



Withdrawal time in colonoscopy, past, present, and future, a narrative review

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Background and Objective: Colonoscopy is a time proven, safe, and gold standard screening method for colorectal cancer (CRC). In order to achieve its objectives, quality markers have been defined for colonoscopy, including withdrawal time (WT). WT is defined as the time spent from reaching the cecum or terminal ileum till the end of procedure in colonoscopies without any additional interventions. This review aims to provide evidence on WT efficacy and future directions.

Methods: We conducted a comprehensive literature search of articles evaluating WT. Search was limited to English language articles from all peer-reviewed journals.

Key Content and Findings: The seminal study by Barclay *et al.*, led to setting of a minimum WT of 6 minutes as the recommended amount for colonoscopy, per 2006 American College of Gastroenterology (ACG) taskforce. Since then, many observational studies have confirmed the efficacy of 6 minutes. Recently, multiple large multicenter trials suggest WT of 9 minutes as the alternative for better outcomes. Recently, novel Artificial Intelligence (AI) models have shown promise in improving WT and other outcomes and proved an exciting tool in the armamentarium of gastroenterologists. Some of these tools encourage the endoscopists to check the blind spots and clean the residual stool. This has shown to improve both WT and ADR. We recommend an improvement of these models to consider risk factors like adenoma detection in current and prior scopes to guide endoscopists spend time in each segment.

Conclusions: In conclusion, new evidence demonstrates that WT of 9 minutes is better than 6 minutes. Future trends point toward an individualized AI-based approach combining real time and baseline data and guiding the endoscopist on how much time to spend in every segment of the colon in every colonoscopy procedure.

Keywords: Screening colonoscopy; artificial intelligence (AI); adenoma; withdrawal time (WT)

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Introduction

Colorectal cancer (CRC) is the second most common cause of death from cancer worldwide. Ninety-five percent of CRC cases originate from tubular adenomas of the colon therefore high-quality colonoscopy screening with adequate adenoma detection rate (ADR) is the gold standard modality to prevent CRC (1). Back-to-back colonoscopy studies

have shown that as much as 24% of tubular adenomas are missed in colonoscopies (2). The majority of interval CRCs are due to missed lesions secondary to inadequate bowel prep leading to difficulty in finding small and flat lesions and differences in endoscopists ability to find adenomas (3). Therefore, ADR, cecal intubation rate, complete polypectomy rate, quality of bowel prep, and withdrawal

Table 1 The search strategy summary

Items	Specification
Date of search	Feb 28, 2023
Databases and other sources searched	PubMed/MEDLINE
Search terms used	Colonoscopy, withdrawal time
Timeframe	Jan 1, 1999 to Feb 28, 2023
Inclusion and exclusion criteria	Inclusion: Observational and randomized trials in English language Exclusion: case reports and case series less than 10 subjects
Selection process	HH and NZ conducted the search independently and consensus was obtained with discussion with MA

time (WT) have been shown to correlate with rates of interval CRC (4). ADR, defined as the number of cases with at least one adenoma detected, has been used as a primary indicator of quality of colonoscopy (5). Studies show that lower-quality colonoscopies reflected by lower ADRs are associated with increased rate of interval CRCs (6). Among the factors studied that can affect the ADR is WT. There is a knowledge gap on the ideal duration of WT since literature has been evolving in this dynamic topic. Moreover, artificial intelligence (AI) is providing new avenues for endoscopists. The objective of this review is to illustrate available evidence for WT efficacy and demonstrate the future direction and potentials of WT in colonoscopy. We present this article in accordance with the Narrative Review reporting checklist (available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-8/rc>) (7).

Methods

We conducted a comprehensive search of PubMed/MEDLINE using the search term “withdrawal time” and “colonoscopy”. The search was restricted to articles in English language only. We included all peer-reviewed observational studies and randomized controlled trials (RCTs). Society guidelines were also reviewed for historical and current recommendations on WT. All studies were cross-referenced to include relevant articles (*Table 1*).

WT

Definition and recommendations

WT is calculated as the duration of time from reaching the cecum or terminal ileum till the end of procedure in

normal colonoscopies without any interventions. The majority of the mucosal inspection is carried out during this period. Increasing WT by spending more time for a detailed colonoscopy through inspecting behind folds and cleaning the colon can lead to increased ADR (8,9). 2021 American Gastroenterological Association (AGA) guidelines recommend endoscopists with lower ADRs, take measures including increasing their WT to achieve an ADR of 30% (5). According to these guidelines, endoscopists should achieve an average WT of at least 6 minutes for normal colonoscopies with an aspirational target of 9 minutes. These recommendations are based on the following available evidence demonstrating that setting a minimum WT ranging from 6 to 9 minutes can increase outcomes including ADR and lower interval CRC compared to WTs less than this amount.

Right colon WT

Colonoscopy has been shown to be more effective in the left colon compared to the right due to presence of serrated lesions in the right colon. Serrated lesions are more difficult to detect due to their flat morphology, fleshy appearance, and having a mucus cap (10). This requires more careful examination with maneuvers like second look in the right colon or retroflexion that can increase the ADR by 5–20% even in cases of adequate prep (11–13). The 2021 AGA guidelines consider a second look of the right colon through forward or retroflexed view best practice especially when polyps are detected on the first look increasing the chance of synchronous lesions (5). Yun *et al.* showed that second look maneuvers in the right colon are time consuming and proposed a need for a WT in the right colon above 3 minutes (14). KASID multicenter study also illustrated

that ADR significantly improves when there is a WT of 2 minutes in the right colon compared to less duration [odds ratio (OR), 2.98; 95% confidence interval (CI), 1.72 to 5.15; $P < 0.001$] (15). Indeed, many studies have shown increased serrated polyp detection rate (SDR) with longer WTs, which brings further evidence that increasing WT is an effective strategy to detect serrated lesions in the right colon (16-18).

Evolving evidence behind WT

Setting an average WT of more than 6 minutes by AGA is based on studies suggesting this number as a quality indicator of achieving a high-quality colonoscopy reflected in higher ADR and lower interval CRC rate. This number was pinpointed by the seminal observational study by Barclay *et al.* in more than seven thousand screening colonoscopies, in which WT more than 6 minutes was found to increase ADR (28.3% *vs.* 11.8%, $P < 0.001$) and advanced ADR (6.4% *vs.* 2.6%, $P = 0.005$) (19). This led to setting the WT of more than 6 minutes as a colonoscopy quality indicator by a 2006 American Society for Gastrointestinal Endoscopy/American College of Gastroenterology task force (20). Since these recommendations, multiple large scale observational studies have supported these findings. Another observational study on 76,810 screening colonoscopies showed improved outcomes with WT of 6 minutes. This study also showed the fewest number of interval CRCs with WT of above 8 minutes (21). Further studies also supported WT of 6 minutes for better outcomes in terms of ADR and interval CRC rates (22-24). A study by Butterly *et al.* on 7,996 colonoscopies found an increase in ADR and also SDR in WT 9 minutes compared to 6 minutes. Regression model showed WT of 9 minutes to be most significant for SDR, with nearly a 30% increase (16). This finding is important as serrated lesions are more prone to be missed. This increases the importance of WT in the right colon and brings up the notion of a dedicated WT for the right colon as discussed in the prior section. A retrospective US study on 31,558 colonoscopy examinations suggested a WT of 11 minutes increased both ADR (OR 1.65, 95% CI: 1.09 to 2.51) and detection rate of proximal serrated polyps (OR 1.81, 95% CI: 1.06 to 3.08) (18). In this study, ADR linearly correlated well with WT ($R = 0.76$, $P < 0.001$). In addition to whole colon WT, there are studies proposing WTs on segments of the colon. Multicenter studies by Jung *et al.* and Kashiwagi *et al.* have shown that setting a minimum WT in each segment of colon of more than

3 minutes also increases the PDR (15,25). The mentioned prior evidence mainly involves observational studies with their adherent bias. Recently, in a large multicenter RCT by Zhao *et al.*, it was noted that increasing WT from 6 to 9 minutes led to significantly improved ADR especially in right colon and for colonoscopists with less experience. This is the first large multicenter RCT that proved superiority of WT of 9 minutes compared to 6 minutes (26). This brings further high-quality evidence for future guideline regarding WT for the procedures.

Interventions to improve WT

Despite recommendations to improve WT, methods to achieve this goal are understudied (4). In order to improve WT, multiple modalities are proposed. Feedback and monitoring have been shown to improve WT (27). Barclay *et al.* in their study on 2053 screening colonoscopies used a digital watch emitting audible signals at 2, 4, 6, and 8 minutes, therefore notifying the endoscopist when they achieved the WT of 8 minutes. This showed to improve detection of neoplasia (34.7% *vs.* 23.5%, $P < 0.0001$) (23). In the era of AI, this new tool has gained interest in improving ADR through various methods including improving WT. In a study on 659 patients by Su *et al.*, a deep convolutional neural network model showed improvement in ADR (0.289 *vs.* 0.165, $P < 0.001$) and WT (7.03 *vs.* 5.68 minutes, $P < 0.001$) (28). The AI had multiple functions including real-time evaluation of withdrawal speed and alerting endoscopist in case speed of withdrawal is too fast. In addition, the software was able to detect bad prep and remind the endoscopist to clean the mucosa and suction the pool of fluid. These secondary functions inadvertently increased the WT while increasing the quality of the colonoscopy. In another RCT by Gong *et al.*, 704 patients underwent AI-assisted colonoscopy with ENDOANGEL AI system (29). ENDOANGEL was developed using deep neural networks to monitor real-time speed of withdrawal in addition to total WT. ENDOANGEL also detected the blind spots not inspected and reminded endoscopists to evaluate those areas. This secondary function increased the quality and secondarily improved the WT. This study found that ADR was significantly higher in the ENDOANGEL group in intention-to-treat analysis (OR 2.30, 95% CI: 1.40-3.77; $P = 0.001$) (29). AI systems solely to detect polyps and not intended to increase WT, have also been shown to inadvertently increase WT. For example, in a recent large RCT on 3059 subjects by Xu *et al.*, an AI system not

intended to increase WT duration, led to an increase in WT (8.3 *vs.* 7.8 minutes; $P=0.004$) (30). This is attributed to longer time spent on endoscopist confirmation of polyps detected by AI during insertion and withdrawal. This study showed improved ADR in AI group however whether the WT prolongation spent on confirming the AI detection of polyps is beneficial or not remains unknown. We believe the recheck of polyps detected by AI is likely a positive aspect as the endoscopist will also inspect the surrounding mucosa secondarily. A recent network meta-analysis by our group showed improvement in both ADR [Relative risk (RR): 1.41, 95% CI: 1.28 to 1.54] and WT [Mean difference (MD): 0.54, 95% CI: 0.10 to 0.97] in AI compared with high-definition colonoscopy without AI (31,32).

Hurdles to WT and future directions

In daily life, there is more to WT than just a number. First, there are external factors that will affect the WT. If faced with external pressure of a large number of endoscopies scheduled in a limited time, for reasons including economic incentives, the endoscopists may not adhere to the minimum WT (33). Second, it is the time spent actively looking behind folds and cleaning the puddles that will improve the ADR rather than the WT, per se. Moreover, there are differences in the difficulty of colonoscopies that will require different time allocated for each individual. For example, a long colon with fair prep in a high-risk obese male with family history of CRC requires longer time than a short colon with excellent prep in an individual with no risk factors. This has led to recent proposals to change the WT of 6 minutes. Since the findings of Zhao *et al.*, Butterly has proposed a “mean” WT of 9 minutes and a minimum WT of 6 minutes (34). Per her suggestion, the providers should strive to have WT of all colonoscopies take more than 6 minutes and the mean WT of all the procedures exceed the 9-minute threshold. We propose an individualized approach based on risk factors. There are risk factors identified for occurrence of CRC. These can be divided to background factors, lifestyle, personal and family history (*Figure 1*) (1). Risk factors like obesity, tobacco, alcohol, low fiber diet in addition to personal and family history of polyps and CRC each increase the probability of CRC. There is a need for future studies determining a scoring system based on the patient’s preexisting risk factors of CRC and the difficulty of the procedure including the anatomy of the colon and quality of the bowel prep. In the era of AI, the AI model should be

able to combine the baseline risk factors and the real-time data including the difficulty of the procedure and determine the speed of withdrawal and time spent in each segment. For example, studies have shown that finding an adenoma in a segment increases risk of synchronous or metachronous adenomas in the same segment (35–37). Therefore, finding an adenoma in a segment should lead to a more careful inspection of the same segment, a recommendation that can be reinforced with AI models similar to that used by Liu *et al.* (38). The AI model will recommend relook in the right colon in high-risk population. Moreover, it will not allow withdrawal from the high-risk segment until three minutes mark and reinforce evaluation of all blind spots behind folds, proper distension, and cleaning residual stool, the four components of good technique (38). There is a need for future studies to prove the efficacy of this approach and develop the appropriate AI models to guide the endoscopist to spend more time inspecting the area of interest based on baseline data prior to colonoscopy and real-time input gathered during the procedure (*Figure 1*).

Limitations and strengths

This review had some limitations. First, it was a narrative review and not a systematic review for literature which may not cover all the available studies. Despite this, the authors conducted a comprehensive review of literature and references of the studies and covered the main studies in this field. Due to the novelty of the subject and its evolution within the last two decades, we believe the search was able to cover the major breakthroughs in the area. Second, there has been heterogeneity in the studies regarding the definition of outcomes due to wide geographic and chronologic variety of the studies. Nevertheless, this can be considered as a strength since this narrative review was not aiming at pooling the data, rather providing the evidence, unrestricted by heterogeneity. Last, some studies were observational with their inherent biases. At the same time, some studies were high-quality RCTs without the aforementioned biases that confirmed the results seen in the observational studies. There is need for updated meta-analysis of the high-quality RCTs to evaluate the effects of the AI in improving WT and ADR.

Conclusions

To conclude, a large body of evidence suggests setting a minimum WT of 6 to 9 minutes can lead to better

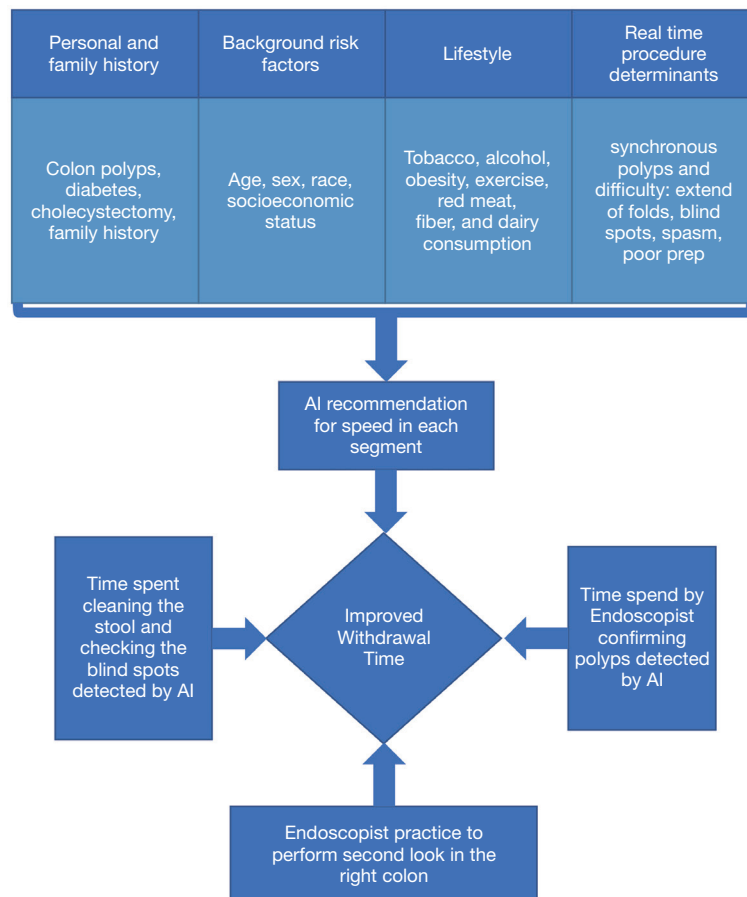


Figure 1 The proposed future of withdrawal time. A combination of background and real-time data help AI determine how much time the endoscopist should spend in each segment and in total. In addition, reminding the endoscopist to clean the stool and check the blind spots, and the time spent on confirming polyps will lead to improved WT. AI, artificial intelligence; WT, withdrawal time.

colonoscopy outcomes including higher ADR and lower interval CRCs. Data on methods to achieve the WT are limited, however, AI models are showing great potential. The future of the WT would be the development of AI models to guide colonoscopists to spend time on high-risk patients and the segmentation of interest based on prior and real time data. This “smart” effective withdrawal still requires a minimum WT likely between 6 to 9 minutes in majority of the procedure. Therefore, WT should be individualized based on difficulty and pretest probability of CRC rather than setting a WT number for all procedures.

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