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MINIREVIEWS

When should we perform colonoscopy to increase the adenoma detection rate?

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Abstract

The rate of adenoma detection is the most reliable quality indicator of colonoscopy. Studies have reported that colonoscopy performed in morning has a higher adenoma detection rate (ADR) than that performed in the afternoon. These studies have explained that several physician-related factors such as undergoing an emergency procedure the night before colonoscopy, accumulated workload, and increased fatigue level in the afternoon might have led to such finding. However, several opposing articles have indicated that the time of day and ADR is not quite related. Complex confounding factors can impact study results. Colonoscopy withdrawal time and bowel preparation quality are key factors. However, queue list numbers, participation of academic fellows, nurses' assistance, and the number of colonoscopies allocated *per* hour are also notable factors. Recently, an attempt has been made to homogenize the ADR in the morning and afternoon through artificial intelligence-assisted colonoscopy. This review article introduces the history of this long-debated topic, discusses points to consider in real-world practice, and suggests new ideas for planning future research. By understanding this issue, the rate of adenoma detection during colonoscopy is expected to be improved further.

Key Words: Colonoscopy; Colorectal cancer; Time of endoscopy; Afternoon colonoscopy; Adenoma detection rate

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Core Tip: Adenoma detection rate is the most reliable indicator of colonoscopy quality. Studies suggest that colonoscopy performed in the morning is associated with a higher detection rate of adenoma than the procedure performed in the afternoon. However, it is important to endeavor not only to improve patients' bowel preparation quality in the

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afternoon, but also to create an environment conducive to adenoma detection by physicians during afternoon sessions.

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INTRODUCTION

According to the statistics from the World Health Organization (WHO)[1], colorectal cancer is the third most common cancer around the world, with approximately 1.93 million newly diagnosed cases in the year 2020. It is the second most commonly diagnosed cancer in women and the third most common cancer in men, accounting for 9.4% (2nd) of the total number of cancer deaths. In the United States, the mortality due to colorectal cancer has substantially declined over the past few decades mainly due to a decrease in the incidence of colorectal cancer thanks to a sensitive detection[2] and the removal of adenomas by colonoscopy[3].

Since more than 95% of colon cancers originate from colorectal adenomas, the rate of adenoma detection [adenoma detection rate (ADR)] during colonoscopy is concerned as the most reliable benchmark quality assessment indicator for determining adequate screening efficacy[3,4]. Some studies have reported that patients examined by endoscopists with ADR of less than 20% have over ten times greater risk of interval colorectal cancer[5,6].

Factors associated with ADRs include nonmodifiable factors (such as age, gender, race, body mass index, and comorbidities) and modifiable factors such as scope withdrawal time (WT) and bowel preparation[7-9]. However, most of these factors are either technical or patient-related factors. On the other hand, studies regarding endoscopist-related factors are scarce. Since the first report by Sanaka *et al*[10] showing that there might be a difference in ADR between morning and afternoon colonoscopies in 2006, several studies have shown that physician's fatigue in the afternoon is related to ADR. However, conflicting results have also been reported. Therefore, we are still uncertain whether colonoscopies performed in the morning show better ADR than those performed in the afternoon.

This review article will introduce the history of this long-debated topic with the latest study results and discuss points to consider when planning future research.

THE BEGINNING OF THE DEBATE

Previous studies have shown that fatigue of medical professionals, including anesthesiologists[11], surgeons[12] and resident trainees[13] has a negative impact on patient safety outcomes. This phenomenon is not only observed for medical personnel, but also observed for non-medical employees such as pilots[14] and truck drivers[15].

In the early 2000s, several retrospective studies have reported that fatigue caused by doctors' sleep deprivation can affect laparoscopic performance[13], and that patients who are hospitalized at weekend have higher mortality than weekday patients in some disease entities[16]. These were the first reports showing that a patient's treatment outcome could vary by the day of the week. In 2004, a study suggested that a decrease in the detection rate of polyps of more than 9 mm was due to the practice pattern with a rapid increase in the number of screening colonoscopy after July based on the National Endoscopic Database[17]. As a result, it has been hypothesized that if the number of colonoscopy procedures by the time increases, the polyp detection rate (PDR) may be inversely affected. This result has been thought to be related to the fatigue of endoscopists.

The first article suggesting that an endoscopist's fatigue during the day might affect colonoscopic cecal intubation rate (CIT) was published in 2006[10]. The authors investigated colonoscopic incompleteness rates through a retrospective chart review of total 2087 colonoscopies (1084 in the morning and 999 in the afternoon). As a result, a significantly higher failure rate in the afternoon (6.5% vs 4.1%) was found. Even after

correcting for poor bowel cleansing quality in the afternoon, the afternoon failure rate was still significantly higher (5.0% vs 3.2%). The authors explained that the time of day could possibly be an independent predictor of the completion rate of colonoscopy. Considering such result, the time factor could also lead to a decrease in the afternoon WT, which was expected to reduce ADR consequently. In a retrospective study[18] of 3619 colonoscopies, ADR was found to be significantly higher in morning colonoscopies than in afternoon colonoscopies (29.3% vs 25.3%). In addition, there was a trend toward declining ADR for each subsequent hour of the day.

A prospective study of Veteran's administration teaching hospital[19] has shown comparable results. Data were analyzed both as a dichotomous time period ("early-morning case" vs "later case") and as a continuous variable (start time). In univariate analysis, early-morning cases yielded 27% more polyps *per* patient than later cases. Numbers of hyperplastic and adenomatous polyps decreased hour-by-hour as the day progressed. These early studies were pioneer studies for many subsequent community-based studies (Table 1 and Figure 1).

TIME OF DAY MAY NOT AFFECT ADR

However, several articles have indicated that the time of the day and ADR are not quite actually related. According to retrospective studies of single center hospitals that used a 3-h colonoscopy shift schedule[20] or an assigned time of 45 min *per* colonoscopy[21], PDR was the highest during the mid-day (shift 2)[20], showing no decrease in PDR as the day progressed[21]. In these studies, patients with poor bowel preparation were relatively less included using exclusion criteria and split-dose preparation methods. In addition, these studies could not reflect various amounts of workload among endoscopists for each institution.

In a retrospective study[22] based on a tertiary medical center where only attending physicians (excluding fellows) participated, PDR showed a decreasing trend for both half and all-day shifts (OR: 0.67, 95%CI: 0.44-1.00). However, due to related small numbers of confirmed adenomas, it could not demonstrate a significant difference in ADR. This result implicates that even in tertiary medical centers where endoscopists suffer high workload, the time of day alone may not have a strong influence on ADR as previously reported.

ENDOSCOPIST FATIGUE AND ADR

Despite these negative results, studies focusing on physician's fatigue and ADR were steadily published in 2014 and 2015. One study has compared ADR between a control group and cases of on-call duty or emergency procedure the night before screening colonoscopy[23]. Interestingly, overnight on-call duty was irrelevant to ADR. However, undergoing an emergency procedure the night before colonoscopy resulted in a significant decrease (24%) in ADR compared to the control group, indicating the influence of sleep deprivation on procedural outcomes. In a prospective, multi-center study[24] on screening colonoscopies when endoscopist fatigue was measured using a Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire with a cutoff score of 25, ADR was found to be lower for fatigued endoscopists than for the non-fatigued group. FACIT-F was 3.6 time higher for the ADR in a multivariate regression analysis.

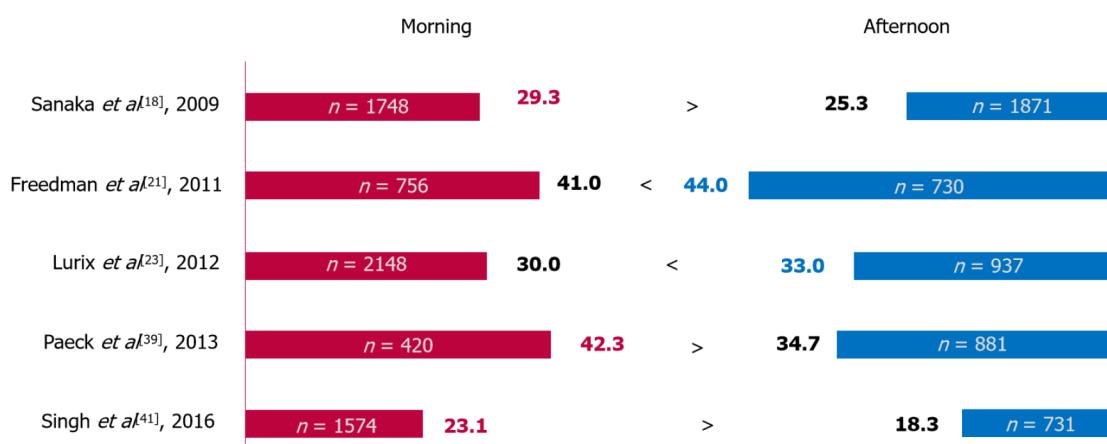
LATEST RESEARCH

A prospective observational study[25] performed in 2016 analyzed the influence of endoscopist-related characteristics on quality indicators for colonoscopy. In that study, factors associated with ADR were found to be age and life-long number of colonoscopies. Only exclusive dedication to endoscopy practice was found to be independently related to adenoma detection of proximal colon. Besides, none of other endoscopist characteristics, including the number of hours/week or annual volume of colonoscopies, was associated with a higher ADR. This was also supported by a following large community-based study[26] including more than 76000 colonoscopies with the aim to objectively reflect procedure related fatigue, considering both the number of colonoscopy procedures and the complexity of the procedure using

Table 1 Study characteristics (including evaluated adenoma detection rate result)

Ref.	Country	Study design	Investigated blocks	Physician (Fellow inclusion: O, X)	Bowel preparation	No. of a.m./p.m. procedure	ADR (%)
Sanaka et al[18], 2009	United States	Retrospective	Full day	Certified endoscopist (O)	Single PEG 4 L or oral fleet	1748/1871	AM (29.3); PM (25.3)
Chan et al[19], 2009	United States	Prospective	Full day	Certified endoscopist (O)	Single PEG 4 L or oral fleet	432/15	AM (49.2); PM (45.1)
Freedman et al [21], 2011	United States	Retrospective	Full day	Certified endoscopist (X)	Split dose PEG 4 L	756/730	AM (41); PM (44)
Long et al[22], 2011	United States	Retrospective	Full day	Certified endoscopist (X)	Single PEG 4 L	2219/1202	24.9
Lurix et al[23], 2012	United States	Retrospective	Half day. Full day	Certified endoscopist (O)	Single or Split PEG 4 L	2148/937	AM (30); PM (33)
Paeck et al[39], 2013	South Korea	Retrospective	Half day. Full day	Certified endoscopist (O)	Single PEG 4 L	420/881	AM (42.3); PM (34.7)
Subramanian et al [40], 2015	United Kingdom	Retrospective	Half day. Full day	Certified endoscopist (O)	Single PEG. Sodium picosulphate	1091/994 (evening:489)	27.6
Singh et al[41], 2016	United States	Retrospective	Full day	Certified endoscopist (O)	Split dose PEG 4 L	1574/731	AM (23.1); PM (18.3)
Teng et al[42], 2016	Singapore	Prospective	Full day	Certified endoscopist (X)	Single PEG (morning); Split-dose PEG (afternoon)	270/263	AM (29); PM (21)
Lei et al[27], 2020	China	Retrospective	Full day	Certified endoscopist (O)	Split-dose PEG	261/223	AM (36); PM (35)

Detection of adenoma was assisted by computer-aided detection (CADe). ADR: Adenoma detection rate.

**Figure 1 Comparison of morning and afternoon adenoma detection rates of studies with more than 1000 patients.**

consensus weights and relative value units. As a result, there was no association between ADR and endoscopist fatigue. Increasing levels of fatigue did not impact ADR, even after adjusting for confounding factors at patient-level and provider-level in multivariable regression analyses.

Meanwhile, the latest study has determined whether there is a difference in ADR between morning and afternoon colonoscopies assisted by artificial intelligence[27]. It was a prospective, single-center study with 484 colonoscopies through computer-aided detection (CAD) for polyps. There seemed to be no significant difference in ADR between morning and afternoon colonoscopies. Indeed, deep learning algorithm with real-time computer-aided polyp detection was proven to produce a significant increase in the detection of smaller adenomas compared to conventional colonoscopy (RR: 1.69; 95%CI: 1.48-1.84), according to a recent systemic review and meta-analysis[28]. It is expected that AI technology will be an effective tool minimizing the influence of 'endoscopist-related' factors in ADR.

Since 2006, numerous works have been done on whether colonoscopies performed in the afternoon are below the standard quality. It is not as easy as expected to conclude because various confounding variables such as patient, physician, assistant nurse, and the type of hospital are all factors that can affect the detection of adenomas during colonoscopy.

COMPLEX CONFOUNDERS

Increasing colonoscopy WT is thought to be able to improve ADR. A minimum WT of over 6 min during a normal colonoscopy is widely recommended[29]. A prospective observational study has been performed to determine how endoscopist fatigue can affect performance quality according to continuous and embedded volumes of colonoscopies[30]. It was found that WT and ADR remained stable while median CIT was lengthened as the repetitive procedure progressed. According to a prospective study (BECOP-3) that analyzed endoscopist factors related to ADR, WT within 6 to 11 min was not related to a reduced ADR[31]. However, ADR showed a significant reduction regardless of sufficient WT when a physician performed an emergency overnight procedure the day before the index colonoscopy[32]. If a physician sacrifices the WT to make up for a longer insertion time, less adenomas is expected to be found.

Along with WT, another substantial factor for ADR is bowel preparation quality. As it is crucial for adenoma detection, afternoon colonoscopies are known to be associated with both inadequate bowel preparation and lower ADR. There is no difference in the detection of adenomas by the time of day in studies when bowel preparation quality in the afternoon is maintained relatively well using a split-dose method[21] or statistically corrected for bowel cleanliness[33]. Another study has stated that bowel preparation is an inevitable confounder in assessing the quality of colonoscopy[34]. Therefore, various ways need to be investigated to improve the preparation quality of afternoon colonoscopies.

Other possible confounding factors include hospital system-related issues such as the participation proportion of academic fellows in endoscopy[34], queue list numbers that differ quite a lot for each endoscopic clinic[35], overnight duty systems for endoscopists or nurses[32], and the number of colonoscopies allocated every hour[20] (Table 2). If an endoscopist is in state of sleep deprivation or if an awaited patient comes in right after a previous laborious colonoscopy, it would be reasonable to question the procedural quality. However, if a highly skilled physician who performs more than 200 colonoscopies a year and if WT can be secured to be over 6 min, ADR can remain stable throughout the day[31]. Factors that might interfere with concentration on endoscopic procedures such as attending educational conferences, replying to frequent consultations, and educating medical students should be emphasized[25, 36]. "Social influencing" using notice or posters, personal auditing reports, and physical or electronic reminders are emerging as part of efforts to prevent deterioration of polyp and ADRs due to fatigue in the afternoon in busy academic teaching institutions[37].

Finally, how many hours of the day the endoscopist devotes to colonoscopies is another issue that should be pointed out. Some physicians may only work in the morning or afternoon (half-day block), while others may perform colonoscopies the entire day (full-day block). This can significantly affect study results. However, it has been poorly controlled across studies. For example, only half-day blocks were included in some studies, whereas full-day and half-day blocks of work were all taken into account in other studies. It seems inappropriate to compare these studies on the same line[33].

WHERE DO WE STAND? AND WHAT'S NEXT?

Meta-analyses on whether a morning colonoscopy is superior to an afternoon colonoscopy have shown cautious but consistent results. According to a study that analyzed a total of 16 eligible publications (14 retrospective studies and two prospective studies), ADRs for morning and afternoon colonoscopies were similar. However, the PDR of the afternoon was significantly less than that of the morning. Since it is generally considered that PDR does not significantly affect the quality of colonoscopy, there should be no change in the quality of colonoscopies throughout the day. Interestingly, the authors also concluded that fellow participation did not impact ADR difference between morning and afternoon colonoscopies. Barakat et al[38]

Table 2 Factors related with higher adenoma detection rate

Category	Factors
Patient-related	Good Bowel preparation Age (Older age), gender (male) Obesity (Higher body mass index)
Endoscopist-related	Withdrawal time (> 6 min) Assist from nurses/additional observer Queue list numbers (Small) Overnight duty (Less or none) Number of colonoscopies allocated <i>per</i> hour (Less) Half-day or Full-day schedule (Half-day) Attending CMEs, conferences, frequent consultations (Less)
Device-related	Higher definition processors, endoscopes

analyzed the effect of the time of day on ADR through multiple subgroup analyses in 2020, showing that the net effect of the time of day did not impact ADR in general. In addition, there was no difference in ADR between morning and afternoon not only for physicians with a half-day block schedule, but also for endoscopists who continuously performed full-day colonoscopies by the same operator.

These meta-analyses have strengths, including a large number of studies with a large sample size with a diverse international population. However, due to relatively high heterogeneity existed in data used for the analysis (allotted time for a colonoscopy, WT, indications for colonoscopy), homogenization of the study design is required. In addition, it must be acknowledged that the unevenness of data among included studies in terms of different fellow participation and bowel preparation quality might affect the interpretation of results. Besides, as these meta-analyses did not estimate operator fatigue, results reflecting a physician's various stamina levels and the complexity of previous procedures might come out differently.

Every colonoscopy is performed under different circumstances. There would be the first procedure of the day, some might be performed after a number of arduous duties. Performing 'full-day' colonoscopies may not necessarily lead to a less careful procedure. The physician who performs colonoscopy until the afternoon may receive additional financial compensation accordingly, which will increase the operator's motivation. Therefore, it is presumable that 'financial compensation policy' of each institution should be also considered as one of the various factors affecting ADR in the afternoon. On the other hand, from experience, the procedural result is not good from time to time when the following colonoscopy is forced to be started immediately after a difficult therapeutic endoscopy due to long waiting patients. We hope that future well-designed studies will be able to evaluate effects of previous endoscopies on ADR. Besides, it will be interesting to see if ADR in the morning and afternoon can be differently affected by the experience of endoscopists (novice/experienced), weekday or weekend, and gender of patients through subgroup analysis.

NO EFFECT OF TIME OF THE DAY ON ADR

Several studies indicated the lack of correlation between the time of the day and the ADR. Single-center retrospective studies at hospitals based on 3-h colonoscopy shift schedule or an assigned time of 45 min *per* colonoscopy revealed that PDR was the highest during the mid-day (shift 2), without decreasing as the day progressed. In these studies, relatively few patients with poor bowel preparation were included based on exclusion criteria and split-dose preparation methods. In addition, these studies failed to reflect various levels of workload among endoscopists at each institution. In a retrospective study based on a tertiary medical center involving only attending physicians (excluding fellows) as the participants, the PDR showed a decreasing trend in both half and full-day shifts (OR: 0.67, 95%CI: 0.44-1.00). However, due to the small number of confirmed adenomas, the study failed to demonstrate a

significant difference in ADR, suggesting that even in tertiary medical centers with endoscopists ensuring increased workload, the time of day alone may not have a strong influence on ADR as previously reported.

CONCLUSION

In conclusion, data up to date did not demonstrate a significant difference in the quality of colonoscopies by the time of the day in either a full day setting or in a half-day block setting. Despite negative results, we believe it is still too early to conclude on this issue. Future systematic randomized clinical trials that can control for confounding factors mentioned above and analyze an endoscopist's fatigue level more objectively might change conclusions on this subject. For now, considering that the PDR (or maybe ADR) in the afternoon may get deteriorated in the full-day block schedule, it is important to make efforts not only to improve patients' bowel preparation quality in the afternoon, but also to create an environment that a physician can focus solely on detecting adenomas during afternoon colonoscopy sessions.

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