the ADR remained at least 5 months after training [33]. When the study was expanded to include a larger number of sites, the ADR increased at the participating sites. However, it was not clear to what extent the training program was responsible for the changes, because raw ADRs also increased at the control sites, albeit to a lesser extent [34]. Educational training significantly increased the detection of sessile serrated adenomas [35]. Simply attending more continuing medical education sessions could have a positive influence on ADR [29].

Dynamic position changes

Position changes to facilitate adequate distention of the colon during barium enema and computer tomography colonography [36,37] inspired the assessment of position changes in colonoscopy during withdrawal to improve visibility. The right colon was examined in the left lateral decubitus position, the transverse colon in the supine position, and the left colon in the right lateral decubitus position [38]. Initial studies showed encouraging results with increased ADR, especially in the transverse colon [39]. Subsequent studies showed that the increase occurred only in endoscopists with a low detection rate [40] or did not occur at all [41]. The drawbacks included difficulty in rotating deeply sedated patients, a raised risk of aspiration in the supine position, and increased withdrawal time not dedicated to mucosal inspection [41]. Therefore, dynamic position changes can be more easily applied in unsedated or

minimally sedated patients, who are abundant in Taiwan where National Health Insurance does not cover the sedation fee.

Polypectomy during insertion

Small polyps visualized during insertion may be difficult to find again during withdrawal. This may be due to different anatomical conformations of the colon during instrument insertion, when the colon is stretched by the instrument, and withdrawal, when the colon is shortened and pleated over the scope [42]. Wildi *et al*. randomized patients when a polyp was first detected into two groups: those with polyps <10 mm removed during insertion and withdrawal (n = 150) and those removed during withdrawal only (n = 151). Of 389 polyps, 13 with a mean size of 3.2 mm were missed in 7.3% of patients when removing polyps only during withdrawal [43]. However, Hewett *et al*., who randomized patients to either insertion inspection for 3 min in addition to withdrawal inspection or withdrawal inspection alone, found no improvement in the ADR [42]. Similarly, Sanaka *et al*., who randomized patients between polypectomy during insertion and withdrawal versus during withdrawal only, found no benefit for detecting more polyps [44].

Retroflexion in the right colon

Recent case–control studies consistently demonstrated that protection by colonoscopy against right-sided colon cancer, ranging from 40% to 60%, was lower than the 80% protection attained in the left colon [45-47]. Proximal colorectal neoplasms with advanced histology frequently are smaller than the ones in the left colon or have a nonpolypoid appearance [48,49]. These findings highlight the need for special efforts to improve the ADR in the right colon. Retroflexion in the right colon has been proposed to facilitate detection of adenomas located on the proximal sides of the haustral folds which are difficult to detect by forward viewing. The maneuver entails placing the colonoscope tip in the cecum, moving the up/down control to the maximum up and the right/left control to the maximum left position, and then rotating the insertion tube counterclockwise. In experienced hands, successful retroflexion could be achieved in more than 90% of cases with a complication rate of 0.03% [50]. This was indirectly supported by a prospective, observational study of 1000 patients, showing that a second pass in the right colon in the retroflex view had a 9.8% per-adenoma miss rate [51]. However, RCTs indicated that a second examination of the right colon in the forward view was just as effective as performing a second examination in retroflexion increasing polyp detection [52,53]. Adding to the confusion, a recent study showed colonoscopic retroflexion in the proximal colon resulted in increased detection of adenomas, even after two consecutive forward-view examinations [54].

Impact of Water Exchange on the Adenoma Detection Rate Based on Analysis of Secondary Outcome Variables in Published Randomized Controlled Trials

Analysis of secondary outcome variables in published RCTs showed an increase in the ADR with WE compared to that with AI. Pooled data from two parallel RCTs in veterans accepting scheduled, unsedated colonoscopy or the option of sedation on demand showed that WE enhanced detection of proximal diminutive lesions (adenoma and hyperplastic polyp <10 mm) in screening colonoscopy (WE vs. AI, 31% vs. 6%, P = 0.0012) and yielded a significantly higher proximal diminutive ADR (28.3% vs. 14.4%, P = 0.0298) in unsedated patients [55,56]. An RCT with head-to-head comparison of WE, WI, and AI found that the WE group had a numerically higher overall ADR (56.7%) than the AI (43.3%) and WI (45.6%) groups. When the right colon (cecum and ascending colon) was considered, the ADR in the WE group (26.7%) was significantly higher than that in the AI (11.1%) and WI (14.4%) groups (P = 0.015) [8]. Another Italian study showed that WE had a significantly higher overall ADR (25.8% vs. 19.1%; P = 0.041), proximal ADR (10.1% vs. 4.8%; P = 0.014), and proximal <10 mm ADR (7.7% vs. 3.9%; P = 0.046) than AI [57]. Taken together, WE appeared to enhance ADR while WI did not as compared with traditional AI.

Impact of water exchange on adenoma detection rate in studies using adenoma detection rate as the primary outcome

Three studies using ADR as the primary outcome were published in 2017. A large Chinese study of 3303 patients comparing WE (n = 1653) to AI (n = 1650) showed an overall ADR of 18.3% with WE and 13.4% with AI (relative risk: 1.45, 95% confidence interval [CI]: 1.20–1.75, P < 0.001). Reproducible enhancement of ADR and adenoma per colonoscopy with WE was observed across all eight participating investigators [58]. The second study, conducted in Taiwan by our group, randomized 651 patients into three groups with a 1:1:1 ratio (217 patients per group). Overall ADR met quality standards: WE 49.8% (95% CI: 43.2%–56.4%), AI 37.8% (95% CI: 31.6%–44.4%), and WI 40.6% (95% CI: 34.2%–47.2%). WE significantly increased the ADR compared with AI (P = 0.016). There was no significant difference in the ADR between WI and WE or between WI and AI. Subgroup analysis found that WE significantly increased the ADR in propofol-sedated patients [10]. The third RCT, also comparing ADR among AI, WI, and WE, was conducted in Europe with blinded colonoscopists, that is, after the cecum had been reached, a second colonoscopist who was blinded to the insertion technique performed the withdrawal. Compared with AI, WE achieved a significantly higher ADR in the whole colon (49.3% vs. 40.4%, P = 0.03) and in the right colon (24.0% vs. 16.9%, P = 0.04). WE showed a comparable overall ADR versus WI (43.4%, P = 0.28). The design with blinded observers strengthened the validity of the observation that WE, but not WI, could achieve a significantly higher ADR than AI [11]. WE has consistently showed an increased ADR compared with AI among different ethnic groups and with varied study designs.

ADR has been criticized for its inability to assess thoroughness. For example, it does not detect a faulty "one and done" practice of a colonoscopist who performs a less than optimal examination after finding the first adenoma. To overcome the drawbacks of ADR, additional metrics such as

adenomas per colonoscopy (APC) and adenomas per positive colonoscopy (APPC) have been recommended [59,60]. Similar to the pattern of ADR, WE showed significantly higher APC than conventional AI [10,58]. There was, however, no significant difference in APPC between WE and AI groups, somewhat reflecting that the participating endoscopists in these studies used similar withdrawal techniques in both groups. Furthermore, there are no data to support a link between APC or APPC and ICs or reduction in cancer mortality. Only ADR has been so linked [2,61]. Indeed, overall ADR rather than screening-only ADR, APC, or APPC was recommended for comparing the quality of colonoscopies by an overseas expert on colonoscopy and CRC screening [62].

Potential mechanism of increased adenoma detection rate with water exchange

The mechanism responsible for the increased ADR with WE is largely unknown. First, the most obvious explanation is that WE improves bowel preparation. Split-dose bowel preparation regimens were administered in the three RCTs using ADR as the primary outcome [10,11,58]. The Boston Bowel Preparation Scale (BBPS) score was significantly higher in the WE group than in the AI group, suggesting that WE further enhanced BBPS scores even in patients receiving split-dose preparations. Second, the underwater insertion phase of WE offers a totally different perspective from its withdrawal phase in air. The magnifying effect of water makes slight discoloration or changes in vasculature of a nonpolypoid neoplasm more obvious [63]. The bowel is less distended when filled with water than with gas, and polyps appear less flattened and even float up [63] [Figure 1]. In an RCT comparing AI, WI, and WE, Hsieh *et al*. showed that a significantly higher insertion ADR was achieved based on the polyps seen during insertion and removed during withdrawal with rates for AI 14%, WI 14%, and WE 22% [8]. The third and final theory is that there is less distraction with infusion and suction during withdrawal with WE [64]. When traditional insertion methods (such as air or carbon dioxide insufflation) or WI are used, intraprocedural cleaning is carried out during withdrawal, at the expense of part of the withdrawal time being devoted to infusion and suction of water for cleaning [65]. The endoscopist might get distracted from the main task of inspecting the colon mucosa to find polyps. In blinded analysis of video recordings in an RCT comparing WE and AI, compared with insertion cleaning, withdrawal cleaning increased the number of distractions (median [interquartile range]), namely, water infusion 0 (1) versus 1 (4) and suction 2 (2.5) versus 4 (4) during withdrawal, and was associated with fewer polypectomies and biopsies, 0 (0) versus 1 (2) [66].

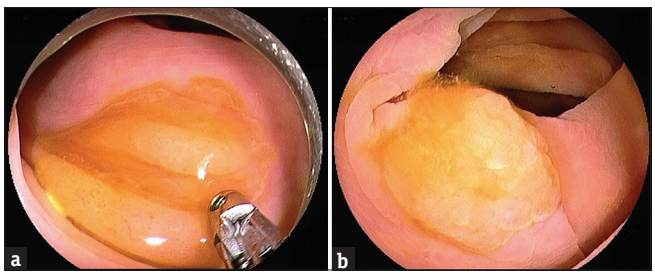

Figure 1: (a) A sessile serrated adenoma appears to be flattened and is easily mistaken as a mucus stain in the ascending colon in air. (b) The same polyp has floated up to assume a sessile appearance with a mucus cap in water

The drawbacks of water exchange

The longer insertion time of WE is perceived by critics as its major drawback [67,68]. The longer insertion time might be compensated by a shorter time spent on infusing and suctioning water during withdrawal [8]. With practice, the insertion time can be reduced to only a few minutes above the endoscopists' baseline AI insertion time [69,70]. Using a transparent cap mounted on the tip of the colonoscope [71] and a water pump with a higher flow rate [72] has recently been shown to reduce the insertion time. In our previous studies, we used the accessory channel for both infusing and suctioning water. Therefore, the water had to be suctioned or infused alternatively. Newer colonoscopes are equipped with two separate channels, allowing for infusing and suctioning simultaneously and thus reducing insertion time. On the other hand, the pain reduction effect of WE diminished the need for sedation [73] and increased the proportion of patients completing colonoscopy without sedation [9], which saved the cost of sedation, reduced sedation-related complications, and eliminated the need for escort and recovery both in the hospital and after returning home. A study that analyzed the cost effectiveness of WE has been reported, showing that at one United States Veterans Affairs medical center a difference of approximately US$58 per procedure, favoring the unsedated alternative, regardless of whether AI or WE was used [74].

The practical view is that the very low payment/reimbursement for colonoscopy and the same payment regardless of the number of adenomas resected (no incentive for detecting and resecting more adenomas) are potential barriers to implementing WE in daily practice by endoscopists in Taiwan. To provide financial incentives to increase ADR tying bonus payments from the National Health Insurance to a by higher ADR might be considered. In addition, charging an extra fee out of the patients' own pocket based on the added time and skills required might also encourage colonoscopists to perform WE.

Learning the water exchange method

In contrast to the traditional AI colonoscopy, WE entails a new set of maneuvers with the complete exclusion of air during insertion [75]. A learning curve with >90% successful cecal intubation is easily achievable after 50–100 cases [68,76]. Direct coaching by a knowledgeable trainer appears to facilitate understanding of the nuances of the WE method [77]. One approach for those who have a set number of procedures to perform on a very tight schedule is to set aside a fixed amount of time, for example, 5 min, to the per-patient allotted time to learn and practice the WE technique and then turn on the air pump when time elapses [69].

Summary

There is room for improvement in the ADR for colonoscopists in Taiwan. Several methods can potentially enhance the ADR without the need to procure fancy adjunct tools or add costs. Optimal withdrawal techniques coupled with sufficient

Table 1: Approaches without the need for an adjunct tool

	Description	Benefits	limitations
Withdrawal time [15,27-29]	Time from cecum to anus, aim for 6-0 min or more	Increased withdrawal time correlates with higher ADR in multiple studies, well defined and easy to measure	Lack of correlation with ADR in some studies potentially due to poor examination technique, mandated increase in withdrawal time does not necessarily increase ADR
Withdrawal techniques [16,30]	Quality criteria: (1) fold examination, (2) adequate distention, (3) adequacy of cleansing	Can be included in educational programs	Difficult to measure
Training to recognize subtle polyps [17,32-35]	Image and video examples focusing on recognition of subtle characteristics of flat lesions	Finds more subtle lesions, especially flat ones Dain in ADR remains after training	A large study including multiple sites showed inconclusive results
Changes in patient position [38-41]	(1): Right colon: Left lateral decubitus; (2) Transverse colon: supine;(3) Left colon: Right lateral decubitus	Increased ADR, especially in the transverse colon Easier for unsedated or minimally sedated patients	Time-consuming Difficult in heavily sedated patients Raises risk of aspiration in supine position
Insertion polypectomy [42-44]	Remove polyps found during insertion	Avoids missing small polyps during withdrawal	RCTs showed no increase in ADR
Right colon retroflexion [50-54]	Move up/down control to the maximum up and right/left control to the maximum left positions, then rotate the insertion tube counterclockwise	Finds additional polyps on proximal side of folds	Complication rate 0.03%
Water exchange [8,10,11,55-58]	Uses water in lieu of air; infuses clean water and removes dirty water during insertion	Reduces insertion pain in addition to increasing ADR	Requires a learning curve Requires more time than air insufflation (mean increase about 4 min)

ADR: Adenoma detection rate

Table 2: Approaches with the need for an adjunct tool and addition costs

Enhanced imaging	Description	Benefits	Limitations
NBI	Narrow spectrum of wavelength enhances visualization of blood vessels and mucosal pit pattern	Helps delineate pathology and depth of invasion in early cancer	Inconsistent impact on ADR Training required
FICE, i-scan	Image enhancement by proprietary postprocessing computer algorithms applied to the white-light images		Additional time required, especially with chromoendoscopy
Chromoendoscopy	Colonic spraying of dye to enhance contrast and accentuate epithelial surface changes		
Third eye retroscope	Slim endoscope passes through biopsy channel and reverses direction 180°	Helps find polyps behind folds	Reduction of suction capacity and need to remove retroscope to perform polypectomy
Full-spectrum endoscopy	330° view on 3 screens		The wide angle of view pertains only to the right-left direction and not the up-down direction Training needed
Fold-flattening devices	Attached to end or tip of colonoscope		Except for the transparent cap, most of these devices are not readily available in Taiwan
Transparent cap	Transparent cap	Shorter insertion time and higher intubation rates	
Endocuff	Flexible cuff with 1 or 2 rows of flexible wings	The most promising device showing increased ADR in multiple studies, especially the second generation (endocuff vision)	Causes a minor increase in discomfort on anal intubation Might cause mucosal abrasions
Endorings	Short tube-like core and several layers of flexible circular rings		
G-eye	Integrated inflatable, reusable balloon		

NBI: Narrow band imaging, FICE: Fujinon intelligent chromoendoscopy

withdrawal time can increase ADR and reduce adenoma miss rate. Training endoscopists with emphasis on the importance of ADR, techniques and methods to increase ADR, and multimedia examples focusing on recognition of subtle characteristics of flat lesions can help. Dynamic position changes during the withdrawal phase of colonoscopy can augment ADR, especially in the transverse colon. Removing small polyps found during insertion reduces the likelihood of missing or spending more time searching for them during withdrawal. There are conflicting data related to the impact of colonoscopic retroflexion in the proximal colon. Analyses of both primary and secondary outcome variables in published RCTs showed that WE yielded higher ADR than AI, especially proximal, diminutive ADR. The aforementioned approaches are summarized in Table 1. For comparison, a brief summary of approaches to increase the ADR with the need for an adjunct tool is presented in Table 2.

Conclusion

Colonoscopists participating in the nationwide CRC screening program in Taiwan should consider applying one or more of the above measures to improve ADR and hopefully reduce ICs.

Financial support and sponsorship

This study was supported in part by VA medical Research Funds and a Tzu Chi Medical Lecture Grant from the Tzu Chi Medical Foundation.

Conflicts of interest

There are no conflicts of interest.

References

1. Chiu SY, Chuang SL, Chen SL, Yen AM, Fann JC, Chang DC, et al. Faecal haemoglobin concentration influences risk prediction of interval cancers resulting from inadequate colonoscopy quality: Analysis of the Taiwanese nationwide colorectal cancer screening program. Gut 2017;66:293-300.
2. Corley DA, Jensen CD, Marks AR, Zhao WK, Lee JK, Doubeni CA, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med 2014;370:1298-306.
3. Rex DK. Polyp detection at colonoscopy: Endoscopist and technical factors. Best Pract Res Clin Gastroenterol 2017;31:425-33.
4. Moons LM, Gralnek IM, Siersema PD. Techniques and technologies to maximize mucosal exposure. Gastrointest Endosc Clin N Am 2015;25:199-210.
5. ASGE Technology Committee, Konda V, Chauhan SS, Abu Dayyeh BK, Hwang JH, Komanduri S, et al. Endoscopes and devices to improve colon polyp detection. Gastrointest Endosc 2015;81:1122-9.
6. Leung F, Harker J, Leung J, Siao-Salera R, Mann S, Ramirez F, et al. Removal of infused water predominantly during insertion (water exchange) is consistently associated with a greater reduction of pain score – Review of randomized controlled trials (RCTs) of water method colonoscopy. J Interv Gastroenterol 2011;1:114-20.
7. Leung FW, Hu B, Wu J. Comparative effectiveness of water immersion and water exchange versus air insufflation for colonoscopy. J Interv Gastroenterol 2013;3:100-10.
8. Hsieh YH, Koo M, Leung FW. A patient-blinded randomized, controlled trial comparing air insufflation, water immersion, and water exchange during minimally sedated colonoscopy. Am J Gastroenterol 2014;109:1390-400.
9. Cadoni S, Sanna S, Gallittu P, Argiolas M, Fanari V, Porcedda ML, et al. A randomized, controlled trial comparing real-time insertion pain during colonoscopy confirmed water exchange to be superior to water immersion in enhancing patient comfort. Gastrointest Endosc 2015;81:557-66.
10. Hsieh YH, Tseng CW, Hu CT, Koo M, Leung FW. Prospective multicenter randomized controlled trial comparing adenoma detection rate in colonoscopy using water exchange, water immersion, and air insufflation. Gastrointest Endosc 2017;86:192-201.
11. Cadoni S, Falt P, Rondonotti E, Radaelli F, Fojtik P, Gallittu P, et al. Water exchange for screening colonoscopy increases adenoma detection rate: A multicenter, double-blinded, randomized controlled trial. Endoscopy 2017;49:456-67.
12. van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E, et al. Polyp miss rate determined by tandem colonoscopy: A systematic review. Am J Gastroenterol 2006;101:343-50.
13. Chen SC, Rex DK. Endoscopist can be more powerful than age and male gender in predicting adenoma detection at colonoscopy. Am J Gastroenterol 2007;102:856-61.
14. Imperiale TF, Glowinski EA, Juliar BE, Azzouz F, Ransohoff DF. Variation in polyp detection rates at screening colonoscopy. Gastrointest Endosc 2009;69:1288-95.
15. Barclay RL, Vicari JJ, Doughty AS, Johanson JF, Greenlaw RL. Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. N Engl J Med 2006;355:2533-41.
16. Rex DK. Colonoscopic withdrawal technique is associated with adenoma miss rates. Gastrointest Endosc 2000;51:33-6.
17. Saitoh Y, Waxman I, West AB, Popnikolov NK, Gatalica Z, Watari J, et al. Prevalence and distinctive biologic features of flat colorectal adenomas in a North American population. Gastroenterology 2001;120:1657-65.
18. Pickhardt PJ, Nugent PA, Mysliwiec PA, Choi JR, Schindler WR. Location of adenomas missed by optical colonoscopy. Ann Intern Med 2004;141:352-9.
19. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 2003;349:2191-200.
20. Heresbach D, Barrioz T, Lapalus MG, Coumaros D, Bauret P, Potier P, et al. Miss rate for colorectal neoplastic polyps: A prospective multicenter study of back-to-back video colonoscopies. Endoscopy 2008;40:284-90.
21. Froehlich F, Wietlisbach V, Gonvers JJ, Burnand B, Vader JP. 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.
22. East JE, Saunders BP, Burling D, Boone D, Halligan S, Taylor SA, et al. Surface visualization at CT colonography simulated colonoscopy: Effect of varying field of view and retrograde view. Am J Gastroenterol 2007;102:2529-35.
23. Soon MS, Kozarek RA, Ayub K, Soon A, Lin TY, Lin OS, et al. Screening colonoscopy in Chinese and Western patients: A comparative study. Am J Gastroenterol 2005;100:2749-55.
24. Rex DK, Schoenfeld PS, Cohen J, Pike IM, Adler DG, Fennerty MB, et al. Quality indicators for colonoscopy. Am J Gastroenterol 2015;110:72-90.
25. Zorzi M, Senore C, Da Re F, Barca A, Bonelli LA, Cannizzaro R, 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.
26. Lee TJ, Rutter MD, Blanks RG, Moss SM, Goddard AF, Chilton A, et al. Colonoscopy quality measures: Experience from the NHS bowel cancer screening programme. Gut 2012;61:1050-7.
27. Lee TJ, Blanks RG, Rees CJ, Wright KC, Nickerson C, Moss SM, et al. Longer mean colonoscopy withdrawal time is associated with increased adenoma detection: Evidence from the bowel cancer screening programme in England. Endoscopy 2013;45:20-6.

28. Sawhney MS, Cury MS, Neeman N, Ngo LH, Lewis JM, Chuttani R, et al. Effect of institution-wide policy of colonoscopy withdrawal time > or = 7 minutes on polyp detection. Gastroenterology 2008;135:1892-8.
29. Adler A, Wegscheider K, Lieberman D, Aminalai A, Aschenbeck J, Drossel R, et al. Factors determining the quality of screening colonoscopy: A prospective study on adenoma detection rates, from 12,134 examinations (Berlin colonoscopy project 3, BECOP-3). Gut 2013;62:236-41.
30. Lee RH, Tang RS, Muthusamy VR, Ho SB, Shah NK, Wetzel L, et al. Quality of colonoscopy withdrawal technique and variability in adenoma detection rates (with videos). Gastrointest Endosc 2011;74:128-34.
31. Yotsumoto Y, Sekuler R. Out of mind, but not out of sight: Intentional control of visual memory. Mem Cognit 2006;34:776-86.
32. Coe SG, Crook JE, Diehl NN, Wallace MB. An endoscopic quality improvement program improves detection of colorectal adenomas. Am J Gastroenterol 2013;108:219-26.
33. Ussui V, Coe S, Rizk C, Crook JE, Diehl NN, Wallace MB, et al. Stability of increased adenoma detection at colonoscopy. Follow-up of an endoscopic quality improvement program-EQUIP-II. Am J Gastroenterol 2015;110:489-96.
34. Wallace MB, Crook JE, Thomas CS, Staggs E, Parker L, Rex DK, et al. Effect of an endoscopic quality improvement program on adenoma detection rates: A multicenter cluster-randomized controlled trial in a clinical practice setting (EQUIP-3). Gastrointest Endosc 2017;85:538-45.
35. Li D, Woolfrey J, Jiang SF, Jensen CD, Zhao WK, Kakar S, et al. Diagnosis and predictors of sessile serrated adenoma after educational training in a large, community-based, integrated healthcare setting. Gastrointest Endosc 2018;87:755-650.
36. Chen SC, Lu DS, Hecht JR, Kadell BM. CT colonography: Value of scanning in both the supine and prone positions. AJR Am J Roentgenol 1999;172:595-9.
37. Yee J, Kumar NN, Hung RK, Akerkar GA, Kumar PR, Wall SD, et al. Comparison of supine and prone scanning separately and in combination at CT colonography. Radiology 2003;226:653-61.
38. East JE, Suzuki N, Arebi N, Bassett P, Saunders BP. Position changes improve visibility during colonoscope withdrawal: A randomized, blinded, crossover trial. Gastrointest Endosc 2007;65:263-9.
39. East JE, Bassett P, Arebi N, Thomas-Gibson S, Guenther T, Saunders BP, et al. Dynamic patient position changes during colonoscope withdrawal increase adenoma detection: A randomized, crossover trial. Gastrointest Endosc 2011;73:456-63.
40. Lee SW, Chang JH, Ji JS, Maeong IH, Cheung DY, Kim JS, et al. Effect of dynamic position changes on adenoma detection during colonoscope withdrawal: A randomized controlled multicenter trial. Am J Gastroenterol 2016;111:63-9.
41. Ou G, Kim E, Lakzadeh P, Tong J, Enns R, Ramji A, et al. A randomized controlled trial assessing the effect of prescribed patient position changes during colonoscope withdrawal on adenoma detection. Gastrointest Endosc 2014;80:277-83.
42. Hewett DG, Rex DK. Inspection on instrument insertion during colonoscopy: A randomized controlled trial. Gastrointest Endosc 2012;76:381-7.
43. Wildi SM, Schoepfer AM, Vavricka SR, Fruehauf H, Safroneeva E, Wiegand N, et al. Colorectal polypectomy during insertion and withdrawal or only during withdrawal? A randomized controlled trial. Endoscopy 2012;44:1019-23.
44. Sanaka MR, Parsi MA, Burke CA, Barnes D, Church J, Rizk M, et al. Adenoma detection at colonoscopy by polypectomy in withdrawal only versus both insertion and withdrawal: A randomized controlled trial. Surg Endosc 2015;29:692-9.
45. Baxter NN, Warren JL, Barrett MJ, Stukel TA, Doria-Rose VP. 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.
46. Nishihara R, Wu K, Lochhead P, Morikawa T, Liao X, Qian ZR, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med 2013;369:1095-105.
47. Doubeni CA, Weinmann S, Adams K, Kamineni A, Buist DS, Ash AS, et al. Screening colonoscopy and risk for incident late-stage colorectal cancer diagnosis in average-risk adults: A nested case-control study. Ann Intern Med 2013;158:312-20.
48. Rondagh EJ, Bouwens MW, Riedl RG, Winkens B, de Ridder R, Kaltenbach T, et al. Endoscopic appearance of proximal colorectal neoplasms and potential implications for colonoscopy in cancer prevention. Gastrointest Endosc 2012;75:1218-25.
49. Gupta S, Balasubramanian BA, Fu T, Genta RM, Rockey DC, Lash R, et al. Polyps with advanced neoplasia are smaller in the right than in the left colon: Implications for colorectal cancer screening. Clin Gastroenterol Hepatol 2012;10:1395-401.
50. Cohen J, Grunwald D, Grossberg LB, Sawhney MS. The effect of right colon retroflexion on adenoma detection: A systematic review and meta-analysis. J Clin Gastroenterol 2017;51:818-24.
51. Hewett DG, Rex DK. Miss rate of right-sided colon examination during colonoscopy defined by retroflexion: An observational study. Gastrointest Endosc 2011;74:246-52.
52. Kushnir VM, Oh YS, Hollander T, Chen CH, Sayuk GS, Davidson N, et al. Corrigendum: Impact of retroflexion vs. second forward view examination of the right colon on adenoma detection: A comparison study. Am J Gastroenterol 2015;110:942.
53. Harrison M, Singh N, Rex DK. Impact of proximal colon retroflexion on adenoma miss rates. Am J Gastroenterol 2004;99:519-22.
54. Lee HS, Jeon SW, Park HY, Yeo SJ. Improved detection of right colon adenomas with additional retroflexion following two forward-view examinations: A prospective study. Endoscopy 2017;49:334-41.
55. Leung J, Mann S, Siao-Salera R, Ransibrahmanakul K, Lim B, Canete W, et al. A randomized, controlled trial to confirm the beneficial effects of the water method on U.S. veterans undergoing colonoscopy with the option of on-demand sedation. Gastrointest Endosc 2011;73:103-10.
56. Leung FW, Harker JO, Jackson G, Okamoto KE, Behbahani OM, Jamgotchian NJ, et al. A proof-of-principle, prospective, randomized, controlled trial demonstrating improved outcomes in scheduled unsedated colonoscopy by the water method. Gastrointest Endosc 2010;72:693-700.
57. Cadoni S, Gallittu P, Sanna S, Fanari V, Porcedda ML, Erriu M, et al. A two-center randomized controlled trial of water-aided colonoscopy versus air insufflation colonoscopy. Endoscopy 2014;46:212-8.
58. Jia H, Pan Y, Guo X, Zhao L, Wang X, Zhang L, et al. Water exchange method significantly improves adenoma detection rate: A Multicenter, randomized controlled trial. Am J Gastroenterol 2017;112:568-76.
59. Wang HS, Pisegna J, Modi R, Liang LJ, Atia M, Nguyen M, et al. Adenoma detection rate is necessary but insufficient for distinguishing high versus low endoscopist performance. Gastrointest Endosc 2013;77:71-8.
60. Aniwan S, Orkoonsawat P, Viriyautsahakul V, Angsuwatcharakon P, Pittayanon R, Wisedopas N, et al. The secondary quality indicator to improve prediction of adenoma miss rate apart from adenoma detection rate. Am J Gastroenterol 2016;111:723-9.
61. Kaminski MF, Wieszczy P, Rupinski M, Wojciechowska U, Didkowska J, Kraszewska E, et al. Increased rate of adenoma detection associates with reduced risk of colorectal cancer and death. Gastroenterology 2017;153:98-105.
62. Rex DK, Ponugoti PL. Calculating the adenoma detection rate in screening colonoscopies only: Is it necessary? Can it be gamed? Endoscopy 2017;49:1069-74.
63. Cammarota G, Cesaro P, Cazzato A, Cianci R, Fedeli P, Ojetti V, et al. The water immersion technique is easy to learn for routine use during EGD for duodenal villous evaluation: A single-center 2-year experience.

J Clin Gastroenterol 2009;43:244-8.

64. Yung VY, Leung JW, Mann SK, Wilson MD, Leung FW. Validation of a novel method for analyzing video recordings of the withdrawal phase of air insufflation and water exchange colonoscopy – Documentation of distractions from focused mucosal inspection. J Interv Gastroenterol 2014:4;8-12.
65. MacPhail ME, Hardacker KA, Tiwari A, Vemulapalli KC, Rex DK. Intraprocedural cleansing work during colonoscopy and achievable rates of adequate preparation in an open-access endoscopy unit. Gastrointest Endosc 2015;81:525-30.
66. Yen AW, Leung JW, Mann SK, Wilson MD, Leung FW. Insertion water exchange minimizes endoscopist multitasking during withdrawal inspection – A plausible explanation for enhanced polyp detection in the right colon. J Interv Gastroenterol 2015;1:3-9.
67. Rex DK. Water exchange vs. water immersion during colonoscope insertion. Am J Gastroenterol 2014;109:1401-3.
68. Sugimoto S, Mizukami T. Diagnostic and therapeutic applications of water-immersion colonoscopy. World J Gastroenterol 2015;21:6451-9.
69. Ramirez FC, Leung FW. The water method for aiding colonoscope insertion: The learning curve of an experienced colonoscopist. J Interv Gastroenterol 2011;1:97-101.
70. Fischer LS, Lumsden A, Leung FW. Water exchange method for colonoscopy: Learning curve of an experienced colonoscopist in a U.S. community practice setting. J Interv Gastroenterol 2012;2:128-32.
71. Tseng CW, Koo M, Hsieh YH. Cecal intubation time between cap-assisted water exchange and water exchange colonoscopy: A randomized-controlled trial. Eur J Gastroenterol Hepatol 2017;29:1296-302.
72. Bayupurnama P, Ratnasari N, Indrarti F, Triwikatmani C, Maduseno S, Nurdjanah S, et al. Endoscope-connected water pump with high flow rates improves the unsedated colonoscopy performance by water immersion method. Clin Exp Gastroenterol 2018;11:13-8.
73. Leung JW, Mann SK, Siao-Salera R, Ransibrahmanakul K, Lim B, Cabrera H, et al. A randomized, controlled comparison of warm water infusion in lieu of air insufflation versus air insufflation for aiding colonoscopy insertion in sedated patients undergoing colorectal cancer screening and surveillance. Gastrointest Endosc 2009;70:505-10.
74. Granados-Savatgy L, Bradham DD, Blohm L, Siao-Salera R, Leung JW, Leung FW. Cost benefit analysis and cost estimating: Sedated vs. unsedated colonoscopy at one VAMC. Am J Clin Med 2010;7:147-50.
75. Leung FW, Leung JW, Mann SK, Friedland S, Ramirez FC. The water method significantly enhances patient-centered outcomes in sedated and unsedated colonoscopy. Endoscopy 2011;43:816-21.
76. Hsieh Y, Leung FW. Water exchange and suction removal of all residual air in the colonic lumen both contribute to attenuation of insertion pain in a learning curve study. J Interv Gastroenterol 2013;3:2-6.
77. Leung F, Cheung R, Fan R, Fischer L, Friedland S, Ho S, et al. The water exchange method for colonoscopy-effect of coaching. J Interv Gastroenterol 2012;2:122-5.